OCT - 7 2003

K030886

510(K) SUMMARY

July 11, 2003

a. Applicant's Name and Address

Respironics Novametrix Inc.
5 Technology Drive
Wallingford, CT 06492

b. Contact Person

Michael J. Malis
Q.A. and Regulatory Manager
(203) 697-6442
(203) 284-0753 (facsimile)

c. Name of Device

Device Names (Proprietary/Trade Names):	NICO, Model 7300
Device Name (Common Name):	multiparameter monitor (monitoring spirometer, CO_2 monitor, pulse oximeter and cardiac output monitor with partial rebreathing valve).
Classification:	Class II, 21 C.F.R. 868.1850, 868.1400, 870.2700, 868.5675

d. Equivalent Devices

Substantial equivalence to the following legally marketed predicate devices with the same or similar indications for use has been demonstrated by a comparison of product features as described in the labeling and promotional literature for predicate devices and for the Model 7300, as well as testing to accepted industry standards. In addition, controlled hypoxia studies were conducted to establish the Model 7300 pulse oximetry accuracy and to ensure that the sensors meet their currently published accuracy specifications with the Model 7300. The predicate devices are as follows:

1. CO2SMO Plus! with NICO, Model 8200 (K982499)
2. MARSPO2, Model 2001 (K993979, K000794).

e. Device Description

The NICO monitor Model 7300 is intended for non-invasive monitoring of the inspired and expired airflow and airway pressure of intensive care unit (ICU), anesthesia and emergency room (ER) patients, as well as capnography and pulse oximetry in all of these clinical settings. As is its predicate device *CO_2SMO Plus! with NICO*, *NICO with MARS* is designed to use neonatal, pediatric, and adult combined CO_2/flow sensors and single patient use or reusable pulse oximetry sensors. It non-invasively calculates cardiac output using established physiological principles by the application and removal of a rebreathed volume in a patient's breathing circuit and the analysis of that response. The *NICO with MARS* is intended to provide cardiac output monitoring in mechanically ventilated patients in the operating room and intensive care units. It is intended to serve the same purposes as the CO_2SMO Plus! with NICO and MARSPO_2, Model 2001.

Oxygen saturation is measured with ratiometric technique using red and infrared absorbance of oxy- and deoxyhemoglobin and pulse rate is measured using the time between successive pulses. The O_2 saturation sensors are already legally marketed as accessories to the Model 2001 monitor. As the Model 2001 monitor, the Model 7300 with MARS consists of a dual microprocessor based data acquisition system that measures oxygen saturation data. The firmware for the second microprocessor, a digital signal processor, performs the filtering, pulse rate and saturation calculations of the existing algorithms and additional calculations which analyze the incoming signals and perform noise reduction on that signal when the presence of noise is detected.

The Model 7300 can be powered by either an internal power supply operating on AC or by a sealed rechargeable lead-acid gel battery. Audible and visual alarms for high/low saturation and pulse rate are available. There is also a serial port that provides user configurable data output capable of communicating with printers and other devices.

f. Intended Use

The intended use of the NICO monitor, Model 7300 is to provide:

- cardiac output monitoring via the method of partial rebreathing in adult patients receiving mechanical ventilation during general anesthesia and in the intensive care unit (ICU).

- spirometric and carbon dioxide monitoring in neonatal, pediatric and adult patients during general anesthesia and in the intensive care unit (ICU) and the emergency department (ED). Separate combination CO_2/flow sensors are provided for adult, pediatric and neonatal use.

- continuous, non-invasive monitoring of functional arterial oxygen saturation and pulse rate in neonatal, pediatric and adult patients during both no motion and motion conditions and for patients who are well or poorly perfused during general anesthesia and in the intensive care unit (ICU) and the emergency department (ED).

The use of the NICO monitor Model 7300 for cardiac output monitoring is contraindicated in patients in which a small rise (3-5 mmHg) in their arterial partial pressure of CO_2 level cannot be tolerated. The intended use, patient population and environments of use are the same or similar to the predicate devices, CO_2SMO Plus! with NICO, Model 8200 and MARSPO$_2$, Model 2001

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g. Technological Characteristics

The *NICO with MARS* uses flow sensors that are considered to be a fixed orifice, target flowmeters and as such the pressure drop is proportional to the square of the flow. Combination CO_2/flow sensors are available in three flow ranges that are tailored for neonates, pediatric patients and adults.

The *NICO with MARS* uses an infrared absorption (IR) technique for monitoring CO_2. The principle is based on the fact that CO_2 molecules absorb infrared light energy of specific wavelengths, with the amount of energy absorbed being directly related to the CO_2 concentration Solid state CO_2 sensors (such as the Capnostat) use a beam splitter to simultaneously measure the IR light at two wavelengths: one which is absorbed by CO_2

and one which is not. The wavelength which is not absorbed by CO_2 is related to the intensity of the IR light source. Also, the IR light source is electronically pulsed (rather than interrupting the IR beam with a chopper wheel) in order to eliminate effects of changes in electronic components.

The *NICO with MARS* measures oxygen saturation and pulse rate with sensors that contain red and infrared light sources. Since oxygen saturated blood absorbs different amounts of light at each wavelength (red and infrared) as compared with unsaturated blood, the amount of light absorbed at each wavelength by the blood in each pulse can be used to calculate oxygen saturation. The light energy from red (660 nm) and infrared (940 nm) LEDs is beamed through a sample cell- a pulsating vascular bed, the patient's finger or toe for example. The remaining light energy not absorbed by the sample cell reaches a photodiode, on the opposing side of the sensor. The signal received by the photodiode is split into its red and infrared components, sampled, software filtered and displayed as a numerical value for oxygen saturation and as a waveform, the plethysmogram.

Functional saturation represents the amount of oxyhemoglobin as a percentage of the hemoglobin that can be oxygenated. Dysfunctional hemoglobin (COHb and METHb) are not included in the measurement of functional saturation. Pulse rate is calculated by measuring the time interval between the peaks of the infrared light waveform. The *NICO with MARS* must be used in conjunction with the Novametrix SuperBright™ series of oxygen saturation sensors. MARS technology exploits the computational power of the digital signal processing to replace the pulse rate interval and rate-based decision tree algorithm of prior devices with a more robust frequency-based algorithm.

A variation on the traditional rebreathing methods, the non-invasive differential Fick partial re-breathing technique is used in the NICO with MARS monitor. The change in VCO_2 and the change in end-tidal CO_2 in response to a change in ventilation is used to determine pulmonary capillary blood flow. This value is then corrected for the effect of shunt to determine cardiac output.

h. Certification Statement

In accordance with the requirements of 21 CFR 807.87(j), the following certification is provided:

Respironics Novametrix, Inc. believes that all data and information submitted in this premarket notification are truthful and accurate and no material fact has been omitted.

M. Malis 7/10/03

Michael J Malis
Q.A. and Regulatory Manager

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

OCT - 7 2003

Mr. Michael Malis
Regulatory and QA Manager
Respironics Novametrix Incorporated
5 Technology Drive
Wallingford, CT 06492

Re: K030886
Trade/Device Name: NICO with MARS, Model 7300
Regulation Number: 868.1400
Regulation Name: Carbon Dioxide Gas Analyzer, Gaseous-Phase
Regulatory Class: II
Product Code: CCK, BZK, DQA
Dated: July 11, 2003
Received: July 14, 2003

Dear Mr. Malis:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies.

You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Office of Compliance at (301) 594-4646. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its Internet address http://www.fda.gov/cdrh/dsma/dsmamain.html.

Sincerely yours,

Chiu Lin, Ph.D.
Director
Division of Anesthesiology, General Hospital,
Infection Control and Dental Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Enclosure

510(k) Number (if known): K030886

Device Name: NICO with MARS

Indications For Use:

The intended use of the NICO monitor, Model 7300 is to provide:

- cardiac output monitoring via the method of partial rebreathing in adult patients receiving mechanical ventilation during general anesthesia and in the intensive care unit (ICU).
- spirometric, and carbon dioxide monitoring in neonatal, pediatric and adult patients during general anesthesia and in the intensive care unit (ICU) and the emergency department (ED). Separate combination CO_2/flow sensors are provided for adult, pediatric and neonatal use.
- continuous, non-invasive monitoring of functional arterial oxygen saturation and pulse rate in neonatal, pediatric and adult patients during both no motion and motion conditions and for patients who are well or poorly perfused during general anesthesia and in the intensive care unit (ICU) and the emergency department (ED).

The use of the NICO monitor Model 7300 for cardiac output monitoring is contraindicated in patients in which a small rise (3-5 mmHg) in their arterial partial pressure of CO_2 level cannot be tolerated.

(PLEASE DO NOT WRITE BELOW THIS LINE - CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

(Division Sign-Off)
Division of Anesthesiology, General Hospital,
Infection Control, Dental Devices

510(k) Number: K030886

Prescription Use ✓ **OR** **Over-The-Counter Use** _____
(Per 21 CFR 801.109)

(Optional Format 1-2-96)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

OCT - 7 2003

Mr. Michael Malis
Regulatory and QA Manager
Respironics Novametrix Incorporated
5 Technology Drive
Wallingford, CT 06492

Re: K030886
Trade/Device Name: NICO with MARS, Model 7300
Regulation Number: 868.1400
Regulation Name: Carbon Dioxide Gas Analyzer, Gaseous-Phase
Regulatory Class: II
Product Code: CCK, BZK, DQA
Dated: July 11, 2003
Received: July 14, 2003

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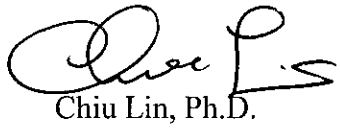
Sincerely yours,



Chiu Lin, Ph.D.
Director
Division of Anesthesiology, General Hospital,
Infection Control and Dental Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Enclosure

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510(k) Number (if known): K030886

Device Name: NICO with MARS

Indications For Use:

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(PLEASE DO NOT WRITE BELOW THIS LINE - CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

(Division Sign-Off)
Division of Anesthesiology, General Hospital,
Infection Control, Dental Devices

510(k) Number: K030886

Prescription Use ✓ **OR** **Over-The-Counter Use** _____
(Per 21 CFR 801.109)

(Optional Format 1-2-96)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

JUN 17 2003

Mr. Michael Malis
Regulatory and QA Manager
Respironics Novametrix Incorporated
5 Technology Drive
Wallingford, CT 06492

Re: K030886
NICO with MARS, Model 7300
Dated: March 17, 2003
Received: March 21, 2003

Dear Mr. Malis:

We have reviewed your Section 510(k) notification of intent to market the device referenced above. We cannot determine if the device is substantially equivalent to a legally marketed predicate device based solely on the information you provided. To complete the review of your submission, we require the following information:

(b)(4)

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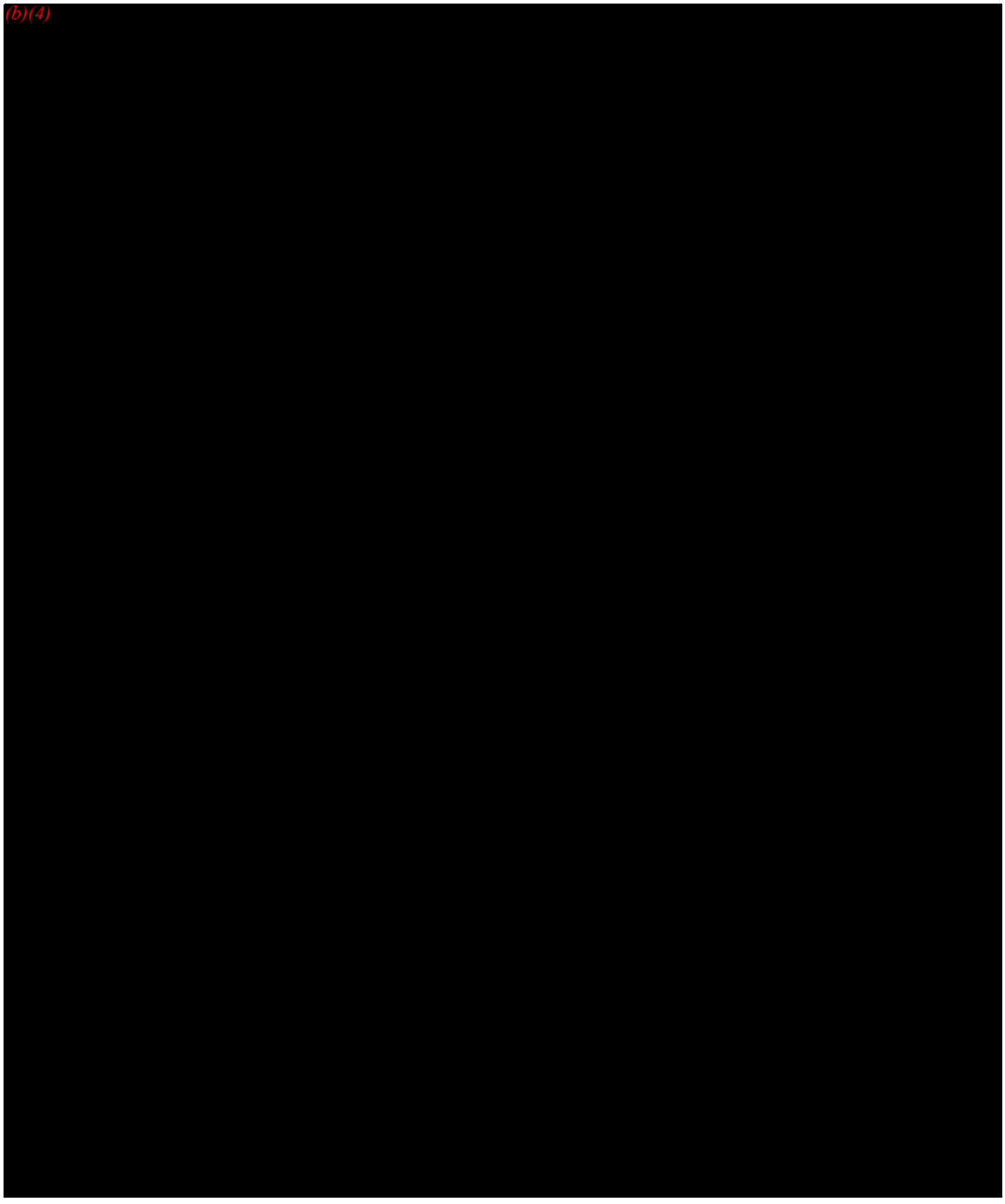
(b)(4)

[redacted]

(b)(4)



(b)(4)

[redacted]

(b)(4)

[redacted]

The deficiencies identified above represent the issues that we believe need to be resolved before our review of your 510(k) submission can be successfully completed. In developing the deficiencies, we carefully considered the statutory criteria as defined in Section 513(i) of the Federal Food, Drug, and Cosmetic Act for determining substantial equivalence of your device. We also considered the burden that may be incurred in your attempt to respond to the deficiencies. We believe that we have considered the least burdensome approach to resolving these issues. If, however, you believe that information is being requested that is not relevant to the regulatory decision or that there is a less burdensome way to resolve the issues, you should follow the procedures outlined in the "A Suggested Approach to Resolving Least Burdensome Issues" document. It is available on our Center web page at:
http://www.fda.gov/cdrh/modact/leastburdensome.html.

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You may not market this device until you have provided adequate information described above and required by 21 CFR 807.87(l), and you have received a letter from FDA allowing you to do so. If you market the device without conforming to these requirements, you will be in violation of the Federal Food, Drug, and Cosmetic Act (Act). You may, however, distribute this device for investigational purposes to obtain clinical data if needed to establish substantial equivalence. Clinical investigations of this device must be conducted in accordance with the investigational device exemption (IDE) regulations.

If the information, or a request for an extension of time, is not received within 30 days, we will consider your premarket notification to be withdrawn and your submission will be deleted from our system. If you submit the requested information after 30 days it will be considered and processed as a new 510(k); therefore, all information previously submitted must be resubmitted so that your new 510(k) is complete.

The requested information, or a request for an extension of time, should reference your above 510(k) number and should be submitted in duplicate to:

Food and Drug Administration
Center for Devices and
Radiological Health
Document Mail Center (HFZ-401)
9200 Corporate Boulevard
Rockville, Maryland 20850

If you have any questions concerning the contents of the letter, please contact Lisa E. Harris at (301) 443-8611. If you need information or assistance concerning the IDE regulations, please contact the Division of Small Manufacturers, International and Consumer Assistance (DSMICA) at its toll-free number (800) 638-2041 or at (301) 443-6597, or at its Internet address http://www.fda.gov/cdrh/dsma/dsmamain.html.

Sincerely yours,

for Susan Runner, DDS, MA
Interim Director
Division of Anesthesiology, General Hospital,
Infection Control and Dental Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

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DEPARTMENT OF HEALTH AND HUMAN SERVICES Public Health Service

Food and Drug Administration
Center for Devices and
Radiological Health
Office of Device Evaluation
Document Mail Center (HFZ-401)
9200 Corporate Blvd.
Rockville, Maryland 20850

March 21, 2003

RESPIRONICS NOVAMETRIX, INC.
5 TECHNOLOGY DRIVE
WALLINGFORD, CT 06492
ATTN: MICHAEL MALIS

510(k) Number: K030886
Received: 21-MAR-2003
Product: NICO WITH MARS, MODEL 7300

The Food and Drug Administration (FDA), Center for Devices and Radiological Health (CDRH), has received the Premarket Notification you submitted in accordance with Section 510(k) of the Federal Food, Drug, and Cosmetic Act (Act) for the above referenced product. We have assigned your submission a unique 510(k) number that is cited above. Please refer prominently to this 510(k) number in any future correspondence that relates to this submission. We will notify you when the processing of your premarket notification has been completed or if any additional information is required. YOU MAY NOT PLACE THIS DEVICE INTO COMMERCIAL DISTRIBUTION UNTIL YOU RECEIVE A LETTER FROM FDA ALLOWING YOU TO DO SO.

The Act, as amended by the Medical Device User Fee and Modernization Act of 2002 (MDUFMA)(Public Law 107-250), authorizes FDA to collect user fees for premarket notification submissions. (For more information on MDUFMA, you may refer to our website at http://www.fda.gov/oc/mdufma).

Please remember that all correspondence concerning your submission MUST be sent to the Document Mail Center (DMC)(HFZ-401) at the above letterhead address. Correspondence sent to any address other than the one above will not be considered as part of your official premarket notification submission. Also, please note the new Blue Book Memorandum regarding Fax and E-mail Policy entitled, "Fax and E-Mail Communication with Industry about Premarket Files Under Review". Please refer to this guidance for information on current fax and e-mail practices at www.fda.gov/cdrh/ode/a02-01.html.

You should be familiar with the manual entitled, "Premarket Notification 510(k) Regulatory Requirements for Medical Devices" available from DSMICA. If you have other procedural or policy questions, or want information on how to check on the status of your submission, please contact DSMICA at (301) 443-6597 or its toll-free number (800) 638-2041, or at their Internet address http://www.fda.gov/cdrh/dsmamain.html or me at (301)594-1190.

Sincerely yours,

Marjorie Shulman
Supervisory Consumer Safety Officer
Office of Device Evaluation
Center for Devices and Radiological Health

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CDRH SUBMISSION COVER SHEET

Date of Submission: 3/17/2003 **FDA Document Number:** K030886

Section A — Type of Submission

PMA	PMA Supplement	PDP	510(k)	Meeting
Original Submission ☐ Modular Submission ☐ Amendment ☐ Report ☐ Report Amendment	☐ Regular ☐ Special ☐ Panel Track ☐ 30-day Supplement ☐ 30-day Notice ☐ 135-day Supplement ☐ Real-time Review ☐ Amendment to PMA Supplement	☐ Presubmission Summary ☐ Original PDP ☐ Notice of intent to start clinical trials ☐ Intention to submit Notice of Completion ☐ Notice of Completion ☐ Amendment to PDP ☐ Report	Original Submission: X Traditional ☐ Special ☐ Abbreviated ☐ Additional Information: ☐ Traditional ☐ Special ☐ Abbreviated ☐ Report Amendment	☐ Pre-IDE mtg. ☐ Pre-PMA mtg. ☐ Pre-PDP mtg. ☐ 180-Day mtg. ☐ Other (specify):

IDE	Humanitarian Device Exemption	Class II Exemption	Evaluation of Automatic Class III Designation	Other Submission
☐ Original submission ☐ Amendment ☐ Supplement	☐ Original submission ☐ Amendment ☐ Supplement ☐ Report	☐ Original Submission ☐ Additional Information	☐ Original Submission ☐ Additional Information	Describe Submission:

Section B — Applicant or Sponsor

Company/Institution Name: Respironics Novametrix Inc.		Establishment registration number: 1219324	
Division Name (if applicable):		Phone number (include area code): 203-697-6442	
Street Address: 5 Technology Drive		Fax number (include area code): 203-284-0753	
City: Wallingford	State/Province: CT	Zip code: 06492	Country: USA
Contact Name: Michael Malis	Michael Malis 3/17/03		
Contact Title: RA & QA		Contact e-mail address: Michael.Malis@respironics.com	

Section C — Submission Correspondent (if different from above)

Company/Institution Name:		Establishment registration number:	
Division name (if applicable)		Phone number (include area code):	
et Address:		Fax number (include area code):	
City:	State/Province:	Zip Code:	Country
Contact Name:			

Section D1 — Reason for Submission – PMA, PDP, or HDE

☐ New Device
☐ Withdrawal
☐ Additional or Expanded Indications
☐ Licensing Agreement

☐ Change in design, component, or specification:
- ☐ Software
- ☐ Color Additive
- ☐ Material
- ☐ Specifications
- ☐ Other (specify below)

☐ Location Change:
- ☐ Manufacturer
- ☐ Sterilizer
- ☐ Packager
- ☐ Distributor

☐ Processing Change:
- ☐ Manufacturing
- ☐ Sterilization
- ☐ Packaging
- ☐ Other (specify below)

☐ Labeling Change:
- ☐ Indications
- ☐ Instructions
- ☐ Performance Characteristics
- ☐ Shelf Life
- ☐ Trade Name
- ☐ Other (specify below)_

☐ Report Submission:
- ☐ Annual or Periodic
- ☐ Post Approval Study
- ☐ Adverse Reaction
- ☐ Device Defect
- ☐ Amendment

☐ Response to FDA correspondence:
- ☐ Request for applicant hold
- ☐ Request for removal of applicant hold
- ☐ Request for extension
- ☐ Request to remove or add manufacturing site

☐ Change in Ownership
☐ Change in correspondent

☐ Other Reason (specify):

Section D2 — Reason for Submission - IDE

☐ New device
☐ Addition of institution
☐ Expansion/extension of study
☐ IRB certification
☐ Request hearing
☐ Request waiver
☐ Termination of study
☐ Withdrawal of application
☐ Unanticipated adverse effect
☐ Notification of emergency use
☐ Compassionate use request
☐ Treatment IDE
☐ Continuing availability request

Change in:
- ☐ Correspondent
- ☐ Design
- ☐ Informed consent
- ☐ Manufacturer
- ☐ Manufacturing process
- ☐ Protocol – feasibility
- ☐ Protocol – other
- ☐ Sponsor

☐ Response to FDA letter concerning:
- ☐ Conditional approval
- ☐ Deemed approval
- ☐ Deficient final report
- ☐ Deficient progress report
- ☐ Deficient investigator report
- ☐ Disapproval
- ☐ Request extension for time to respond to FDA
- ☐ Request meeting

☐ Report Submission:
- ☐ Current investigator
- ☐ Annual progress
- ☐ Site waiver limit reached
- ☐ Final

☐ Other reason (specify):

Section D3 — Reason for Submission – 510(k)

☐ New Device
☐ Additional or expanded indications
X Other reason (specify):

☐ Change in technology
☐ Change in design

☐ Change in materials
☐ Change in manufacturing process

The NICO with Mars is a combination of the CO2SMO PLUS! with NICO, which was found substantially equivalent by FDA (K982499) and MARSpO2 Model 2001, which was found substantially equivalent by FDA (K993979 & K000794).

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Section E **Additional Information on 510(k) Submissions**

Product codes of devices to which substantial equivalence is claimed:				Summary of, or statement concerning safety and effectiveness data: X 510(k) summary attached ☐ 510(k) statement
1 74 DQA	2 73 BYW	3 73 BZC	4	
5	6	7	8	

Information on devices to which substantial equivalence is claimed:

510(k) Number	Trade of Proprietary or model name	Manufacturer
1 K982499	1 CO2SMO PLUS!	1 Novametrix Medical Inc.
2 K993979	2 MARSpO2 Model 2001	2 Novametrix Medical Inc.
3 K000794	3 MARSpO2 Model 2001	3 Novametrix Medical Inc.
4	4	4
5	5	5
6	6	6

Section F **Product Information – Applicable to All Applications**

Common or usual name or classification name: Multi-parameter monitor (monitoring spirometer, CO2 monitor, pulse oximeter and cardiac output monitor with partial rebreathing valve)

Trade or proprietary or model name	Model Number
1 NICO with MARS	1 Model 7300
2	2
3	3
4	4
5	5

FDA document numbers of all prior related submissions (regardless of outcome):

1 K982499	2 K993979	3 K000794	4	5	6
7	8	9	10	11	12

Data included in submission: X Laboratory Testing X Animal Trials X Human Trials

Section G **Product Classification – Applicable to All Applicants**

Product code:	C.F.R. Section 868.1850, 868.1400, 870.2700, 868.5675	Device Class: ☐ Class I X Class II ☐ Class III ☐ Unclassified
Classification Panel: Cardiovascular Device		

Indications (from labeling):

ote: Submission of this information does not affect the need to submit a 2891 or 2891a Device Establishment Registration form.	FDA Document Number:

Section H **Manufacturing/Packaging/Sterilization Sites Relating to a Submission**

X Original ☐ Add ☐ Delete	FDA establishment registration number: 1219324	X Manufacturer ☐Contract Sterilizer ☐ Contract Manufacturer ☐ Repackager/relabeler	
Company/Institution name: Respironics Novametrix Inc.		Establishment registration number: 1219324	
Division name (if applicable):		Phone number (include area code): 203-697-6442	
Street address: 5 Technology Drive		FAX number (include area code): 203-284-0753	
City Wallingford	State/Province CT	Zip code: 06492	Country USA
Contact name: Michael Malis			
Contact title: RA & QA			

☐ Original ☐ Add ☐ Delete	FDA Establishment registration number:	☐ Manufacturer ☐ Contract Sterilizer ☐ Contract Manufacturer ☐ Repackager/relabeler	
Company/Institution Name: as above		Establishment registration number:	
Division name (if applicable):		Phone number (include area code):	
Street address:		FAX number (include area code):	
City:	State/Province:	Zip code:	Country:
Contact name:			
Contact title:	Contact e-mail address:		

☐ Original ☐ Add ☐ Delete	FDA Establishment registration number:	☐ Manufacturer ☐Contract sterilizer ☐ Contract Manufacturer ☐Repackager/relabeler	
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Division name (if applicable):		Phone number (include area code):	
et address:		FAX number (include area code):	
City:	State/Province:	Zip code:	Country:
Contact name:			

March 17, 2003

Food and Drug Administration
Center for Devices and Radiological Health
Document Mail Center (HFZ-401)
9200 Corporate Boulevard
Rockville, MD 20850

Attention: Division of Anesthesiology, General Hospital,
Infection Control, and Dental Devices

2003 MAR 21 11:10

Re: 510(k) Premarket Notification for the Respironics Novametrix NICO, Model 7300 with MARS

Dear Sir or Madam:

In accordance with section 510(k) of the Federal Food, Drug and Cosmetic Act, Respironics Novametrix, Inc. submits this Premarket notification to provide notice of its intent to market a combination device, the NICO® Cardiopulmonary Management System, Model 7300 with MARS™ technology (Motion Artifact Rejection System) (also known as "NICO with MARS"). The NICO with MARS is a combination of the CO_2SMO Plus! with NICO, which was found substantially equivalent by FDA by letter dated October 16, 1998 (510(k) No. K982499) and MARSpO_2™ Model 2001 which was found substantially equivalent by FDA by letters dated 2/22/2000 and 04/10/2000 (510(k) No.s K993979 and K000794). The NICO with MARS is intended to provide cardiac output monitoring in mechanically ventilated patients in the operating room and intensive care units. In addition, the NICO with MARS is intended to provide all of the existing capabilities of the CO_2SMO Plus! with NICO of spirometric, arterial oxygen saturation and CO_2 monitoring in the operating and emergency rooms and intensive care units. Also, the NICO with MARS is intended to provide improved capabilities of arterial oxygen saturation monitoring consistent with the MARSpO_2™ Model 2001 monitor.

The NICO with MARS is substantially equivalent to the respective predicate devices in all respects, including labeling.

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The following summary information is provided as a quick reference for the initial reviewer. For a complete reference to the material in this 510(k) submission, please refer to the table of Contents.

Device Names (Proprietary/Trade Names):	NICO with MARS
Device Name (Common Name):	multiparameter monitor (monitoring spirometer, CO_2 monitor, pulse oximeter and cardiac output monitor with partial rebreathing valve)
Establishment Registration Number:	1219324
Classification:	Class II, 21 C.F.R. 868.1850, 868.1400, 870.2700, 868.5675
Classification Panel:	Cardiovascular Device Classification Panel

Performance and Other Standards: No performance standards have been promulgated under section 514 for monitoring spirometers, CO_2 monitors, pulse oximeters, cardiac output monitors or rebreathing valves. No special controls apply. The fittings of the flow sensors and CO_2 airway adapters comply with (ISO 5356-1:1987(E)). The NICO with MARS complies with IEC 601-1 and the requirements for EMC (EN60601-1-2 (2001)).

Proposed Labeling: A draft operator's manual is provided in Appendix 1A; draft literature, draft pouch labeling, and draft front and rear panel labeling are provided in Appendices 1B, 1C, 1D, respectively.

Legally Marketed Devices to Which Substantial Equivalence is Claimed: The NICO with MARS is substantially equivalent to the CO_2SMO! Plus with NICO and MARSpO2 Model 2001.

510(k) Summary: The summary appears in a separate section of the 510(k) submission and is identified as such in the Table of Contents.

510(k) Certification: This certification appears in a separate section of the 510(k) submission and is identified as such in the Table of Contents.

The information in this submission provides all the information needed to process this 510(k) submission according to 21 C.F.R. pt. 807 subpt. E, the "checklist" under the Office of Device Evaluation's refuse-to-accept policy, and other guidance documents known at the time of the submission. Please refer to the Table of Contents for a complete listing of the information included in this 510(k).

The pages of this submission stamped "Confidential" constitute trade secret or confidential commercial information and Respironics Novametrix therefore claims for each of these pages the protections afforded by 21 U.S.C. § 331(j), 21 C.F.R. §§ 807.95 and 20.61, 5 U.S.C. § 552(b)(4), and 18 U.S.C. 1905.

Please refer any communications regarding this application to the undersigned.

Sincerely,

Michael Malis

Michael J. Malis
Regulatory & QA Manager
(203) 697-6442
(203) 284-0753 (facsimile)

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510(k) Number (if known):_____

Device Name: **NICO with MARS**

Indications For Use:

The intended use of the NICO monitor, Model 7300 is to provide:

- cardiac output monitoring via the method of partial rebreathing in adult patients receiving mechanical ventilation during general anesthesia and in the intensive care unit (ICU).
- spirometric, and carbon dioxide monitoring in neonatal, pediatric and adult patients during general anesthesia and in the intensive care unit (ICU) and the emergency department (ED). Separate combination CO_2/flow sensors are provided for adult, pediatric and neonatal use.
- continuous, non-invasive monitoring of functional arterial oxygen saturation and pulse rate in neonatal, pediatric and adult patients during both no motion and motion conditions and for patients who are well or poorly perfused during general anesthesia and in the intensive care unit (ICU) and the emergency department (ED).

The NICO monitor Model 7300 and its sensors are intended to be used by trained operators when spirometric, capnographic, pulse oximetry, or cardiac output monitoring is indicated in the judgement of a physician.

The fittings of the combination CO_2/flow sensors comply with ISO [5356-1: 1987 (E)]. The combination CO_2/flow sensors may be used in conjunction with endotracheal tubes, face masks, and breathing circuit devices that also comply with the same fitting specification.

The combination CO_2/flow sensors and NICO sensors are single patient use devices.

The use of the NICO monitor Model 7300 for cardiac output monitoring is contraindicated in patients in which a small rise (3-5 mmHg) in their arterial partial pressure of CO_2 level cannot be tolerated.

(PLEASE DO NOT WRITE BELOW THIS LINE - CONTINUE ON ANOTHER PAGE IF NEEDED)

_____ _____ _____ _____ _____ _____ _____ _____

Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use_____ **OR** **Over-The-Counter Use**_____
(Per 21 CFR 801.109)

(Optional Format 1-2-96)

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TABLE OF CONTENTS

I. GENERAL DESCRIPTION

A. Applicant's Name and Address

Respironics Novametrix Inc. (formerly known as Novametrix Medical Systems, Inc.)
5 Technology Drive
Wallingford, CT 06492

B. Contact Person

Michael J. Malis
Q.A. and Regulatory Manager
(203) 697-6442
(203) 284-0753 (facsimile)

C. Manufacturer's Names and Address

Respironics Novametrix Inc.
5 Technology Drive
Wallingford, CT 06492

D. Establishment Registration Number: 1219324

E. Device Names (Proprietary/Trade Names): NICO, Model 7300

F. Device Name (Common Name): multiparameter monitor (monitoring spirometer, CO_2 monitor, pulse oximeter and cardiac output monitor with partial rebreathing valve).

G. Classification: Class II, 21 C.F.R. 868.1850, 868.1400, 870.2700, 868.5675

H. Performance and Other Standards:

No performance standards have been promulgated under section 514 for monitoring spirometers, carbon dioxide monitors, pulse oximeters, cardiac output monitors or rebreathing valves. No special controls apply. The fittings of the flow sensors and CO_2 airway adapters comply with ISO 5356-1:1987(E). The NICO monitor, Model 7300 complies with IEC 601-1 and the requirements for EMC (such IEC 1000-3-2, 1000-3-3, 1000-4-2, 1000-4-3).

I. Company Overview

Respironics Novametrix, Inc. was acquired in April 2002 by Respironics, Inc. and now is the cardiopulmonary operating unit of the Hospital division of Respironics, Inc. The Novametrix division is a medical device manufacturing company that commenced operation in 1978. Operations consist of the design, manufacturing, distribution and servicing of high tech medical monitoring devices.

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INTENDED USE

Intended Use

The intended use of the NICO monitor, Model 7300 is to provide:

- cardiac output monitoring via the method of partial rebreathing in adult patients receiving mechanical ventilation during general anesthesia and in the intensive care unit (ICU).

- spirometric, and carbon dioxide monitoring in neonatal, pediatric and adult patients during general anesthesia and in the intensive care unit (ICU) and the emergency department (ED). Separate combination CO_2/flow sensors are provided for adult, pediatric and neonatal use.

- continuous, non-invasive monitoring of functional arterial oxygen saturation and pulse rate in neonatal, pediatric and adult patients during both no motion and motion conditions and for patients who are well or poorly perfused during general anesthesia and in the intensive care unit (ICU) and the emergency department (ED).

The NICO monitor Model 7300 and its sensors are intended to be used by trained operators when spirometric, capnographic, pulse oximetry, or cardiac output monitoring is indicated in the judgement of a physician.

The fittings of the combination CO_2/flow sensors comply with ISO [5356-1: 1987 (E)]. The combination CO_2/flow sensors may be used in conjunction with endotracheal tubes, face masks, and breathing circuit devices that also comply with the same fitting specification.

The combination CO_2/flow sensors and NICO sensors are single patient use devices.

The use of the NICO monitor Model 7300 for cardiac output monitoring is contraindicated in patients in which a small rise (3-5 mmHg) in their arterial partial pressure of CO_2 level cannot be tolerated.

Proposed Labeling and Instructions for Use

The draft user's manual, product literature, pouch labeling and front, top and rear panel labeling may be found in Appendices 1A, 1B, 1C, and 1D, respectively.

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III: DEVICE DESCRIPTION, INCLUDING PHOTOGRAPHS AND ENGINEERING DRAWINGS

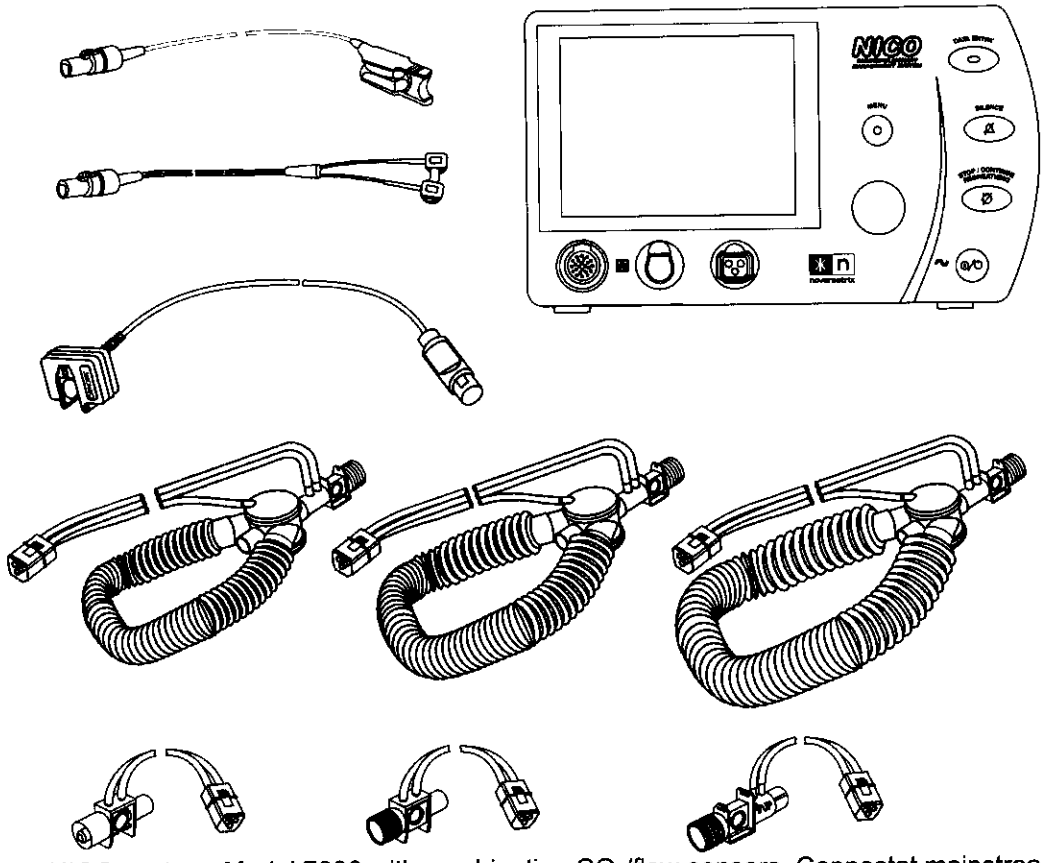


Figure III-1 - NICO system, Model 7300 with combination CO_2/flow sensors, Capnostat mainstream gas sensor, NICO sensors, and oxygen saturation probes.

A. REASON FOR SUBMISSION

The reason for this submission is to notify the FDA that Novametrix plans to market a device, the NICO Model 7300 with MARS which is the combination of two previously cleared devices. The predicate devices are the CO_2SMO Plus! with NICO, Model 8200 (510(k) No. K982499 dated 10/16/98) and MARSPO_2, Model 2001 (510(k) No.s K993979 date 2/22/00 and K000794 dated 04/10/2000).

B. INTRODUCTION

Pulse oximetry (non-invasive monitoring of oxygen saturation) and capnography (non-invasive measurement of airway carbon dioxide) are routinely monitored in critically ill patients and during surgery. Additionally, short term monitoring of the critically ill patient's airflow has become routine in many institutions. Continuous spirometry monitoring is presently used in both the intensive care unit and the operating room as well as any other area of the hospital where respiratory monitoring is indicated. Invasive cardiac output monitoring with a pulmonary artery catheter using bolus thermodilution has become commonplace since its introduction in the 1970's. Continued questions about its effect on morbidity and mortality have led to an increased interest in the application of non-invasive methods for cardiac output monitoring. These non-invasive methods have included Fick-based rebreathing methods and Doppler based methods using transducers located externally at the xiphoid process or internally in the esophagus or trachea.

The *NICO with MARS*, Model 7300 is intended for non-invasive monitoring of the inspired and expired airflow and airway pressure of intensive care unit (ICU), anesthesia and emergency room (ER) patients, as well as capnography and pulse oximetry in all of these clinical settings. It is also intended for cardiac output monitoring via the method of partial rebreathing in adult patients receiving mechanical ventilation during general anesthesia and in the intensive care unit (ICU). It is intended to serve the same purposes as the *CO_2SMO Plus! with NICO* and *MARSPO_2*, Model 2001.

In the NICO system, combination CO_2 adapter/flow sensors (neonatal, pediatric, adult) are connected with a male pneumatic connector to the NICO monitor. The principal function of the flow portion of these sensors are to provide a differential pressure signal related to flow and airway pressure relative to atmospheric pressure. These sensors are often placed in the breathing circuit between the endotracheal tube and the ventilator circuit Y piece and may also be used in conjunction with a face mask or mouthpiece. The CO_2 airway adapter portion of these sensors, allow the Novametrix CO_2 mainstream gas sensor, the Capnostat®, to attach to it and measure the concentration of CO_2 in the airway using infrared technology. When CO_2 measurements are combined with airway flow and volume measurements, other parameters such as CO_2 production and dead space can be calculated.

The NICO monitor (see block diagram) consists of a microprocessor-based data acquisition system that measures flow, pressure, CO_2 and oxygen saturation data. Flow is measured with a fixed orifice differential flow sensor. Airway and barometric pressure are measured with absolute pressure transducers. Airway pressure is measured relative to the barometric pressure. CO_2 is measured by a mainstream infrared absorption (IR) technique with a solid state sensor. Oxygen saturation is measured with ratiometric technique based using red and infrared absorbance of oxy- and deoxyhemoglobin. The combination flow/CO_2 sensors and O_2 saturation sensors are already legally marketed as accessories of 510(k) cleared Novametrix predicate devices.

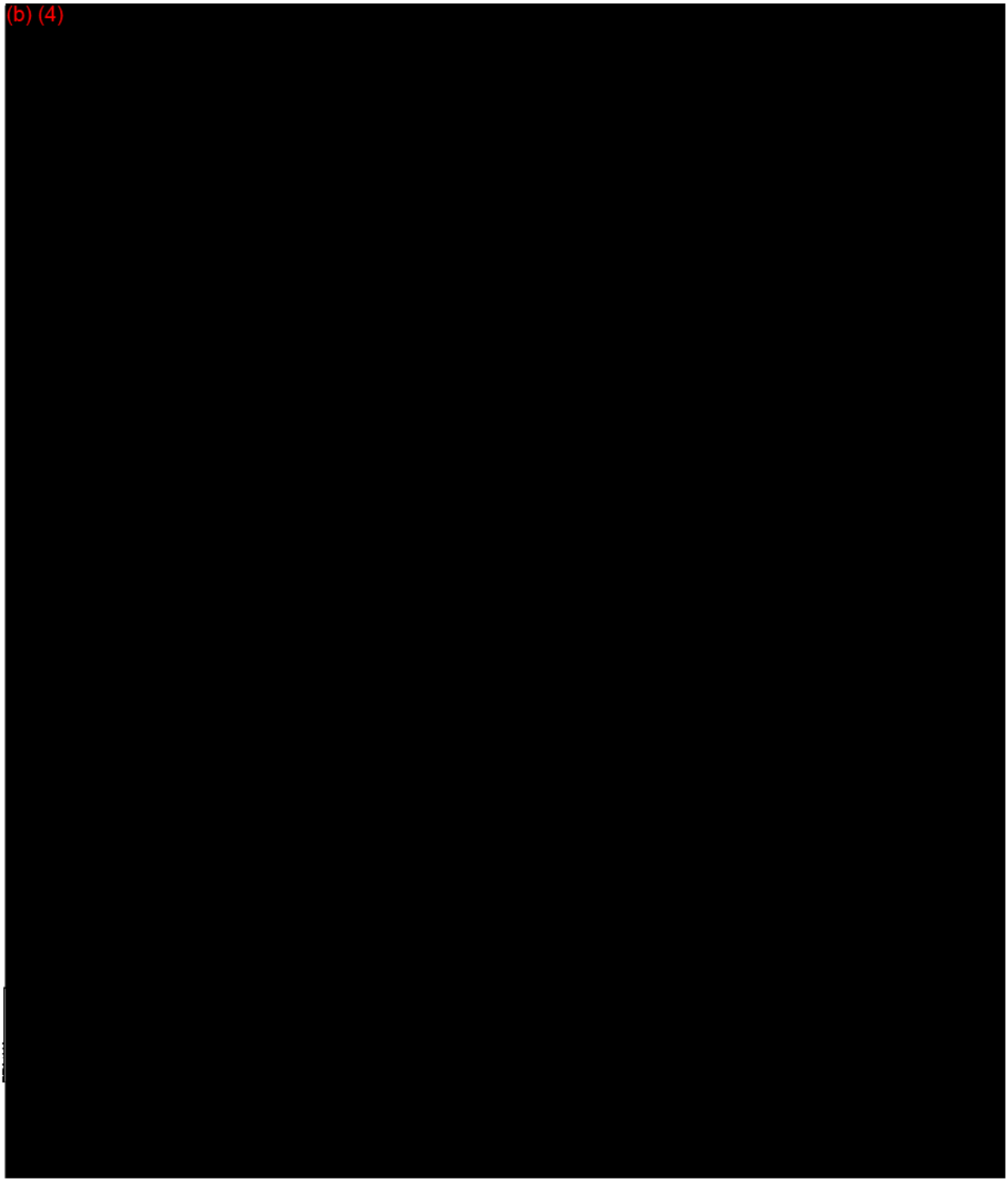
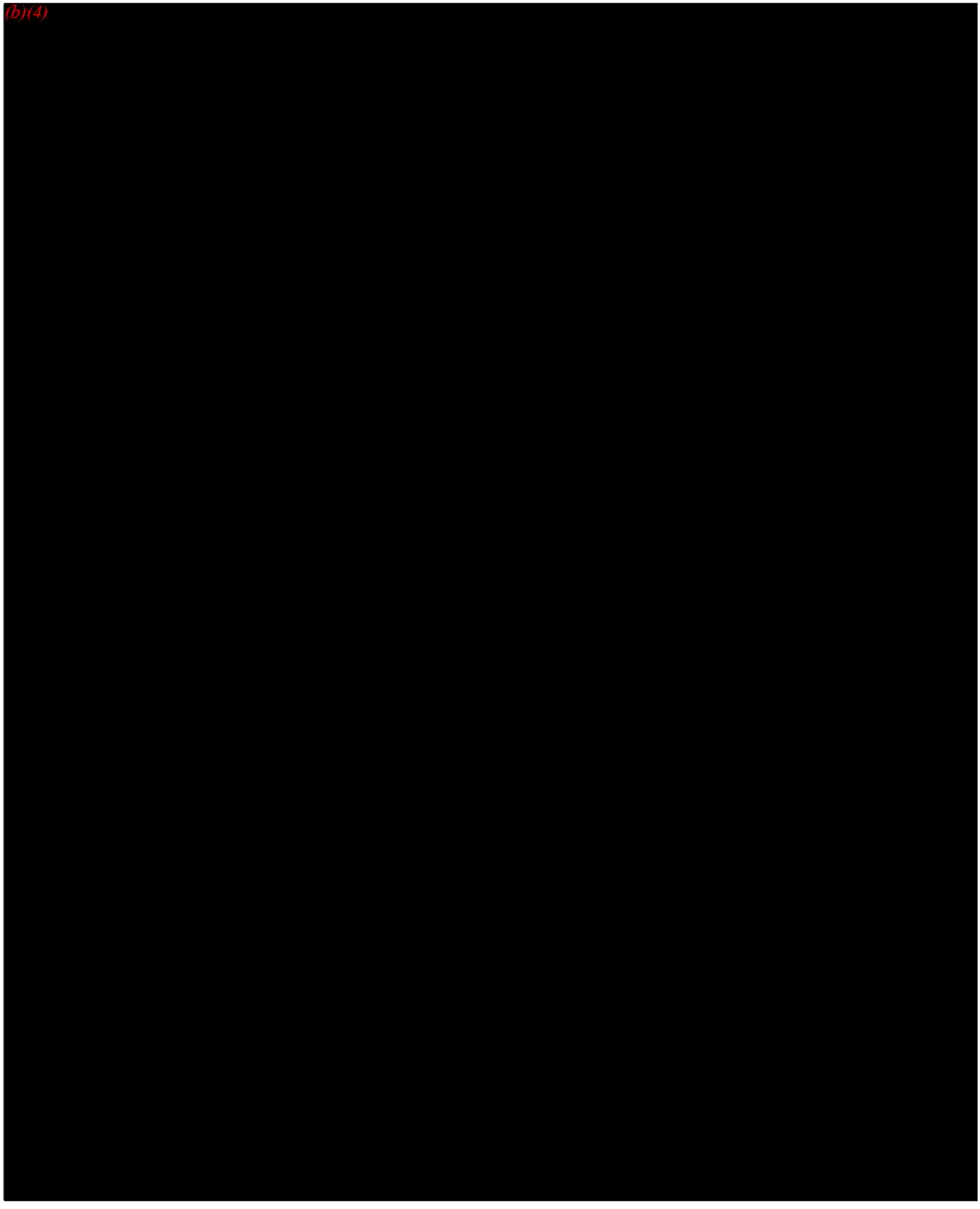


Figure III-1 - Overall System Block Diagram

The firmware in the NICO module acquires data from the flow, pressure, SpO_2 and CO_2 sensors. The monitor calculates parameters and displays waveforms, loops, trends and numeric data.

C. Technical Description - NICO

(b)(4)



C. Technical Description - NICO

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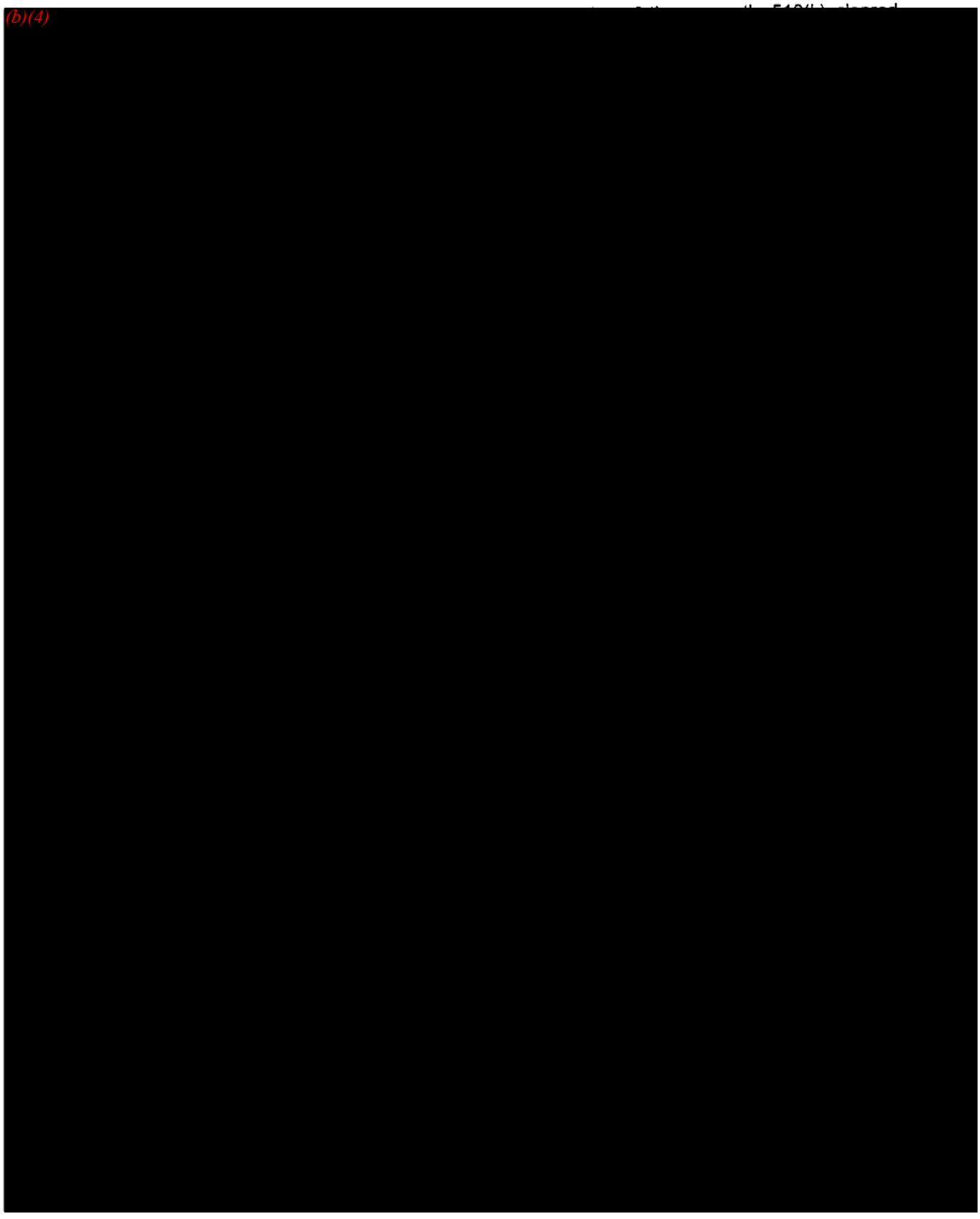

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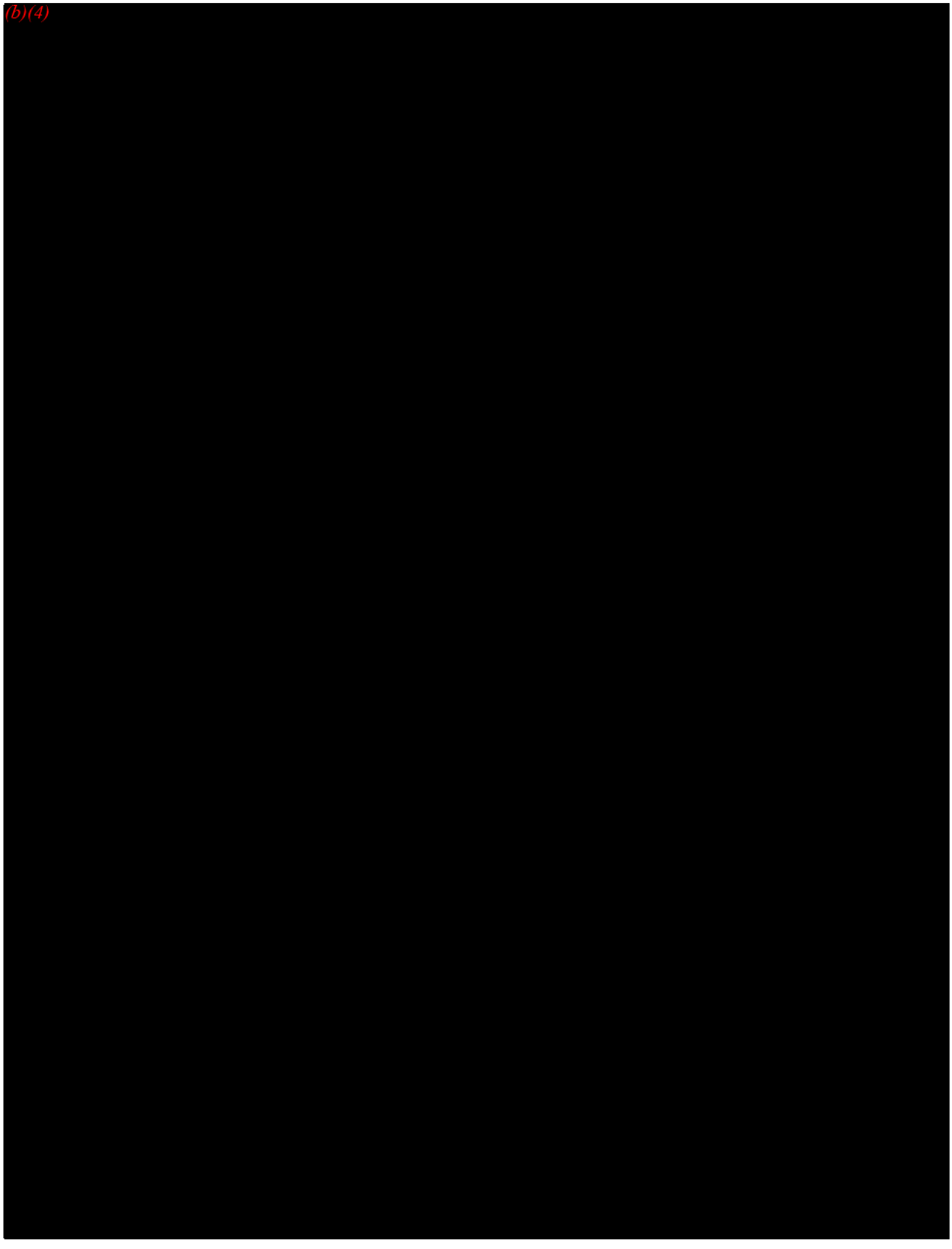

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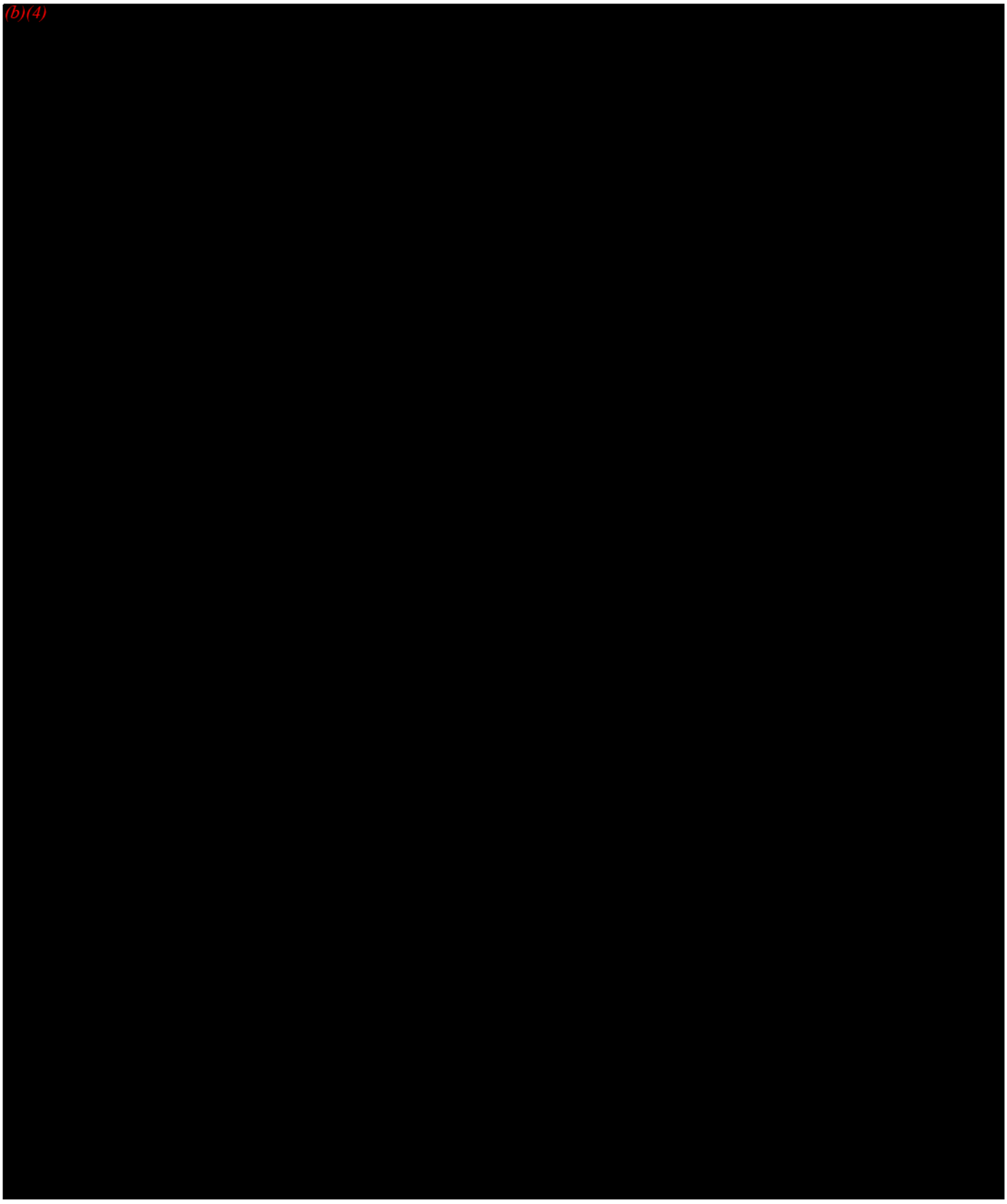

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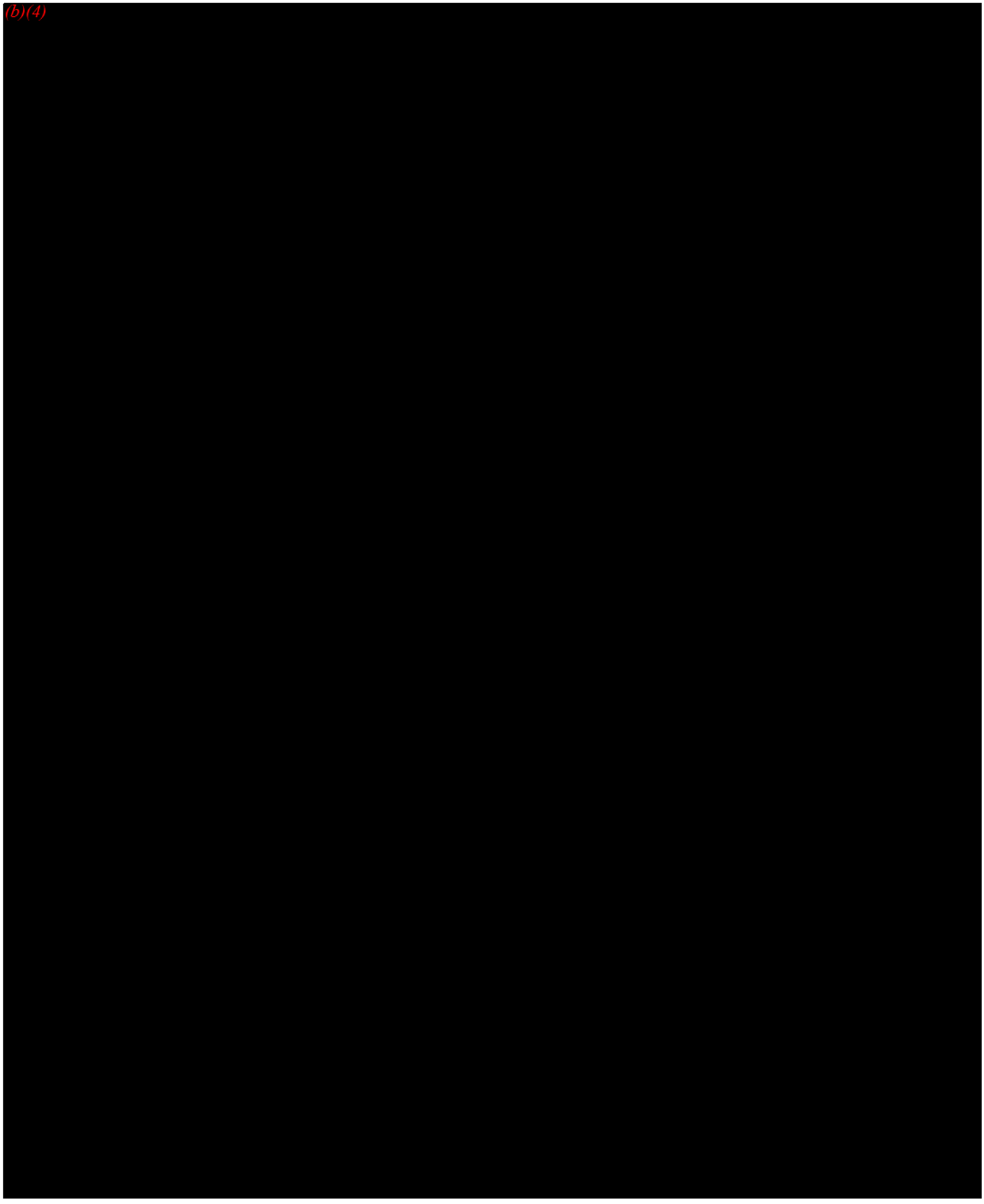

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Table 1 – Selected NICO Studies*

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[redacted]

Table 2- Bolus Thermodilution to Baxter Intellicath CCO System

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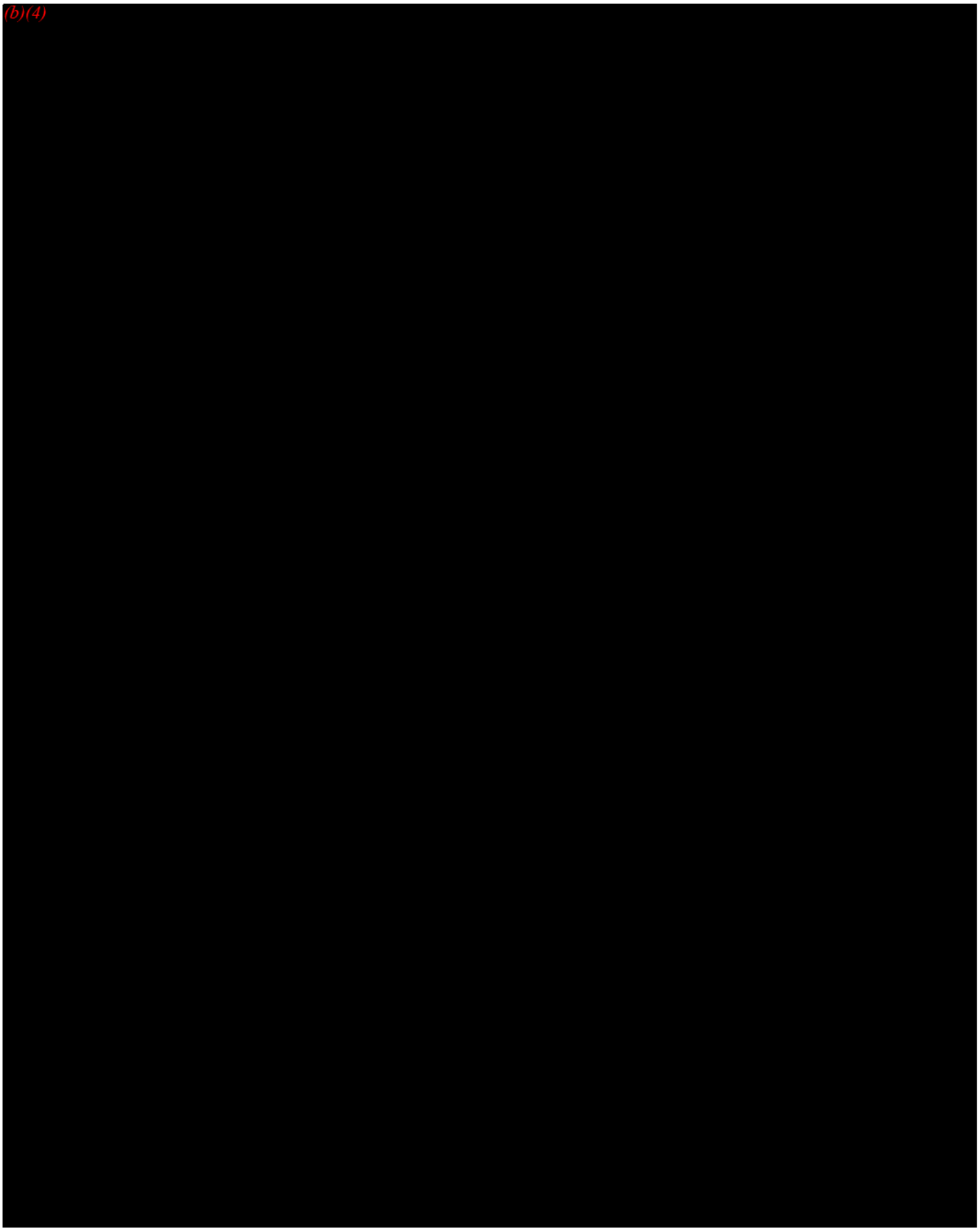

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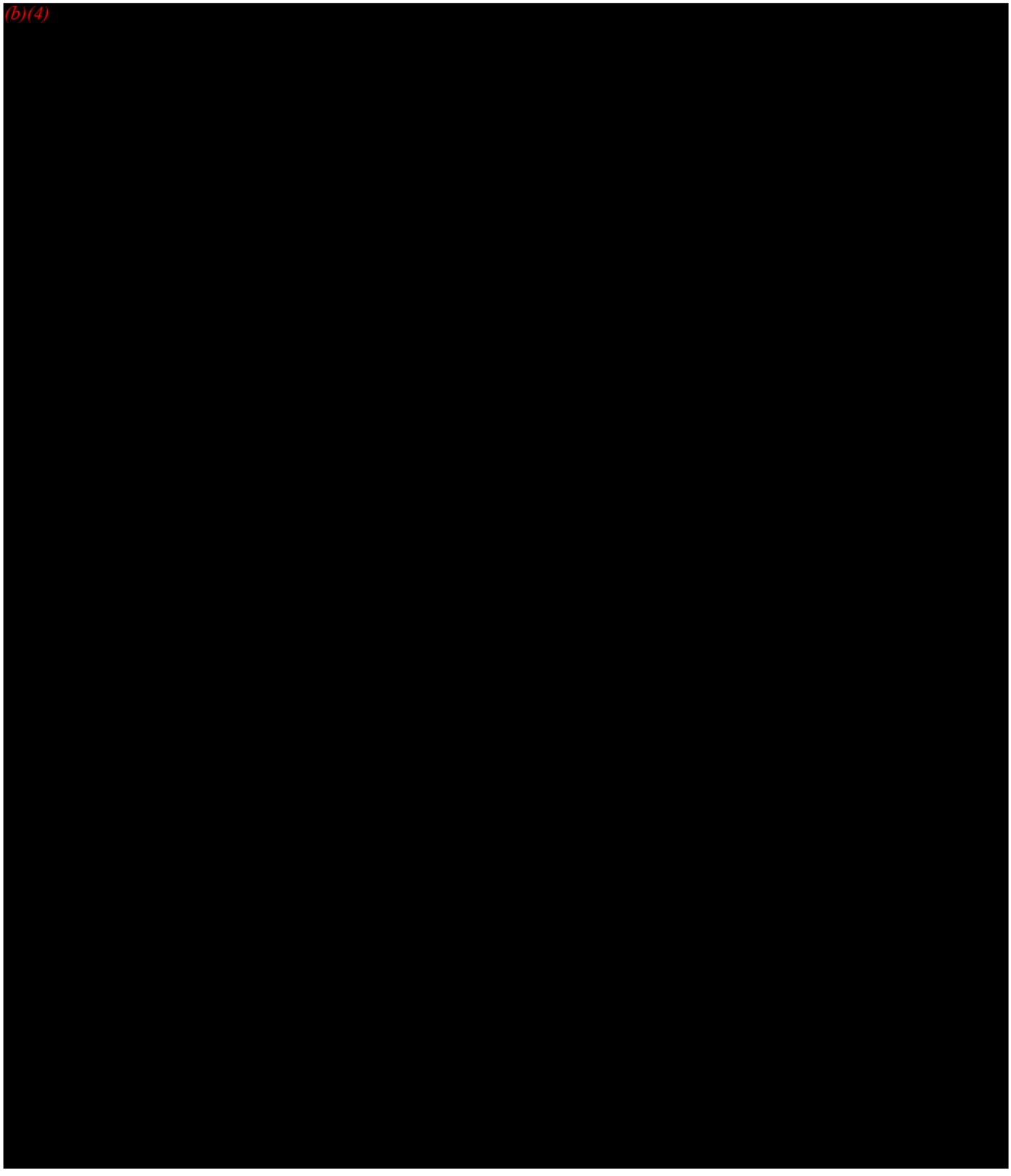

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D. USE OF DEVICE

PURPOSE AND ENVIRONMENT

Function and Patient Population

The *NICO with MARS*, Model 7300 provides cardiac output monitoring in the mechanically ventilated pediatric/adult patient during general anesthesia and in the ICU. It also provides spirometric, CO_2, and pulse oximetry monitoring during general anesthesia, in the ICU and in the ER. Three NICO sensors with different expandable loop sizes covering tidal volume ranges of 200-500 ml, 400-1000 ml, and 750-1500 ml each with the same combination CO_2/flow sensor and valve body are provided. Separate combination CO_2/flow sensors are provided for neonatal, pediatric and adult use.

Other User Environment Information

NICO with MARS is a prescription device that is not labeled or intended for home use. It is intended to be used by qualified personnel.

Typical Application

Intubated patients - The combination CO_2/flow sensors are placed between the endotracheal tube and Y piece. The Capnostat CO_2 sensor attaches to the CO_2 airway adapter and measures the concentration of CO_2 of the patient's respired gases inside the airway adapter using infrared technology. The interconnected tubing in these circuits use tapered sections of tubing specified in ISO standards to provide dependable connections. The ends of the CO_2 airway adapters have tapers to assure reliable connections.

Intubated patients (cardiac output monitoring) - The combined CO_2/flow sensor with a rebreathing valve and loop (known as the NICO sensor) is placed between the endotracheal tube and Y piece. This valve is controlled pneumatically and is periodically actuated to increase the rebreathed volume. Using flow and CO_2 data from the period before rebreathing and during rebreathing, cardiac output may be calculated. The state of the rebreathing and valve is monitored by the system which is measuring the pressure in the valve control line and amount of CO_2 rebreathed.

Nonintubated patients - The Capnostat is attached to an airway adapter connected to a mouthpiece or facemask.

Oxygen Saturation - The SpO_2 Finger sensor is intended for use on adult or pediatric patients. It is clipped to the patient's finger. The Y-sensor is a multi-site sensor which can be used on all patient populations on sites including the finger, ear, hand, foot or toe. The sensor is applied using either foam, tape or cloth applicators which are available in various sizes for each patient population. The tape applicators included a release liner that allows the sensor to be assembled with the tape prior to the removal of the liner. The liner consists of two parts with release tabs for the clinical staff to pull to release the liner prior to applying to the patient. Additionally, there are slits in the liner which allow the liner to be "peeled around" the assembled sensor. The three variations of applicators with release liners - butterfly, strip and foam wrap allow the sensor applied to patients ranging from neonates to adults. The individual tapes of each type are connected end-to-end by a perforation and packaged in a dispenser box such as 100 parts wound on 2 inch ID per package. The Single Patient Use SpO_2 Sensors are designed for use on all patient populations and can be applied to the finger, hand, foot or toe. A Velcro strip holds the sensor onto the site.

Patient Contact (Cleaning, Disinfecting, and Sterilizing)

Combination CO_2/Flow Sensors - The combination CO_2/flow sensors are not in direct contact with the patient in normal use. The airway adapters are labeled as single patient use and are not intended to be cleaned, disinfected, sterilized, or reused for another patient.

NICO Sensor - The combination CO_2/flow sensor and valve assembly portions are not in contact with the patient in normal use. NICO sensors are labeled as single patient use and are not intended to be cleaned, disinfected, sterilized, or reused for another patient.

SpO_2 Probes- The SpO_2 Finger sensor can be wiped down with a cloth dampened with 70% isopropyl alcohol, 10% bleach solution or gluteraldehyde solution followed by wiping with water. The Y-sensor can be immersed (up to but not including the connector) in a 10% bleach solution or gluteraldehyde solution followed by rinsing with water. The Single Patient Use SpO_2 Sensors are not intended to be cleaned, disinfected, sterilized or reused for another patient.

E. PRODUCT LIFE

The combination CO_2/flow sensors are intended to be used as a single patient use device and are not shipped as a sterile device. The NICO sensor (combination CO_2/flow sensor and valve assembly) is intended to be used as a single patient use disposable device and is packaged as a non-sterile device. Reusable SpO_2 sensors can be cleaned and sterilized and can last 3-24 months, depending upon care and usage. Single patient use SpO_2 sensors are labeled as such and not intended to be cleaned or sterilized or reused on another patient.

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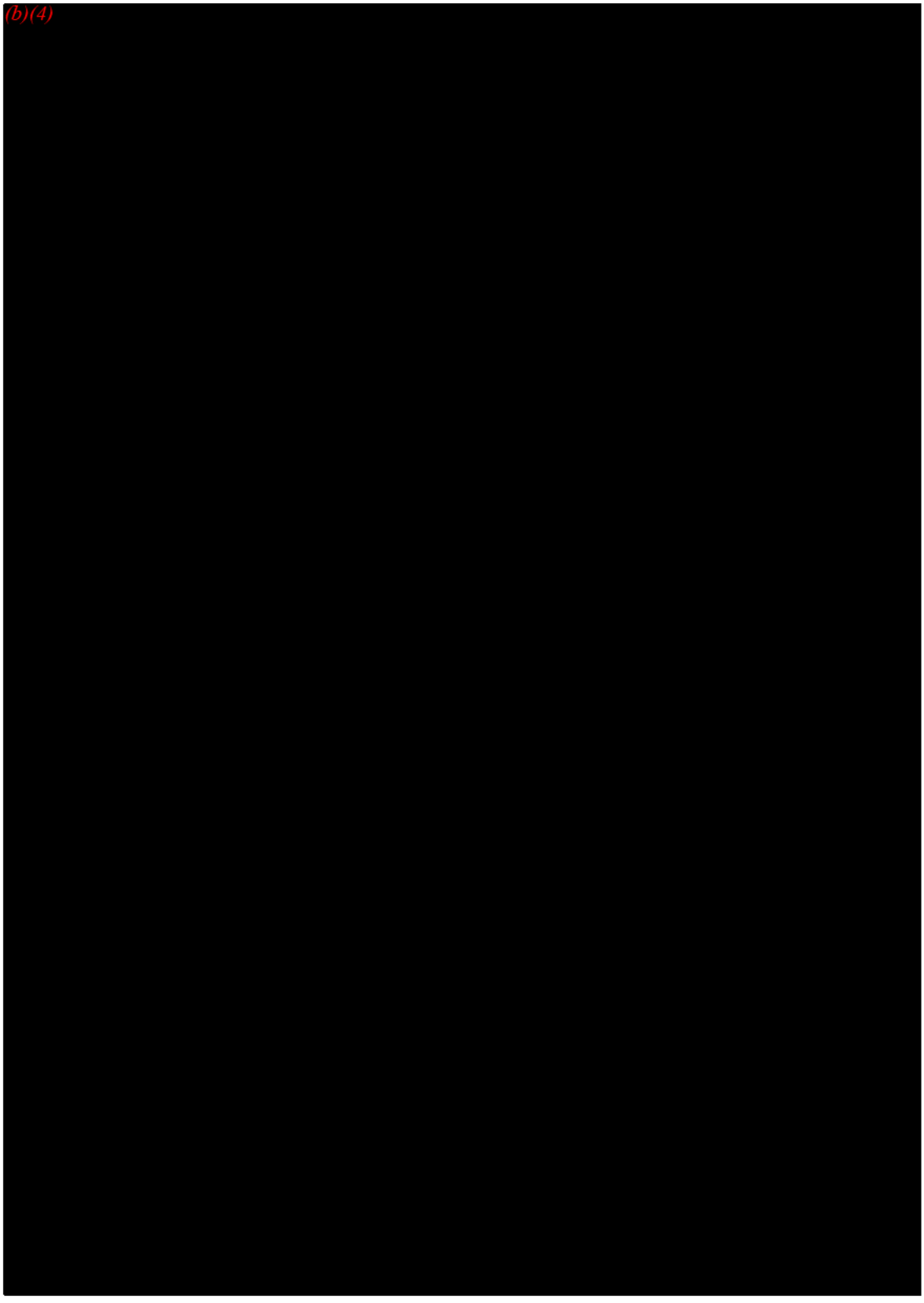
F. DESCRIPTION OF DEVICE CONSTRUCTION

MATERIALS

(b)(4)



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ASSEMBLY PROCESS

(b) (4)

ENGINEERING DRAWINGS

See the drawings listed in Table III-1.

Table III-1 - Drawings

Drawing	Section
Combination CO_2/flow sensor, pediatric/adult	III
Combination CO_2/flow sensor, pediatric	III
Combination CO_2/flow sensor, neonatal	III
Partial Rebreathing valve	III
Partial Rebreathing valve assembly and pouch	III
SpO_2 sensor - Y-sensor	III
SpO_2 sensor finger sensor	III
Neonatal/pediatric SPU SpO2 sensor pouch drawings	III
Pediatric/adult SPU SpO2 sensor pouch drawings	III
Pediatric/adult combination CO_2/Flow sensor assembly and pouch	III
Pediatric combination CO_2/Flow sensor assembly and pouch	III
Neonatal combination CO_2/Flow sensor assembly and pouch	III
Wiring Diagram	III
Pneumatics Diagram	III
Front panel overlay	Appendix 1
Rear panel overlay	Appendix 1
Top Cover	Appendix 1

*SPU - Single Patient Use

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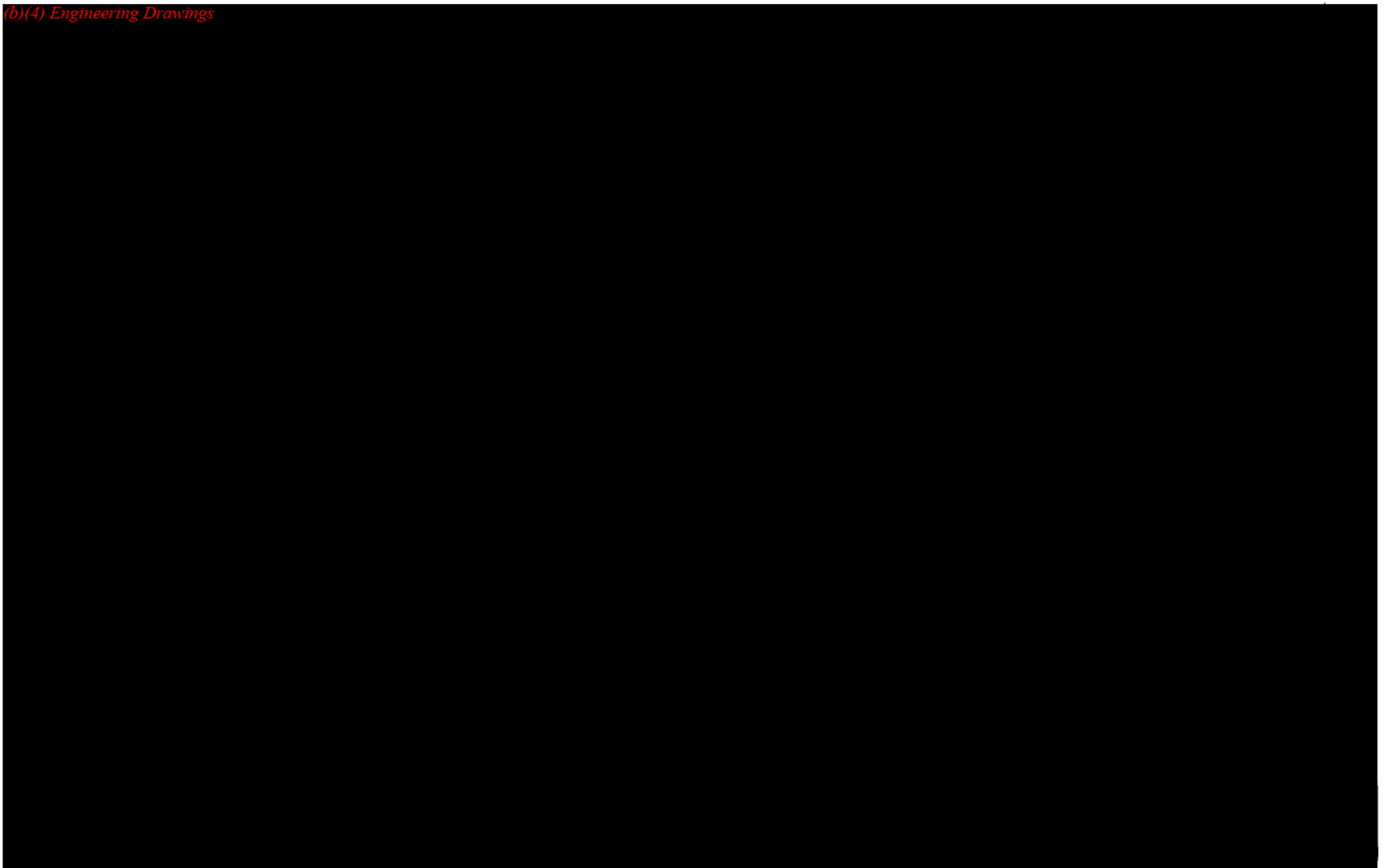
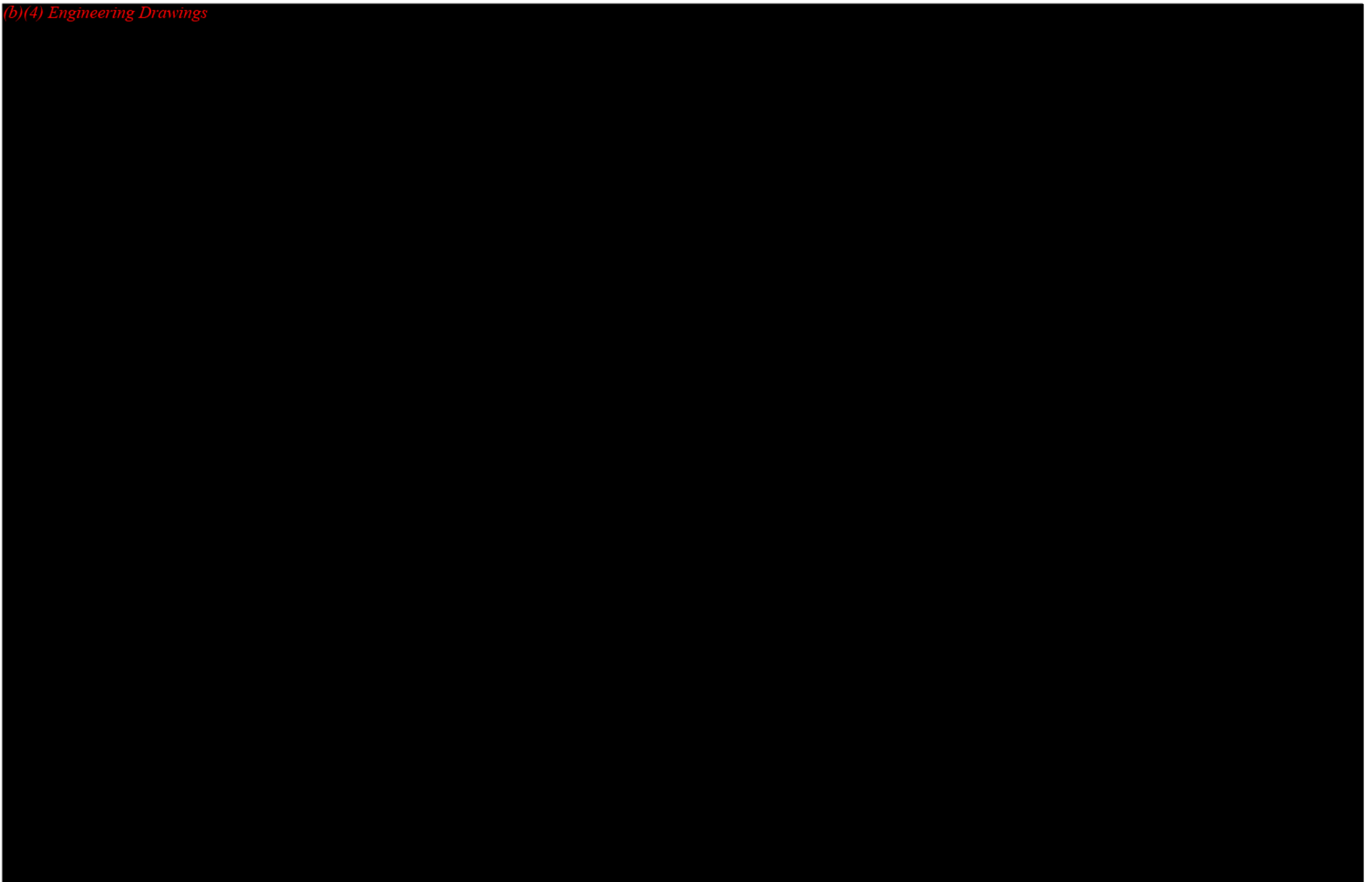
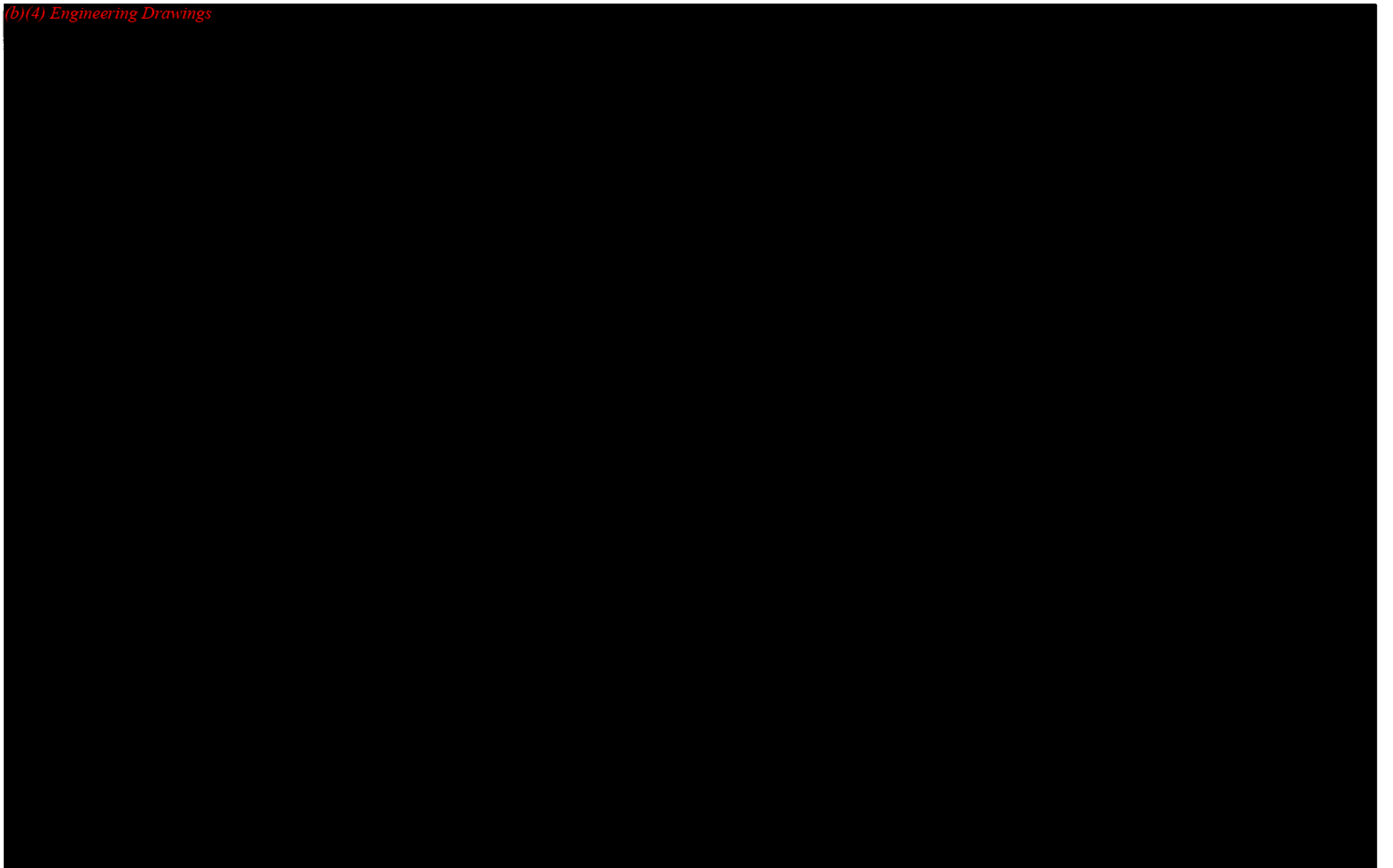
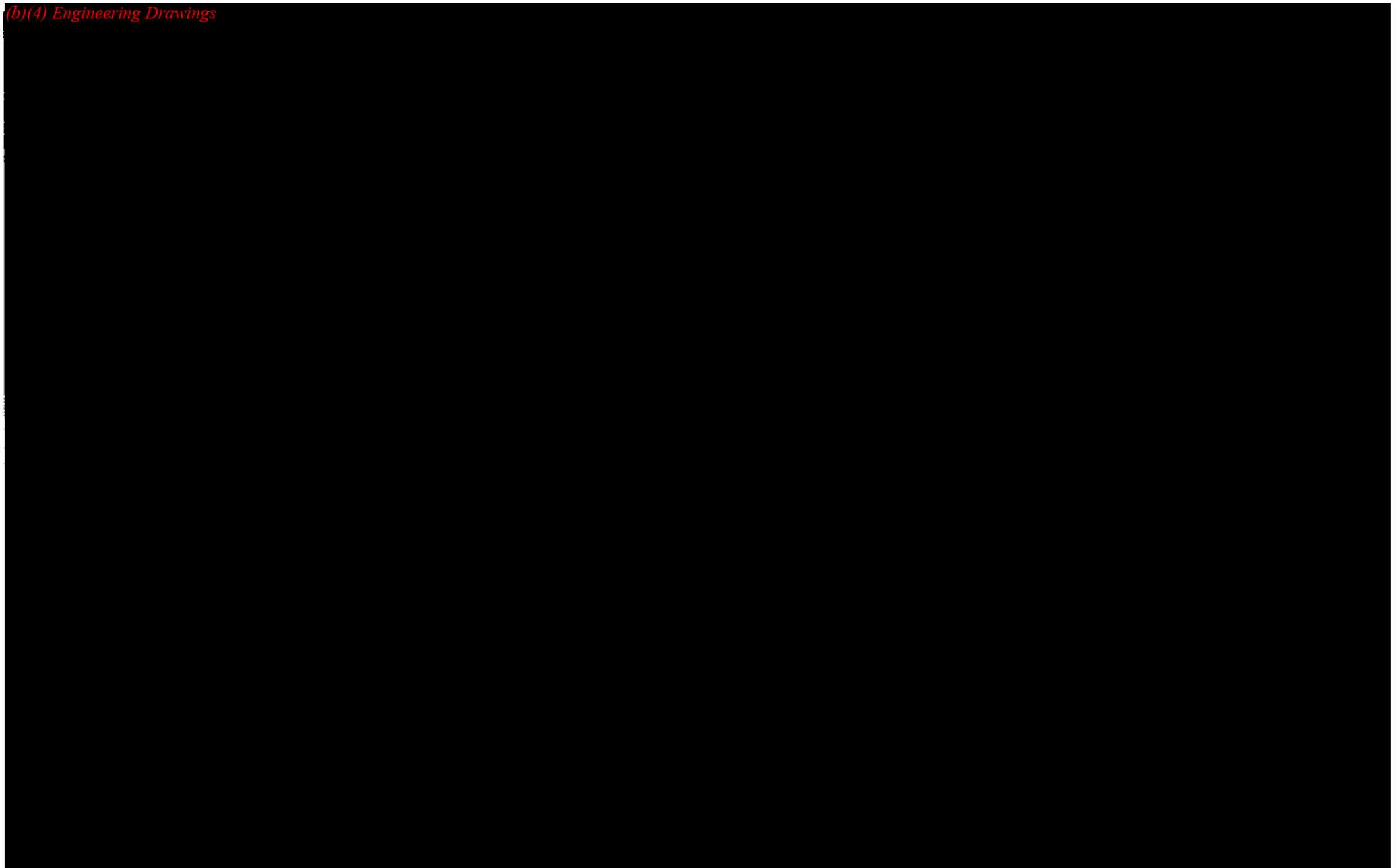
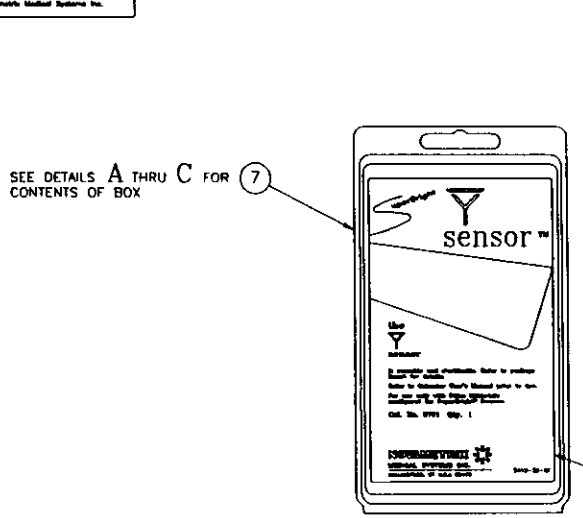










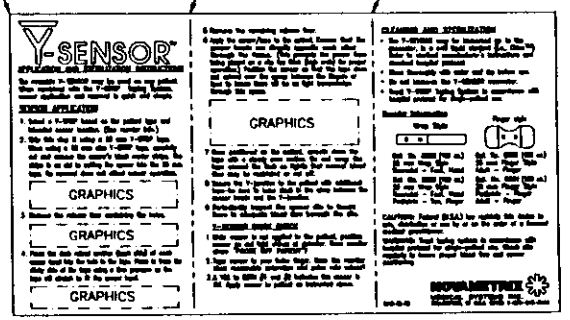
SEE DETAILS A THRU C FOR CONTENTS OF BOX (7)

(1) NOTE ORIENTATION OF LABEL AND LOCATE ON TOP OF TRAY COVER APPROX AS SHOWN

FOLD IN THIRDS AND PLACE IN BOX FIRST (2)

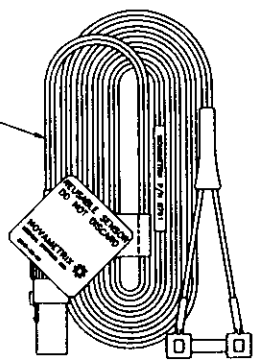
FIRST FOLD LINE

SECOND FOLD LINE



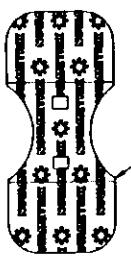
DETAIL B

PLACE SENSOR IN BOX ON TOP OF TAPES (3)



DETAIL A

PLACE TAPE ON TOP OF INSTRUCTION SHEET (5)



(6) PLACE TAPE ON TOP OF INSTRUCTION SHEET

DETAIL C

22

CONFIDENTIAL

REV		
05	M337	20Sep95
04	M331	23Sep93
03	M286	14JAN93
02	M247	29JUL92
01	M218	23OCT91

02 SATURATION SUPERBRIGHT Y-SENSOR

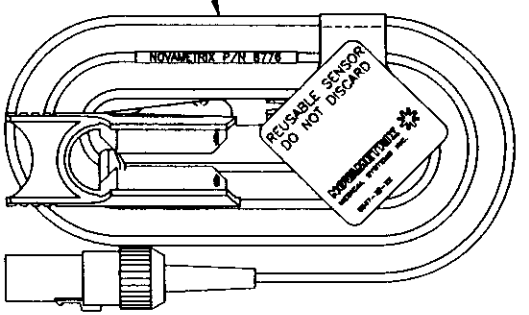
NOVAMETRIX MEDICAL SYSTEMS INC.

D | 8791 | 00 | 05

SEE DETAILS A & B FOR CONTENTS OF BOX (1)

(3)

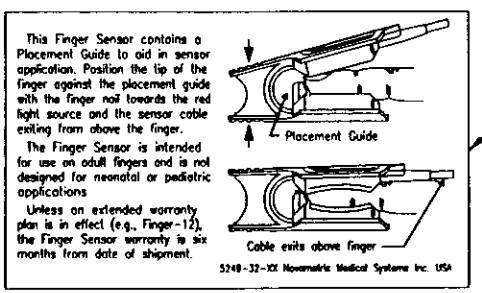
(2)



DETAIL A

CONFIDENTIAL

221



(4) PLACE IN BOX FIRST

DETAIL B

REV	R NO.	DATE
07	N278	16Mar92
06	N262	5Sep90
05	N247	2Jul90
04	N209	27Jul89
03	N182	23Jan89
02	N167	21Nov88
01	P19	9Sep88

DO NOT SCALE
UNLESS OTHERWISE SPECIFIED DIMENSIONS ARE IN INCHES (mm)
BREAK ALL SHARP EDGES
TOLERANCES
DEC ± – (mm) ± –
FRAC ± – (mm) ± –
HOLES +.007 -.003 (mm) (+.18 -.08)
ANG ± –
MATERIAL ——
FINISH ——

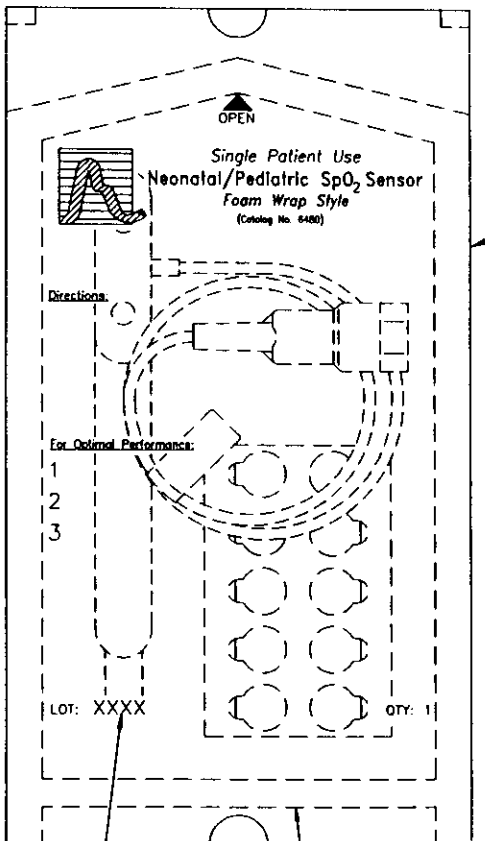
TITLE: O2 SATURATION FINGER SENSOR, SUPERBRIGHT

DRAWN GB 9Sep88 mrt | CHECKED SM 28Sep88
MFG ENGR MW 2Nov88 | APPROVED ST 18Nov88
USED ON: –

NOVAMETRIX MEDICAL SYSTEMS INC. WALLINGFORD, CT U.S.A. 06492

SIZE	DRAWING NO	CODE	REV
C	8776	00	07

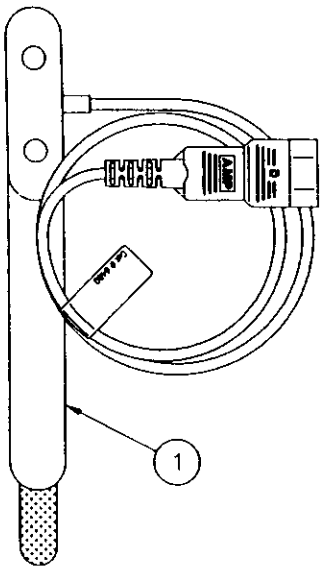
SCALE: 1/1 SHEET 1 OF 1



2 SEE NOTE 1 FOR ASSY PROCEDURE

LOT NUMBER

SEAL THIS END



DETAIL A

CONFIDENTIAL

NOTES:

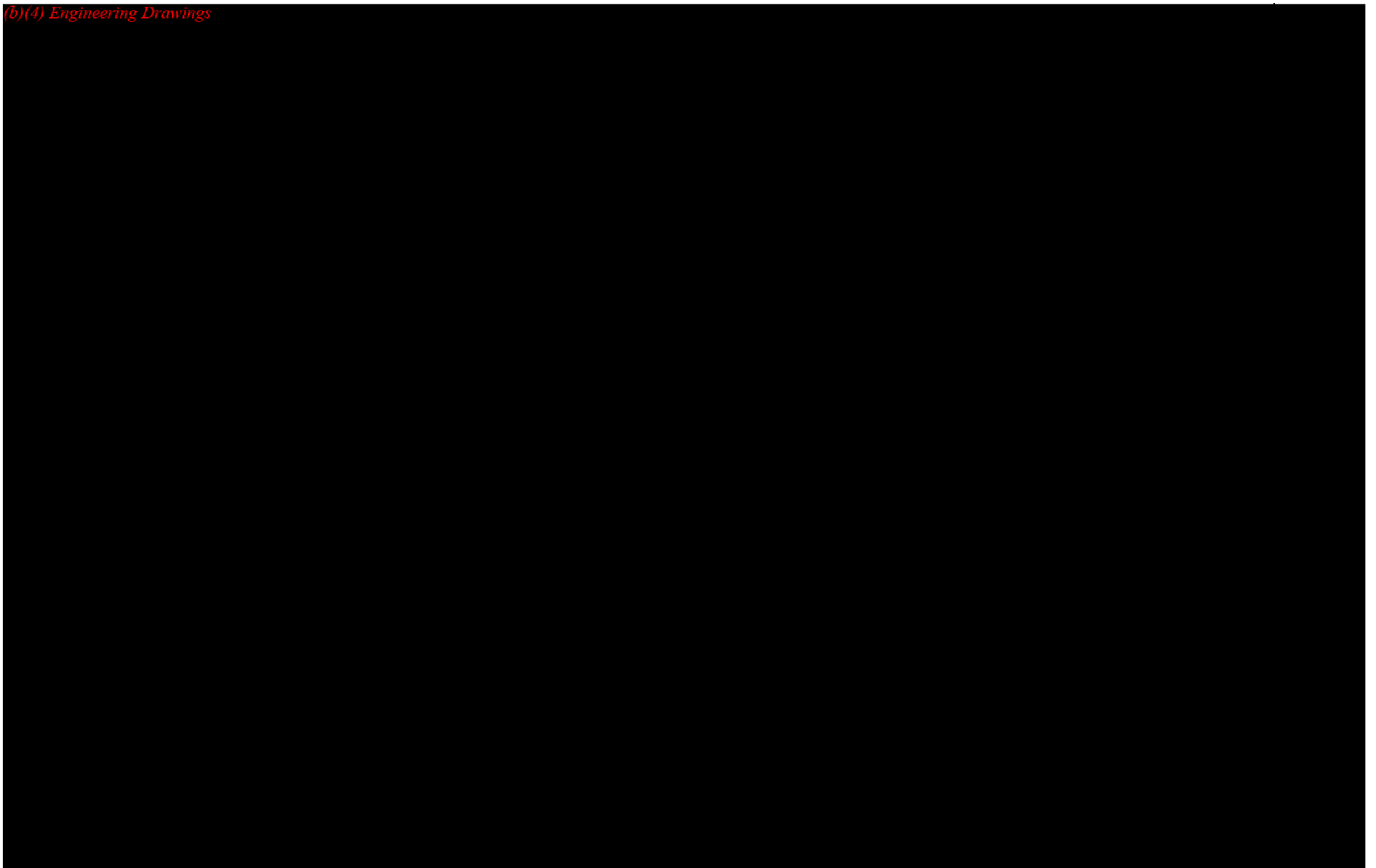
1. ASSY PROCEDURE:
   A. MARK LOT NO. ON POUCH (ITEM 2) IN AREA INDICATED.
   B. PLACE SPU SPO2 SENSOR (ITEM 1) REF DETAIL A AND 1 SHEET OF APPLICATION DOTS, ITEM 3 INTO POUCH.
   C. SEAL POUCH APPROX AS SHOWN.

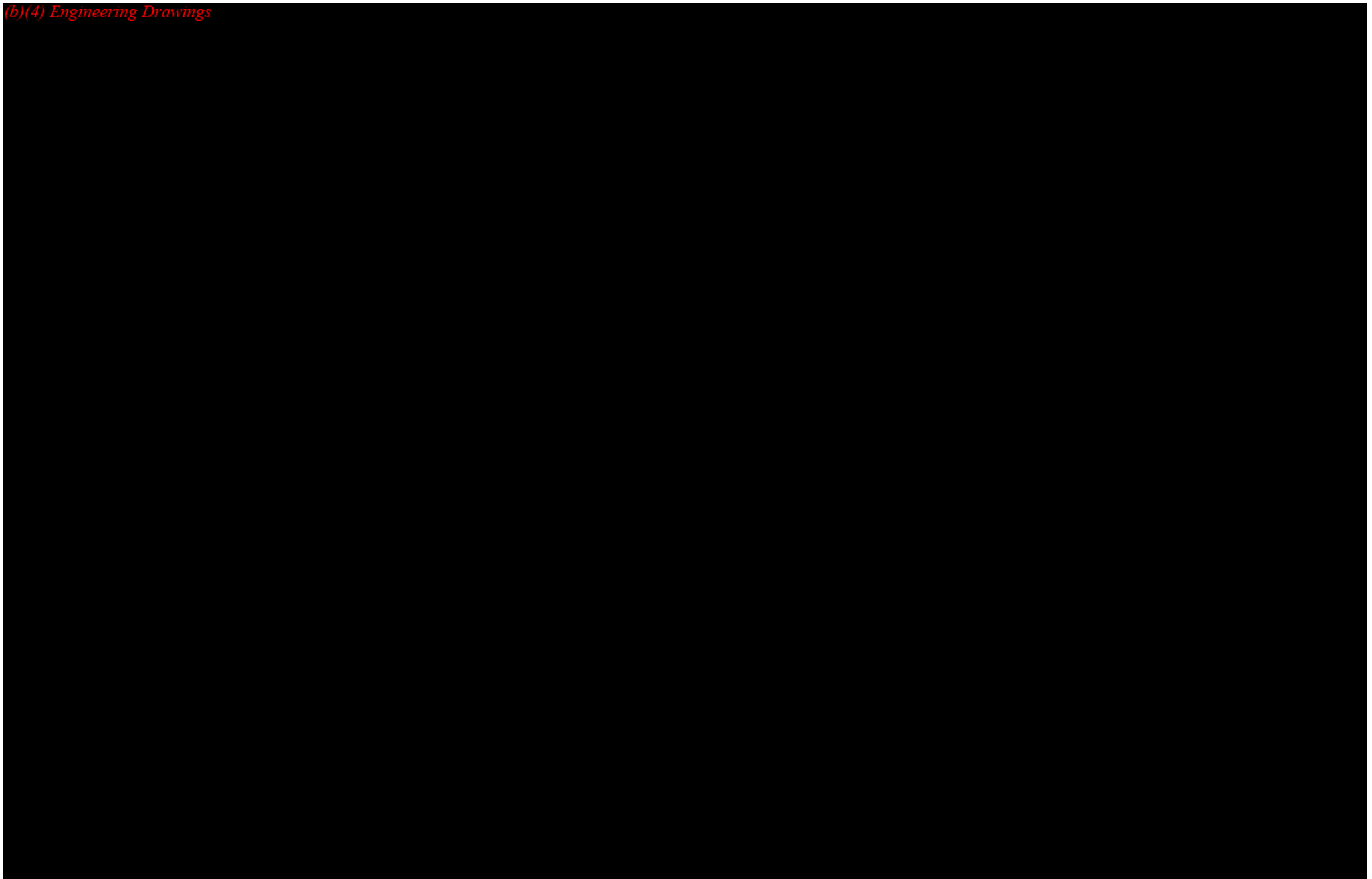
REV	R NO.	DATE	DO NOT SCALE UNLESS OTHERWISE SPECIFIED DIMENSIONS ARE IN INCHES (mm) BREAK ALL SHARP EDGES TOLERANCES DEC ± ~ (mm) (± ~) FRAC ± ~ (mm) (± ~) HOLES ± .007 -.003 (mm) (± ~) ANG ± ~ MATERIAL ~ FINISH ~	TITLE: NEONATAL/PEDIATRIC SENSOR & POUCH ASSY, SPU SPO2 SENSOR	NOVAMETRIX MEDICAL SYSTEMS INC. WALLINGFORD, CT U.S.A. 06492
				DRAWN BL 8Dec95 / CHECKED MRL 18Dec95	
				MFG ENGR WT 12/18/95 / APPROVED HW 12/18/95	SIZE C / DRAWING NO. 6480 / CODE 01 / REV 00
				USED ON 6480-00 & 6480-25	SCALE: 1/1 / SHEET 1 OF 1

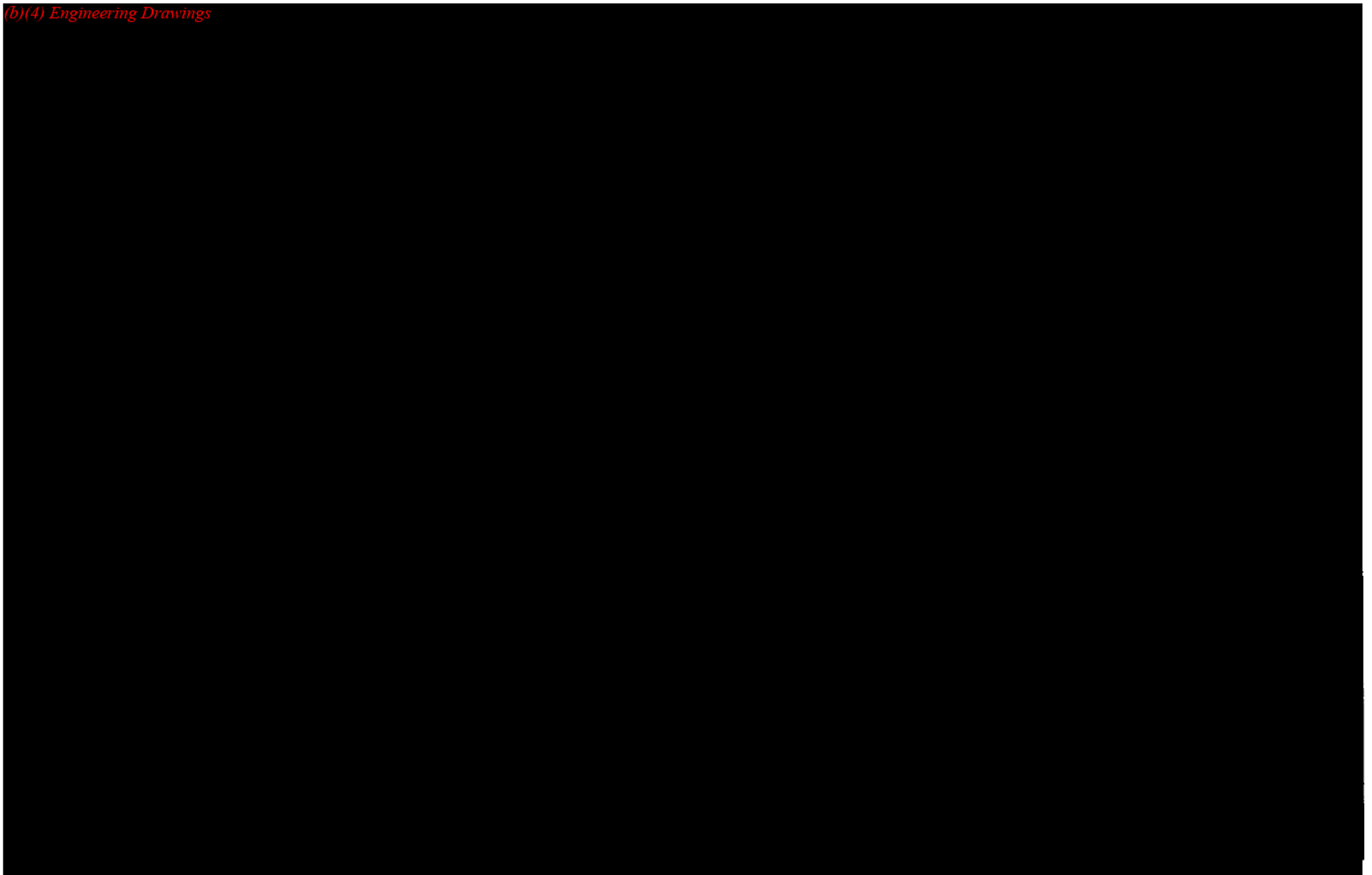
(b) (4)

(b)(4) Engineering Drawings

[redacted]







IV - 510(K) "Substantial Equivalence"

The analysis below follows the definition of substantial equivalence in section 513(i) of the Federal Food, Drug and Cosmetic Act. The *NICO Model 7300 with MARS* is a *combination* of the currently 510(k)-cleared *CO_2SMO Plus! with NICO* and MARSpO2 Model 2001. The *NICO Model 7300* is judged to be substantially equivalent in safety and effectiveness in its intended use to legally marketed devices. In addition, performance of all parameters associated with the safety and effectiveness of the device were validated through testing and reference is made to the test results and analysis.

A. NICO Model 7300 with MARS Substantial Equivalence

QUESTION	SUMMARY RESPONSE	REFERENCES
1. Does new device have same indication statements?	**YES**: *NICO* with MARS has the same intended use and indications as the *CO_2SMO Plus! with NICO* and MARSpO_2 monitors	• Appendix 3: Substantial Equivalence Comparison Charts
2. Does new device have same technological characteristics?	**YES**: The answer is "Yes" for the following: *Sensor(s)* (a) The combination adult, pediatric and neonatal CO_2/flow sensors and SpO_2 sensors are identical or similar to those used in the CO_2SMO Plus! with NICO system. *System* (a) The front-end circuitry, signal processing for the CO_2 are identical to those used in the CO_2SMO Plus! with NICO system. (b) The front-end circuitry, signal processing for the flow are similar to those used in the CO_2SMO Plus! with NICO system. (c) The front-end circuitry, signal processing for the SpO_2 and all oxygen saturation parameter calculations are identical to those used in the MARSpO_2 system. *Software* (a) The parameter calculations for flow, CO_2 and derived calculations such as respiratory mechanics and VCO_2 are identical to the CO_2SMO Plus! with NICO. (b) The cardiac output algorithm is similar to the CO_2SMO Plus! with NICO.	• Appendix 3: Substantial Equivalence Comparison Charts
	NO: The answer is "No" for the following: *System* (a) The front-end of the flow measurement system of CO_2SMO Plus! with NICO system uses a four gain stage approach with a 12 bit A/D while the NICO monitor uses a single gain stage with 20 bit A/D.	Appendix 3: Substantial Equivalence Comparison Charts

	(b) The single board design of the CO2SMO Plus! with NICO was repackaged as a three board set and the display was enlarged. *Software* (a) The NICO algorithm has been improved to make it more robust. (b) The rebreathing interval has been reduced from 50 seconds to 35 seconds. There are no other technological characteristics of any significance known that require validation.	
3. Do differences in technology raise new or novel questions of safety or effectiveness from those raised by the predicate devices?	From above: *System* (a) The front-end of CO_2SMO Plus! with NICO system uses a four gain stage approach with a 12 bit A/D while the NICO monitor uses a single gain stage with 20 bit A/D. **NO:** The use of a 20 bit A/D improves system linearity and noise.	Appendix 3: Substantial Equivalence Comparison Charts See also Sect. III Device Description
	(b) The single board design of the CO2SMO Plus! with NICO was repackaged as a three board set and the display was enlarged. **NO:** The power, digital and analog functions were split into three separate boards for electrical and mechanical packaging reasons. *Software* (a) The NICO algorithm has been improved to make it more robust. **NO:** Improved algorithm extension of existing algorithm and yields equivalent if not improved correlation with "gold standard." (b) The rebreathing interval has been reduced from 50 seconds to 35 seconds. **NO:** The reduction in rebreathing has been shown not to impact system performance and at the same time improves patient comfort.	See also Sect III Device Description See Appendix 4E – Clinical Testing -Report See Appendix 4E – Clinical Testing – Report
4. Are the descriptive characteristics precise enough to ensure equivalence?	**YES** Comparison to predicate devices and comparative bench and clinical tests has demonstrated equivalence to the predicate devices.	(a) see Appendix 4 : performance data and Appendix 3: Substantial Equivalence Comparison Charts

"Substantially Equivalent" Determination

Substantial Equivalence Decision Summary: The *NICO Model 7300 with MARS* is substantially equivalent to the 510(k)-cleared *CO_2SMO Plus! with NICO Model 8200* and *MARSpO_2 Model 2001* devices. This conclusion is based on the decision table and upon the specification validation tests, inter-device comparisons and clinical tests and their results.

V. Summary of Performance Data

The testing of the *NICO, Model 7300 with MARS* consisted of (a) bench specification tests, (b) bench inter-device comparisons, (c) environmental tests, (d) biocompatability tests and (e) clinical tests. The tests performed for (a) through (e) are summarized in this section.

A. SPECIFICATION TESTS

Test Name	Summary
(b)(4)	[redacted]

231

B. INTER-DEVICE COMPARISONS

The following inter-device tests were performed. The NICO with MARS was compared to the currently shipping software version in the CO_2SMO Plus! and was found to be equivalent.

Test	Variables Compared
(b)(4)	[redacted]

232

C. ENVIRONMENTAL TESTS

The environmental testing has been structured in accordance with Appendix A - Performance Requirements, Reviewer Guidance for Premarket Notification Submissions, Anesthesiology and Respiratory Devices Branch, November 1993. Tests of dielectric withstand, and leakage current were found to meet the requirements of IEC 601-1. Electromagnetic compatability tests per EN60601-1-2 (2001) of the *NICO with MARS* system was found to pass. Test reports are enclosed in appendix 4. High, low temperature, humidity and surface temperature tests per IEC 601-1 were conducted and found to pass. Vibration testing and package drop tests were performed and found to pass.

D. BIOCOMPATABILITY TESTS

The biocompatability testing requirements for the flow/ CO_2 sensors, partial rebreathing valve and SpO_2 sensors were determined with reference to the FDA Tripartite Biocompatability Guidance and to the International Standard (ISO 10993-1: 1992) Biological Evaluation of Medical Devices. In both documents the Test Chart (or Guidance for Initial Evaluation Tests) reference Body Contact and further define subcategories as Surface (or External Devices), External Communicating Devices and Implant Devices. These sensors do not directly fit into any of the listed categories, it was decided to use the Surface (or External Devices), Intact Skin as an acceptable reference of tests to be conducted. Therefore the Biocompatability Testing for the sensors included Irritation, Sensitization and Cytotoxicity Tests. All of the sensors did not identify any biocompatability concerns. See appendix 4D for more details and test reports for all of the sensors.

233

E. CLINICAL TESTS

(b)(4)

234

VI: SUMMARY OF SOFTWARE VALIDATION AND VERIFICATION

(b)(4)

235

(b)(4)

236

Product Functions

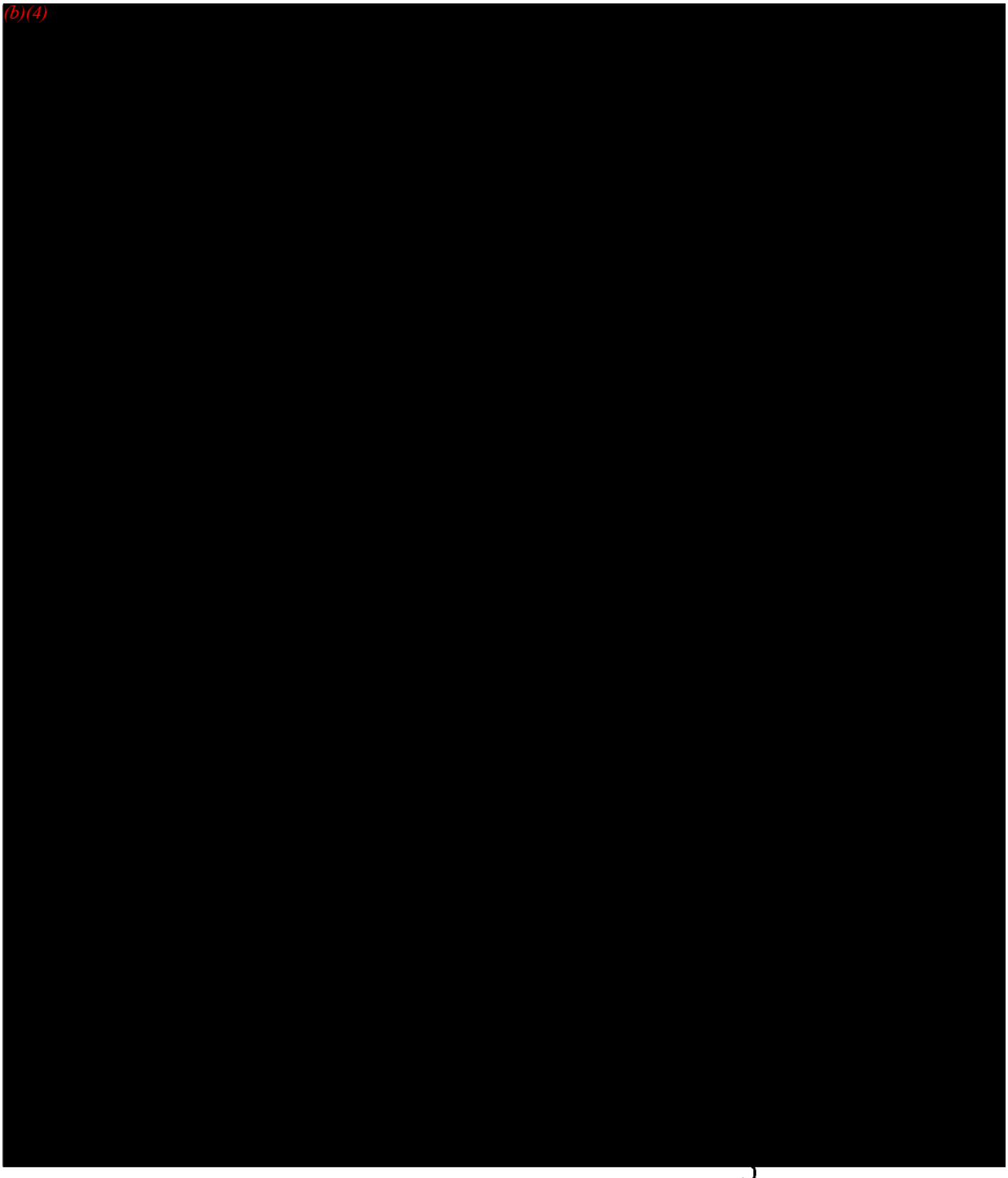
The functions of the NICO Model 7300 monitor are subdivided as follows:

REQUIREMENTS	SPECIFICATION
(b)(4)	[redacted]

237

C. Software Design Description Summaries for *NICO with* (b)(4)

(b)(4)



238

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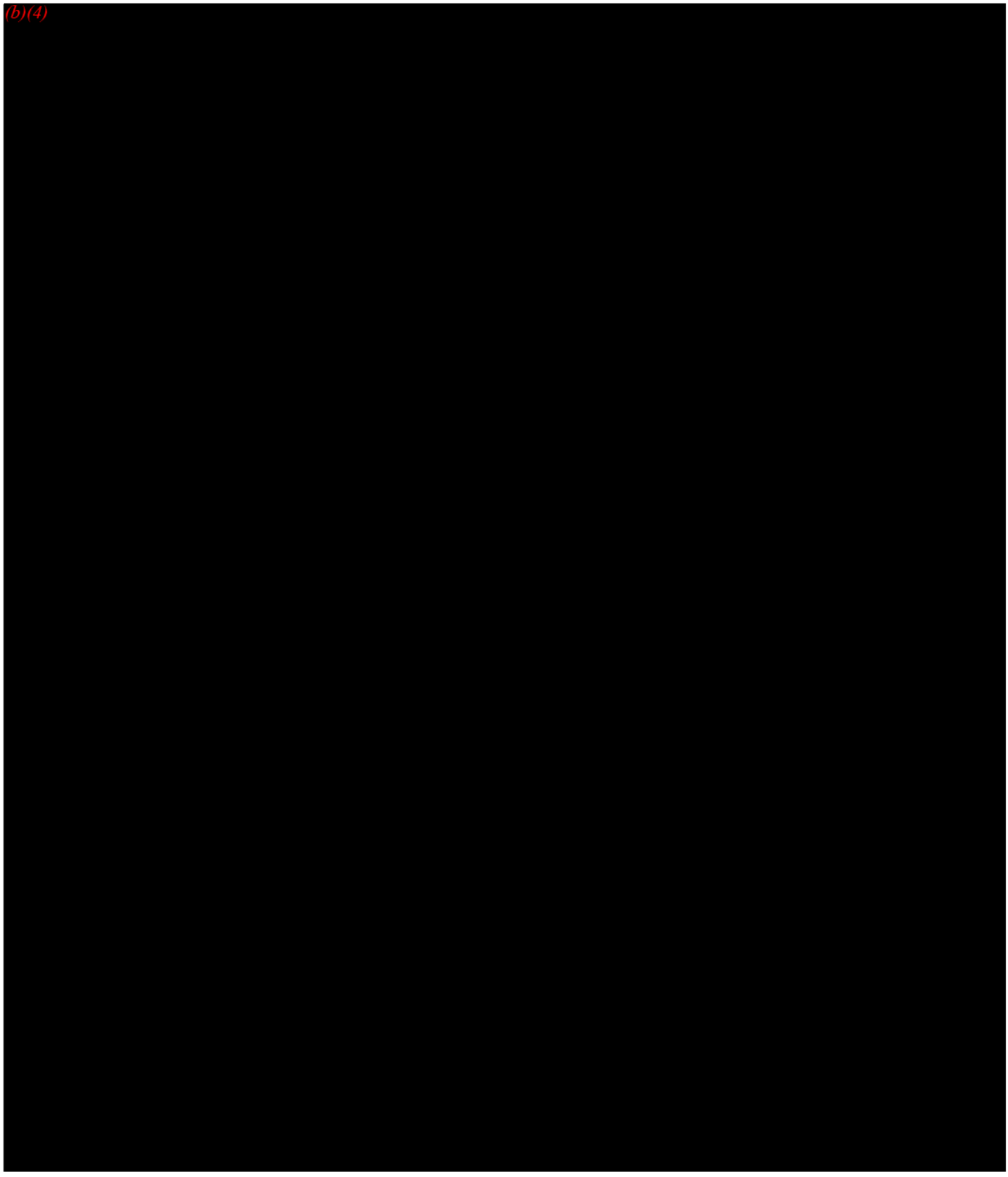

239

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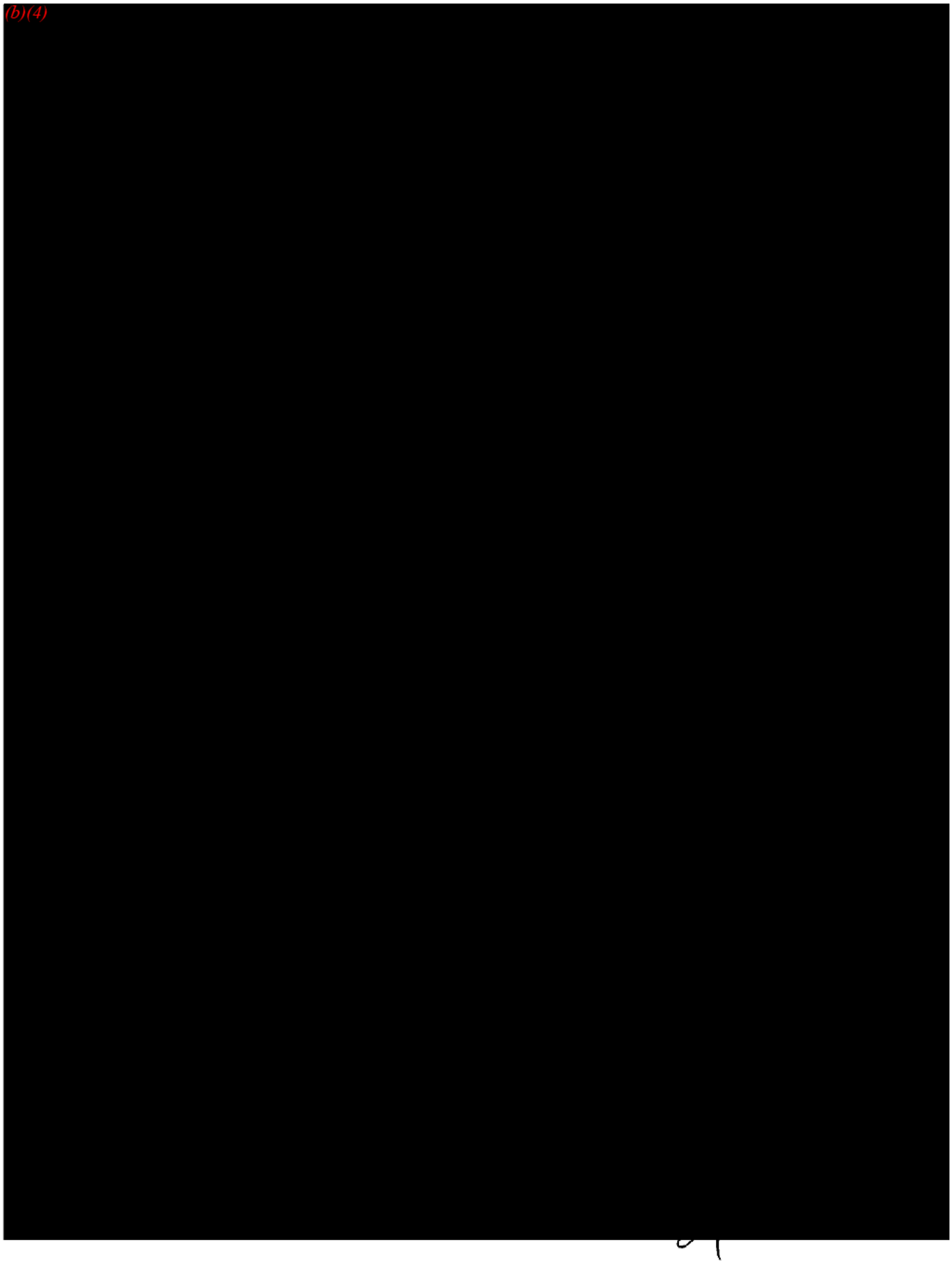

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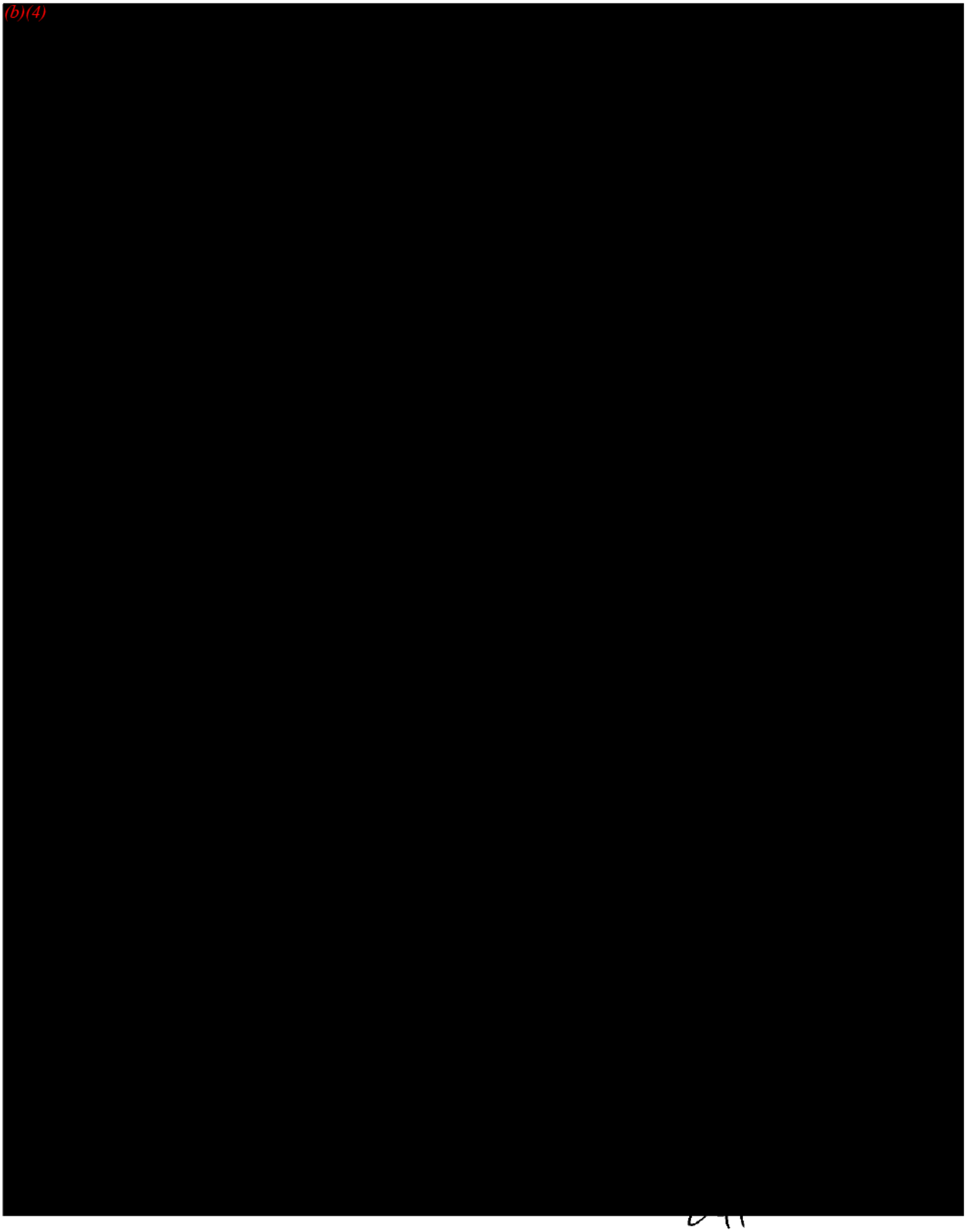

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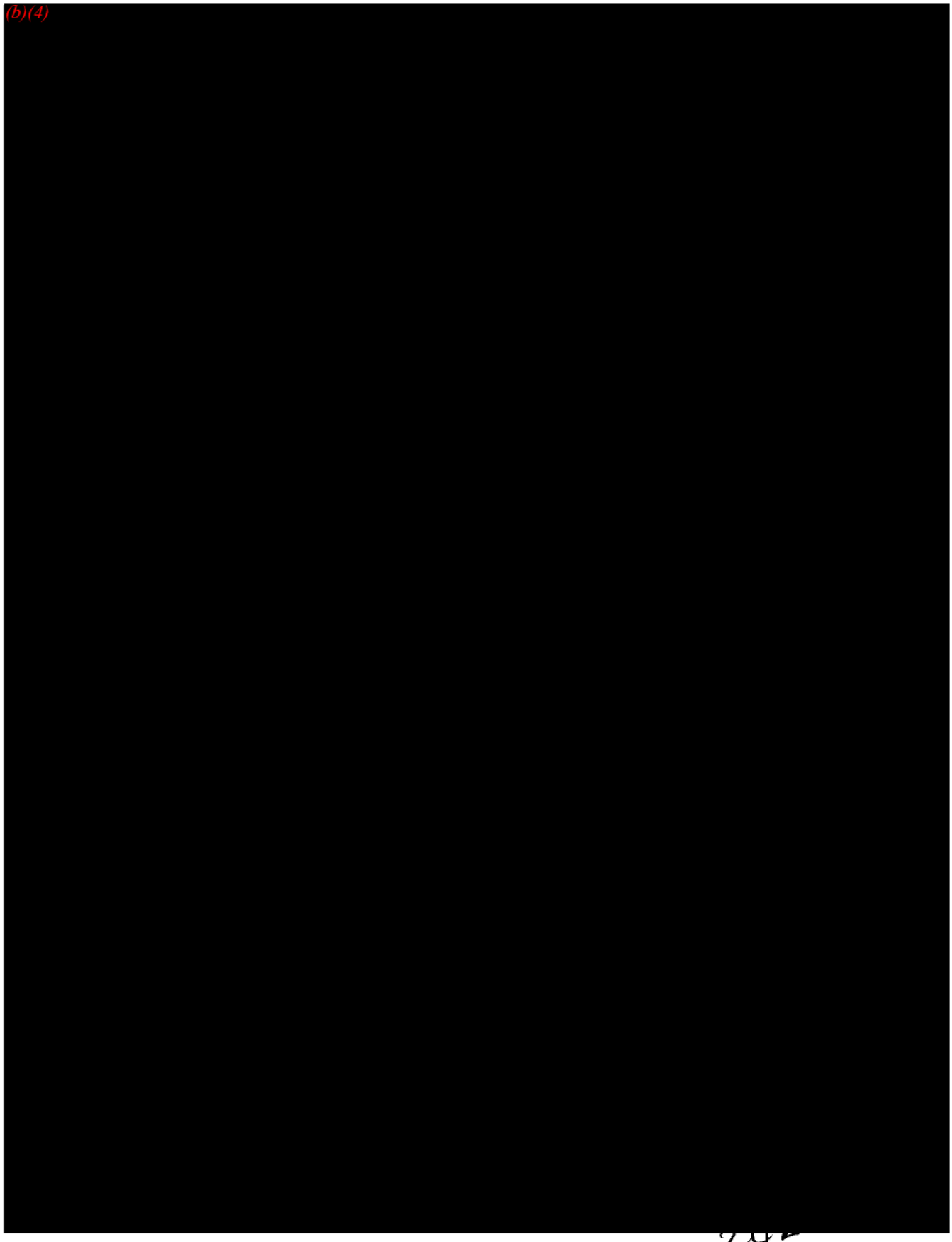

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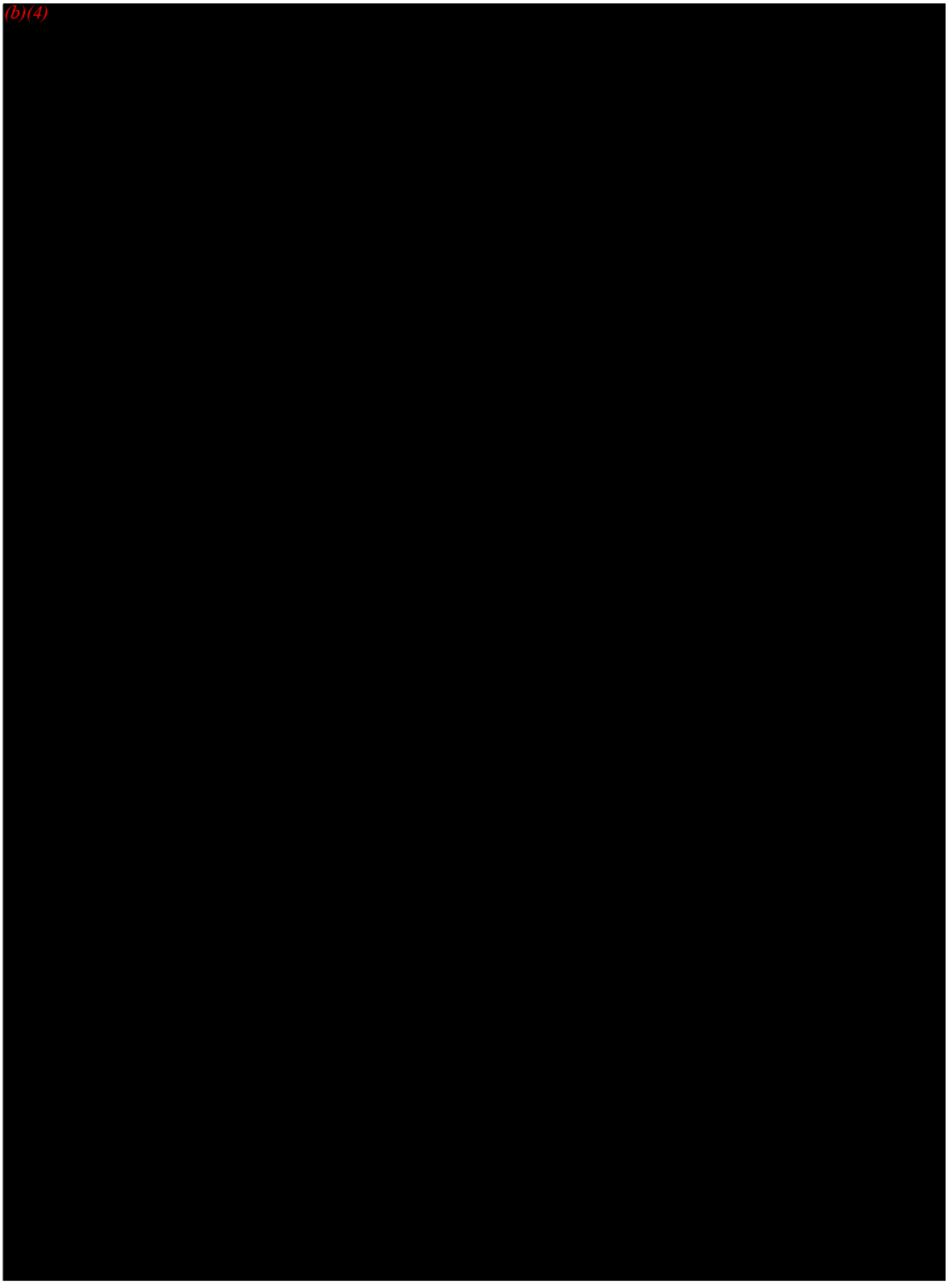

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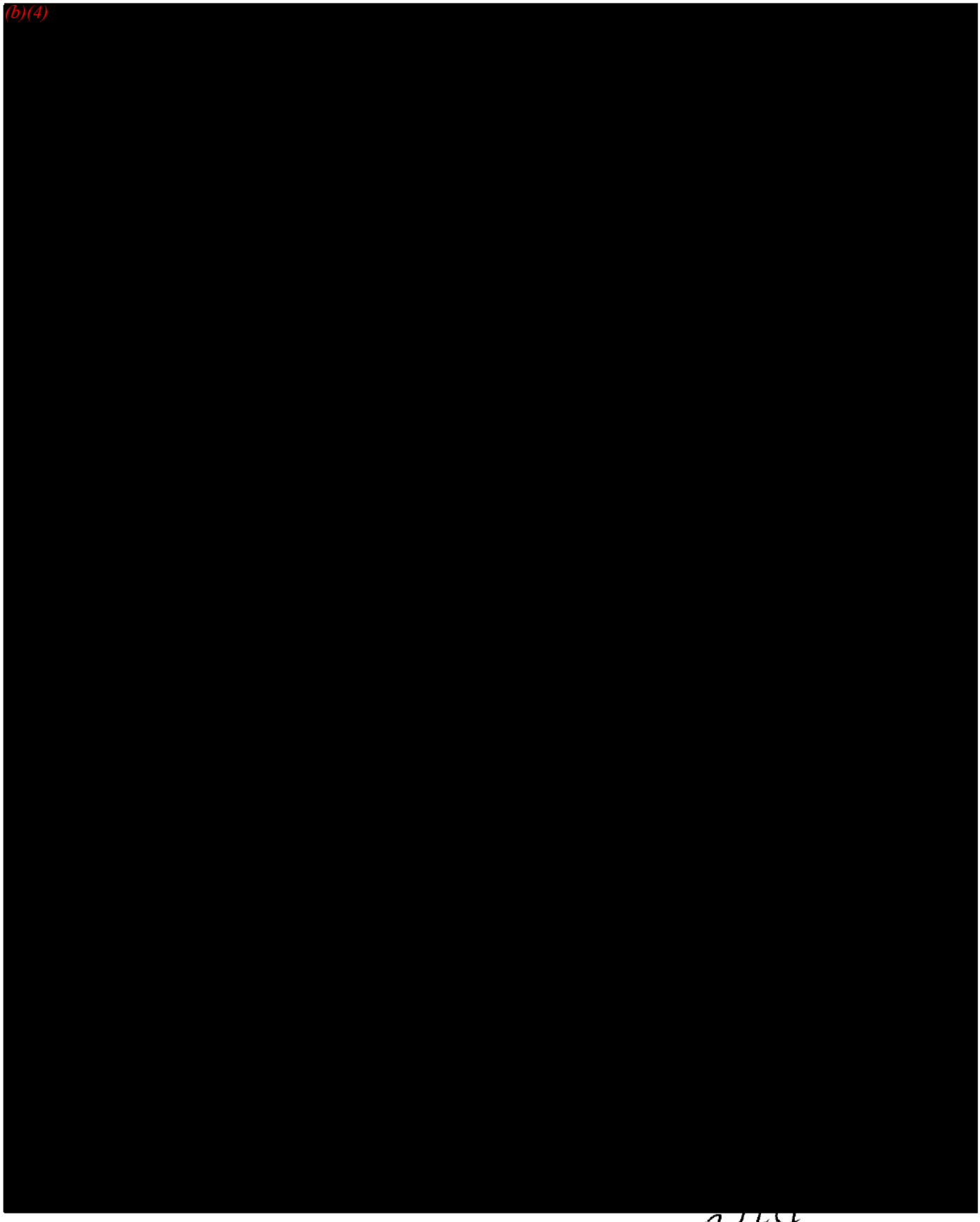


(b)(4)

[redacted]

(b)(4)

[redacted]

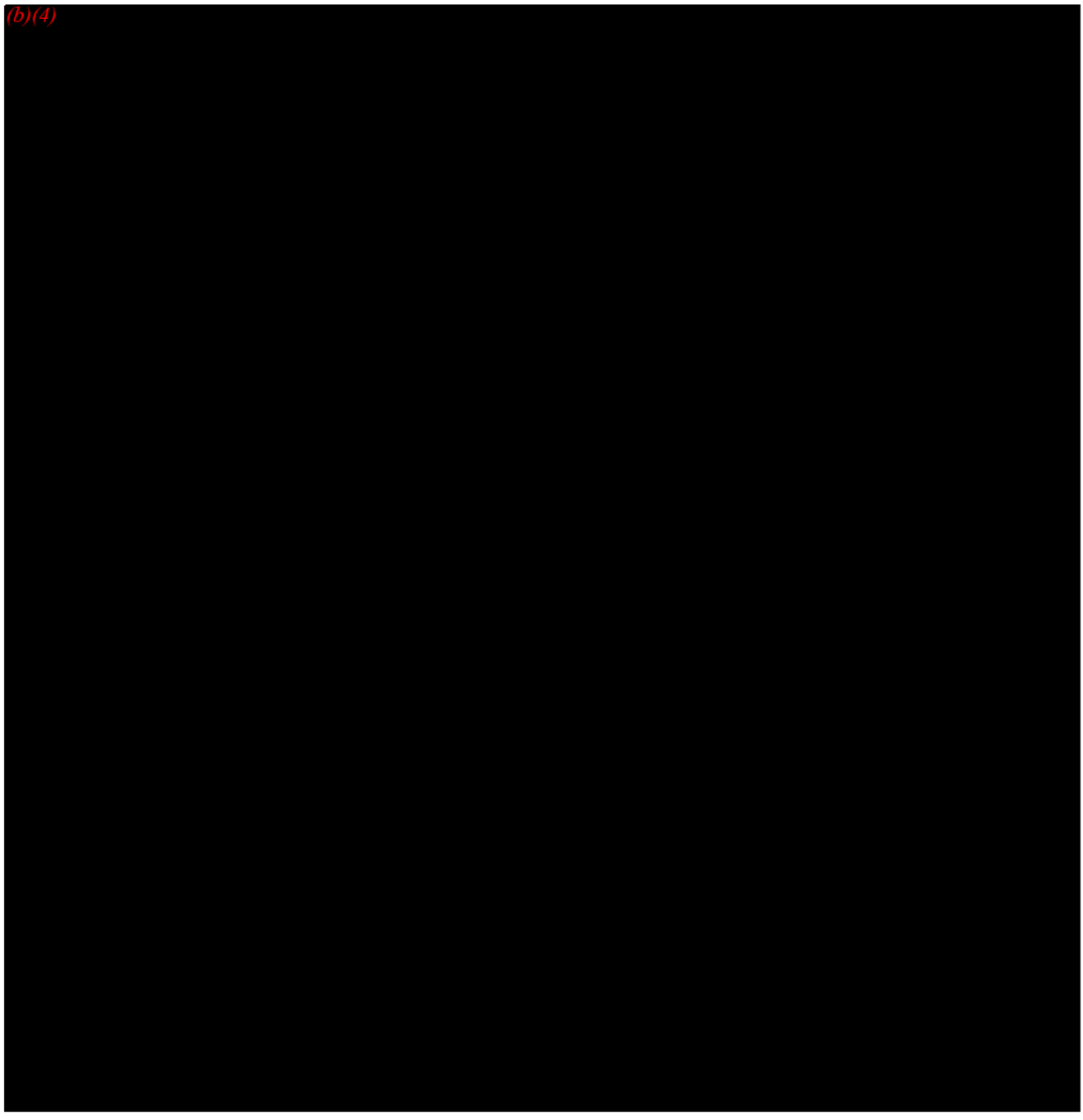
D. Testing of the *NICO with* (b)(4)

(b)(4)

[redacted]

246

(b)(4)



247

E. Summary of results of testing

The following test cases are described in detail in appendix 5.

Test Case	Test Types	Phase
(b) (4)		

Test Case	Test Type	Phase
(b) (4)		

Test Case	Test Types	Phase
(b) (4)		

250

Test Case	Test Type	Phase
(b) (4)		

F. Certification

It is hereby certified that the aforementioned software development procedures were followed; that quality assurance procedures were adhered to; that software verification and validation completed; that the testing described demonstrates that the functional requirements were met and that system specifications were fulfilled.

EP Wigforss 3-19-03

Eric Wigforss
Project Manager

252

VII: Hazard Analysis

(b)(4)

EPD 98236
System Hazard Analysis for NICO Model 7300

Author: Dave Rich
Editor: Rich Daniels, Eric Wigforss

Approvals:

(b) (6)

Engineering:

Project Manager	Date	4-Mar-03
Quality Engineering	Date	6-Mar-03
Clinical Research	Date	3-5-03
Director of Engineering	Date	5-Mar-03

Marketing:

Product Manager	Date	3/10/03

Regulatory:

RA/QA	Date	3/11/03

Revision Record

(b) (4)

Revision	Date	Prepared By

254

1.0 Purpose

(b)(4)

[redacted]

2.0 Reference Documents

(b)(4)

[redacted]

3.0 Hazard Analysis

(b)(4)

[redacted]

258

(b)(4)

[redacted]

256

(b)(4)

Ref. No.	Section	Requirement	Response	Section Ref.
			Internal high voltage parts are labeled	PV138-9226-00 *UL-544 Test*

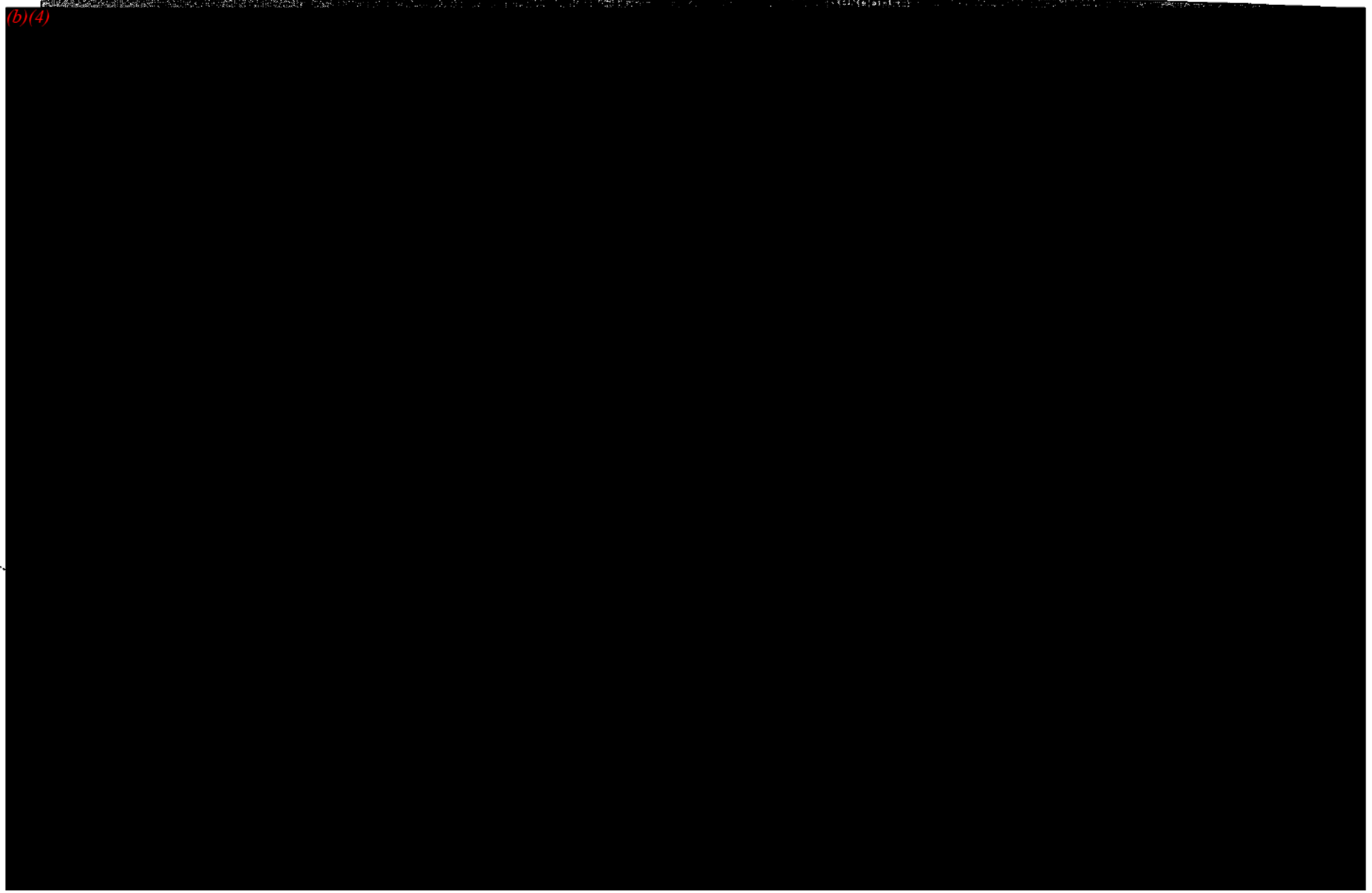
(b)(4)

[redacted]

Ref No.	Hazard	Cause	Effect
(b)(4)			

Ref No.	Hazard	Cause	Init.	Resp.	Remarks	Effective
(b)(4)					Passages adequate for specified flow	EPD00084 – NICO Sensor

(b)(4)



(b)(4)

(b)(4)

[redacted]

(b)(4)

[redacted]

Ref [illegible] Hazard [illegible] Risk [illegible]

(b)(4)

[redacted]

285

(b)(4)

(b)(4)

Ref No.	Hazard	Cause	Risk	Response	Response	Reference
[redacted]						

(b)(4)

Ref No.					
(b)(4)					

Ref	Hazard	Cause	Risk Index	Response Type	RC Status	RC Comments

(b)(4)

(b)(4)

[redacted]

(b)(4)

[redacted]

nkt

Revision Record

(b)(4)

[redacted]

EPD98140
Software Hazard Analysis for *NICO Model* 7300

Authors: Eric Wigforss and Paul Gunneson

Approvals:

Engineering:

Project Manager [redacted] Date 6 Mar 03

Director of Engineering [redacted] Date 10-Mar-03

Software Coordinator [redacted] Date 10 MAR 2003

Regulatory:

RA Manager [redacted] Date 3/11/03

Revision Record

Revision	Date	Prepared By
[redacted]		

274

1.0 Purpose

(b)(4)

[redacted]

2.0 Reference Documents

(b)(4)

[redacted]

275

3.0 Hazard and Risk Analysis

(b)(4)

[redacted]

276

(b)(4)

(b)(4)

[redacted]

(b)(4)

[redacted]

(b)(4)

[redacted]

(b)(4)

[redacted]

187

(b)(4)

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(b)(4)

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(b)(4)

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(b)(4)

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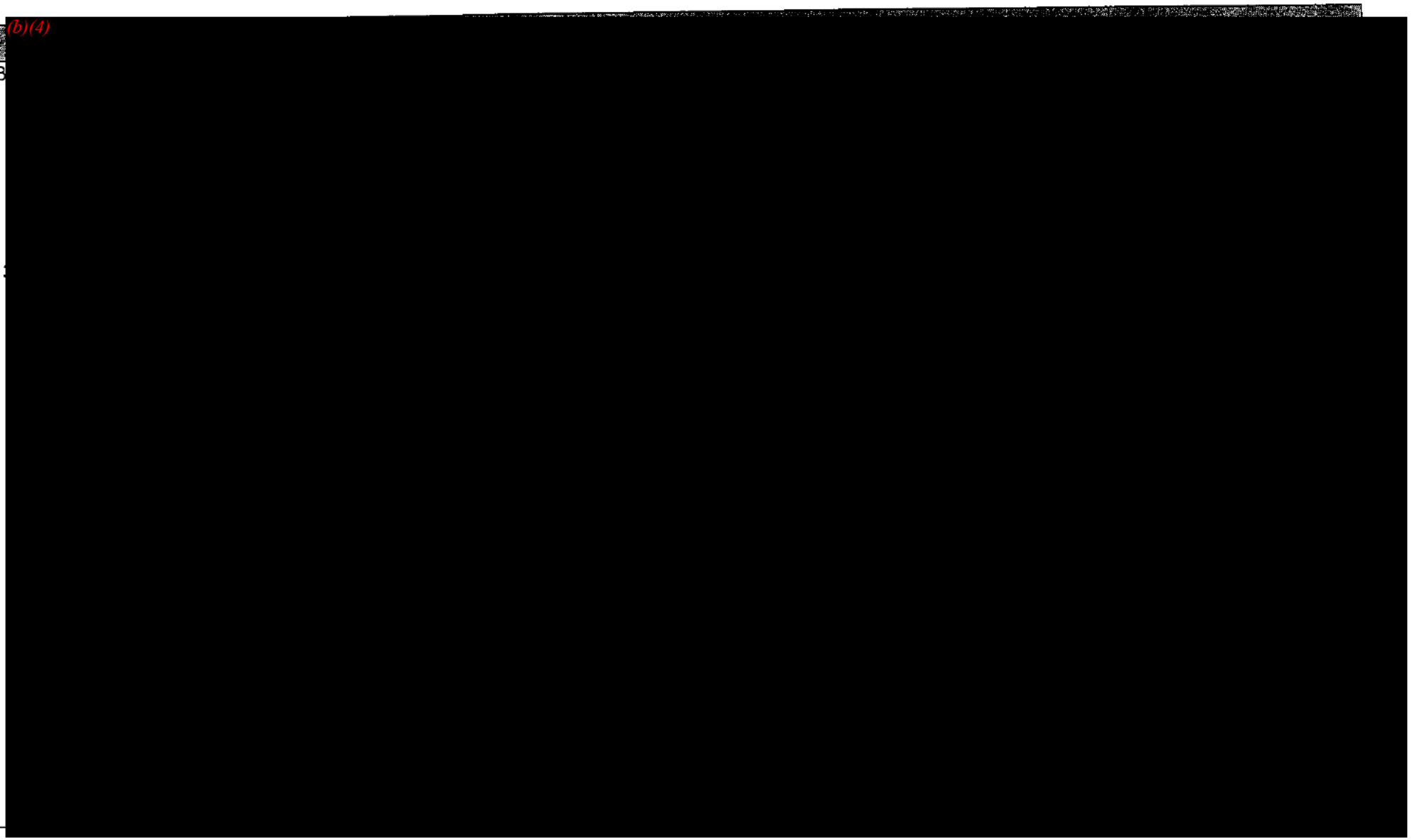
(b)(4)

[redacted]

(b)(4)



(b)(4)

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(b)(4)

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(b)(4)

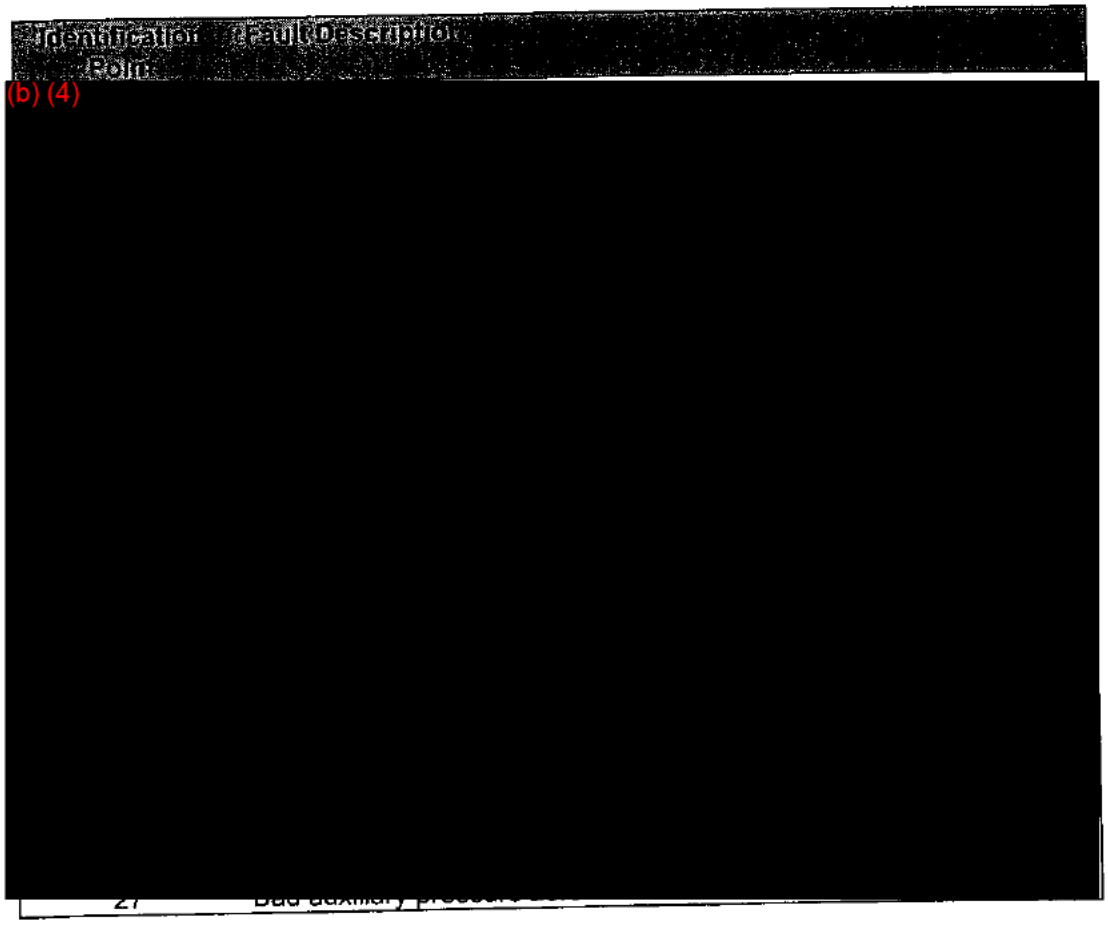
[redacted]

(b)(4)

(b)(4)

[redacted]

4.0 Fault Tree Analysis



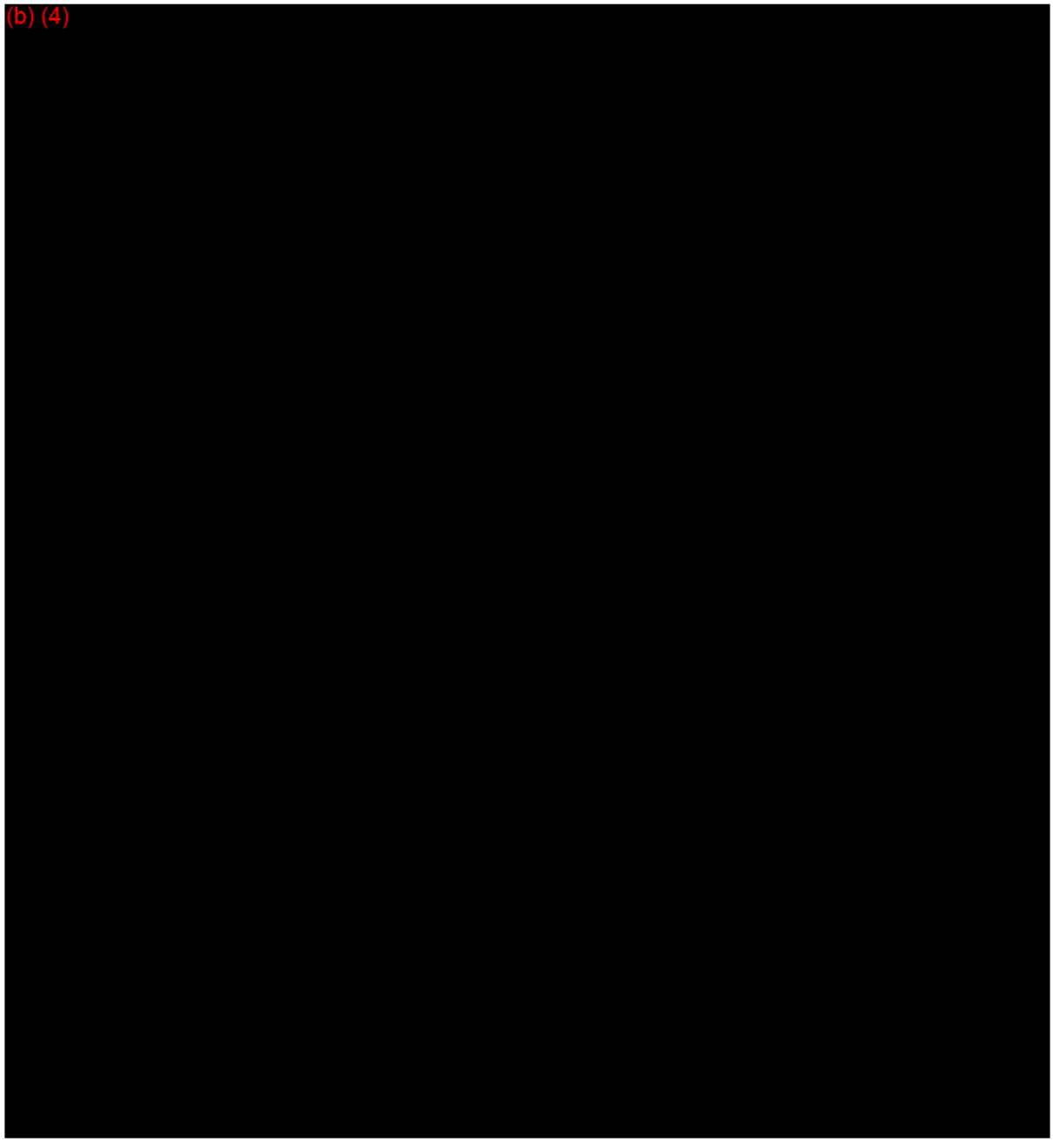
296

(b) (4)

(b) (4)

298

(b) (4)



(b) (4)

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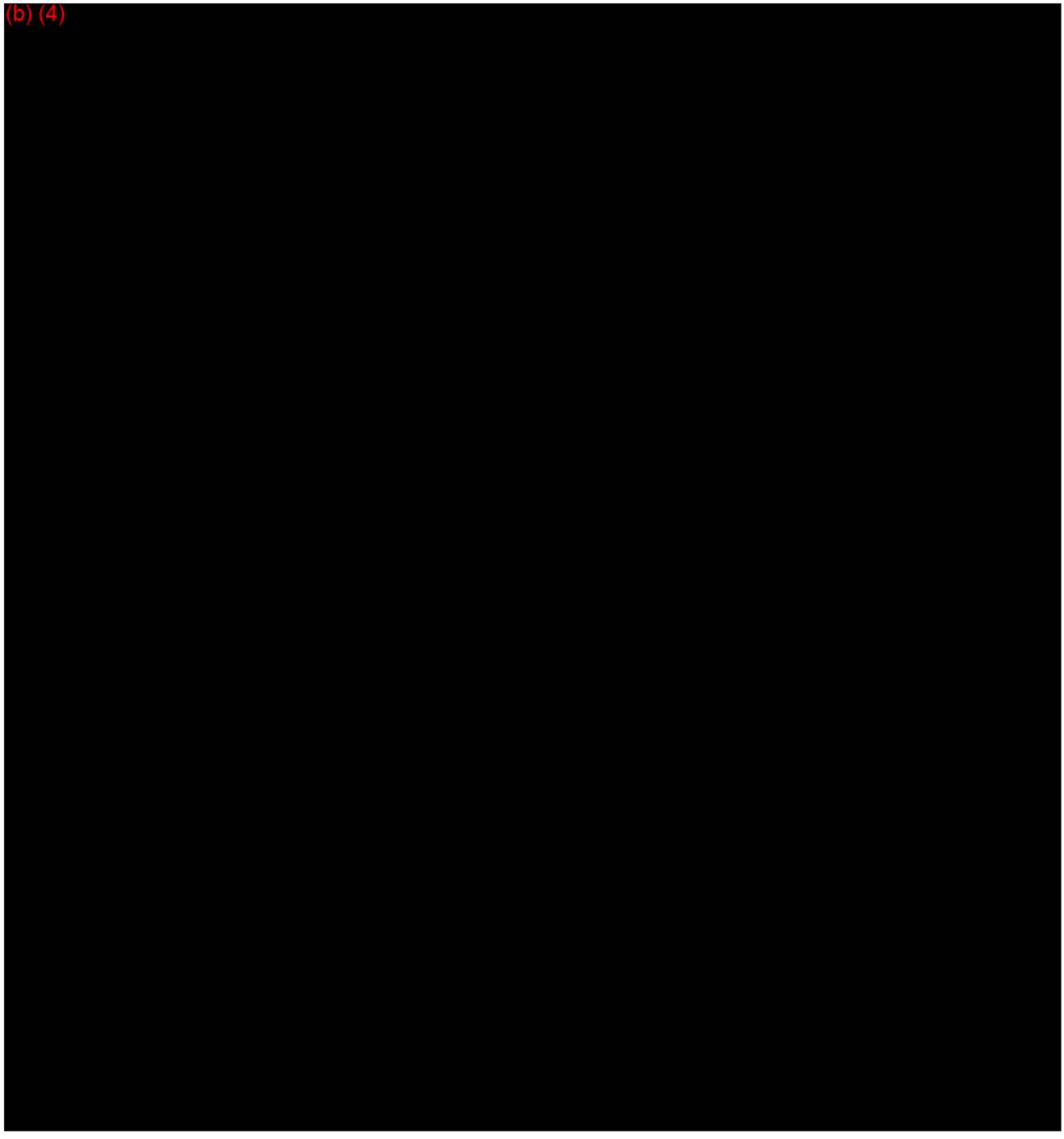
300

(b) (4)



301

Revision Record

(b)(4)

[redacted]

(b)(4)

EPD00084
Hazard Analysis for NICO Sensors

Author: John Triunfo

Approvals:

Engineering:

(b) (6)

Project Manager Date 14 Feb 02

Quality Engineering Date 21-Feb-02

Director of Engineering Date 22-Feb-02

Marketing:

Product Manager Date 22 Feb 02

Regulatory:

Quality Assurance Date 2/26/02

Revision Record

Revision	Date	Prepared By
(b) (6), (b) (4)		

1.0 Purpose

(b)(4)

[redacted]

2.0 Reference Documents

(b)(4)

[redacted]

3.0 Hazard Analysis

(b)(4)

306

Ref No.	Hazard	Cause	Response Type	Response	Risk	Reference
(b)(4)						

Ref No.	Hazard	Cause	Response Type	Response	Risk	Reference
(b)(4)						

308

Ref No.	Hazard	Cause	Response	Response	Risk	Reference
(b)(4)						

b3 c7

Ref No.	Hazard	Cause	Response	Response	Risk	Ref
(b)(4)						

Ref No.	Hazard	Cause	Response Type	Response	Risk	Reference
(b)(4)						

Ref No.	Hazard	Cause	Response Type	Response	Risk	Reference
(b)(4)						

Ref No.	Hazard	Cause	Response Type	Response	Risk	Reference
(b)(4)						

213

Ref No.	Hazard	Cause	Response Type	Response	Risk	Reference
(b)(4)						

314

Ref No.	Hazard	Cause	Response Type	Response	Risk	Reference
(b)(4)						

Revision Record

(b)(4)

[redacted]

EPD00085
Hazard Analysis for 3-Port CO_2/Flow Sensors

Author: John Triunfo

Approvals:

Engineering:

(b) (6)

Project Manager Date 24 Jan 2001

Quality Engineering Date 26-Jan-01

Director of Engineering Date 26-Jan-01

Marketing:

Product Manager Date 1/24/01

Regulatory:

Quality Assurance Date 1/24/01

Revision Record

Revision	Date	Prepared By
(b) (6), (b) (4)		

1.0 Purpose

(b)(4) [redacted]

2.0 Reference Documents

(b)(4) [redacted]

3.0 Hazard Analysis

(b)(4) [redacted]

(b)(4)

[redacted]

Ref No.	Hazard	Cause	Risk Index	Response Type	Response	Reference
(b)(4)						

Ref No.	Hazard	Cause	Risk Index	Response Type	Response	Reference
(b)(4)						

321

Ref No.	Hazard	Cause	Risk Index	Response Type	Response	Reference
(b)(4)						

3.2.2

Ref No.	Hazard	Cause	Risk Index	Response Type	Response	Reference
(b)(4)						

323

Ref No.	Hazard	Cause	Risk Index	Response Type	Response	Reference
(b)(4)						

324

Ref No.	Hazard	Cause	Risk	Response	Response	Reference
(b)(4)						

329

Revision Record

(b)(4)

[redacted]

EPD00074
Hazard Analysis for Flow Sensors Connector Plug

(b)(4) [redacted]

Author: John Sandor

Approvals:

Regulatory:

(b) (6) [redacted]

Quality Assurance Date 1/26/01

Engineering:

Project Engineer Date: 26 JAN 01

Quality Engineering Date: 26-Jan-01

Director of Engineering Date: 6-Feb-01

Marketing:

Product Manager Date: 26-Jan-01

Revision Record

Revision	Date	Prepared By
(b) (6), (b) (4) [redacted]		

1.0 Purpose

(b)(4) [redacted]

2.0 Referenced Documents

(b)(4) [redacted]

3.0 Hazard Analysis

(b)(4) [redacted]

(b)(4)

[redacted]

	Hazard	Cause	Risk Index	Type	Response	Reference
(b)(4)						

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	Hazard	Cause	Risk	Type	Response	Reference
(b)(4)						

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Revision Record

(b)(4)

[redacted]

510(K) SUMMARY

March 17, 2003

a. Applicant's Name and Address

Respironics Novametrix Inc.
5 Technology Drive
Wallingford, CT 06492

b. Contact Person

Michael J. Malis
Q.A. and Regulatory Manager
(203) 697-6442
(203) 284-0753 (facsimile)

c. Name of Device

Device Names (Proprietary/Trade Names):	NICO, Model 7300
Device Name (Common Name):	multiparameter monitor (monitoring spirometer, CO_2 monitor, pulse oximeter and cardiac output monitor with partial rebreathing valve).
Classification:	Class II, 21 C.F.R. 868.1850, 868.1400, 870.2700, 868.5675

d. Equivalent Devices

Substantial equivalence to the following legally marketed predicate devices with the same or similar indications for use has been demonstrated by a comparison of product features as described in the labeling and promotional literature for predicate devices and for the Model 7300, as well as testing to accepted industry standards. In addition, controlled hypoxia studies were conducted to establish the Model 7300 pulse oximetry accuracy and to ensure that the sensors meet their currently published accuracy specifications with the Model 7300. The predicate devices are as follows:

1. CO2SMO Plus! with NICO, Model 8200 (K982499)
2. MARSPO2, Model 2001 (K993979, K000794).

e. Device Description

The NICO monitor Model 7300 is intended for non-invasive monitoring of the inspired and expired airflow and airway pressure of intensive care unit (ICU), anesthesia and emergency room (ER) patients, as well as capnography and pulse oximetry in all of these clinical settings. As is its predicate device *CO_2SMO Plus! with NICO, NICO with MARS* is designed to use neonatal, pediatric, and adult combined CO_2/flow sensors and single patient use or reusable pulse oximetry sensors. It non-invasively calculates cardiac output using established physiological principles by the application and removal of a rebreathed volume in a patient's breathing circuit and the analysis of that response. The *NICO with MARS* is intended to provide cardiac output monitoring in mechanically ventilated patients in the operating room and intensive care units. It is intended to serve the same purposes as the CO_2SMO Plus! with NICO and MARSPO$_2$, Model 2001.

Oxygen saturation is measured with ratiometric technique using red and infrared absorbance of oxy- and deoxyhemoglobin and pulse rate is measured using the time between successive pulses. The O_2 saturation sensors are already legally marketed as accessories to the Model 2001 monitor. As the Model 2001 monitor, the Model 7300 with MARS consists of a dual microprocessor based data acquisition system that measures oxygen saturation data. The firmware for the second microprocessor, a digital signal processor, performs the filtering, pulse rate and saturation calculations of the existing algorithms and additional calculations which analyze the incoming signals and perform noise reduction on that signal when the presence of noise is detected.

The Model 7300 can be powered by either an internal power supply operating on AC or by a sealed rechargeable lead-acid gel battery. Audible and visual alarms for high/low saturation and pulse rate are available. There is also a serial port that provides user configurable data output capable of communicating with printers and other devices.

f. Intended Use

The intended use of the NICO monitor, Model 7300 is to provide:

- cardiac output monitoring via the method of partial rebreathing in adult patients receiving mechanical ventilation during general anesthesia and in the intensive care unit (ICU).

- spirometric and carbon dioxide monitoring in neonatal, pediatric and adult patients during general anesthesia and in the intensive care unit (ICU) and the emergency department (ED). Separate combination CO_2/flow sensors are provided for adult, pediatric and neonatal use.

- continuous, non-invasive monitoring of functional arterial oxygen saturation and pulse rate in neonatal, pediatric and adult patients during both no motion and motion conditions and for patients who are well or poorly perfused during general anesthesia and in the intensive care unit (ICU) and the emergency department (ED).

The NICO monitor Model 7300 and its sensors are intended to be used by trained operators when spirometric, capnographic, pulse oximetry, or cardiac output monitoring is indicated in the judgement of a physician. The fittings of the combination CO_2/flow sensors comply with ISO [5356-1: 1987 (E)]. The combination CO_2/flow sensors may be used in conjunction with endotracheal tubes, face masks, and breathing circuit devices that also comply with the same fitting specification. The combination CO_2/flow sensors and NICO sensors are single patient use devices. The use of the NICO monitor Model 7300 for cardiac output monitoring is contraindicated in patients in which a small rise (3-5 mmHg) in their arterial partial pressure of CO_2 level cannot be tolerated. The intended use, patient population and environments of use are the same or similar to the predicate devices, CO_2SMO Plus! with NICO, Model 8200 and MARSPO$_2$, Model 2001

g. Technological Characteristics

The *NICO with MARS* uses flow sensors that are considered to be a fixed orifice, target flowmeters and as such the pressure drop is proportional to the square of the flow. Combination CO_2/flow sensors are available in three flow ranges that are tailored for neonates, pediatric patients and adults.

The *NICO with MARS* uses an infrared absorption (IR) technique for monitoring CO_2. The principle is based on the fact that CO_2 molecules absorb infrared light energy of specific wavelengths, with the amount of energy absorbed being directly related to the CO_2 concentration Solid state CO_2 sensors (such as the Capnostat) use a beam splitter to simultaneously measure the IR light at two wavelengths: one which is absorbed by CO_2 and one which is not. The wavelength which is not absorbed by CO_2 is related to the intensity of the IR light source. Also, the IR light source is electronically pulsed (rather than interrupting the IR beam with a chopper wheel) in order to eliminate effects of changes in electronic components.

The *NICO with MARS* measures oxygen saturation and pulse rate with sensors that contain red and infrared light sources. Since oxygen saturated blood absorbs different amounts of light at each wavelength (red and infrared) as compared with unsaturated blood, the amount of light absorbed at each wavelength by the blood in each pulse can be used to calculate oxygen saturation. The light energy from red (660 nm) and infrared (940 nm) LEDs is beamed through a sample cell- a pulsating vascular bed, the patient's finger or toe for example. The remaining light energy not absorbed by the sample cell reaches a photodiode, on the opposing side of the sensor. The signal received by the photodiode is split into its red and infrared components, sampled, software filtered and displayed as a numerical value for oxygen saturation and as a waveform, the plethysmogram.

Functional saturation represents the amount of oxyhemoglobin as a percentage of the hemoglobin that can be oxygenated. Dysfunctional hemoglobin (COHb and METHb) are not included in the measurement of functional saturation. Pulse rate is calculated by measuring the time interval between the peaks of the infrared light waveform. The *NICO with MARS* must be used in conjunction with the Novametrix SuperBright™ series of oxygen saturation sensors. MARS technology exploits the computational power of the digital signal processing to replace the pulse rate interval and rate-based decision tree algorithm of prior devices with a more robust frequency-based algorithm.

A variation on the traditional rebreathing methods, the non-invasive differential Fick partial re-breathing technique is used in the NICO with MARS monitor. The change in VCO_2 and the change in end-tidal CO_2 in response to a change in ventilation is used to determine pulmonary capillary blood flow. This value is then corrected for the effect of shunt to determine cardiac output.

h. Certification Statement

In accordance with the requirements of 21 CFR 807.87(j), the following certification is provided:

Respironics Novametrix, Inc. believes that all data and information submitted in this premarket notification are truthful and accurate and no material fact has been omitted.

Michael J Malis
Q.A. and Regulatory Manager

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PREMARKET NOTIFICATION
TRUTHFUL AND ACCURATE CERTIFICATION
[As required by 21 CFR 807.87 (j)]

I certify that, in my capacity as Quality Assurance and Regulatory Manager of Respironics Novametrix, Inc., I believe to the best of my knowledge, that all data and information submitted in this premarket notification are truthful and accurate and that no material fact has been omitted.

Michael Malis

(Signature)

Michael J. Malis
Q.A. and Regulatory Manager

3/17/03

(Dated)

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APPENDIX 1: PROPOSED LABELING AND INSTRUCTIONS FOR USE

1A. Draft User's Manual for the NICO Model 7300 with MARS

1B. Draft Product Literature for NICO Model 7300 with MARS

1C. Pouch Labeling

- NICO Sensor (small) — Catalog No. 8950-00
- NICO Sensor (standard) — Catalog No. 8951-00
- NICO Sensor (large) — Catalog No. 8952-00
- Adult Combined CO_2/Flow Sensor — Catalog No. 9767-00
- Pediatric Combined CO_2/Flow Sensor — Catalog No. 9766-00
- Neonatal Combined CO_2/Flow Sensor — Catalog No. 9765-00

1D. Sensor and Y Sensor Applicator Labeling

Sensor

- SpO_2 SuperBright Finger Sensor — Catalog No. 8776
- SpO_2 SuperBright Y Sensor™ — Catalog No. 8791

Y Sensor Applicators

- Neonatal/Pediatric Y-Strip™ — Catalog No. 8828
  - Carton Artwork (5461-02)
  - Artwork- Tape Strip (8828-02)
- Adult Y-Strip™ — Catalog No. 8829
  - Carton Artwork (5459-02)
  - Artwork- Tape Strip (8828-02)
- Pediatric Butterfly Wrap — Catalog No. 8831
  - Carton Artwork (6133-02)
  - Artwork- Small Finger (9968-02)
  - Artwork- Release Liner (9969-02)
- Adult Butterfly Wrap — Catalog No. 8832
  - Carton Artwork (5460-02)
  - Artwork- Large Finger (9970-02)
  - Artwork- Release Liner (9971-02)
- Non-adhesive Foam Wrap - Large — Catalog No. 8836
  - Package Artwork (8836-02)
- Non-adhesive Foam Wrap – Small — Catalog No. 8943
  - Package Artwork (8843-02)
- Adhesive Foam Wraps, Large — Catalog No. 6929
  - Carton Artwork (6929-02)
  - Artwork- Release Liner (9953-02)
- Adhesive Foam Wraps, Small — Catalog No. 6968
  - Carton Artwork (6968-02)
  - Artwork- Release Liner (9952-02)
- Ear Clip — Catalog No. 6131
  - Package Artwork (8928-02)

1E. Front and Rear Panel Labeling

- Front Panel Overlay
- Rear Panel Overlay
- Top Cover Labeling

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NICO®

CARDIOPULMONARY MANAGEMENT SYSTEM

User's Manual

NICO with MARS

Cardiopulmonary Management System
Model 7300

March 4, 2003

Catalog No. 9226-23-10

PRELIMINARY

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NICO®

Thank you ...

Thank you for purchasing the NICO® Cardiopulmonary Management System from Novametrix.

The NICO® monitor measures cardiac output through respiratory gas analysis based on the well accepted Fick Principle, providing continuous and accurate display of cardiac output. The monitor also operates in Respiratory Mechanics-only mode, providing the clinician with a respiratory profile of the patient through a combination of capnography, airway flow and pressure, and pulse oximetry.

We expect that you will find the application and use of the NICO® monitor extremely simple, making it easy to adopt this exciting technology into your clinical practice. The NICO® monitor can provide accurate cardiac output values without the need for invasive procedures, benefitting the patient, the clinician, and the health care system in general.

We appreciate your patronage and look forward to developing a long-term relationship with you and your institution.

Sincerely,

novametrix™

Respironics, Inc.
Customer Service & Product Support:

USA and Canada
Phone 1-800-345-6443
Customer Service Fax 1-800-886-0245
Product Support Fax 1-724-387-5236

International
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Respironics Novametrix, Inc.

5 Technology Drive
Wallingford, CT 06492

CE 0086

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NICO®

Introduction

About this manual

This manual is written for clinical personnel using the Novametrix NICO® Cardiopulmonary Management System, Model 7300, and the sensors and accessories intended for use with the monitor.

NICO® Monitor Technical Description

Per requirements of IEC 601-1, the NICO® monitor is classified as class II equipment, internally powered, with type BF applied part, and an enclosure protection rating of IPX0. The NICO® monitor is Year 2000 compliant.

Transport/Storage: -10 to +55° C (14-131° F), 10-95% R.H. non-condensing
Operating Conditions: 10 to +40° C (50 to 104° F), 10-90% R.H. non-condensing

The NICO® monitor, Model 7300, contains no user serviceable parts. Refer servicing to qualified service personnel. A technical Service Manual is available for use by technical personnel.

Manufacturing Quality & Safety

The Novametrix Medical Systems Inc. manufacturing facility is certified to both ISO 9001 and EN46001 (MDD93/42/EEC Annex II). Novametrix' products bear the "CE 0086" mark. The product is certified by Underwriter's Laboratories (UL) to bear the UL mark; and tested by TÜV Rheinland to IEC 601-1/EN60601-1.

Declaration of Conformity with European Union Directive

The Authorized Representative for Novametrix equipment is:

D.R.M. Green
European Compliance Services Limited,
Oakdene House,
Oak Road,
Watchfield
Swindon, Wilts SN6 8TD
United Kingdom

Trademarks and Patents

CAPNOSTAT, NICO, $NICO_2$ and the stylized $NICO_2$ with CO_2 shadow are registered trademarks (®); MARS, MARSpO_2, CObar (cardiac output confidence bar), SuperBright and Y-Sensor are trademarks (™) of Respironics Novametrix Inc. Other trademarks and registered trademarks are the property of their respective owners.

The NICO® monitor and its sensors and accessories are covered by the following USA patents: 4,859,858, 4,859,859, 4,914,720, 4,958,075 5,146,092, 5,153,436, 5,190,038, 5,251,121, 5,347,843, 5,369,277, 5,379,650, 5,398,680, 5,448,991, 5,535,633, 5,616,923, 5,693,944, 5,789,660, 5,793,044, 5,820,550, 5,891,026, 5,999,834, 6,042,550, 6,059,732, 6,073,038 6,098,622, 6,099,481, 6,126,610, 6,179,784, 6,200,271, 6,210,342, 6,227,196, 6,238,351, 6,241,681, 6,258,038, 6,306,098, 6,312,389, 6,393,311, 6,408,848, 6,471,658, 6,519,486, D424,193. Other patents pending.

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Manual Revision History

11-Mar-99 Release at Rev. 00.
23-Mar-99 Revision 01.
05-Oct-99 Revision 02. R-N677
20-Mar-00 Revision 03. R-N741
19-Oct-00 Revision 04, R-N807
01-Feb-01 Revision 05, R-N850
20-Jun-01 Revision 07, R-N906, R-N915
28-Sep-01 Revision 08, R-N941
05-Feb-02 Revision 09, R-N984
04-Mar-03 Revision 10, PRELIMINARY

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NICO®

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Welcome

General Description

NICO®, a Cardiopulmonary Management System from Novametrix Medical Systems Inc., non-invasively measures and displays cardiac output (C.O.). The NICO monitor, Model 7300, also displays cardiac index, stroke volume and pulmonary capillary blood flow, as well as various respiratory monitoring parameters including CO_2 elimination (VCO_2) and alveolar minute ventilation. In Respiratory Mechanics mode, the NICO system can be used as a respiratory profile monitor, without cardiac output displayed. In either mode, the monitor provides the clinician with important information to aid in precise and efficient patient management.

Indications

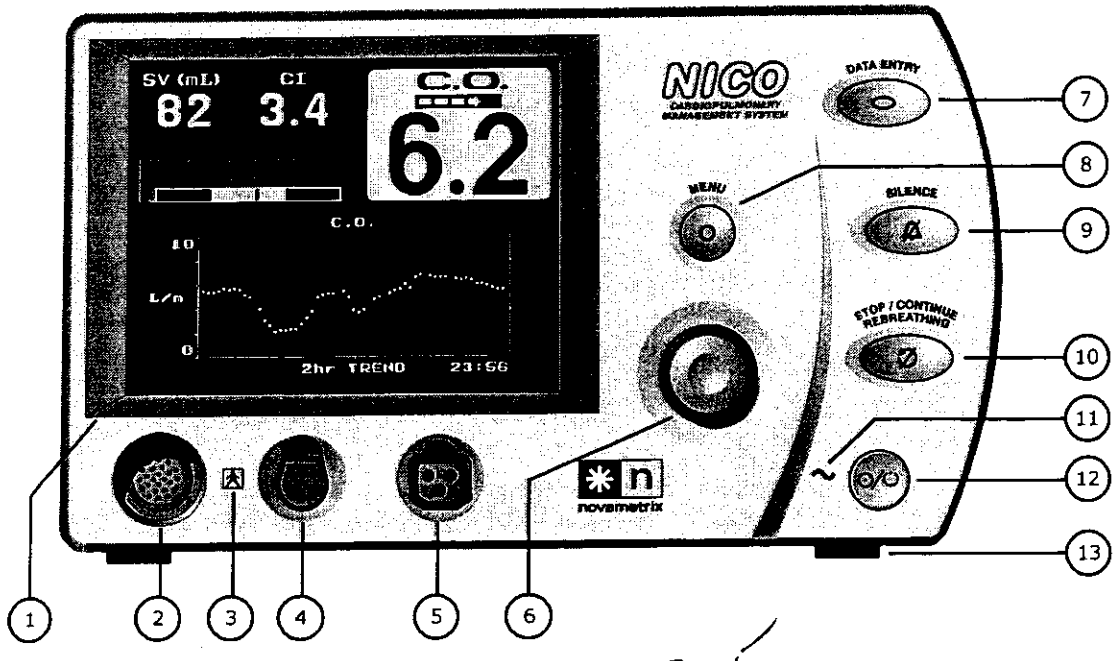
The NICO monitor is indicated for use by technically skilled clinical personnel. In Cardiac Output mode, the monitor is used for the monitoring of cardiac output and various respiratory parameters of adult patients receiving mechanical ventilation. In Respiratory Mechanics mode, the NICO monitor is used for monitoring the respiratory parameters of adult, pediatric and neonatal patients. The pulse oximeter in the NICO monitor is intended to be used for monitoring oxygen saturation and pulse rate in all critical monitoring environments including ventilatory support and anesthesia. It is designed to monitor all patient areas including adult, pediatric and neonatal. The NICO monitor is not intended for any other purpose.

Contraindications

In Cardiac Output mode, use of the NICO monitor is contraindicated in patients in whom a small rise (3-5 mmHg, 0.4-0.67 kPa) in their $PaCO_2$ level cannot be tolerated.

Front Panel

The NICO monitor's front panel includes a display screen, sensor input connectors, a control knob, and operational push button keys and indicators that are explained below.



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1 **Display Screen**. The screen displays cardiac output data, respiratory mechanics, trends, waveforms and messages, along with setup and configuration data.

2 **CAPNOSTAT® CO_2 Sensor Input Connector**. Connect only a Novametrix CAPNOSTAT® CO_2 Sensor, Catalog Number 9567-00 here.

3 **Connector Isolation Icon.** Identifies the connector to either side of this icon as a type BF patient isolation connection.

4 **Pulse Oximetry Sensor Input Connector**. Connect only Novametrix pulse oximetry sensors and extension cables approved for use with the NICO monitor.

5 **NICO Sensor Input Connector**. Connect only Novametrix NICO Sensors, Catalog Number 8950-00, 8951-00 and 8952-00 or Novametrix CO_2/Flow sensors, Catalog Number 9765-00, 9766-00 and 9767-00.

6 **KNOB**. The **KNOB** is used to select monitoring screens, scroll through menus and to change or enter values. The **KNOB** is generally turned to access different monitoring screens and to highlight menu options, and pressed to accept or change those selections.

7 **DATA ENTRY key**. Press to activate the **DATA ENTRY** screen and illuminate the key's green icon. Press the key again to return to the previously displayed screen. From the **DATA ENTRY** screen, you can enter patient information including height, weight and respiratory gas mixture, and access the **ABG DATA ENTRY** screen.

8 **MENU key**. Press to activate the **SELECT A SCREEN** menu and illuminate the key's green icon. Press the key again to return to the previously displayed screen. From the **SELECT A SCREEN** menu you can, by turning the knob, highlight the screen you wish to display. Press the **MENU** key or the **KNOB** to display that selected screen.

9 **SILENCE key**. The **SILENCE** key is used to mute/prevent audible alerts. It also visually indicates the presence of a "High Priority Alert". The Silence feature operates in two modes; a temporary "2 Minute Silence" mode and an "Audio Disabled" mode.

- 2 Minute Silence — Press and release to activate or deactivate the two minute silence. The key's icon illuminates amber when active and audible alerts will be muted for two minutes, after which the icon turns off and any audible alert will sound.
- Audio Disabled — Press and hold for one second to prevent or allow any audible alerts. The key's icon illuminates and beeps twice to indicate that all audible alerts are being suppressed.
- High Priority Alerts — (See "Alert Priorities" on page 61) The **SILENCE** key's icon illuminates and flashes red to indicate High Priority Alert is active. The icon alternately flashes red and amber if the audio is disabled and a High Priority Alert is active.

10 **STOP/CONTINUE REBREATHING key**. Press to start cardiac output monitoring and the automatic rebreathing process. Subsequent presses will stop (amber indicator illuminated) or continue (amber indicator off) the rebreathing process. Press and hold for two seconds to clear the values in the C.O. averaging memory. The **STOP/CONTINUE REBREATHING** key will be amber and inactive in Respiratory Mechanics mode.

11 **AC Mains Power Indicator.** This icon illuminates green to indicate AC Mains power is applied to the monitor. To illuminate the icon, the monitor must be plugged into the AC outlet and the monitor's rear panel power switch must be on ("|").

12 **OPERATE/STANDBY key.** Press this key to turn the monitor on. If connected to the AC outlet, the monitor uses AC power, otherwise it powers up using its internal battery (provided the battery is charged). Press the **OPERATE/STANDBY** key again to put the monitor into Standby mode (if using AC power) or to turn it off (if using battery power).

13 **Kickstand** (front and rear). The NICO monitor can be positioned for better viewing from above or below by extending the kickstand at the front or rear of the monitor.

Rear Panel

The NICO monitor's rear panel includes an AC Mains power input module, three RS232 serial communications ports, an analog input/output port, equipotential connector, fan and ventilation slots, and the monitor's serial number label. These are explained below.

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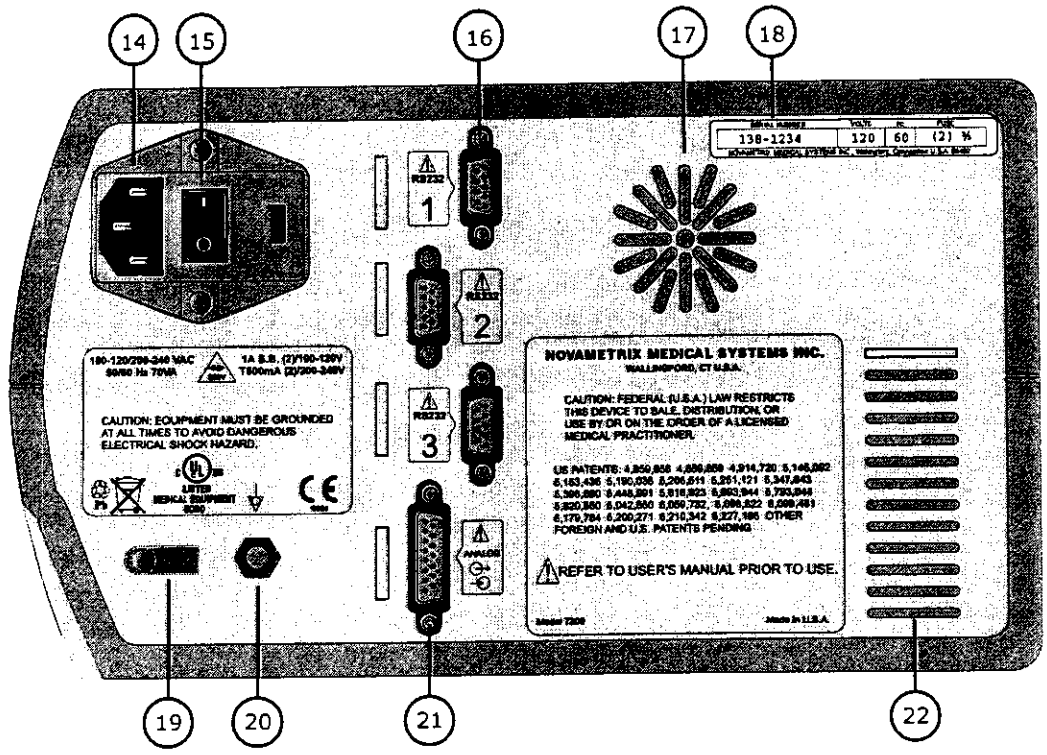

14 **AC Mains Power Cord Connection**. Connect only approved hospital-grade line cords to this connector.

15 **AC Mains Power Switch**. This switch controls the flow of AC current into the NICO monitor. Press the "|" portion of the switch to supply the monitor with AC power, or the "O" portion of the switch to interrupt the flow of AC power. If supplied with AC power, the monitor illuminates the front panel AC Mains Power Indicator, energizes the fan and recharges the internal battery.

16 **RS232 Communications Ports.** Three 9-pin serial communications ports provide for digital communications with the NICO monitor (see "RS232 Communications").

17 **Fan**. The fan draws air in through the monitor. Do not block the fan's air intake slots.

18 **Serial Number Label**. The NICO monitor's serial number is shown here. Refer servicing to qualified personnel.

19 **Power cord retaining clip**. If desired, remove the screw, slip the cord through the clip and insert and tighten the screw. Use only the supplied screw to secure the clip.

20 **Equipotentiality**. Connection to the monitor's chassis (earth ground system).

21 **Analog Input/Output Port**. This 15-pin connector provides analog signal output capability for the NICO monitor (Input reserved for future use).

22 **Ventilation Slots**. Do not block the air ventilation slots.

Symbols

These symbols may be found on the NICO monitor, its sensors, accessories and documentation.

Attention
Consult manual for detailed information.

Single Patient Use
Treat in accordance with protocol for "single patient use" items.

Patient Isolation
Identifies the patient isolation connection as type BF.

AC Mains Power Switch
"|" ON-connection to mains;
"O" OFF-disconnection from mains

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Mains Fuse Rating
Mains rating for replacement fuses

Separate collection
Take appropriate steps to ensure that spent batteries are collected separately when disposed of. This symbol is found on the internal battery and the monitor enclosure.

Recyclable item
This symbol is found on the internal battery and the monitor enclosure.

Equipotentiality
Connection to monitor's chassis.

Heavy Metal Content
Indicates heavy metal content, specifically lead. This symbol is found on the internal battery and the monitor enclosure.

AC/Battery Operation

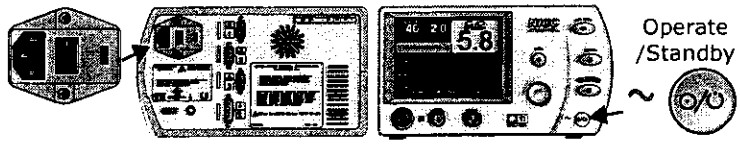
The NICO monitor is designed to be operated from AC Mains power. An internal battery provides uninterrupted monitoring and trending capability for short periods (no more than 45 minutes) if the AC power is removed.

AC Mains Operation

To operate the monitor from AC Mains power:

1 Plug the line cord into the rear panel connector and the AC Mains power outlet.

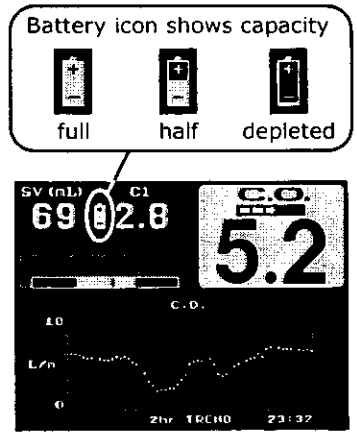
2 Set the rear panel power switch to the On "|" position.
- The front panel AC Mains Power indicator illuminates.
- The monitor's fan turns on.
- The internal battery starts to recharge.



3 Press the front panel **Operate/Standby** key to turn the monitor on and off.

Battery Operation

The NICO monitor automatically switches to battery power from AC Mains power if the AC source is removed. A fully charged battery will power the monitor for up to 45 minutes. While on battery power, the NICO monitor displays a battery icon that "drains" as power is consumed.



The battery icon starts to flash when approximately 5 minutes of battery power remain. An audible alert tone also sounds.

Reconnect to AC Mains power or the monitor will automatically shut off. A depleted battery may require 12-16 hours to fully recharge.

To operate the NICO monitor on battery power:

1 Unplug the line cord or set the rear panel power switch to the Off "O" position.
- The front panel AC Mains Power indicator turns off.

2 Press the front panel **Operate/Standby** key to turn the monitor on and off.

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Parameter List

Cardiac Output mode The NICO monitor displays the parameters described in this table.

Label	Parameter	Range/Units	Description	Screen Display
C.O.	Cardiac Output	0.5-19.9 L/min	Volume of blood pumped by the heart each minute	All except Trend
CO-a	Average Cardiac Output	0.5-19.9 L/min	C.O. averaged value.	Trend & Tabular Data
CO-f	Fast-mode Cardiac Output	0.5-19.9 L/min	Unaveraged C.O. value from the last completed cycle	Trend & Tabular Data
Cdyn	Dynamic Compliance	0-500 ml/cmH_2O	Volume the lungs expand for a given pressure Note that if the ventilator is set for an inspiratory pause that is detected by NICO, Cdyn becomes Cstat.	Numerics & Tabular Data
CI	Cardiac Index	0-9.9 L/min/m^2	C.O. divided by body surface area	All
$ETCO_2$	End Tidal Carbon Dioxide	0-150 mmHg 0-20.0 % 0-20.0 kPa	Maximum CO_2 plateau value at the end of the breath (reflects alveolar CO_2)	Numerics, CO_2/SpO_2, Volumetric CO_2, Trend, rebreathing curves & Tabular Data
Insp CO_2	Inspired Carbon Dioxide	3-50 mmHg 0.4-6.7 % 0.4-6.7 kPa	Maximum CO_2 value observed during the baseline portion of the Inspiratory phase of the breath (baseline shift above zero point)	General Message Area (if above 3 mmHg for 10 sec (0.4 % or kPa))
MAP	Mean Airway Pressure	0-100 cmH_2O	Mean (average) pressure in the airway throughout the breath	Numerics, Trend & Tabular Data
MV	Minute Volume	2-60 L/min Adult	Volume (in liters) of gas delivered to the patient per minute	Numerics, Trend & Tabular Data
MV alv	Alveolar Minute Volume	0.05-16 L/min	MV less deadspace (wasted) ventilation	Numerics & Tabular Data
NIP	Negative Inspiratory Pressure	0 to -120 cmH_2O	Maximum negative pressure during inspiration	Respiratory Numerics
PCBF	Pulmonary Capillary Blood Flow	0.5-19.9 L/min	Portion of the cardiac output that is effective in gas exchange	All except Trend
PCBFa	Average Pulmonary Capillary Blood Flow	0.5-19.9 L/min	PCBF averaged value	All except Trend
PCBFf	Fast-mode Pulmonary Capillary Blood Flow	0.5-19.9 L/min	Unaveraged PCBF from last completed cycle	All except Trend
$PeCO_2$/ $FeCO_2$	Mixed expired CO_2	0-100 mmHg, 0-13.2 kPa or %	Volume weighted average CO_2 in the breath	Tabular Data
PEEP	Positive End Expiratory Pressure	0-99 cmH_2O	Pressure in the lungs at the end of expiration	Numerics, Flow/ Pressure, Trend & Tabular Data
PEF	Peak Expiratory Flow	2-180 L/min	Highest absolute flow rate during expiration	Trend & Tabular Data
PIF	Peak Inspiratory Flow	2-180 L/min	Highest absolute flow rate during inspiration	Trend & Tabular Data
PIP	Peak Inspiratory Pressure	0-120 cmH_2O	Peak (highest) pressure in the airway during inspiration	Numerics, Flow/ Pressure, Trend & Tabular Data

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Label	Parameter	Range/Units	Description	Screen Display
Pplat	Pressure plateau	0-99 cmH_2O	Pressure held during an end-inspiratory pause	Respiratory Numerics
☑	Pulse Rate	30-250 bpm	Number of pulse beats per minute	Numerics, CO_2/SpO_2, Trend & Tabular Data
Raw	Airway Resistance	0-100 cmH_2O/L/sec	Pressure required to cause gas flow at a given rate	Numerics & Tabular Data
RR	Respiration Rate	2-120 br/min	Number of breaths per minute	Numerics, CO_2/SpO_2, Trend & Tabular Data
RSBI	Rapid Shallow Breathing Index	0-1000 br/min/L	Respiratory rate divided by average spontaneous tidal volume (only calculated when RR < 57)	Respiratory Numerics & Tabular Data
SpO_2	Oxygen Saturation	0-100 %	Oxyhemoglobin as a percentage of the sum of oxyhemoglobin and deoxyhemoglobin	Numerics, CO_2/SpO_2, rebreathing curves, Trend & Tabular Data
SV	Stroke Volume	0-250 ml	Volume of blood pumped by the heart each beat	All
SVI	Stroke Volume Index	0-125 ml	Stroke volume divided by body surface area	Tabular Data
SVR	Systemic Vascular Resistance	0-9999 dynes sec/ cm^5	Resistance exerted by the blood vessels on blood flow and is an indicator of left ventricular afterload.	SVR Calculation & Tabular Data
SVRI	Systemic Vascular Resistance Index	0-9999 dynes sec/ cm^5	SVR normalized to body surface area	Tabular Data
VCO_2	Carbon Dioxide Elimination	0-3000 ml/min	Volume of CO_2 eliminated through the breath each minute	Numerics, Volumetric CO_2, rebreathing curves, Trend & Tabular Data
Vd Aw	Airway deadspace	0-500 ml	Total airway deadspace, not including NICO Loop.	Respiratory Numerics, Volumetric CO_2, Tabular Data
Vd/Vt	Deadspace to tidal volume ratio	0-1.00	$(PaCO_2-PeCO_2)/PaCO_2$	Respiratory Numerics & ABG Data Entry
Vd alv	Alveolar deadspace	0-500 ml	Difference between physiologic and airway deadspace	Respiratory Numerics & ABG Data Entry
Vt alv	Alveolar tidal volume	0-2400 ml	Tidal volume less airway deadspace	Respiratory Numerics, Volumetric CO_2 & Tabular Data
Vt/kg	Tidal volume per kilogram	0-120 ml/kg	Tidal volume divided by kilogram of body weight	Respiratory Numerics
Vte	Expired Tidal Volume	200-3000 ml	Volume of gas exhaled per breath	Respiratory Numerics, Flow/Pressure, Volumetric CO_2 & Trend
Vte-m	Expired Tidal Volume - mechanical	200-3000 ml	Volume of gas exhaled per breath during mechanical ventilation	Tabular Data
Vte-s	Expired Tidal Volume - spontaneous	200-3000 ml	Volume of gas exhaled per breath during spontaneous ventilation	Tabular Data
Vti	Inspired Tidal Volume	200-3000 ml	Volume of gas inhaled per breath	Respiratory Numerics, Flow/Pressure, Volumetric CO_2 & Trend

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Label	Parameter	Range/Units	Description	Screen Display
Vti-m	Inspired Tidal Volume - mechanical	200-3000 ml	Volume of gas delivered by ventilator, per breath	Tabular Data
Vti-s	Inspired Tidal Volume - spontaneous	200-3000 ml	Volume of gas inhaled by the patient, per breath	Tabular Data

Respiratory Mechanics mode

The NICO monitor displays the parameters described in this table.

Label	Parameter	Range/Units	Description	Screen Display
Cdyn	Dynamic Compliance	0-500 ml/cmH_2O	Volume the lungs expand for a given pressure Note that if the ventilator is set for an inspiratory pause that is detected by NICO, Cdyn becomes Cstat.	Numerics & Tabular Data
$ETCO_2$	End Tidal Carbon Dioxide	0-150 mmHg 0-20.0 % 0-20.0 kPa	Maximum CO_2 plateau value at the end of the breath (reflects alveolar CO_2)	All
I:E	I:E Ratio	1:9.9 or 4:1	Ratio of inspiratory time (ti) to expiratory time (te)	Flow/Pressure
MAP	Mean Airway Pressure	0-100 cmH_2O	Mean (average) pressure in the airway throughout the breath	Numerics, Trend & Tabular Data
MV	Minute Volume	0.4-60 L/min adult 0.06-30 L/min pedi. 0.01-5 L/min neonatal	Volume (in liters) of gas delivered to the patient per minute	All except Flow/ Pressure & Loops
MV alv	Alveolar Minute Volume	0-16 L/min adult 0-8 L/min pediatric 0-4 L/min neonatal	MV less deadspace (wasted) ventilation	Numerics & Tabular Data
NIP	Negative Inspiratory Pressure	0 to -120 cmH_2O	Maximum negative pressure during inspiratory cycle	Loops
$PeCO_2$/ $FeCO_2$	Mixed expired CO_2	0-100 mmHg, 0-13.2 kPa or %	Volume weighted average CO_2 in the breath	Volumetric CO_2 & Tabular Data
PEEP	Positive End Expiratory Pressure	0-99 cmH_2O	Pressure in the lungs at the end of expiration	Numerics, Flow/ Pressure, Trend & Tabular Data
PEF	Peak Expiratory Flow	2-180 L/min adult 0.5-100 L/min pedi. 0.25-25 L/min neo.	Highest absolute flow rate during expiration	Loops, Trend & Tabular Data
PIF	Peak Inspiratory Flow	2-180 L/min adult 0.5-100 L/min pedi. 0.25-25 L/min neo.	Highest absolute flow rate during inspiration	Loops, Trend & Tabular Data
PIP	Peak Inspiratory Pressure	0-120 cmH_2O	Peak (highest) pressure in the airway during inspiration	Numerics, Flow/ Pressure, Trend & Tabular Data
☑	Pulse Rate	30-250 bpm	Number of pulse beats per minute	All

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Label	Parameter	Range/Units	Description	Screen Display
Raw	Airway Resistance	0-100 $cmH_2O/L/sec$ adult/pediatric 0-500 $cmH_2O/L/sec$ neonatal	Pressure required to cause gas flow at a given rate	Numerics & Tabular Data
RR	Respiration Rate	2-120 br/min adult 2-150 br/min pedi. 10-150 br/min neo.	Number of breaths per minute	All
RSBI	Rapid Shallow Breathing Index	0-1000 br/min/L (adult only)	Respiratory rate divided by average spontaneous tidal volume (only calculated when RR < 57)	Loops
SpO_2	Oxygen Saturation (Functional)	0-100 %	Oxyhemoglobin as a percentage of the sum of oxyhemoglobin and deoxyhemoglobin	All
VCO_2	Carbon Dioxide Elimination	1-3000 ml/min adult/pediatric 0-300 ml/min neonatal	Volume of CO_2 eliminated through the breath each minute	All except Flow/ Pressure & Loops
Vd Aw	Airway deadspace	0-500 ml	Total circuit deadspace, not including NICO Loop.	Numerics, Volumetric CO_2, Tabular Data
Vd/Vt	Deadspace to tidal volume ratio	0-1.00 ml	$(PaCO_2\text{-}PeCO_2) / PaCO_2$	Numerics, Volumetric CO_2 & ABG Data Entry
Vd alv	Alveolar deadspace	0-500 ml	Difference between physiologic and airway deadspace	Numerics, Volumetric CO_2 & ABG Data Entry
Vt alv	Alveolar tidal volume	0-2400 ml adult 0-1200 ml pediatric 0-160 ml neonatal	Tidal volume less airway deadspace	Numerics, Volumetric CO_2 & Tabular Data
Vt/kg	Tidal volume per kilogram	0-120 ml/kg adult 0-999.9 ml/kg pediatric 0-999.9 ml/kg neonatal	Tidal volume divided by kilogram of body weight	Respiratory Numerics
Vte	Expired Tidal Volume	200-3000 ml adult 30-400 ml pediatric 1-100 ml neonatal	Volume of gas exhaled per breath	All except Flow/ Pressure & Loops
Vte-m	Expired Tidal Volume - mechanical	200-3000 ml adult 30-400 ml pediatric 1-100 ml neonatal	Volume of mechanically exhaled gas, per breath	Tabular Data
Vte-s	Expired Tidal Volume - spontaneous	200-3000 ml adult 30-400 ml pediatric 1-100 ml neonatal	Volume of spontaneously exhaled gas, per breath	Tabular Data
Vti	Inspired Tidal Volume	200-3000 ml adult 30-400 ml pediatric 1-100 ml neonatal	Volume of gas inhaled per breath	All except Flow/ Pressure & Loops
Vti-m	Inspired Tidal Volume - mechanical	200-3000 ml adult 30-400 ml pediatric 1-100 ml neonatal	Volume of mechanically inhaled gas, per breath	Tabular Data
Vti-s	Inspired Tidal Volume - spontaneous	200-3000 ml adult 30-400 ml pediatric 1-100 ml neonatal	Volume of spontaneously inhaled gas, per breath	Tabular Data

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Principles of Operation

Non-Invasive Cardiac Output

The NICO monitor calculates cardiac output (C.O.) non-invasively based on respiratory gas analysis, using a technique known as "differential Fick partial rebreathing." The key to this technique is a NICO Sensor, consisting of a rebreathing valve and a combined CO_2/Flow sensor placed in the breathing circuit. The NICO Sensor is placed into the ventilator circuit between the patient elbow and ventilator wye. The rebreathing valve is automatically controlled by the monitor. When the valve is activated, the flow of the inspired and expired gas is diverted through a rebreathing NICO Loop. When the valve is deactivated, this additional rebreathing volume is bypassed and normal ventilation resumes. Every three minutes, a baseline, rebreathing and stabilization phase occurs. (See "The NICO Cycle" on page 28.) A non-invasive cardiac output calculation is made following the end of each three minute cycle. The calculation is based on the changes induced in CO_2 elimination and end tidal CO_2 in response to the rebreathing volume. The increase in end tidal CO_2, which reflects the increase in $PaCO_2$, is usually 3-5 mmHg (0.4-0.67 kPa) and returns to baseline in less than 30 seconds.

The Fick equation using CO_2 as an indicator states that cardiac output is equal to CO_2 elimination divided by the venous-arterial difference in the CO_2 content: $VCO_2/(CvCO_2-CaCO_2)$. The partial rebreathing method yields a differential form of the Fick equation, eliminating the need to measure mixed venous CO_2 (assumed constant during the rebreathing period and therefore cancels out of the equation). This indirect Fick method is then corrected for shunt, based on the Nunn's iso-shunt curves using SpO_2 (or entered PaO_2) and a user-entered value for FiO_2 (INSP O_2).

Carbon Dioxide (CO_2)

The NICO monitor uses the CAPNOSTAT® CO_2 Sensor to measure CO_2 by using the infrared absorption technique. The principle is based on the fact that CO_2 molecules absorb infrared (IR) light energy of specific wavelengths, with the amount of energy absorbed being directly related to the CO_2 concentration. When an IR beam is passed through a gas sample containing CO_2, the electronic signal from the photodetector (which measures the remaining light energy) can be obtained. This signal is then compared to the energy of the IR source and calibrated to accurately reflect CO_2 concentration in the sample. The CAPNOSTAT® CO_2 Sensor's response to a known concentration of CO_2 is stored at the factory in the sensor's memory. A reference channel accounts for optical changes in the sensor, allowing the system to remain in calibration without user intervention.

Flow and Pressure

Flow and pressure measurements in the NICO monitor are made by a fixed orifice differential pressure pneumotachometer. Respired gas flowing through the flow sensor causes a small pressure drop across the two tubes connected to the sensor. This pressure drop is transmitted through the tubing to a differential pressure transducer located inside the monitor, and is correlated to flow according to the factory stored calibration. User calibration is not required due to the ability of the plastic injection mold to repeatedly produce precision flow sensors. The pressure transducer is automatically "zeroed" to correct for changes in ambient temperature and electronics. The NICO monitor system software compensations allow accurate flow and volume measurements in the presence of high oxygen concentrations, anesthetic gases and helium-oxygen mixtures. When compensated, gas density and viscosity effects do not cause significant errors in flow measurement.

Carbon Dioxide Elimination (VCO_2)

Measurement of carbon dioxide elimination (VCO_2) is a fundamental component of the system's C.O. calculations. It is calculated based on a mathematical integration of the measured flow and CO_2 signals. These signals are obtained from practically the same point at the patient's airway, thereby insuring optimal accuracy. Both the flow and CO_2 sensors are integral components of the NICO Sensor.

Oxygen Saturation (SpO_2) & Pulse Rate

Oxygen saturation (SpO_2) is used by the NICO monitor to calculate the shunt correction of the NICO calculation, and the pulse rate is used to calculate stroke volume.

SpO_2 is determined using sensors containing red and infrared light emitting diodes (LEDs). The light from each LED is beamed through a pulsating vascular bed such as the patient's finger or toe. The remaining light not absorbed by the tissue reaches a photodiode light receptor in the sensor. Oxygen saturated blood absorbs different amounts of light at each wavelength as compared to unsaturated blood. Therefore, the amount of light absorbed by the blood in each pulse can be used to calculate oxygen saturation.

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The NICO monitor is calibrated to display "functional" saturation. This differs from the "fractional" saturation value displayed by most co-oximeters. Functional saturation represents the amount of oxyhemoglobin as a percentage of the hemoglobin that can be oxygenated. Dysfunctional hemoglobins, (COHb and METHb) are not included in the measurement of functional saturation.

- Functional Saturation = $HbO_2/100-(COHb+METHb)$; HbO_2 is oxyhemoglobin (fractional), COHb is carboxyhemoglobin, and METHb is methemoglobin.

Pulse Rate, derived from the pulse oximetery sensor, is calculated by measuring the time interval between the peaks of the infrared light waveform. The inverse of this measurement is displayed as pulse rate.

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NICO®

Navigating in Cardiac Output mode

Areas of the Display

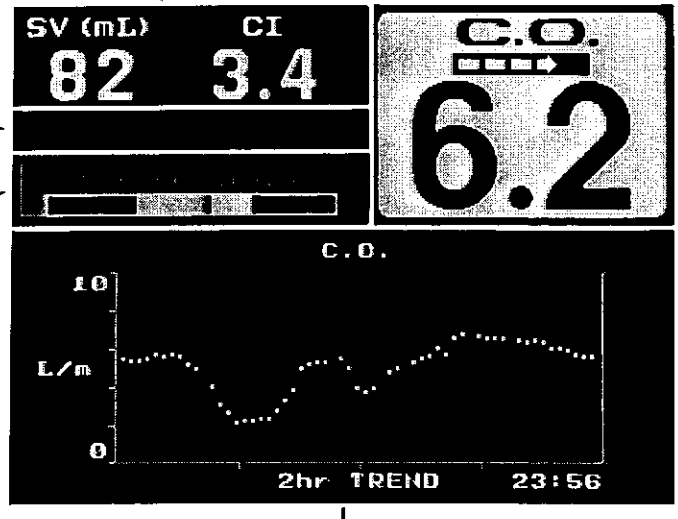
The major sections of the Cardiac Output mode screen are identified below.

Stroke Volume (SV) is displayed in all views. Cardiac Index (CI) or Cardiac Output (C.O.) is displayed. A battery icon also appears if on battery power.

Cardiac Output (C.O.), Cardiac Index (CI), or Pulmonary Capillary Blood Flow (PCBF) value is displayed. The CObar™ confidence indicator, **FAST MODE** or **MANUAL MODE** is displayed above the value.

A General Message area for status, alert and error information. Displayed in all views (here shown blank).

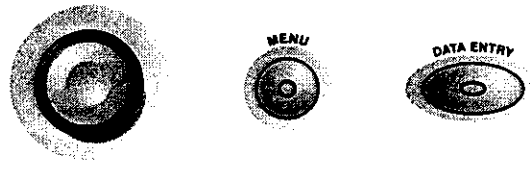
A Cardiac Output Message area for C.O. information is displayed in all views. The Rebreathing Bar is displayed during the rebreathing portion of the cycle.



The lower half of the display presents trend, waveform, respiratory and numeric data to the user. Various data entry, setup and alert menus are also presented here. Use the **KNOB** and the **MENU** and **DATA ENTRY** keys to select the various displays.

Navigating the Display System

Use the **KNOB**, **MENU**, and **DATA ENTRY** keys to navigate the NICO® monitor's display system (as outlined in the following sections).



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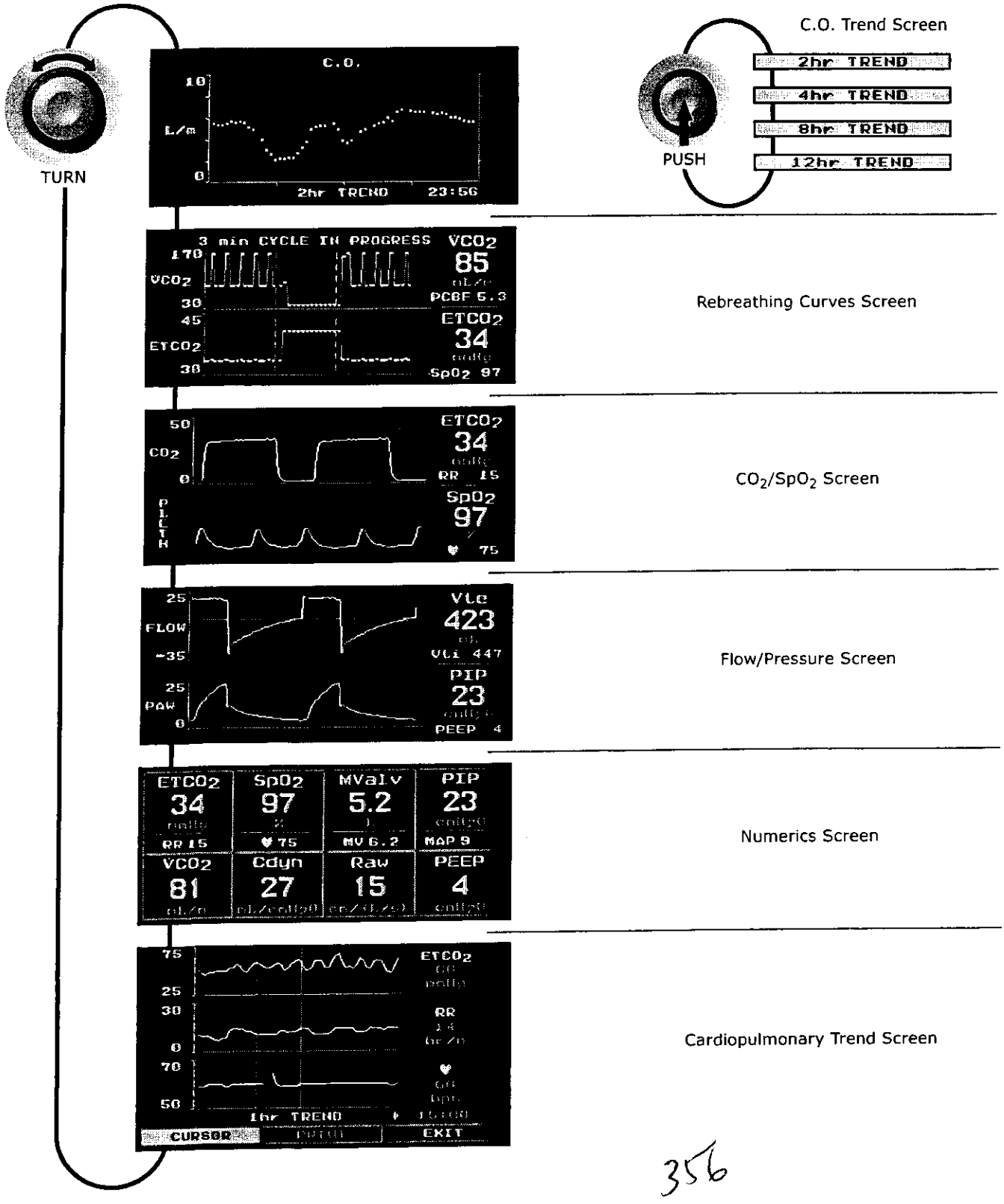
KNOB selectable Monitoring Screens

The **KNOB** is used to page through monitoring screens, scroll through menus and make selections, and to change or enter values. The **KNOB** is generally turned to access different monitoring screens and to highlight menu options, and pressed to accept or change selections. Screens must be enabled from the **CHOOSE SCREENS** menu (see "Enabling Screens" on page 41)



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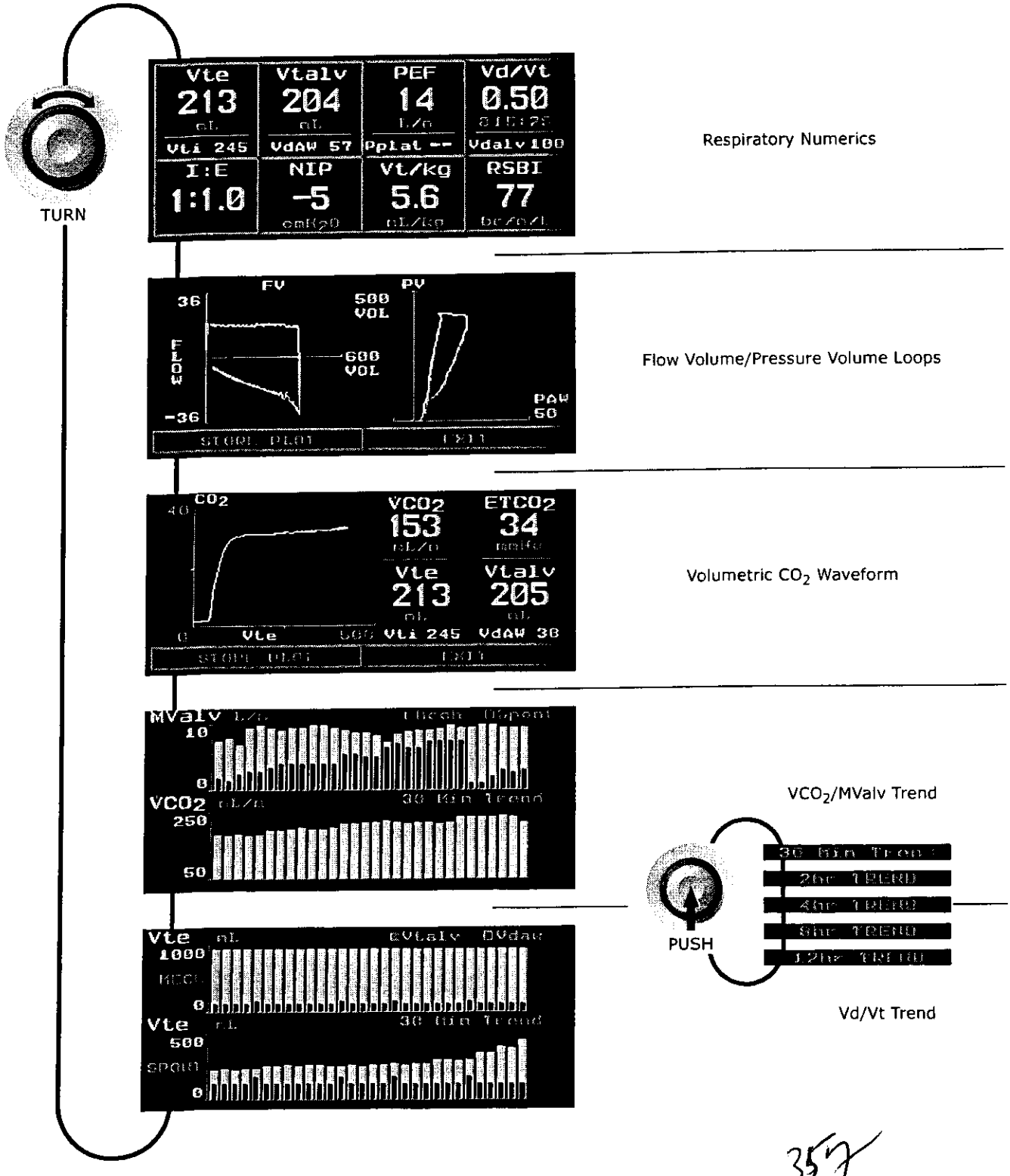
KNOB Selectable Respiratory Screens

The following Respiratory Screens are available in the monitoring mode. Press the **MENU** key and select **RESP SCREENS** from the **SELECT A SCREEN** menu by turning and then pressing the **KNOB**.

From the **SELECT RESPIRATORY SCREENS** menu, highlight and select a screen by turning and then pressing the **KNOB**. Screens can also be displayed by turning the **KNOB** while viewing any monitoring screen. Screens must be enabled from the **CHOOSE SCREENS** menu (see "Enabling Screens" on page 41)



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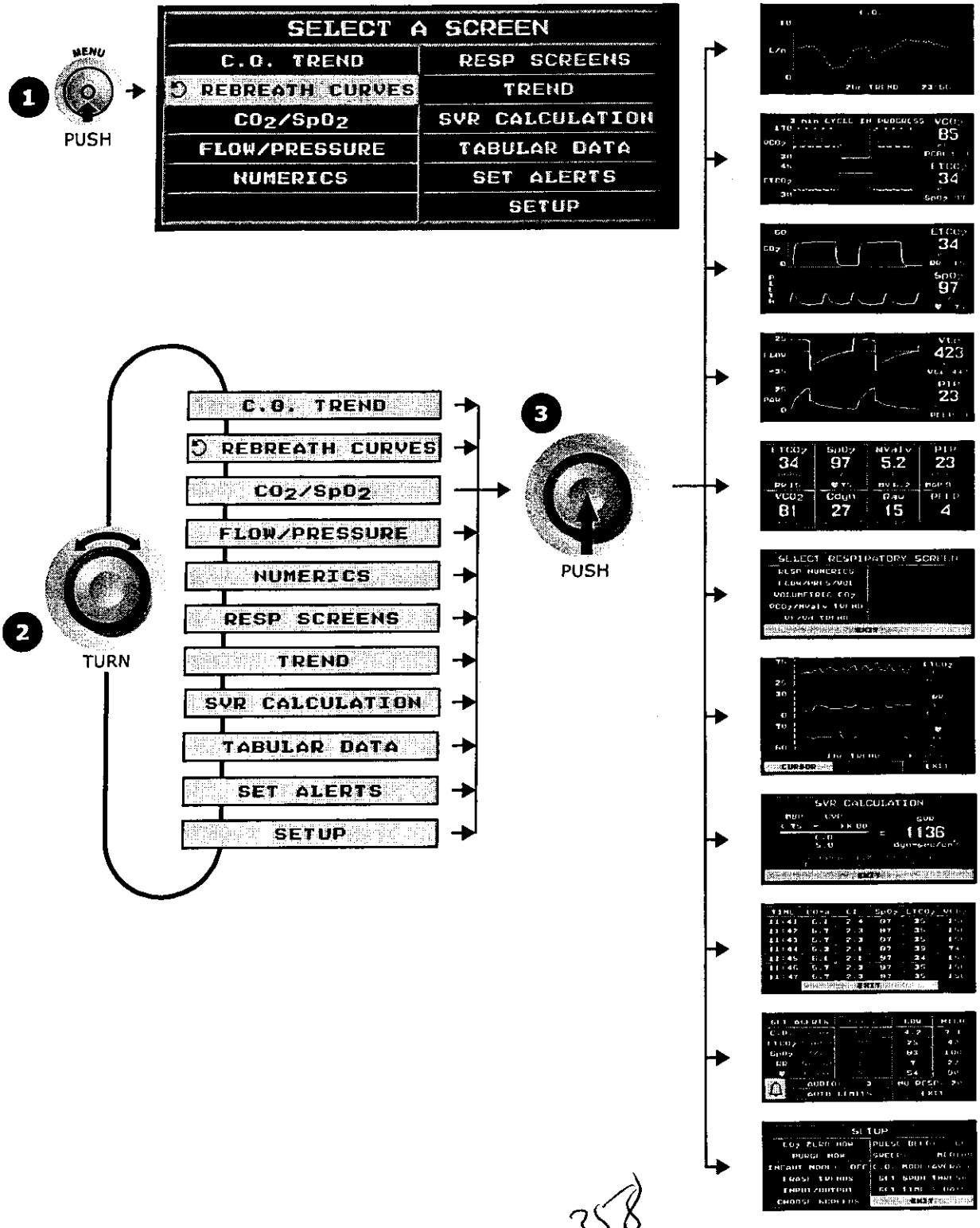
MENU key Screen Displays

Press the **MENU** key to activate the **SELECT A SCREEN** menu and illuminate the key's green icon. Press the key again to return to the previously displayed screen. From the **SELECT A SCREEN** menu turn the **KNOB** to highlight the screen you wish to display. Press the **MENU** key or the **KNOB** to display that selected screen.



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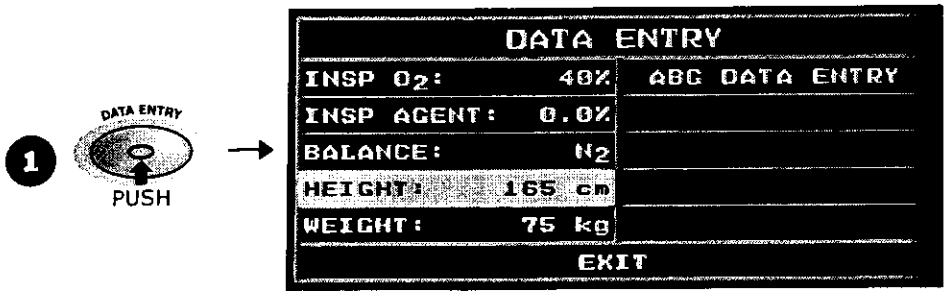
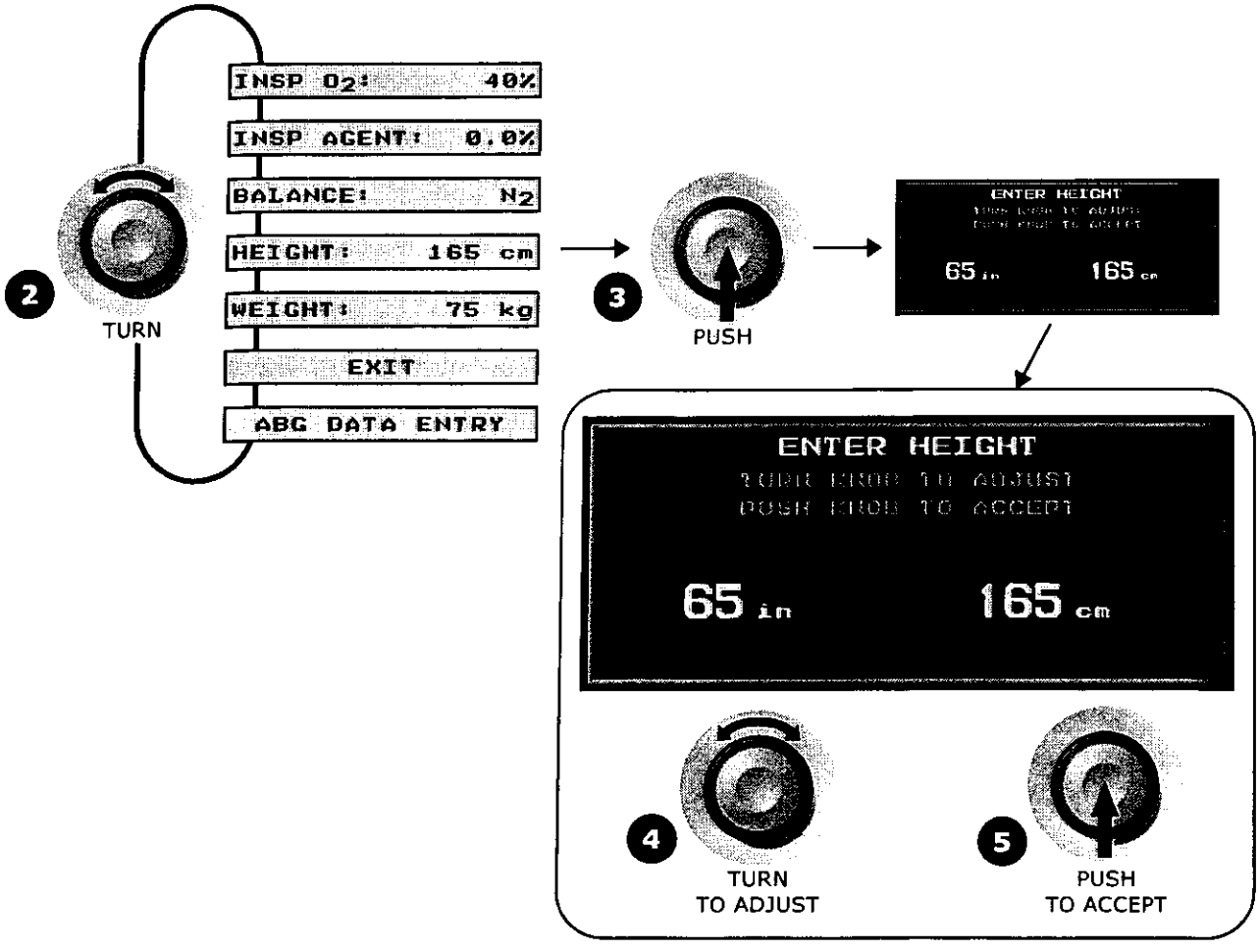
DATA ENTRY key Screen Displays

Press the **DATA ENTRY** key to activate the **DATA ENTRY** screen and illuminate the key's green icon. Press the key again to return to the previously displayed screen. From the **DATA ENTRY** screen, you can enter patient information including height, weight and respiratory gas mixture, and access the **ABG DATA ENTRY** screen. (See "Entering Patient Data" on page 29 for details.)





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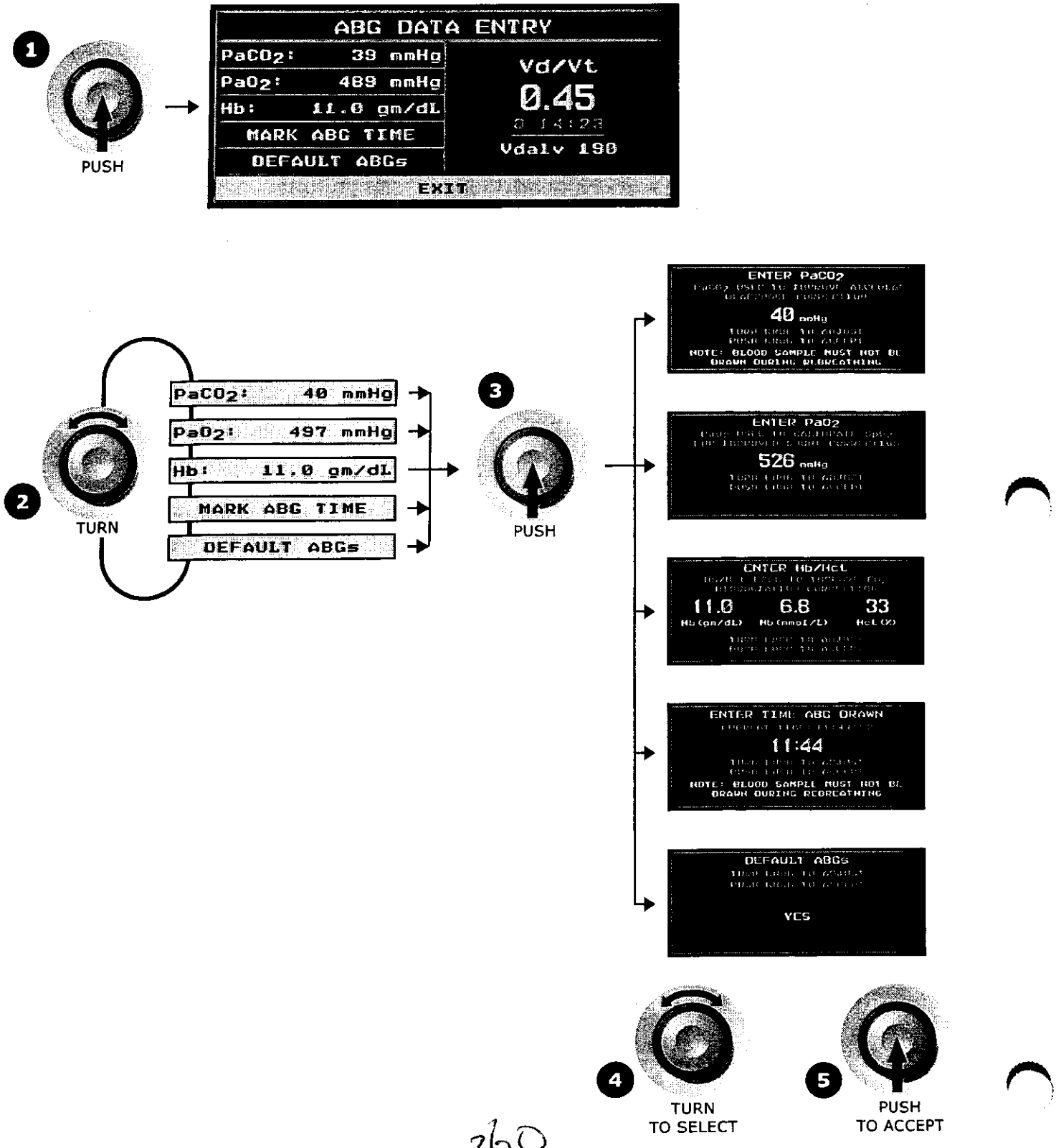
ABG Data Entry Screens

From the **DATA ENTRY** screen, select **ABG DATA ENTRY.** Turn and press the **KNOB** to enter $PaCO_2$, PaO_2, and Hemoglobin entry screens. (See "Entering Patient Data" on page 29 for details.)



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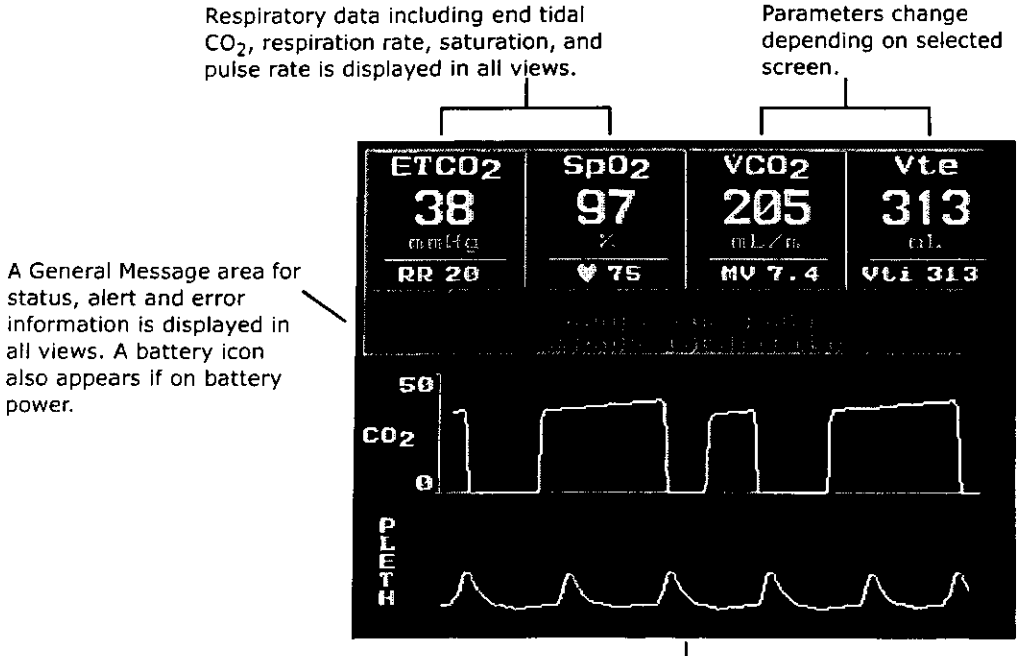
NICO®

Navigating in Respiratory Mechanics mode

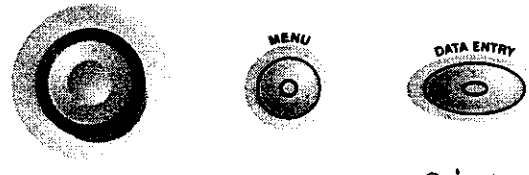
Areas of the Display

The major sections of the Respiratory Mechanics mode screen are identified below.



Navigating the Display System

Use the **KNOB**, **MENU**, and **DATA ENTRY** keys to navigate the NICO® monitor's display system (as outlined in the following sections).



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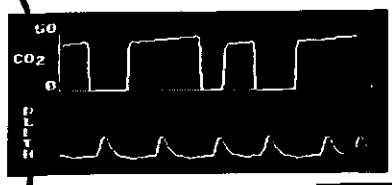
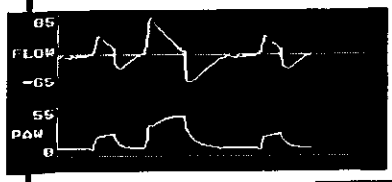
KNOB selectable Monitoring Screens

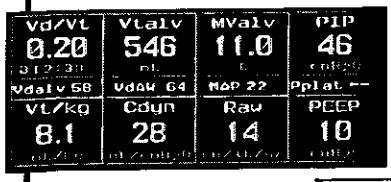
The **KNOB** is used to page through monitoring screens, scroll through menus and make selections, and to change or enter values. The **KNOB** is generally turned to access different monitoring screens and to highlight menu options, and pressed to accept or change selections. Screens must be enabled from the **CHOOSE SCREENS** menu (see "Enabling Screens" on page 41)



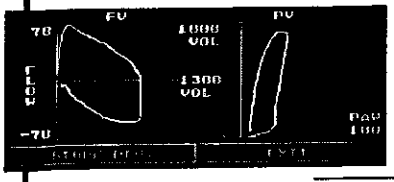
CO_2/SpO_2 Screen



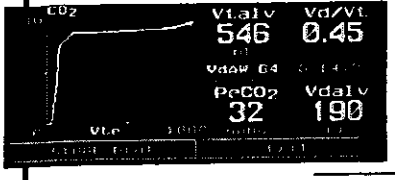
Flow/Pressure Screen



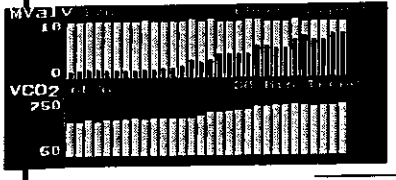
Respiratory Numerics Screen



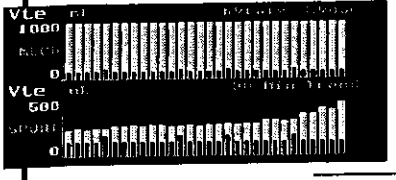
Flow Volume/Pressure Volume Loops



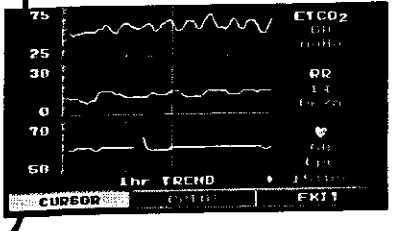
Volumetric CO_2 Screen



VCO_2/MValv Trend



Vtalv/Vdaw Trend



Cardiopulmonary Trend

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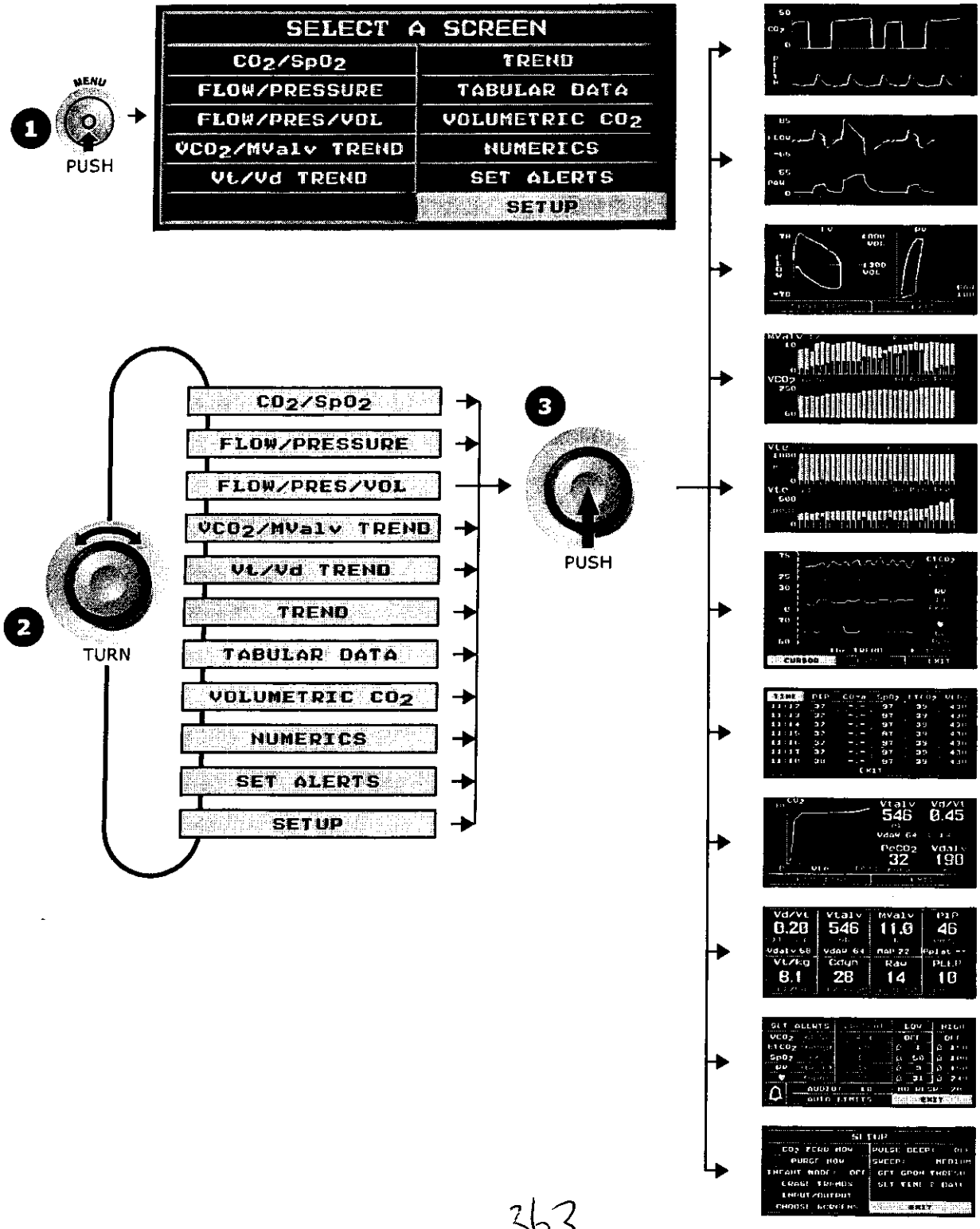
MENU key Screen Displays

Press the **MENU** key to activate the **SELECT A SCREEN** menu and illuminate the key's green icon. Press the key again to return to the previously displayed screen. From the **SELECT A SCREEN** menu turn the **KNOB** to highlight the screen you wish to display. Press the **MENU** key or the **KNOB** to display that selected screen.



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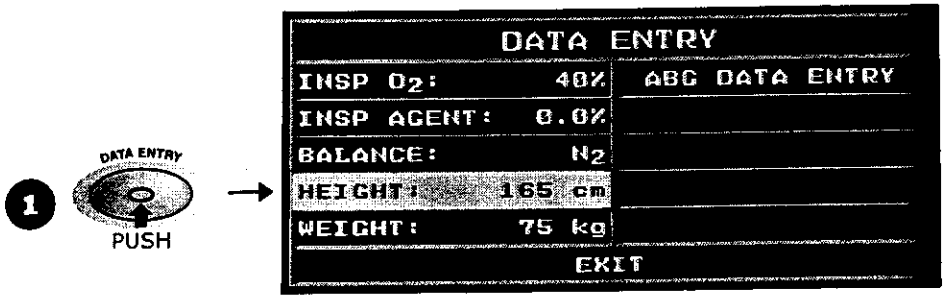
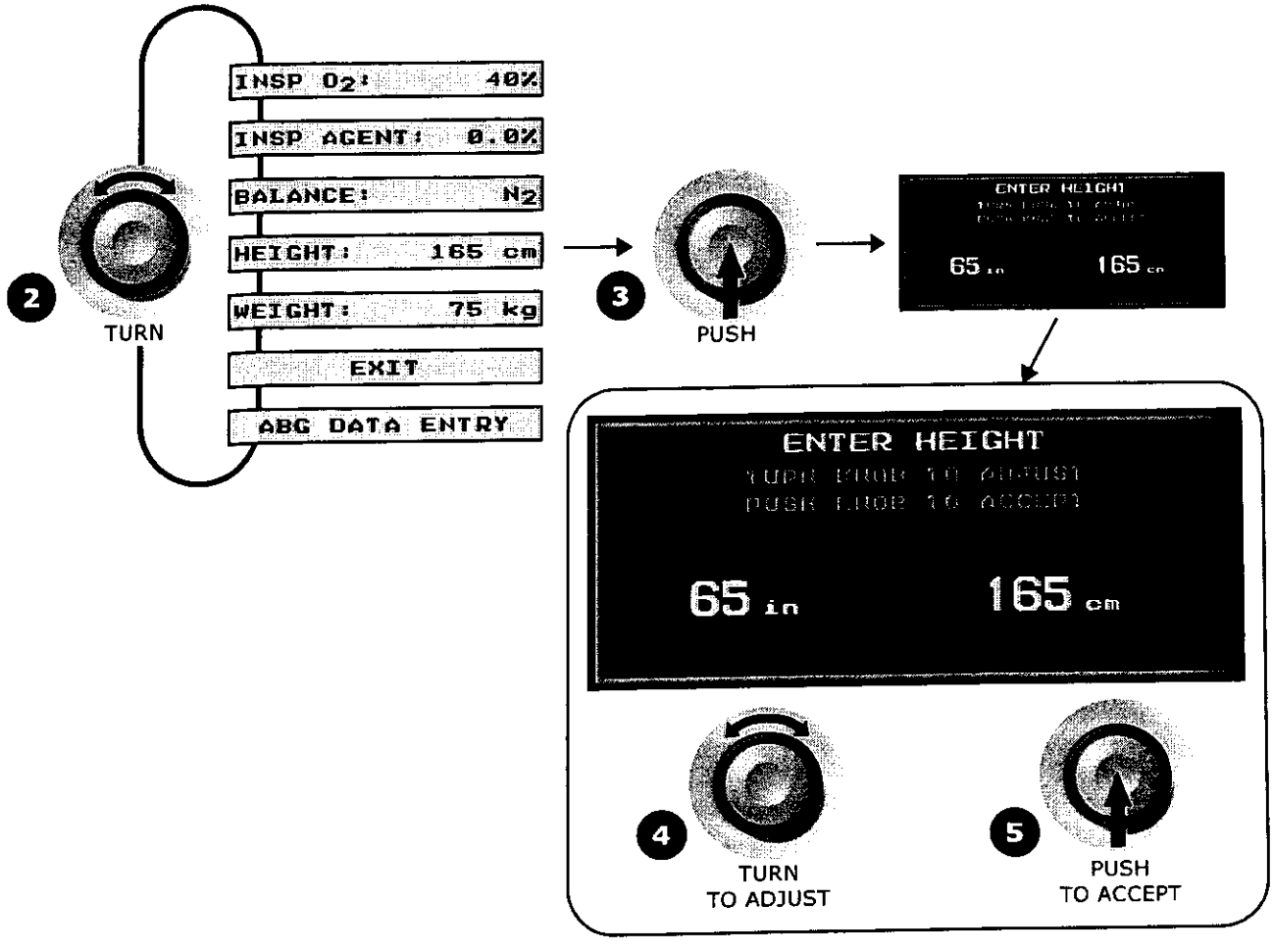
DATA ENTRY key Screen Displays

Press the **DATA ENTRY** key to activate the **DATA ENTRY** screen and illuminate the key's green icon. Press the key again to return to the previously displayed screen. From the **DATA ENTRY** screen, you can enter patient information including height, weight and respiratory gas mixture, and access the **ABG DATA ENTRY** screen. (See "Entering Patient Data" on page 29 for details.)





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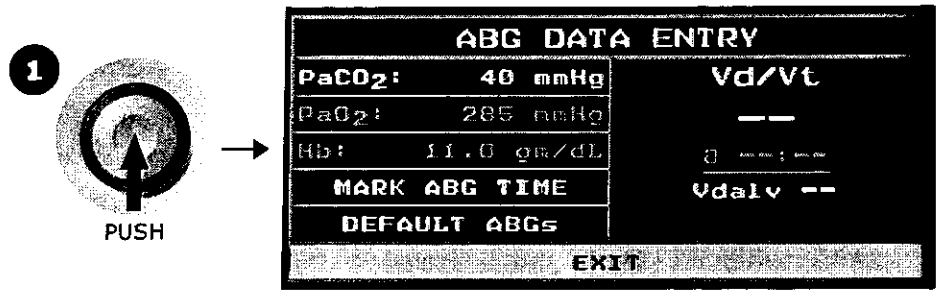
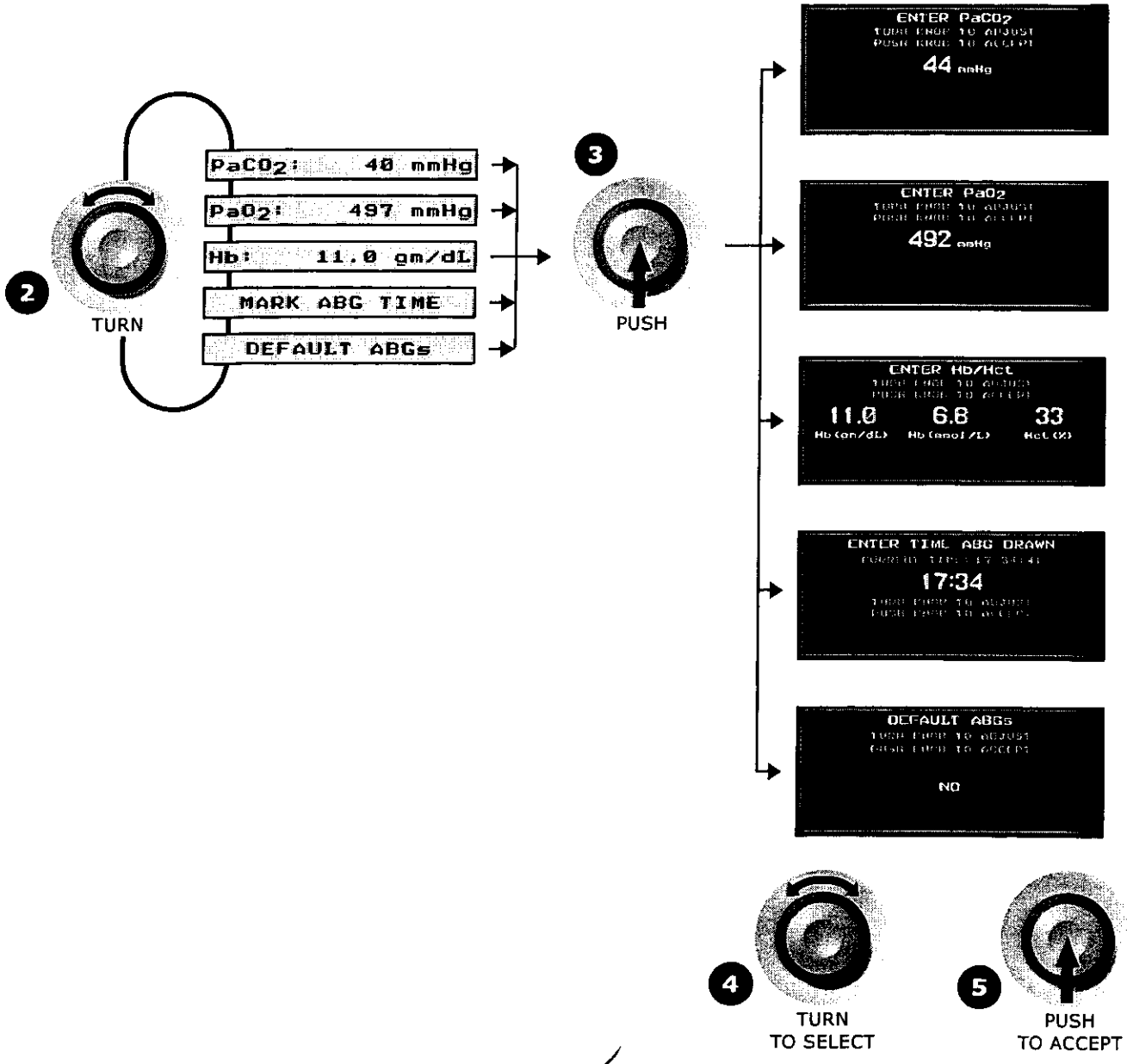
ABG Data Entry Screens

From the **DATA ENTRY** screen, select **ABG DATA ENTRY**. Turn and press the **KNOB** to enter $PaCO_2$, PaO_2, and Hemoglobin entry screens. (See "Entering ABG Data" on page 38 for details.)





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NICO®

Safety

For maximum patient and operator safety, observe the following warnings, cautions and notes.

Warnings

WARNING:

⚠ Indicates a potentially harmful condition that can lead to personal injury.

- Explosion Hazard: Do not use the NICO® monitor in the presence of flammable anesthetics. Use of this instrument in such an environment may present an explosion hazard.
- Electrical Shock Hazard: Always turn the NICO monitor off before cleaning it. Do not use with a damaged external power source. Refer servicing to qualified service personnel.
- Connect the AC Mains power cord to a properly grounded hospital-grade outlet. The NICO monitor should be connected to the same electrical circuit as other equipment in use on the patient. Outlets of the same circuit can be identified by members of the hospital's engineering department.
- Failure of Operation: If the monitor fails to respond as described, do not use it until the situation has been corrected by qualified personnel.
- Reuse (disassembly, cleaning, disinfecting, resterilizing, etc.) of the CO_2, CO_2/Flow and NICO Sensors may compromise device functionality and system performance and cause a potential patient hazard. Performance is not guaranteed if a sensor is reused.
- Inspect the CO_2, CO_2/Flow, SpO_2 and NICO Sensors prior to use.
  - Do not use if they appear to be damaged or broken.
  - Do not attempt to rotate the NICO Sensor in the breathing circuit by grasping the pneumatic tubes exiting the flow sensor.
  - Do not apply excessive tension to any cable or pneumatic tubing.
  - Periodically inspect sensor tubing lines for kinks.
  - Replace the CO_2/Flow or NICO Sensor if excessive moisture or secretions are observed in the tubing.
- The NICO monitor automatically identifies the type of sensor (small, standard or large NICO Sensor, or neonatal, pediatric or adult CO_2/Flow sensor) when it is connected. If a sensor identification message is not displayed when a sensor is first connected, DO NOT use the sensor. If the condition persists, refer the monitor to qualified service personnel.
- Do not use the NICO monitor if it is unable to properly identify a CO_2/Flow sensor or a NICO Sensor. If the condition persists, refer the monitor to qualified service personnel.
- In the event the message **NICO SENSOR FAILURE** is displayed, remove the NICO Sensor from the patient circuit.
- The CO_2/Flow or NICO Sensor connector should be properly inserted into the front panel receptacle prior to connecting a sensor to the breathing circuit, in order to avoid a circuit leak, or occlusion of sensor tubing.
- NICO Sensors increases airway deadspace by 35 cc (minimum). At low tidal volumes, compensatory changes to ventilation protocol should be considered.
- NICO Sensors are not for pediatric use.
- Patient Safety: Care should be exercised with all patients, especially neonates, to assure continued peripheral perfusion distal to the SpO_2 sensor site after application.
  - Inspect the SpO_2 sensor site for adequate circulation at least once every four hours.

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- When applying sensors take note of patient's physiological condition. For example, burn patients may exhibit more sensitivity to heat and pressure and therefore additional consideration such as more frequent site checks may be appropriate.

- Data Validity: The NICO monitor should not be used as a substitute for an ECG monitor. The Pulse Rate display reflects the pulsatile flow found at the patient extremity connected to the sensor. This rate can be affected by many factors and may occasionally be "frozen."
- Periodically check sensors and tubing for excessive moisture or secretion build up. Although the NICO monitor automatically purges the lines, excessive moisture or secretions may still remain.
- While using the sensors, a system leak, such as that caused by uncuffed endotracheal tubes or a damaged sensor may significantly affect flow related readings. These include flow, volume, pressure, deadspace, CO_2 production and other respiratory mechanics parameters.
- Do not position sensor cables or tubing in any manner that may cause entanglement or strangulation.
- The NICO monitor is not intended to be used as an apnea monitor.
- The NICO monitor has no protection against the ingress of water.

Cautions

CAUTION:
Indicates a condition that may lead to equipment damage or malfunction.

- Use only Novametrix approved sensors and accessories with the NICO monitor.
- Do not operate the NICO monitor when it is wet due to spills or condensation.
- Do not operate the product if it appears to have been dropped or damaged.
- Never sterilize or immerse the monitor in liquids.
- Do not sterilize or immerse sensors except as directed in this manual.
- No tension should be applied to any sensor cable or tubing.
- To avoid the effects of excessive moisture in the NICO Sensor, insert it in the ventilator circuit with the pneumatic tubes upright. Excessive moisture in the NICO Sensor may affect the accuracy of the measurements.
- To avoid the effects of excessive moisture in the measurement circuit, insert the CO_2/Flow sensor in the ventilator circuit with the tubes upright. Improper placement may result in erroneous data.
- Excessive moisture in the CO_2/Flow sensor tubing may affect the accuracy of the measurements.
- It is recommended that CO_2/Flow or NICO Sensors be removed from the circuit whenever an aerosolized medication is delivered. These medications may contaminate the sensor windows, causing the sensor to fail prematurely.
- Operate the monitor at temperatures between 10 to +40° C (50 to 104° F), 10-95% R.H. non-condensing.
- Avoid storing the monitor at temperatures less than -10° C or greater than +55° C (<14° F or >131° F) 10-95% R.H. non-condensing
- Observe precautions for electrostatic discharge (ESD) and electromagnetic interference (EMI) to and from other equipment.
- Sudden erratic changes in the CO_2 and pressure waveforms that do not correlate to the physiological condition of the patient may be signs that the monitor is experiencing electromagnetic interference.
- To reduce electromagnetic interference, maximize the distance between electromedical devices.
- The NICO monitor is not intended for use in a hyperbaric chamber or an MRI (Magnetic Resonance Imaging) environment.

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- Where electromagnetic devices (i.e., electrocautery) are used, patient monitoring may be interrupted due to electromagnetic interference. Electromagnetic fields up to 3 V/m will not adversely affect system performance.
- Caution: Federal (U.S.A.) law restricts this device to sale, distribution, or use by or on the order of a licensed medical practitioner.
- The NICO monitor contains no user serviceable parts. Refer servicing to qualified service personnel. A technical Service Manual is available for use by technical personnel.

Notes

NOTE

A point of particular interest or emphasis intended to provide more efficient or convenient operation.

- In order to ensure proper monitoring of oxygenation and ventilation:
  - The use of pulse oximetry is recommended during monitoring with the NICO system.
  - Setting of $ETCO_2$ and SpO_2 alert limits is recommended.
- Before monitoring, confirm settings for delivered oxygen, anesthetic agent, balance gas and hemoglobin by pressing the **DATA ENTRY** key.
- A "NO RESPIRATION" alert is not generated when both the CAPNOSTAT® CO_2 sensor and the NICO Sensor or CO_2/Flow sensor are disconnected from the NICO monitor.
- Be certain that the monitor is not in Demo mode while monitoring. Demo mode can be identified by the flashing **DEMO MODE** label in the General Message area of the display. To exit Demo mode and return to normal monitoring mode, turn the power off and back on.
- Do not attach an SpO_2 sensor distal to a blood pressure cuff. Valid data cannot be processed when the cuff is inflated. Attach the sensor to the limb opposite to the site used for the blood pressure cuff.
- This product and its accessories which have patient contact are free of latex.
- The NICO monitor is Year 2000 compliant.
- Data Validity: Inaccurate SpO_2 and Pulse Rate values may be caused by:
  - Incorrect application or use of a sensor
  - Significant levels of dysfunctional hemoglobin; carboxyhemoglobin or methemoglobin
  - Significant levels of indocyanine green, methylene blue, or other intravascular dyes
  - Exposure to excessive illumination such as surgical lamps—especially ones with a xenon light source, or direct sunlight
  - Excessive patient movement
  - Venous pulsations
  - Electrosurgical interference
  - Use of an IABP.
- The NICO monitor provides C.O. measurements when the following conditions are met:
  - The NICO Sensor assembly is properly installed in the patient's breathing circuit.
  - Valid flow and CO_2 signals are detected with no significant signal artifact.
  - VCO_2 is greater than 20 mL/min.
  - $ETCO_2$ is between 15 and 85 mmHg (2.0 - 11.5 kPa or %) during baseline
  - $ETCO_2$ is between 15 and 100 mmHg (2.0 - 13.5 kPa or %) during rebreathing
  - The tidal volume is greater than 200ml (small and standard sizes)
  - The tidal volume is greater than 400 ml (large size).
  - The respiratory rate is between 3 and 60 br/min.
  - The **STOP/CONTINUE REBREATHING** key is not illuminated.
  - The NICO cycle is not paused by the monitor for any other reason (displayed in the C.O. message area).
- When a new CAPNOSTAT® CO_2 sensor is attached to the monitor, or is moved from one monitor to another, it must be zeroed before use.
- After the life cycle of the equipment and accessories has been met, disposal should be accomplished following national and local requirements.

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NICO®

Monitoring Cardiac Output

This section details the steps needed to begin patient monitoring with the NICO® monitor.

Preparing for Use

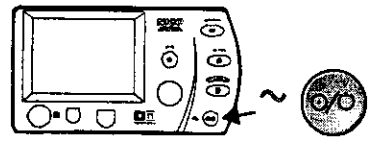
Inspect

Before monitoring, take a few moments to inspect the NICO monitor and its sensors. Check that all items are clean, dry, and physically intact with no broken or damaged components.

Turn on the monitor

Turn the NICO monitor on.

1 Press the **Operate/Standby** key to turn the monitor on and off.
   - The monitor can operate from its internal battery or from the AC Mains. (See "AC/Battery Operation" on page 4 for details.)



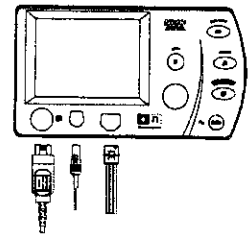
2 The monitor performs a quick self-test.
   - An audible tone sounds, the key indicators illuminate, and a **SELF-TEST IN PROGRESS** message is briefly displayed.

3 The message **PRESS KNOB TO ERASE STORED TRENDS** is displayed for 5 seconds.
   - To erase the contents of the monitor's trend memory, press the knob. **TRENDS ERASED** is briefly displayed.
   - To retain the contents of the monitor's trend memory, do not press the knob. Wait the 5 seconds and **TRENDS RETAINED** is displayed.
   - Note: If the internal battery becomes fully discharged, the message **CHECK DATE/TIME (MENU -> SETUP)** will appear before the **PRESS KNOB TO ERASE STORED TRENDS** message. (See "Setup Screen" on page 49 for details.)

4 The power up sequence is completed and a monitoring screen is displayed.
   - The monitor displays the screen that was displayed when the monitor was last turned off.
   - If the monitor is in Respiratory Mechanics mode, connecting a NICO Sensor will cause the monitor to automatically switch to Cardiac Output mode.
   - The monitor is in a READY state and the parameters will be dashed and alerts will not be active until parameters are calculated and displayed.
   - Parameters will display and their alerts will become active as they are calculated.

Connect and apply the sensors

Connect the sensors to the monitor, ventilator circuit, and patient.



1 Connect the SpO_2 sensor to the monitor and apply it to the patient. (See "Pulse Oximetry Sensors" on page 72.)

2 Connect the CAPNOSTAT® CO_2 Sensor to the monitor. (See "CAPNOSTAT® CO2 Sensor" on page 70.)

3 Select a NICO Sensor, see "Choosing a NICO Sensor size" on page 65.

4 Connect the NICO Sensor to the monitor and attach a CAPNOSTAT® CO_2 Sensor. (See "NICO Sensor" on page 64.)

5 Use the Initial Adjustment Template as a guide and adjust the NICO Loop to match the ventilator's tidal volume setting, then discard the template. (See Instructions on the NICO Sensor template.

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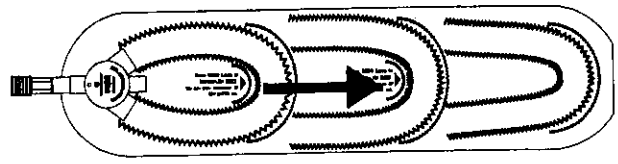
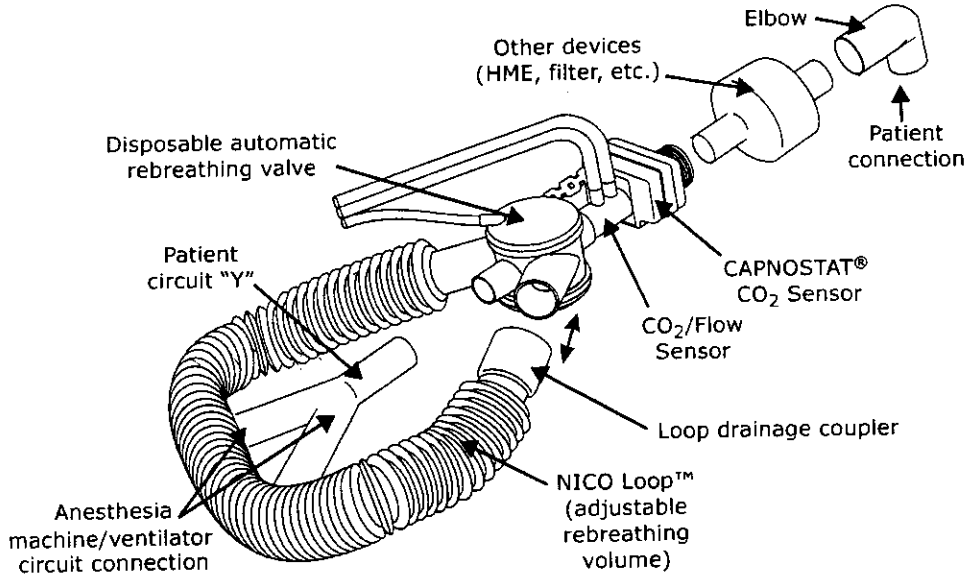


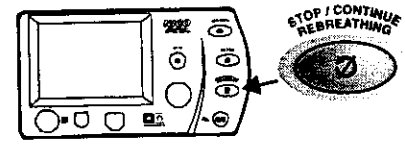
6 For optimal results, place the NICO Sensor into the ventilator circuit between the endotracheal tube and the ventilator circuit wye.
   - Place other devices (HME, filters, etc.) between NICO Sensor and the patient connection.
   - The NICO Sensor increases airway deadspace by 35 cc (minimum). At low tidal volumes, compensatory changes to ventilation protocol should be considered.
   - Placement of a sidestream gas analyzer sampling port between the NICO Sensor and the patient connection may reduce measurement accuracy at low tidal volumes.
   - Sidestream or mainstream gas analyzers placed between the NICO Sensor and the patient circuit "Y" may be inaccurate during the rebreathing phase of the NICO cycle.
   - Place the sensor so that the triple lumen tubing lines exit from the top of the sensor (to help keep them clear and dry).
   - Excess moisture may be removed by temporarily opening the circuit at the loop drainage coupler. Securely reconnect the coupler.

NICO Sensor and CAPNOSTAT® CO_2 Sensor



Begin Cardiac Output monitoring

After the NICO monitor is turned on and the sensors are properly connected and applied, cardiac output monitoring can begin.



1 Press the **STOP/CONTINUE REBREATHING** key to initiate monitoring. Subsequent presses will Stop/Continue the rebreathing process.
   - An icon "Ø" identifies rebreathing status.
   - Ø Illuminated: Rebreathing is DISABLED.
   - Ø Not illuminated: Rebreathing is ENABLED.

2 Enter the patient's height and weight (for cardiac index calculations) and the delivered oxygen, anesthetic agent and balance gas by pressing the **DATA ENTRY** key. (See "Entering Patient Data" on page 29.)

3 If available, enter the patient's $PaCO_2$, PaO_2, hemoglobin and hematocrit in the **ABG DATA ENTRY** screens, then mark the ABG time before exiting. (See "Entering Patient Data" on page 29).

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NOTE: Vd/Vt Phy, Vd Phy, and Vd alv are calculated based on the $PaCO_2$ value last entered, and are not updated until the next time the $PaCO_2$ value is entered or changed.

4 As you begin monitoring, please note the following:

- Reliance on Cardiac Output parameters (C.O., PCBF, SV & CI) should be taken in context with other monitoring parameters and the physiologic condition of the patient.
- Entry of patient height and weight is required to calculate and display Cardiac Index.
- Pulse oximetry is required to calculate and display Stroke Volume (SV).
- Accuracy of cardiac output and related parameters will be affected by the following:
  - Significant fluctuations in mixed venous CO_2 content or metabolic CO_2 production during any three minute measurement period.
  - Sudden release of CO_2 into the bloodstream, such as when releasing a cross clamp.
  - The presence of excessive moisture or secretions in the NICO sensor.
  - Entry of blood gas information.
- Due to the periodic rebreathing for C.O. measurements, the patient's effective ventilation will be reduced by typically 10-15% (depending on the rebreathing volume required). This can be offset by increasing the minute ventilation before monitoring begins.

Rebreathing Bar

The Rebreathing Bar visually indicates the level of patient rebreathing. Under normal monitoring conditions, the ↻ REBREATHING icon and Rebreathing Bar appear in the message center each time the automatic rebreathing cycle begins.

- The Rebreathing Bar represents the total possible range of rebreathing from 0-100%.
- The highlighted area within the bar represents the target rebreathing range (35%-70%) for optimal NICO performance.
- A vertical pointer within the Rebreathing Bar indicates the current rebreathing percentage.
  - The pointer will appear within the highlighted area of the Rebreathing Bar when the NICO Loop is properly sized and providing an acceptable percentage of rebreathing.
  - *Note*: The word "OK" will disappear when the pointer falls within that area of the highlighted bar.

Expand/Retract NICO Loop

- If the NICO Loop is not sufficiently expanded and the Rebreathing Bar pointer falls below 35%, the message **EXPAND LOOP** is displayed during the rebreathing period.

- If the NICO Loop is over-expanded and the Rebreathing Bar pointer is above 70%, the message **RETRACT LOOP** is displayed during the rebreathing period.

To expand or retract the NICO Loop:

1 Grasp the NICO Loop with one hand and the automatic rebreathing valve with the other hand so as not to disturb/disconnect the breathing circuit while adjusting the loop.

2 Expand or retract the NICO Loop 3-6 inches.
- It may take 2-3 additional breaths before the icon changes.
- Note that if the loop is still not appropriately sized by the end of the rebreathing period, the message will be removed and may be displayed again during the next rebreathing period.

Sensor Size Message

If the **EXPAND** or **RETRACT LOOP** message appears for more than three rebreathing cycles, and resizing the NICO Loop was not effective, the NICO monitor will suggest a different sized sensor to correct the condition. See "Status Messages" on page 66.

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The NICO Cycle

Once rebreathing is enabled, the NICO monitor automatically repeats a three-minute cardiac output measurement cycle, unless it is set to **MANUAL MODE** in the **C.O. MODE** screen. In that case, a 3-cycle rebreathing sample is user-initiated by pressing the **STOP/CONTINUE REBREATHING** key.

The NICO cycle has three phases:

- **Baseline:** During the 60-second baseline period, the rebreathing valve inside the NICO Sensor is turned off and the rebreathing volume of the NICO Loop is bypassed. During this time, VCO_2, $PaCO_2$ and $ETCO_2$ will be at baseline values.
- **Rebreathing:** The 35-second rebreathing period starts when the monitor turns on the rebreathing valve inside the NICO Sensor causing the rebreathing volume of the NICO Loop to be added into the circuit. During rebreathing, VCO_2 is reduced, $PaCO_2$ and $ETCO_2$ become elevated (3-5 mmHg, typical) and mixed venous CO_2 remains unchanged.

  NOTE: The rebreathing period will typically induce an increase in $PaCO_2$ by 3-5 mmHg. An ABG blood sample drawn during this period (↻ **REBREATHING** displayed) or during the first twenty seconds of the stabilization period (where **NEXT** ↻ is displayed), may cause $PaCO_2$ values to reflect higher than normal levels.

- **Stabilization:** After completion of rebreathing, an 85-second stabilization period begins, during which time VCO_2, $PaCO_2$ and $ETCO_2$ return to their baseline values.

The NICO monitor updates the displayed C.O. value following the completion of each three minute NICO cycle. The CObar (cardiac output confidence bar) provides an indication of the system's confidence in the displayed value. (See "CObar™ Confidence Indicator" on page 33.)

When the third cycle is completed in **MANUAL MODE**, rebreathing is paused and the **STOP/CONTINUE REBREATHING** key is turned on. To stop rebreathing during the three cycles, press the key again. For details, see "Manual Mode" on page 33.

Rebreathing On/Off or Paused

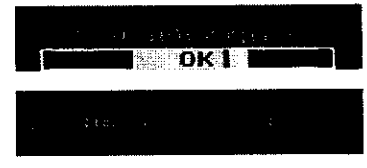
The user can interrupt or resume the rebreathing cycle at any time by pressing the **STOP/CONTINUE REBREATHING** key. The NICO monitor will not automatically restart the rebreathing cycle—that must be initiated by the user pressing the **STOP/CONTINUE REBREATHING** key. Note that once rebreathing is initiated by the user, the monitor will, under certain conditions, pause rebreathing until a specified condition (see below) is corrected—at which time the monitor will restart the rebreathing.

Rebreathing can be Off, On, or Paused as indicated below:

Rebreathing OFF (disabled)

- The monitor starts in this state upon power-up.
- The **STOP/CONTINUE REBREATHING** key is illuminated while in this state.
- The rebreathing cycle can be placed into this state at any time by pressing the **STOP/CONTINUE REBREATHING** key (rebreathing is immediately disabled).
- The rebreathing cycle is automatically turned off for certain monitor/sensor conditions. (See "(Alert Class: H-High Priority, M-Medium Priority, L-Low Priority, S-Status Message. See "Alert Priorities" on page 61 for details." on page 84.)
- Noted in the cardiac output message area as **REBREATHING OFF**.

Rebreathing ON (enabled)



- When the monitor is initially turned on, this state is entered only after pressing the **STOP/CONTINUE REBREATHING** key.
- The **STOP/CONTINUE REBREATHING** key is not illuminated while in this state.
- The cardiac output is calculated and updated while in this state.
- Noted in the cardiac output message area as ↻ **REBREATHING** or **NEXT** ↻.

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Rebreathing Paused

- The NICO monitor automatically pauses the rebreathing cycle and generates a display message under any of these conditions:
  - $ETCO_2$ is less than or equal to 15 mmHg (2.0 kPa or %), or greater than or equal to 85 mmHg (11.5 kPa or %)
  - Respiration rate is less than or equal to 3 or greater than or equal to 60 br/min.
  - VCO_2 is less than or equal to 20 mL/min.
- The rebreathing cycle automatically restarts when the condition is corrected.

Entering Patient Data

NICO monitoring can be enhanced by the entry of key patient specific data including respired gas composition (anesthetic agent, balance gas, and inspired O_2), patient height and weight, and arterial blood gas data ($PaCO_2$, PaO_2, Hb or Hct). Inclusion of ABG data is especially important when gas exchange impairment is expected (i.e., high shunt or deadspace). **ABG samples should not be obtained during the rebreathing phase of the 3-minute NICO cycle.**

Patient data should be updated in the **DATA ENTRY** screen whenever possible. The screen may be accessed at any time by pressing the **DATA ENTRY** key.

DATA ENTRY settings The following table lists the parameters and ranges accessible in the **DATA ENTRY** screens.

Label	Parameter	Default	Range/Units	Description
INSP O_2	Inspired Oxygen	40%	21-100 %	Percent of oxygen in the inspired gas. Must be entered in order for NICO to accurately calculate parameters.
INSP AGENT	Inspired Anesthetic Agent	0%	0-20 %	Percent of anesthetic agent in the inspired gas. Must enter percent delivered in order to accurately calculate parameters.
BALANCE	Gas Balance	N_2	N_2, He, or N_2O	N_2, He or N_2O. Must select the correct balance in the inspired gas in order to accurately calculate parameters.
HEIGHT	Patient Height	--	35-91 in 90-230 cm	Enter patient height for CI calculations.
WEIGHT	Patient Weight	--	55-551 lb 25-250 kg	Enter patient weight for CI calculations.
ABG DATA ENTRY Screen				
$PaCO_2$	Arterial Carbon Dioxide	40 mmHg (5.4 kPa or %) ("--" displayed until an initial value is entered)	0-250 mmHg 0.0-20.0 kPa 0.0-20.0 %	Partial pressure of carbon dioxide in arterial blood. Entering this value can enhance the accuracy of cardiac output parameters (C.O., SV, and CI).
PaO_2	Arterial Oxygen	FiO_2*(Pb-47 mmHg) ("--" displayed until an initial value is entered)	0-750 mmHg 0.0-99.5 kPa 0.0-99.5 %	Partial pressure of oxygen in arterial blood. Entering this value can enhance the accuracy of C.O. parameters cardiac output parameters (C.O., SV, and CI).
Hb	Hemoglobin Concentration or Hematocrit	11.0 gm/dL 6.8 mmol/L 33 % ("--" displayed until an initial value is entered)	Hb: 5.0-20.0 gm/dL Hb: 3.1-12.4 mmol/L Hct: 0-60 %	Concentration of hemoglobin or hematocrit in the blood. Entering this value can enhance the accuracy of cardiac output parameters (C.O., SV, and CI).

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Label	Parameter	Default	Range/Units	Description
MARK ABG TIME	Time when ABG blood sample is drawn	Current Time	hh:mm (hours:minutes)	Enter time ABG is drawn. (Only accepts time since $ETCO_2$ was first detected.)
DEFAULT ABGs	Blood gas values	$PaCO_2$: 5 mmHg (0.7 kPa or %) above the measured $ETCO_2$ value[a] PaO_2: Based on barometric pressure and INSP O_2 value. Hb: 11.0 gm/dL		Resets blood gas settings to default values.

a. 40mmHg (5.4 kPa or %) if $ETCO_2$ is not available.

Entering Patient Data To enter (or view) patient data:

1. Press the **DATA ENTRY** key to activate **DATA ENTRY**. The key's green icon illuminates.
   - Press the key again to return to the previously displayed screen.
2. Highlight the desired data by turning the **KNOB**.
3. Select the highlighted data by pressing the **KNOB**.
4. Turn the **KNOB** to adjust the value as desired.
5. Press the **KNOB** to accept the value.

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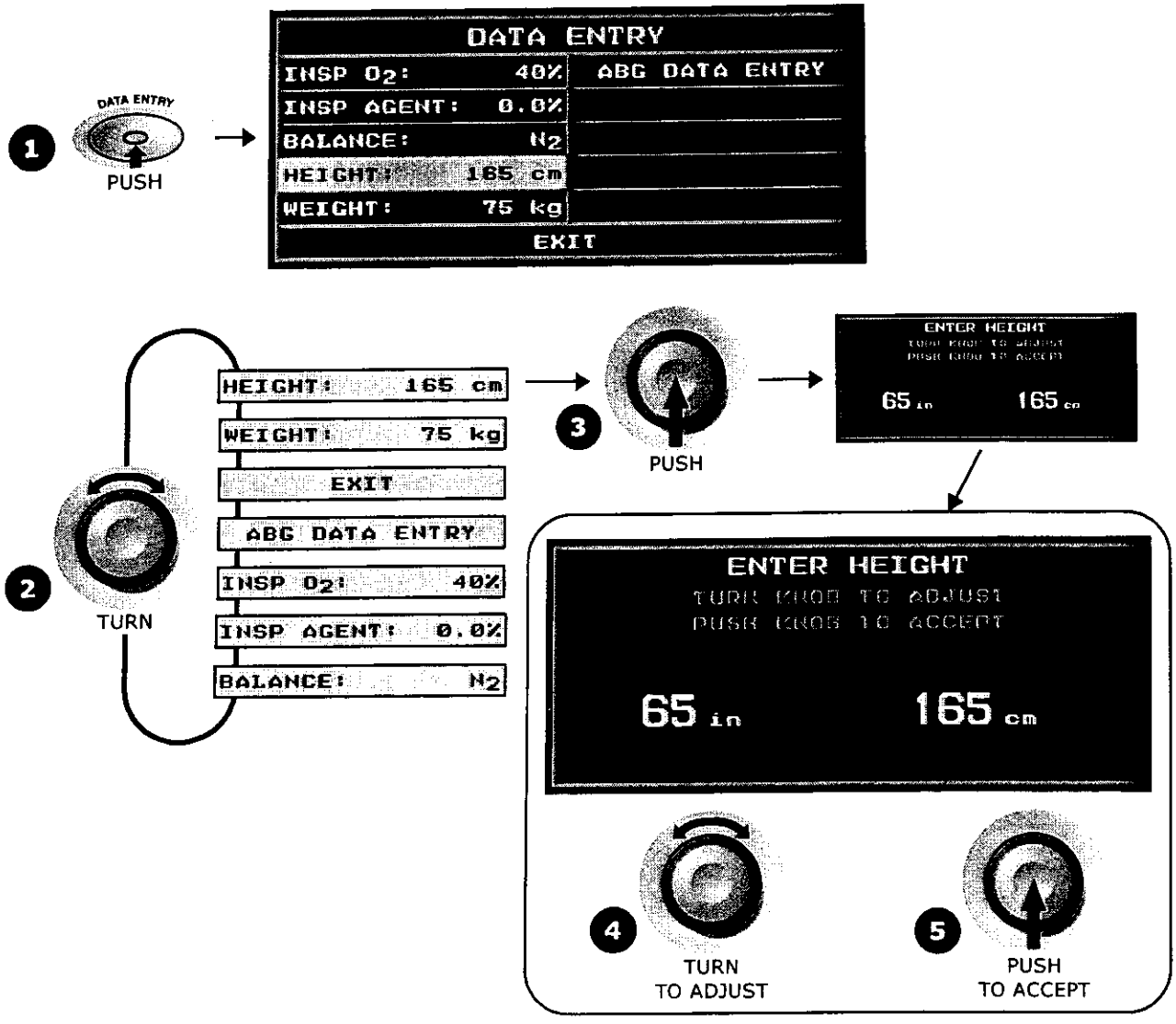
6 Repeat these steps for the other settings.



Entering ABG Data

To enter ABG data:

1 Draw blood sample during the "normal" phase of the NICO cycle, not during the rebreathing phase.
   - The cardiac output message will display how much time before the next rebreathing phase occurs.

2 Press the **DATA ENTRY** key to activate **DATA ENTRY.** The key's green icon illuminates.
   - Press the key again to return to the previously displayed screen.

3 Highlight **ABG DATA ENTRY** by turning the **KNOB.**

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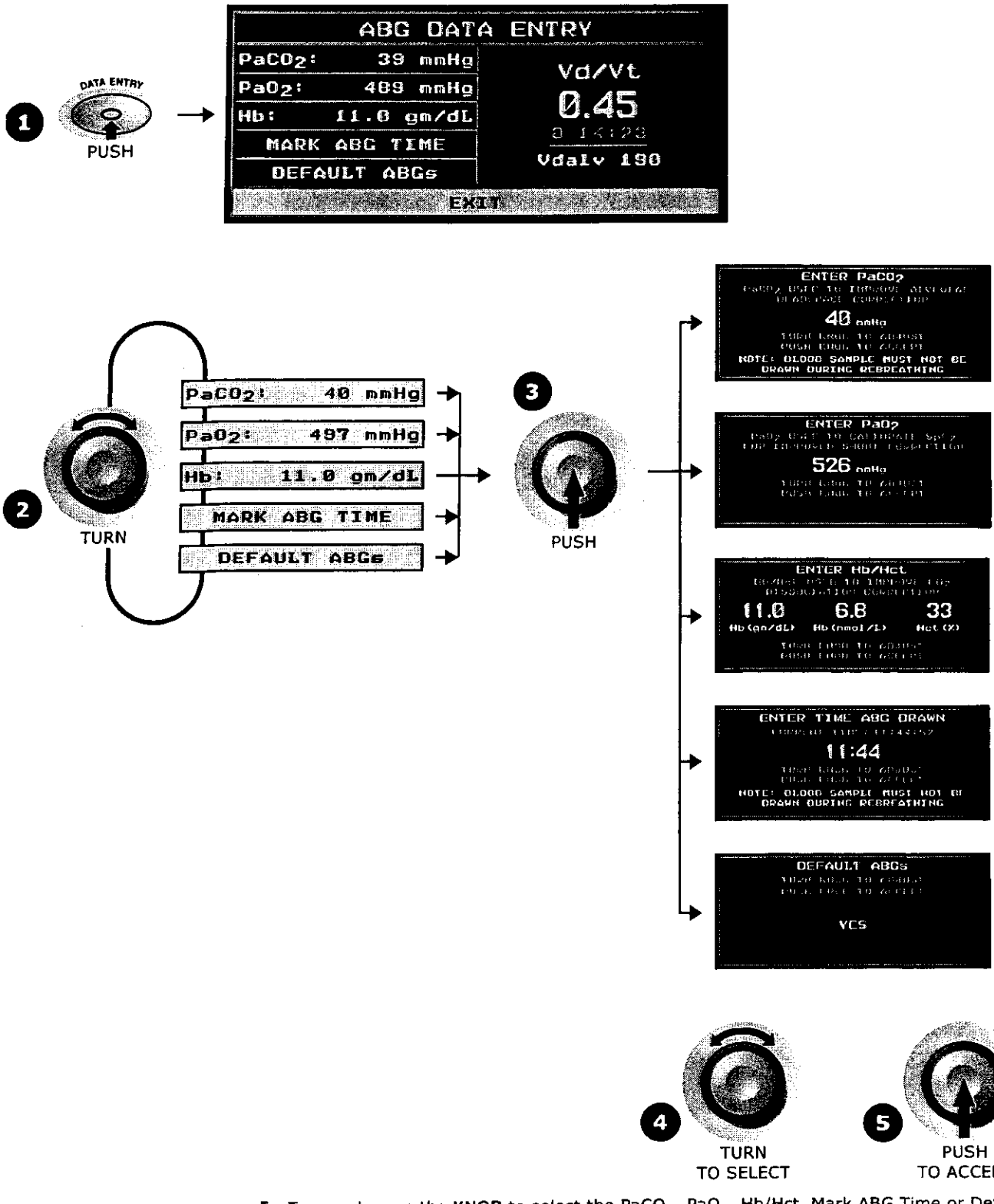
4 Select **ABG DATA ENTRY** by pressing the **KNOB**.



5 Turn and press the **KNOB** to select the $PaCO_2$, PaO_2, Hb/Hct, Mark ABG Time or Default ABG screen.

6 Turn **KNOB** to adjust value.
- ABG Time is required for $PaCO_2$ and PaO_2.

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- Ensure that the monitor's clock is synchronized to the clock used to determine the draw time.

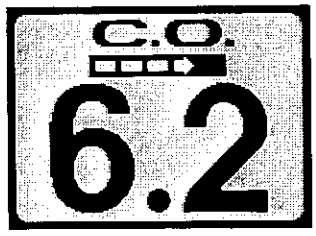
7 Press the **KNOB** to accept the value and return to the **ABG DATA ENTRY** screen.
- Updated Vd/Vt and Vdalv values are displayed.

Averaging Mode

Averaging options (**C.O. MODE**) for C.O., CI, and PCBF are set in the **SETUP** screen.

CObar™ Confidence Indicator

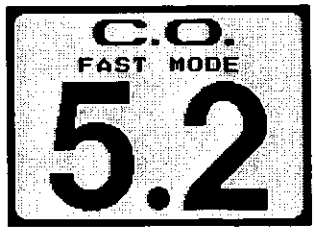
The Cardiac Output Confidence Bar, or CObar™, is an indicator of the system's confidence in the currently displayed C.O., CI or PCBF value (depending upon which is selected in the Configuration Menu). The CObar indicator is located above the value and can contain up to five segments. The degree of confidence (more segments for higher confidence, fewer segments for lower confidence) is based on multiple factors including ventilatory pattern, sizing of the NICO Loop, tidal volume, entry of patient data and breathing circuit integrity.



A lower number of segments indicates that the displayed reading is being averaged more with readings from previous rebreathing cycles. If there is no confidence in the signals, the cardiac output value is not displayed and no segments are displayed in the CObar.

Fast Mode

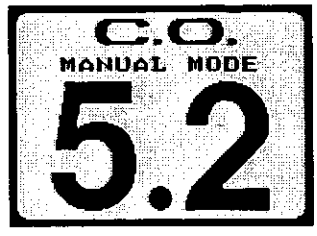
When the **C.O. MODE** is set to **FAST**, the monitor will display the unfiltered cardiac output value (CO-f) or PCBF value (PCBF-f) rather than the averaged value. The text **FAST MODE** will replace the CObar graphic. The stroke volume and cardiac index will be calculated from this value rather than the averaged value.



Averaged and fast values can also be viewed in the **3 MIN CYCLE IN PROGRESS, TREND** and **TABULAR DATA** screens. The values shown vary depending on which parameter and mode is selected for the large display.

Manual Mode

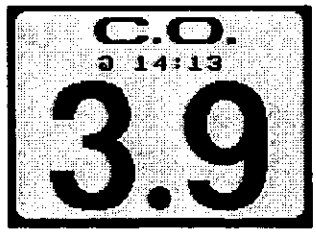
When the **C.O. MODE** is set to **MANUAL**, the text **MANUAL MODE** will replace the CObar. Pressing the **STOP/CONTINUE REBREATHING** key will initiate patient rebreathing for three cycles. Displayed C.O., CI or PCBF will correspond to averaged mode values; the stroke volume and cardiac index will be calculated from the averaged value.



Averaged and fast values can also be viewed in the **3 MIN CYCLE IN PROGRESS, TREND** and **TABULAR DATA** screens. The values shown vary depending on which parameter and mode is selected for the large display.

Display Hold

In all cardiac output modes, when rebreathing is turned off and eight minutes has elapsed, the NICO will dim and hold the large-digit reading for C.O., PCBF or C.I. The CObar™ or text for **FAST MODE** or **MANUAL MODE** is replaced with the time the last cycle was completed.



If the user modifies the monitor settings between C.O., PCBF and C.I., the time stamp will not change and the display will remain dimmed. After 12 hours, the large number display will turn to dashes (--) and the time stamp will be removed.

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NICO®

Respiratory Monitoring

This section details the steps needed to begin patient respiratory mechanics monitoring with the NICO® monitor.

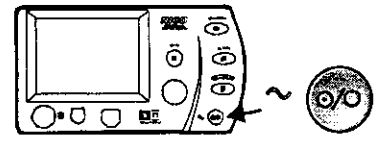
Preparing for Use

Inspect

Before monitoring, take a few moments to inspect the NICO monitor and its sensors. Check that all items are clean, dry, and physically intact with no broken or damaged components.

Turn on the monitor

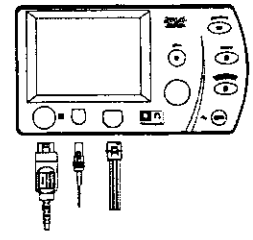
Turn the NICO monitor on.



1 Press the **Operate/Standby** key to turn the monitor on and off.
   - The NICO monitor can operate from its internal battery or from the AC Mains. (See "AC/Battery Operation" on page 4 for details.)
2 The monitor performs a quick self-test.
   - An audible tone sounds, the key indicators illuminate, and a **SELF-TEST IN PROGRESS** message is briefly displayed.
3 The message **PRESS KNOB TO ERASE STORED TRENDS** is displayed for 5 seconds.
   - To erase the contents of the monitor's trend memory, press the knob. **TRENDS ERASED** is briefly displayed.
   - To retain the contents of the monitor's trend memory, do not press the knob. Wait the 5 seconds and **TRENDS RETAINED** is displayed.
   - Note: If the internal battery becomes fully discharged, the message **CHECK DATE/TIME (MENU -> SETUP)** will appear before the **PRESS KNOB TO ERASE STORED TRENDS** message. (See "Setup Screen" on page 49 for details.)
4 The power up sequence is completed and a monitoring screen is displayed.
   - The NICO monitor displays the screen that was displayed when the monitor was last turned off.
   - If the monitor is in Cardiac Output mode, connecting a CO_2/Flow sensor will cause the monitor to automatically switch to Respiratory Mechanics mode.
   - The monitor is in a READY state and the parameters will be dashed and alerts will not be active until parameters are calculated and displayed.
   - Parameters will display and their alerts will become active as they are calculated.

Connect and apply the sensors

Connect the sensors to the monitor, ventilator circuit, and patient.



1 Connect the SpO_2 sensor to the monitor and apply it to the patient. (See "Pulse Oximetry Sensors" on page 72.)
2 Connect the CAPNOSTAT® CO_2 Sensor to the monitor. (See "CAPNOSTAT® CO2 Sensor" on page 70.)
3 Select an appropriate size CO_2/Flow sensor.
4 Connect a CO_2/Flow Sensor to the monitor and attach a CAPNOSTAT® CO_2 Sensor. (See "CO_2/Flow Sensors" on page 67.)

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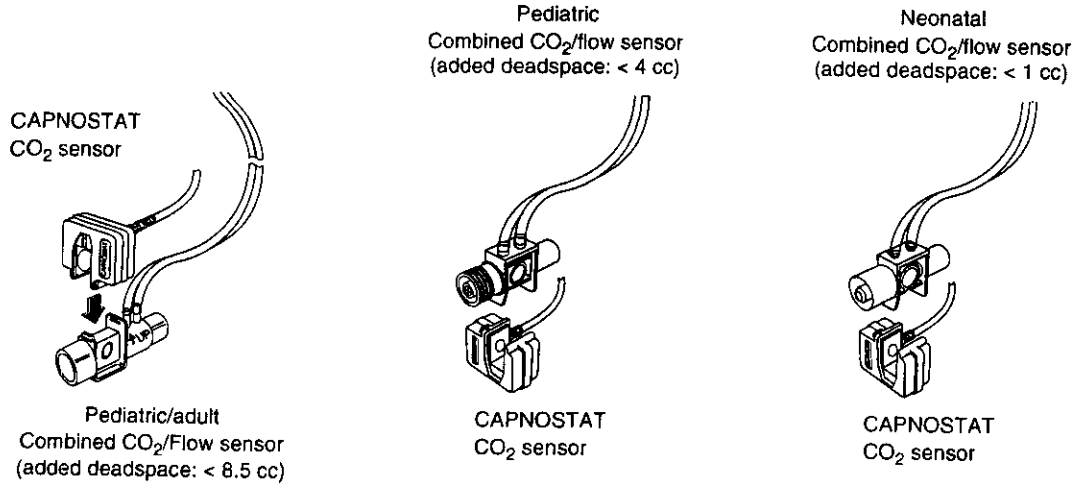
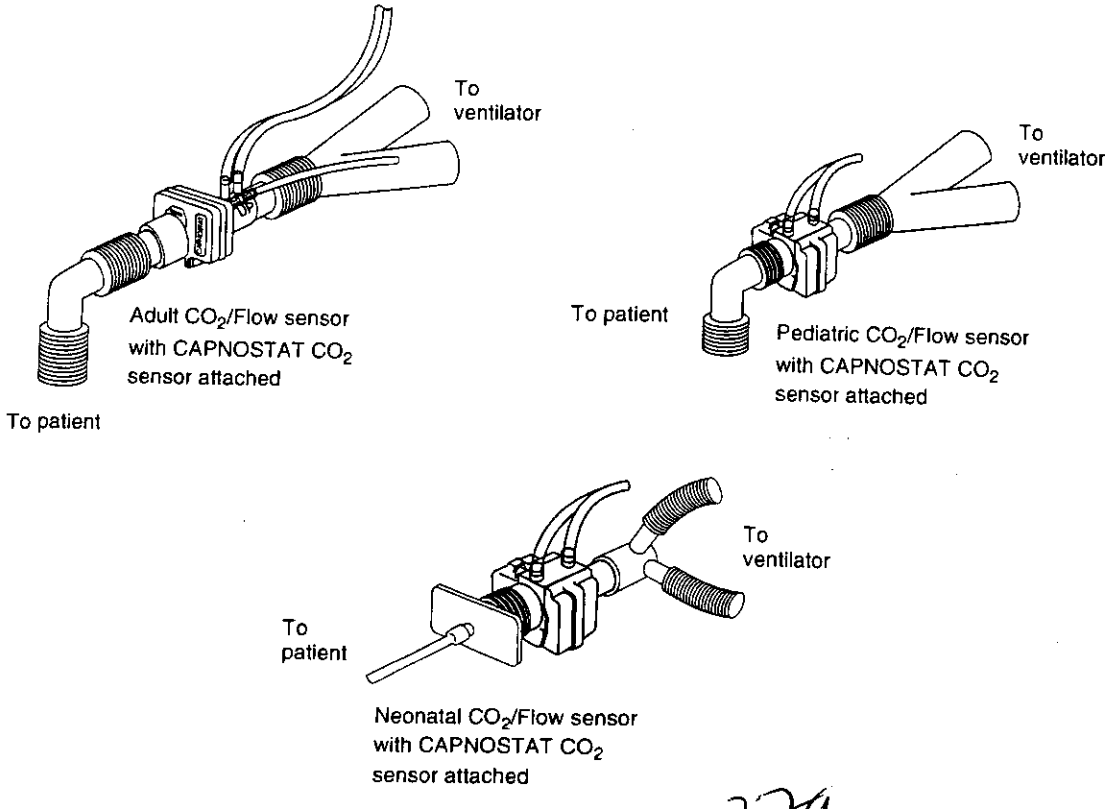
5 Connect the CAPNOSTAT CO_2 sensor to the CO_2/Flow sensor.



6 For optimal results, place the CO_2/Flow sensor in the ventilator circuit between the endotracheal tube and the ventilator circuit wye.
- Place the sensor proximal to the patient if using other devices in the circuit.
- Place the sensor so that the tubing lines exit from the top of the sensor (to help keep them clear and dry).
- Keep the sensor clear of accumulations by proper circuit maintenance.

7 Connect the combined CO_2/Flow sensor to the patient breathing circuit.



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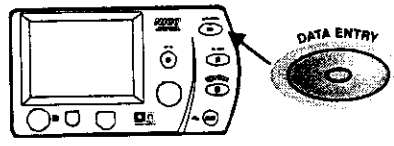
- Do NOT place the CO_2/Flow sensor between the ET tube and the elbow (pediatric/adult circuit), as this may allow patient secretions to block the adapter windows.
- Position the CO_2/Flow sensor with its windows in a vertical and NOT a horizontal position: this helps keep patient secretions from "pooling" on the windows.
- To prevent "rain-out" and moisture from draining into the CO_2/Flow sensor, do NOT place the CO_2/Flow sensor in a gravity dependent position.
- Periodically check the CO_2/Flow sensor and tubing for excessive moisture or secretion build up.
- For routine performance of airway care, separate the system between the ET tube and the airway adapter (neonatal circuit), or between the ET tube and elbow (pediatric/adult circuit). Lavage and suctioning of the airway can then be performed without fluids and mucous accumulating on the CO_2/Flow sensor windows.

Begin Respiratory Monitoring

After the NICO monitor is turned on and the sensors are properly connected and applied, Respiratory Mechanics monitoring can begin.

1 Enter the delivered oxygen and balance gas or anesthetic agent if present, by pressing the **DATA ENTRY** key. (See "Entering Patient Data" on page 36.)



2 As you begin monitoring, please note the following:

- Water that accumulates in the CO_2/Flow sensor or the sensor tubing may cause the reported Tidal Volumes to be higher than set volumes. If reported values are higher (or lower) than expected and water is seen in the line or sensor body, purge the lines. If purging does not clear the water, remove the sensor from the circuit and remove the water by shaking the sensor, or by flowing oxygen or compressed air through the tubing or sensor until the water is removed. Do not use high pressure for water removal.
- To minimize the effects of aerosolized medications on the CO_2/Flow sensor, it is recommended that the CO_2/Flow sensor be removed from the ventilator circuit prior to the delivery of the medication. ***The decision to remove or not remove the CO_2/Flow sensor is the responsibility of the clinician.***
- During the purge cycle the pump will be heard.
- Water will condense in the pressure sense lines at a faster rate when used in cooler ambient temperatures.
- Always keep the CO_2/Flow sensor tubing pointed in an upward position to minimize pooling of water and secretions at the pressure sense line openings.
- The automatic purge mode may not be disabled.
- During a very low battery condition, automatic and manual purging is not allowed.

Entering Patient Data

Respiratory monitoring can be enhanced by the entry of key patient specific data including respired gas composition (anesthetic agent, balance gas, and inspired O_2).

Patient data should be updated in the **DATA ENTRY** screen whenever possible. The screen may be accessed at any time by pressing the **DATA ENTRY** key.

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DATA ENTRY settings The following table lists the parameters and ranges accessible in the **DATA ENTRY** screens.

Label	Parameter	Default	Range/Units	Description
INSP O_2	Inspired Oxygen	40%	21-100 %	Percent of oxygen in the inspired gas. Must be entered in order to accurately calculate parameters.
INSP AGENT	Inspired Anesthetic Agent	0%	0-20 %	Percent of anesthetic agent in the inspired gas. Must enter percent delivered in order to accurately calculate parameters.
BALANCE	Gas Balance	N_2	N_2, He, or N_2O	N_2, He, or N_2O. Must select the correct balance in the inspired gas in order to accurately calculate parameters.
HEIGHT	Patient Height	--	35-91 in 90-230 cm	Enter patient height (unavailable for neonatal patients in Respiratory Mechanics mode).
WEIGHT	Patient Weight	--	Neonatal: 0.22 - 44.09 lb 0.10 - 20.00 kg Pediatric: 0.2 - 220.2 lb 0.1 - 99.9 kg Adult: 55-551 lb 25-250 kg	Enter patient weight for respiratory mechanics calculations.
ABG DATA ENTRY Screen				
$PaCO_2$	Arterial Carbon Dioxide	40 mmHg (5.4 kPa or %) ("--" displayed until an initial value is entered)	0-250 mmHg 0.0-20.0 kPa 0.0-20.0 %	Partial pressure of carbon dioxide in arterial blood. Enter this value for calculation of Vd alv (alveolar deadspace), Vd/Vt (deadspace to tidal volume ratio).
PaO_2	Arterial Oxygen	FiO_2*(Pb-47 mmHg) ("--" displayed until an initial value is entered)	0-750 mmHg 0.0-99.5 kPa 0.0-99.5 %	Partial pressure of oxygen in arterial blood. Enter a value for this parameter if desired; does not affect CO_2/flow calculations.
Hb	Hemoglobin Concentration or Hematocrit	11.0 gm/dL 6.8 mmol/L 33 % ("--" displayed until an initial value is entered)	Hb: 5.0-20.0 gm/dL Hb: 3.1-12.4 mmol/L Hct: 0-60 %	Concentration of hemoglobin or hematocrit in the blood. Enter a value for this parameter if desired; does not affect CO_2/flow calculations.
MARK ABG TIME	Time when ABG blood sample is drawn	Current Time	hh:mm (hours:minutes)	Enter time ABG is drawn. Only accepts time since $ETCO_2$ was first detected.
DEFAULT ABGs	Blood gas values	$PaCO_2$: 5 mmHg (0.7kPa or %) above the measured $ETCO_2$ value[a] PaO_2: Based on barometric pressure and INSP O_2 value. Hb: 11.0 gm/dL		Resets blood gas settings to default values.

a. 40mmHg (5.4 kPa or %) if $ETCO_2$ is not available.

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Entering Patient Data To enter (or view) patient data:

1 Press the **DATA ENTRY** key to activate **DATA ENTRY.** The key's green icon illuminates.
- Press the key again to return to the previously displayed screen.

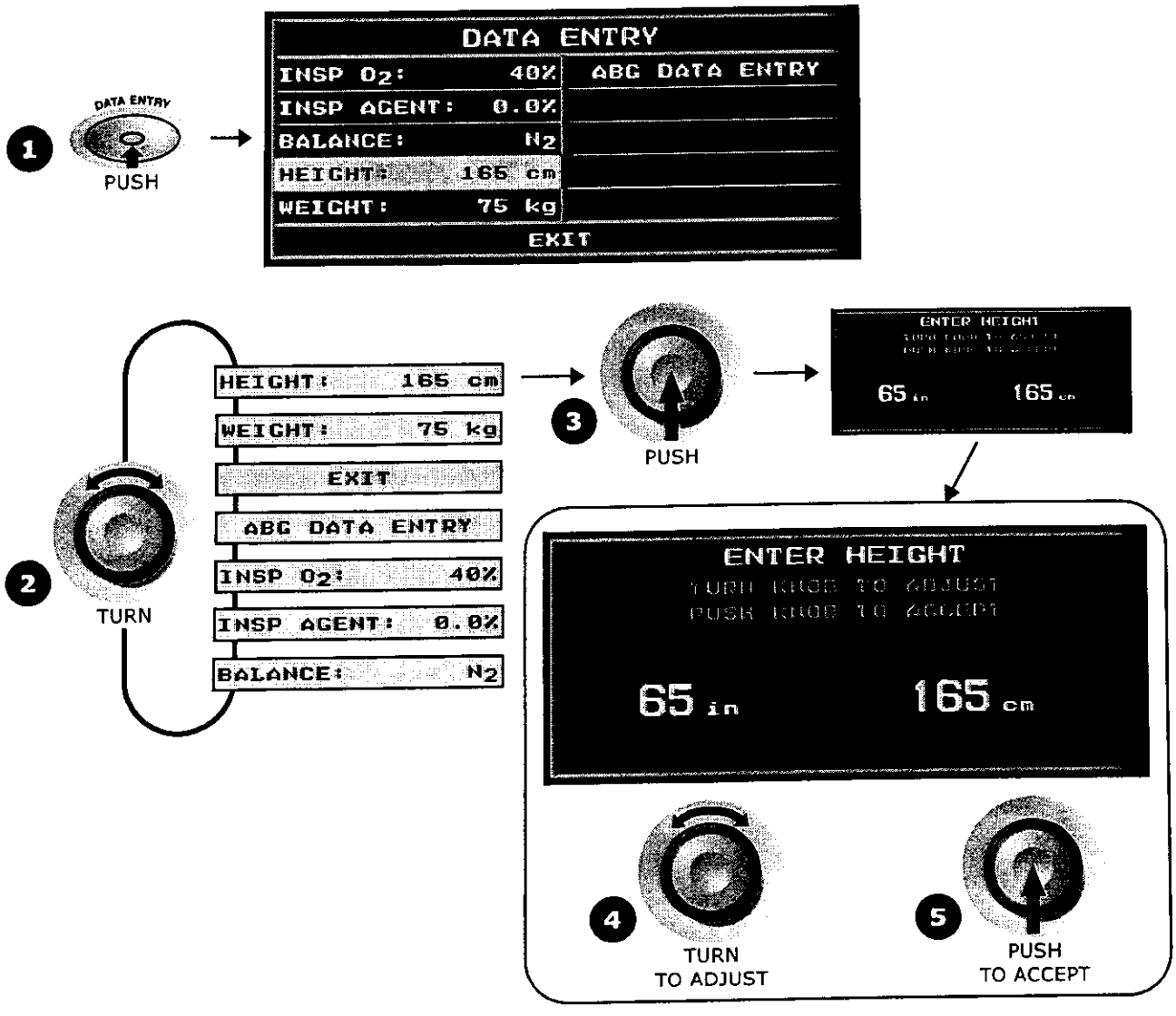
2 Highlight the desired data by turning the **KNOB**.

3 Select the highlighted data by pressing the **KNOB**.

4 Turn the **KNOB** to adjust the value as desired.

5 Press the **KNOB** to accept the value.

6 Repeat these steps for the other settings.



Entering ABG Data

To enter ABG data:

1 Press the **DATA ENTRY** key to activate **DATA ENTRY.** The key's green icon illuminates.
- Press the key again to return to the previously displayed screen.

2 Highlight **ABG DATA ENTRY** by turning the **KNOB**.

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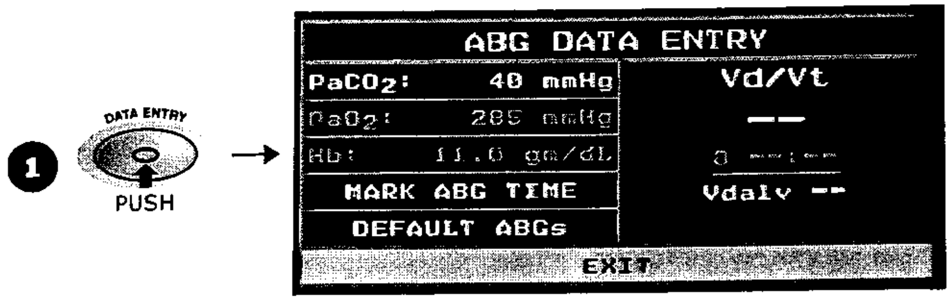
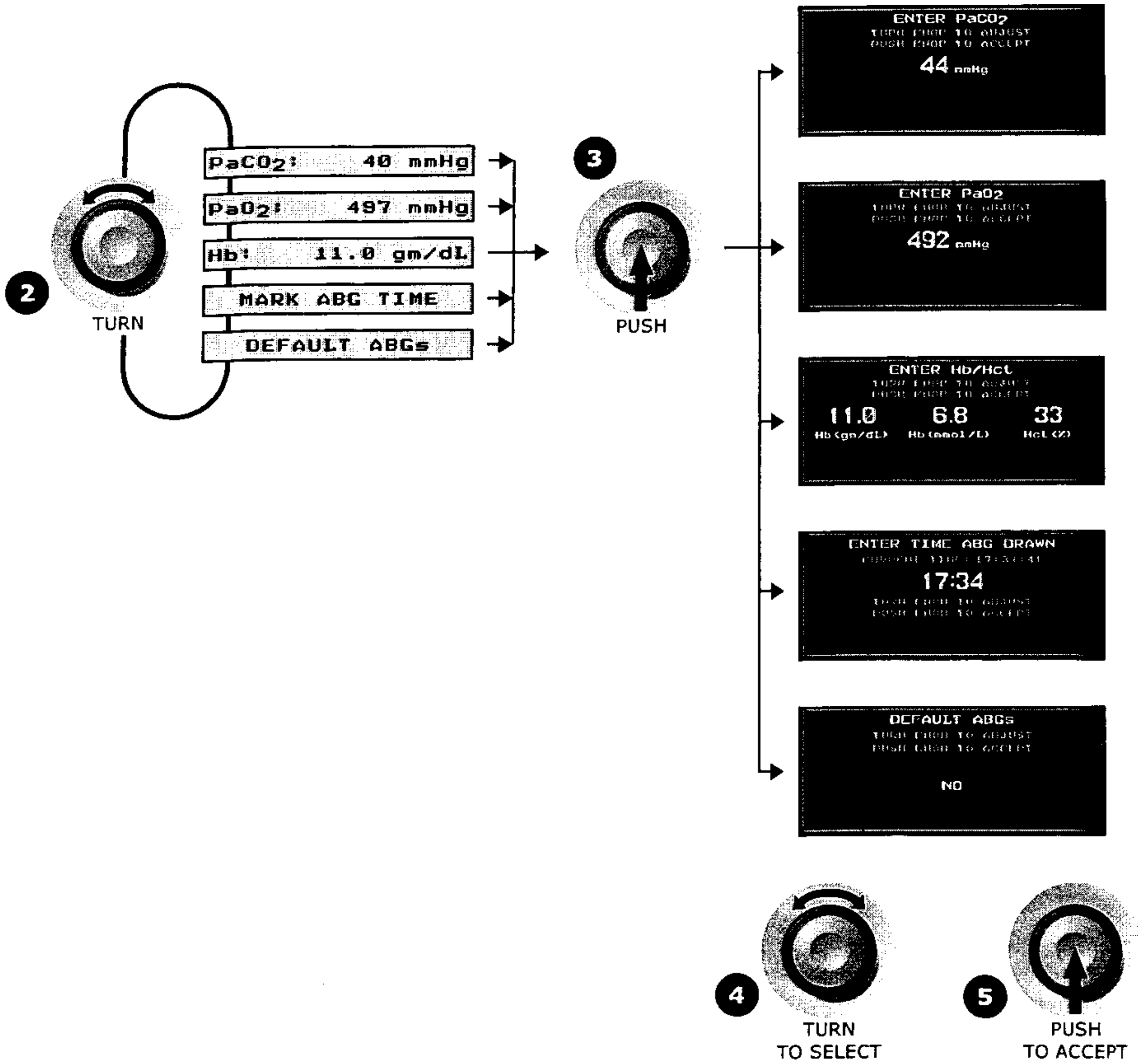
3 Select **ABG DATA ENTRY** by pressing the **KNOB.**





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4 Turn and press the **KNOB** to select the $PaCO_2$, PaO_2, Hb/Hct, Mark ABG Time or Default ABG screen.
NOTE: PaO_2 and Hb selections are dimmed in Respiratory Mechanics mode to denote that, although they are available for data input, the data will not affect parameter calculations.

5 Turn **KNOB** to adjust value.
- ABG Time is required for $PaCO_2$.
- Ensure that the monitor's clock is synchronized to the clock used to determine the draw time.

6 Press the **KNOB** to accept the value.
- Updated Vd/Vt and Vdalv values are displayed.

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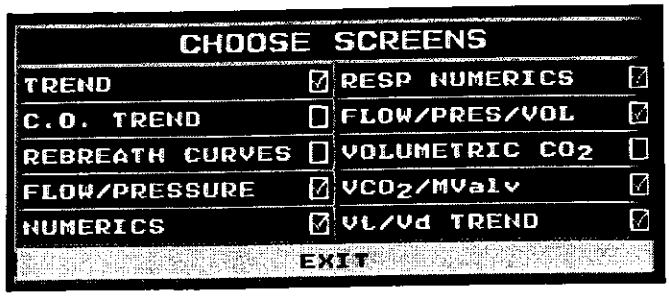
NICO®

Monitoring and Setup Screens

Choose Screens Menu

The **CHOOSE SCREENS** menu allows the user to customize the active screen set for monitoring in Cardiac Output or Respiratory Mechanics modes. In Respiratory Mechanics mode, **C.O. TREND**, **REBREATH CURVES** and **RESP NUMERICS** are unavailable (dimmed). CO_2/SpO_2 is the base screen, it is always available.



Enabling Screens

To enable or disable specific screens, press the **MENU** key to display **SELECT A SCREEN**. Turn the **KNOB** to highlight **SETUP** and push the **KNOB**. From the **SETUP** screen, select **CHOOSE SCREENS** and push the **KNOB**.

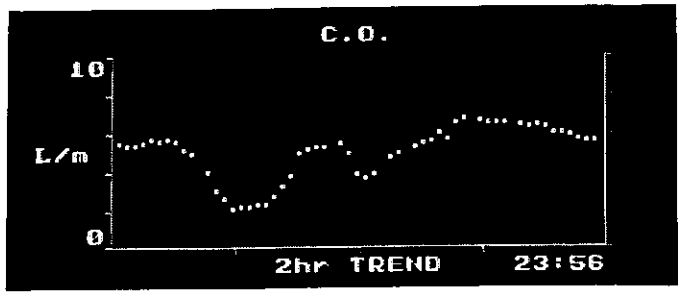
In the **CHOOSE SCREENS** menu, turn and push the **KNOB** to add or remove each monitoring screen from the active screen set. When a screen is enabled, a check is in the checkbox. In monitoring mode, enabled screens will appear with successive turns of the **KNOB**. If a screen is unchecked, it will not appear when the **KNOB** is turned, but can be accessed directly from **SELECT A SCREEN** or **SELECT RESPIRATORY SCREENS**.

Cardiac Output mode

This section provides an overview of monitoring and setup screens in Cardiac Output mode.

C.O. Trend Screen

The Cardiac Output Trend Screen plots cardiac output over time.



The **C.O. TREND** screen can be displayed, when enabled, by turning the **KNOB** while viewing any monitoring screen, or by pressing the **MENU** key and selecting **C.O. TREND**.

- While viewing the **C.O. TREND** screen, each push of the **KNOB** will advance through the available 2, 4, 8 and 12 hour trend displays.

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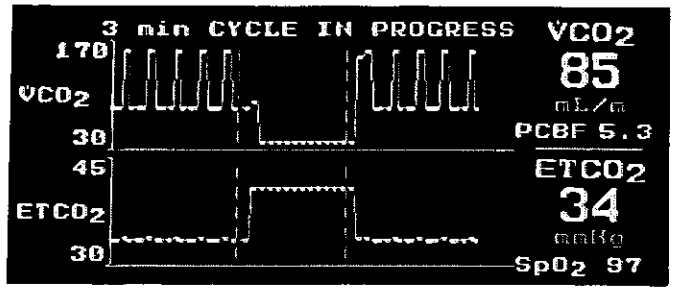
- Data is plotted from left (oldest data) to right (newest data). Once the display is filled, data shifts left so that the oldest data point on the left is pushed out to make room for the newest point entering from the right.
- The current time is shown in the lower right corner of the display and represents time at the right edge of the screen. See "Setup Screen" on page 49 to set the time.
- Each point on the trend (plotted or blank) represents the average C.O. value over a time period. The time periods are: 1 minute average for the 2 hour trend, 2 minutes for the 4 hour trend, 4 minutes for the 8 hour trend, and 6 minutes for the 12 hour trend.
- C.O. trends are automatically scaled to fit 0-5, 0-10, 0-15 and 0-20 L/min scales.
- A two-pixel wide dashed vertical line in the trend is used to denote a power-cycle where the NICO® monitor was turned off and back on, or where the time and date setting was changed.

Rebreathing Curves Screens

The Rebreathing Curves screen displays the current NICO cycle. VCO_2 and $ETCO_2$ values are plotted over time, and numeric displays for VCO_2, $ETCO_2$, PCBF and SpO_2.

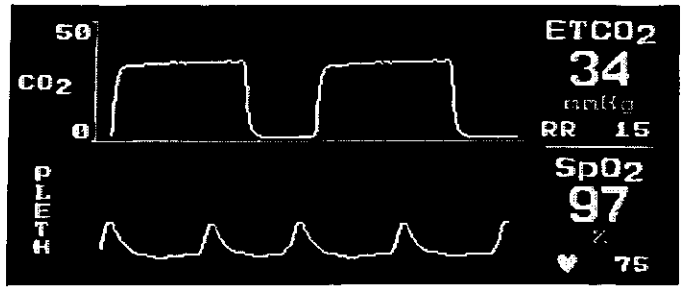


The Rebreathing Curves screen can be displayed, when enabled, by turning the **KNOB** while viewing any monitoring screen, or by pressing the **MENU** key and selecting **REBREATH CURVES**.

- Data is plotted from left (oldest data) to right (newest data).
- Points on the trend (plotted or blank) represent the VCO_2 or $ETCO_2$ value for each breath.
- The curves are automatically scaled to fit the display area.
- Two one-pixel wide dashed vertical lines are used to divide the curve into its baseline, rebreathing and stabilization phases.
- $ETCO_2$ and SpO_2 values will flash if an alert limit is exceeded.

CO_2 and SpO_2 Waveform Screen

The CO_2 and SpO_2 Waveform Screen plots the capnogram and plethysmogram signals as well as providing numeric displays of $ETCO_2$, Respiratory rate, SpO_2 and pulse rate (♥).



The **CO_2/SpO_2** screen can be displayed by turning the **KNOB** while viewing any monitoring screen, or by pressing the **MENU** key and selecting **CO_2/SpO_2**.

- Information is updated in real time and reflects current patient status.
- The capnogram and plethysmogram are automatically scaled.
- The capnogram sweep speed is selectable in the **SETUP** menu.
- $ETCO_2$, RR, SpO_2 and pulse rate values will flash if an alert limit is exceeded.

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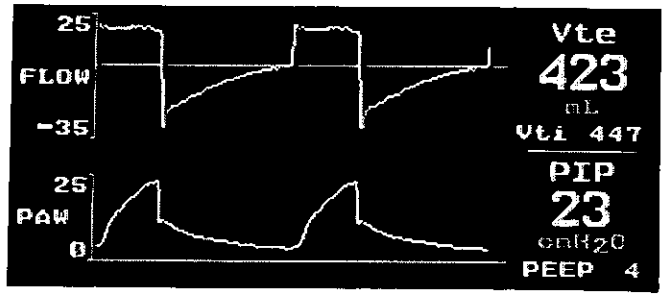
Flow and Pressure Waveform Screen

The Flow and Pressure Waveform screen plots the airway flow and pressure signals over time as well as providing numeric displays of Vte, Vti, PIP and PEEP.

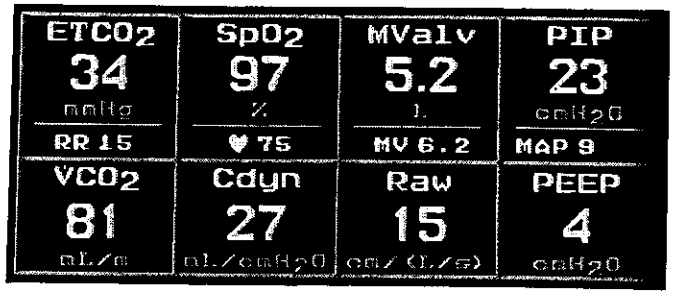


The **FLOW/PRESSURE** screen can be displayed, when enabled, by turning the **KNOB** while viewing any monitoring screen, or by pressing the **MENU** key and selecting **FLOW/PRESSURE**.

- Information is updated in real time.
- The airway flow and pressure waveforms are automatically scaled.
- The waveform sweep speed is selectable in the **SETUP** menu.

Numerics Screen

The **NUMERICS** screen display presents several monitored parameters together in one place.



The **NUMERICS** screen can be displayed, when enabled, by turning the **KNOB** while viewing any monitoring screen, or by pressing the **MENU** key and selecting **NUMERICS**.

- Information is updated in real time.
- The PEEP label is replaced with AUTO if Auto-PEEP (Intrinsic-PEEP) is detected.
- $ETCO_2$, RR, SpO_2 and pulse rate values will flash if an alert limit is exceeded.
- The Cdyn label is replaced with Cst if static lung compliance is detected.

Respiratory Screens

The NICO monitor offers five respiratory screens, displaying Respiratory Numerics, Flow Volume and Pressure Volume Loops, a Volumetric CO_2 Waveform, a VCO_2/MValv Trend and the Vt/Vd Trend. Press the **MENU** key and select **RESP SCREENS** from the **SELECT A SCREEN** menu by turning and then pressing the **KNOB**.

From the **SELECT RESPIRATORY SCREEN** menu, highlight and then select the desired screen by turning and then pressing the **KNOB**. Screens can also be displayed, when enabled, by turning the

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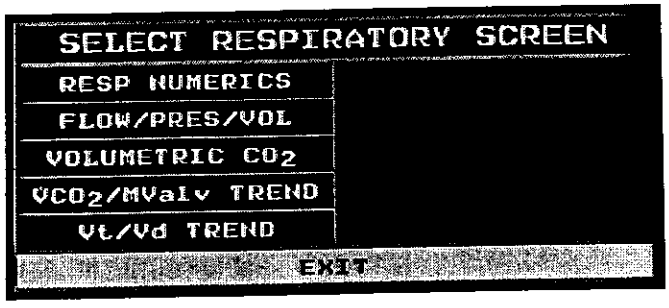
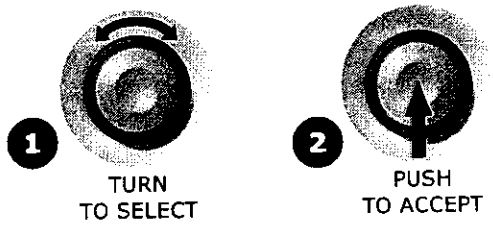
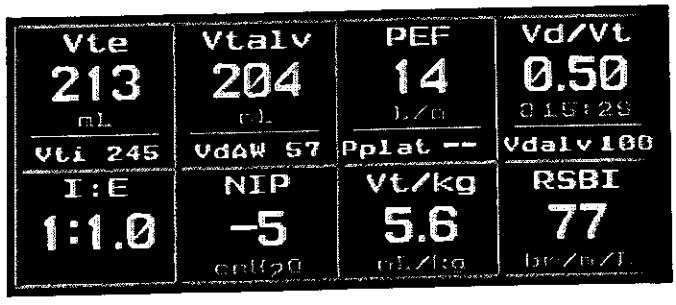
KNOB while viewing any monitoring screen (See "KNOB Selectable Respiratory Screens" on page 13).





Respiratory Numerics

The **RESPIRATORY NUMERICS** screen presents several monitored parameters together in one place.

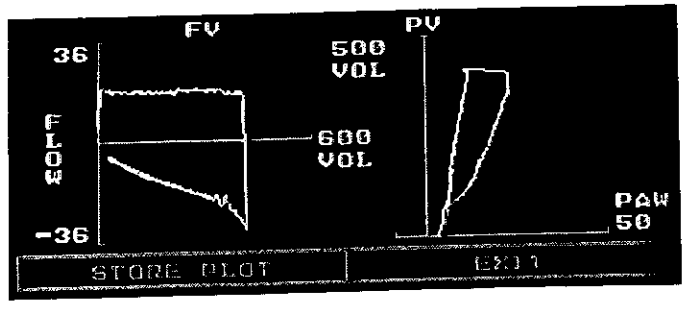


The **RESPIRATORY NUMERICS** screen can be displayed, when enabled, by turning the **KNOB** while viewing any monitoring screen.

- Information is updated in real time.

Flow Volume and Pressure Volume Loops

The Flow Volume and Pressure Volume Loops screen displays a flow versus volume loop and a volume versus peak airway pressure loop.



The Flow Volume and Pressure Volume Loops screen can be displayed, when enabled, by turning the **KNOB** while viewing any monitoring screen.

- The flow-volume loop is plotted in a clockwise direction, comparing flow versus volume for a single patient breath and providing information regarding the condition of the airways.

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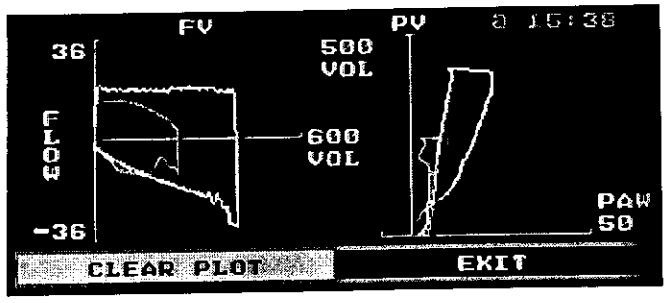
- The pressure-volume loop is plotted in a counter-clockwise direction; the slope from the beginning of inspiration to the end of inspiration depicts compliance while the width of the loop references resistance.
- The curve is automatically scaled to fit the display area.

Store Plot

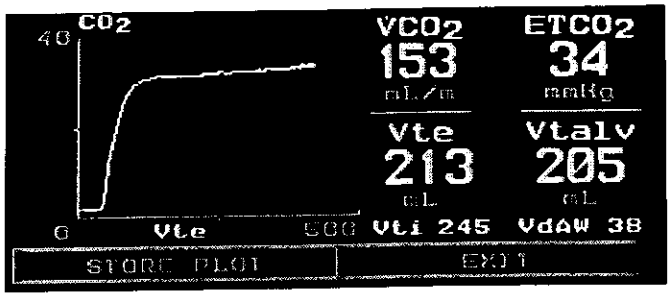
The Store Plot function "freezes" a single breath on the **FLOW/PRES/VOL** screen as a template. Subsequent loops will be drawn over that breath.



- Press the **KNOB** to highlight **STORE PLOT** and again to select the breath.
- Press the **KNOB** to highlight **CLEAR PLOT** and again to erase the selected breath.
- The time stamp above the template wave corresponds to when the plot was set.

Volumetric CO_2 Screen

The **VOLUMETRIC CO_2** screen displays the CO_2 waveform for a single patient breath, as well as providing numeric displays of VCO_2, Vte, $ETCO_2$, Vtalv, Vti, and VdAw.

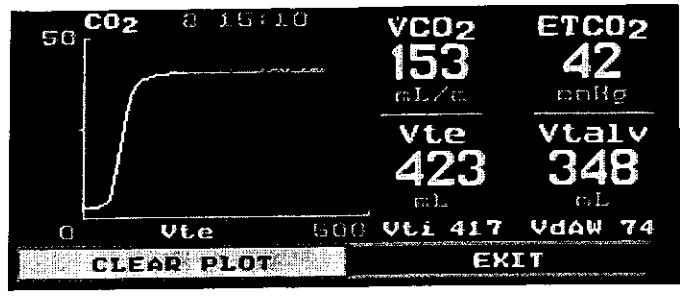


Volumetric CO_2 presents the exhaled concentration of CO_2 versus tidal volume during a single expiration; useful for understanding the ventilation/perfusion relationship. It allows the clinician to detect relative changes in CO_2 production, deadspace, and effective ventilation by observing the shape of the graph.

- The curve is automatically scaled to fit the display area.

Store Plot

The Store Plot function "freezes" a breath on the **VOLUMETRIC CO_2** screen as a template. Subsequent waveforms will be drawn over that breath for comparison.



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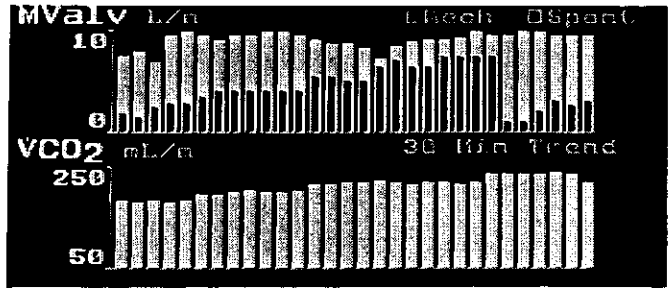
- Press the **KNOB** to highlight **STORE PLOT** and again to select the breath.
- Press the **KNOB** to highlight **CLEAR PLOT** and again to erase the selected breath.
- The time stamp above the template wave corresponds to when the plot was set.

VCO_2/MValv Trend

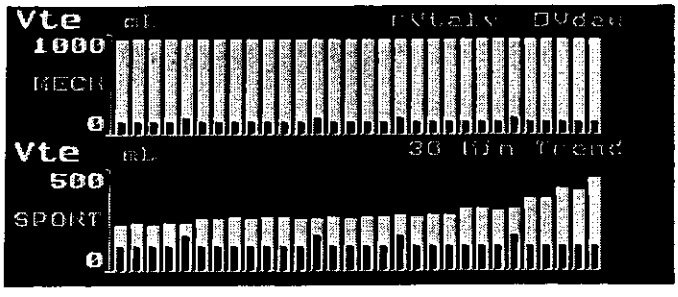
The **VCO_2/MVALV TREND** screen displays trends for alveolar minute ventilation and CO_2 elimination. Monitoring spontaneous versus mechanical alveolar ventilation along with CO_2 elimination provides information on continued success or impending failure when weaning a patient off a ventilator.



- While viewing the **VCO_2/MV ALV TREND** screen, each push of the knob will advance through the available 30 minute, and 2, 4, 8, and 12 hour trend displays.
- Data is plotted from left (oldest data) to right (newest data). Once the display is filled, data shifts left so that the oldest data point on the left is pushed out to make room for the newest point entering from the right.
- Each bar on the trend represents the average MValv or VCO_2 value over a time period. The time periods are; 1 minute average for the 30 minute trend, 4 minute average for the 2 hour trend, 8 minutes for the 4 hour trend, 16 minutes for the 8 hour trend, and 24 minutes for the 12 hour trend.

Vt/Vd Trend Screen

The **Vt/Vd TREND** screen displays trends for mechanical and spontaneous airway deadspace and alveolar tidal volume. Monitoring spontaneous versus mechanical deadspace along with expired tidal volume provides information on continued success or impending failure when weaning a patient off a ventilator.



- While viewing the **Vt/Vd TREND** screen, each push of the knob will advance through the available 30 minute, and 2, 4, 8, and 12 hour trend displays.
- Data is plotted from left (oldest data) to right (newest data). Once the display is filled, data shifts left so that the oldest data point on the left is pushed out to make room for the newest point entering from the right.
- Each bar on the trend represents the average Vtalv or Vdaw value over a time period. The time periods are: 1 minute average for the 30 minute trend, 4 minute average for the 2 hour trend, 8 minutes for the 4 hour trend, 16 minutes for the 8 hour trend, and 24 minutes for the 12 hour trend.

Cardiopulmonary Trend Screen

The Cardiopulmonary **TREND** screen displays two user-selectable numeric parameters and three user-selectable trend graphs. Push then turn the **KNOB** to advance through the displays.

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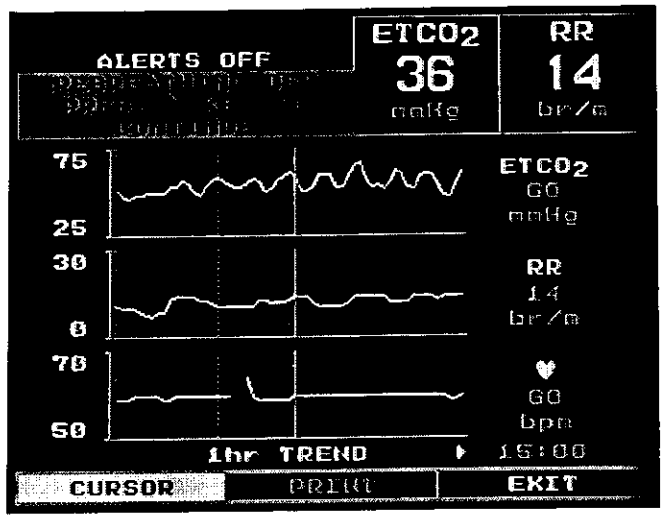
Highlight the desired parameter, trend type or trend duration, then select by turning then pressing the **KNOB**.



- Data is plotted from left (oldest data) to right (newest data). Once the display is filled, data shifts left so that the oldest data point on the left is pushed out to make room for the newest point entering from the right.
- To move between newer and less recent trend data on the graph, press and turn the **KNOB** to highlight the CURSOR. Press and turn the **KNOB** again to view the desired time period. Arrows will appear below the trend graph, to signify that more data is available by turning the **KNOB**. To view the most recent data, scroll to the right using the **KNOB**, to view less recent data, scroll to the left.
- The time periods are: 1 minute average for the 1 hour trend, 2 minute average for the 2 hour trend, 4 minutes for the 4 hour trend, 8 minutes for the 8 hour trend, 12 minutes for the 12 hour trend and 24 minutes for the 24 hour trend.
- VCO_2, $ETCO_2$, RR, SpO_2 and pulse rate values will flash if an alert limit is exceeded.
- A two-pixel wide dashed vertical line in the trend is used to denote a power-cycle where the NICO® monitor was turned off and back on or where the time and date setting was changed.
- A single pixel-wide dotted vertical line in the trend is used to mark the most recent ABG entry.
- Trend reports can be printed from the Cardiopulmonary Trend screen. See "Printing" on page 87 for details.
- The PRINT option is dimmed when HP PRINTER OUTPUT is not selected. To set the monitor to the proper interface, see "Printing" on page 87.

Systemic Vascular Resistance (SVR) Calculation

The SVR CALCULATION screen displays the Systemic Vascular Resistance formula and allows for entering the MBP, CVP and C.O. values for calculating the SVR value. The screen also displays the current time and last SVR value.

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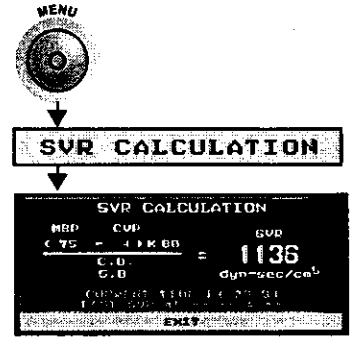
To calculate the SVR value:



1. Press the **MENU** key. The **SELECT A SCREEN** menu appears.
2. Highlight and then select **SVR CALCULATION** by turning and then pressing the knob.
3. The **SVR CALCULATION** screen is displayed.
4. Press then turn the **KNOB** to adjust the setting.
   - **MBP** - Mean Blood Pressure (25 to 300 mmHg).
   - **CVP** - Central Venous Pressure (-9 to 40 mmHg, CVP > MBP).
   - **C.O.** - Cardiac Output (0.5 to 19.9 L/m). This value will correspond to the displayed value (**AVERAGED** or **FAST**) and its value can be manually changed. If manually changed, the value will not be updated to reflect the displayed value.
   - **SVR** - Systemic Vascular Resistance (0 to 9999 dynes sec/cm^5). Appears as "----" until the **MBP** value is entered.
   - **80** - A constant factor used to convert from Wood to VRU units.
5. Press the **KNOB** to accept the displayed value; turn to select the next setting.

$$\frac{(\text{MBP} - \text{CVP}) \times 80}{\text{C.O.}} = \text{SVR dyn-sec/cm}^5$$

Tabular Data Screen

The **TABULAR DATA** screen displays the data collected for all parameters, in one-minute increments, in a table format.

The parameter displayed in each column will vary, depending on the setting chosen by the user.

1. Highlight and select the desired column by turning then pressing the **KNOB**.
2. Turn the **KNOB** to advance through all available parameters.
3. Press the **KNOB** to accept the displayed parameter; turn to select the next column.

TIME	CO-a	CI	SpO_2	$ETCO_2$	VCO_2
11:41	6.1	2.4	97	35	156
11:42	5.7	2.3	97	35	156
11:43	5.7	2.3	97	35	156
11:44	5.3	2.1	97	39	74
11:45	6.1	2.1	97	34	157
11:46	5.7	2.3	97	35	156
11:47	5.7	2.3	97	35	156
		EXIT			

Time Column

With the **TIME** column selected (flashing), turn the **KNOB** to display parameters collected since the beginning of the monitoring session; the most recent records are at the bottom of the table. Three arrows ↓↓↓ will display at the bottom of the column when more records are available.

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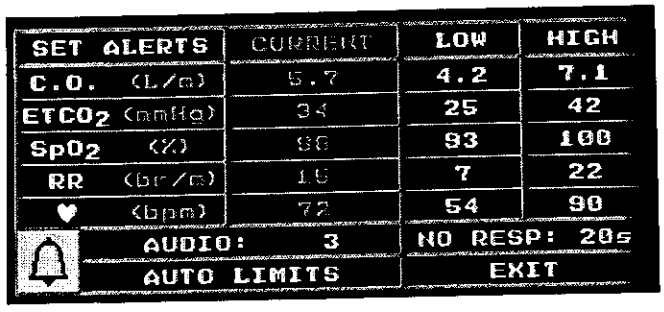
Set Alerts Screen

The **SET ALERTS** screen displays the current patient values as well as the LOW and HIGH alert limit settings for various parameters. This screen also allows adjustment of alert limits, audible alert volume, and of the "No Respiration" alert. See "Alerts" on page 61 for details.



The **SET ALERTS** screen can only be displayed by pressing the **MENU** key and selecting **SET ALERTS.**

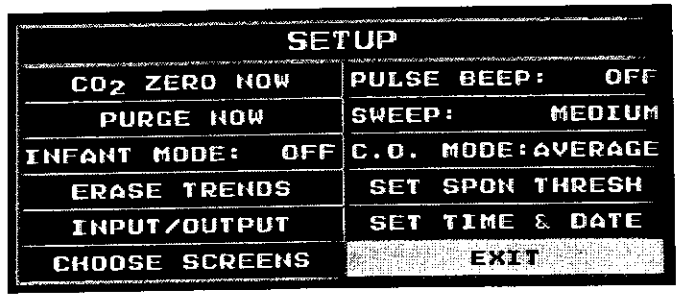
- **CURRENT** - the current patient value for a parameter, shown in real time
- **LOW** and **HIGH** - the values below and above which an alert will be generated. The value will flash when a high or low alert limit is exceeded.
- (Bell with slash) - audible alerts are disabled
- (Bell) - audible alerts are enabled
- **AUDIO** - set the audible alert volume level
- **AUTO LIMITS** - have the NICO monitor bracket alerts around current patient values
- **NO RESP:** - set the No Respiration alert delay timer

Setup Screen

The **SETUP** screen allows the user to perform certain functions, such as a CO_2 Zero, erase trend data, change items like the waveform trace sweep speed and to set the time and date. Once set, the NICO monitor will use these settings until again changed by the user.

To display the **SETUP** screen:

1. Press the **MENU** key to activate **SELECT A SCREEN.** The key's green icon illuminates.
   - Press the key again to return to the previously displayed screen.
2. Highlight and then select **SETUP** by turning and then pressing the **KNOB.**
3. The **SETUP** screen is displayed.
4. Again, turn the **KNOB** to highlight an item and push the **KNOB** to select it.



Items within the **SETUP** screen are described below:

Label	Settings/Range	Description
CO_2 ZERO NOW	Start or Cancel (default: Start)	Displays the **CO_2 ZERO NOW** screen. Place the CAPNOSTAT® CO_2 Sensor onto a clean and dry adapter. Place the adapter in room air and away from all sources of CO_2. Select **START** to begin a CO_2 Zero or **CANCEL** to exit the selection and return to the **SETUP** menu.
PURGE NOW	n/a	The system immediately purges the NICO Sensor tubing. No messages are displayed. The Purge takes approximately 8 seconds. The flow and pressure waveform traces will return to zero during this period.

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Label	Settings/Range	Description
ERASE TRENDS	Yes or No (default: No)	Displays the **ERASE STORED TRENDS?** screen. Turn the **KNOB** to select **NO** (the default setting) or **YES**. Push the **KNOB** to accept your selection and return to the **SETUP** menu.
IABP Intra-Aortic Balloon Pump	ON or OFF	Displays the **SET SpO_2 IABP MODE** screen. Turn the **KNOB** to select **OFF** (default setting) or **ON** to turn off the validator algorithm so that all pulsatile data, including the normally rejected artifact generated by the IABP, are allowed to influence the SpO_2 and Pulse Rate calculations. Push the **KNOB** to accept your selection and return to the **SETUP** menu.
INFANT MODE	ON or OFF	Displays the **SET MARS INFANT MODE** screen. Infant Mode allows the NICO to accommodate neonatal and smaller patients with heart rates greater than 100 bpm. Turn the **KNOB** to select **OFF** (default setting) or **ON**. Push the **KNOB** to accept your selection and return to the **SETUP** menu. When the monitor detects a neonatal CO_2/Flow sensor, **INFANT MODE** is automatically enabled.
INPUT/OUTPUT	ANALOG OUT 1-4 ANALOG CAL. RS232-2/RS232-3	Turn the **KNOB** to select **ANALOG OUT 1** through **ANALOG OUT 4**, **ANALOG CAL.**, **RS232-2** or **RS232-3**. Push the **KNOB** to accept your selection and assign it the desired output parameter.
CHOOSE SCREENS	N/A	Displays the **CHOOSE SCREENS** menu. Turn and press the **KNOB** to select the monitoring screens you want to enable in the active screen set. Turn the **KNOB** to highlight **EXIT** and push to return to the **SETUP** menu.
PULSE BEEP	OFF and 1-10 (default: OFF)	Displays the **SET PULSE BEEP** screen. Turn the **KNOB** to select a volume (1-10 and OFF) for the audible tone to accompany each detected pulse beat. Push the **KNOB** to accept your selection and return to the **SETUP** menu.
SWEEP	Slow, Medium, Fast (default: Medium)	Displays the **SET SWEEP SPEED** screen. Turn the **KNOB** to select how quickly the CO_2, Flow and Pressure waveforms sweep across the display (Plethysmogram is unaffected). Push the **KNOB** to accept your selection and return to the **SETUP** menu.
C.O. MODE	AVERAGE, FAST or MANUAL	Displays the **SET C.O. MODE** screen. Turn the **KNOB** to select **AVERAGE** (CO-a, CObar is displayed), **FAST** (CO-f, FAST MODE is displayed) or **MANUAL** (MANUAL MODE is displayed). Push the **KNOB** to accept your selection and return to the **SETUP** menu.
SET SPON THRESHOLD	0-50 cmH_2O	Displays the **SET SPONTANEOUS THRESHOLD** screen. The spontaneous threshold is the airway pressure chosen to differentiate between a spontaneous (patient-initiated) breath and a mechanical (ventilator) breath. Turn the **KNOB** to adjust the pressure setting indicated by a dashed line. For optimal setting of the spontaneous threshold, the dashed line should be above the peak of spontaneous breaths and below the peak of mechanical breaths. Push the **KNOB** to accept your selection and return to the **SETUP** menu.
SET TIME & DATE	hh:mm dd mmm yyyy	Displays the **SET TIME / DATE** screen. Turn the **KNOB** to highlight the portion of the time/date to change. Push the **KNOB** to select that item—it begins to flash. Turn the **KNOB** to adjust the flashing item, and when correctly set, push the **KNOB** again to accept the value. Repeat for the other time/date entries. Finally, turn the **KNOB** to highlight **EXIT** and push the **KNOB** to return to the **SETUP** menu.

Respiratory Mechanics mode

This section provides an overview of the various monitoring and setup screens in Respiratory Mechanics mode.

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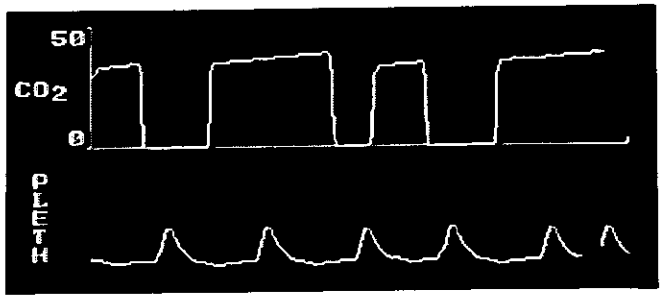
CO_2 and SpO_2 Waveform Screen

The CO_2 and SpO_2 Waveform Screen plots the capnogram and plethysmogram signals.

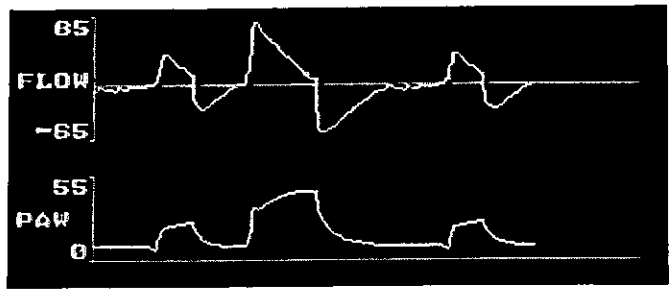


The CO_2/SpO_2 screen can be displayed by turning the **KNOB** while viewing any monitoring screen, or by pressing the **MENU** key and selecting CO_2/SpO_2.

- Information is updated in real time.
- The capnogram and plethysmogram are automatically scaled.
- The capnogram sweep speed is selectable in the **SETUP** menu.

Flow and Pressure Waveform Screen

The Flow and Pressure Waveform screen plots the airway flow and pressure signals over time.

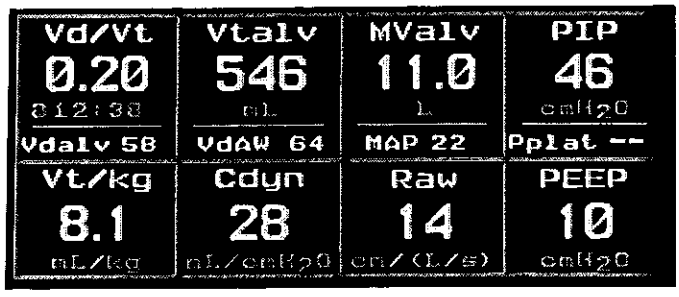


The **FLOW/PRESSURE** screen can be displayed, when enabled, by turning the **KNOB** while viewing any monitoring screen, or by pressing the **MENU** key and selecting **FLOW/PRESSURE**.

- Information is updated in real time.
- The airway flow and pressure waveforms are automatically scaled.
- The waveform sweep speed is selectable in the **SETUP** menu.

Numerics Screen

The **NUMERICS** screen display presents several monitored parameters together in one place.



The **NUMERICS** screen can be displayed, when enabled, by turning the **KNOB** while viewing any monitoring screen, or by pressing the **MENU** key and selecting **NUMERICS**.

- Information is updated in real time.
- The PEEP label is replaced with AUTO if Auto-PEEP (Intrinsic-PEEP) is detected.
- The Cdyn label is replaced with Cst if static lung compliance is detected.

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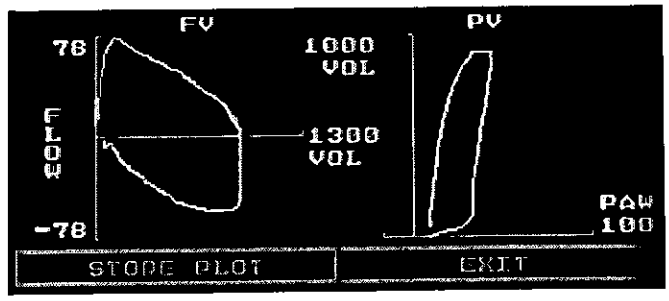
Flow Volume and Pressure Volume Loops screen

The Flow Volume and Pressure Volume Loops screen displays a flow versus volume loop and a volume versus peak airway pressure loop.

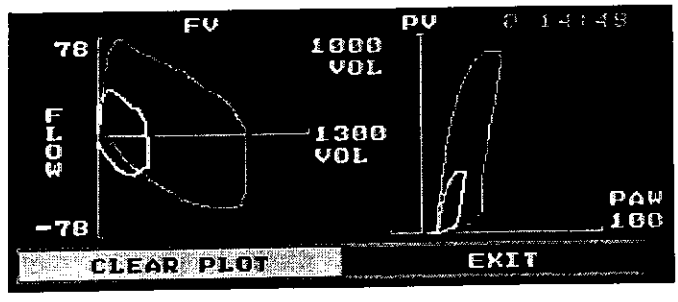


The **FLOW/PRES/VOL** screen can be displayed, when enabled, by turning the **KNOB** while viewing any monitoring screen, or by pressing the **MENU** key and selecting **FLOW/PRES/VOL**.

- The flow-volume loop is plotted in a clockwise direction, comparing flow versus volume for a single patient breath and providing information regarding the condition of the airways.
- The pressure-volume loop is plotted in a counter-clockwise direction; the slope from the beginning of inspiration to the end of inspiration depicts compliance while the width of the loop references resistance.
- The curve is automatically scaled to fit the display area.

Store Plot

The Store Plot function "freezes" a single breath on the **FLOW/PRES/VOL** screen as a template. Subsequent loops will be drawn over that breath.



- Press the **KNOB** to highlight **STORE PLOT** and again to select the breath.
- Press the **KNOB** to highlight **CLEAR PLOT** and again to erase the selected breath.
- The time stamp above the template waveform corresponds to when the plot was set.

Volumetric CO_2 Screen

The **VOLUMETRIC CO_2** screen displays the CO_2 waveform for a single patient breath, as well as providing numeric displays of Vd/Vt, Vtalv, Vdaw, $PeCO_2$, and Vdalv.

Volumetric CO_2 presents the exhaled concentration of CO_2 versus tidal volume during a single expiration; useful for understanding the ventilation/perfusion relationship. It allows the clinician

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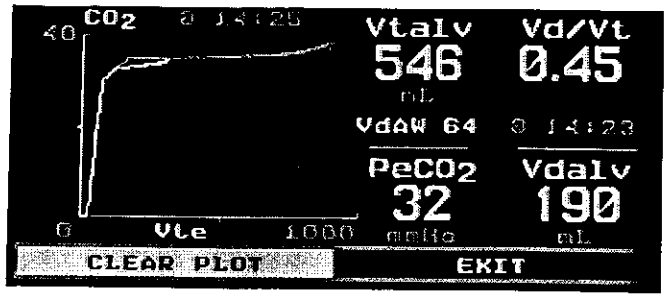
to detect relative changes in CO_2 production, deadspace, and effective ventilation by observing the shape of the graph.

- The curve is automatically scaled to fit the display area.

Store Plot

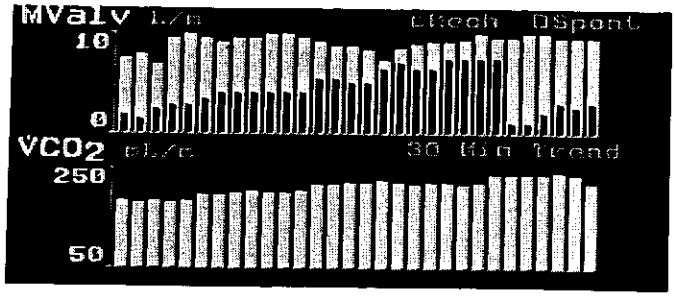
The Store Plot function "freezes" a breath on the **VOLUMETRIC CO_2** screen as a template. Subsequent waveforms will be drawn over that breath.



- Press the **KNOB** to highlight **STORE PLOT** and again to select the breath.
- Press the **KNOB** to highlight **CLEAR PLOT** and again to erase the selected breath.
- The time stamp above the template wave corresponds to when the plot was set.

VCO_2/MValv Trend Screen

The **VCO_2/MVALV** Trend screen displays trends for alveolar minute ventilation and CO_2 elimination. Monitoring spontaneous versus mechanical alveolar ventilation along with CO_2 elimination provides information on continued success or impending failure when weaning a patient off a ventilator.



- While viewing the **VCO_2/MVALV** Trend screen, each push of the knob will advance through the available 30 minute, and 2, 4, 8, and 12 hour trend displays.
- Data is plotted from left (oldest data) to right (newest data). Once the display is filled, data shifts left so that the oldest data point on the left is pushed out to make room for the newest point entering from the right.
- Each bar on the trend represents the average MValv or VCO_2 value over a time period. The time periods are: 1 minute average for the 30 minute trend, 4 minute average for the 2 hour trend, 8 minutes for the 4 hour trend, 16 minutes for the 8 hour trend, and 24 minutes for the 12 hour trend.

Vt/Vd Trend Screen

The **Vt/Vd TREND** screen displays trends for mechanical and spontaneous airway deadspace and alveolar tidal volume. Monitoring spontaneous versus mechanical deadspace along with expired

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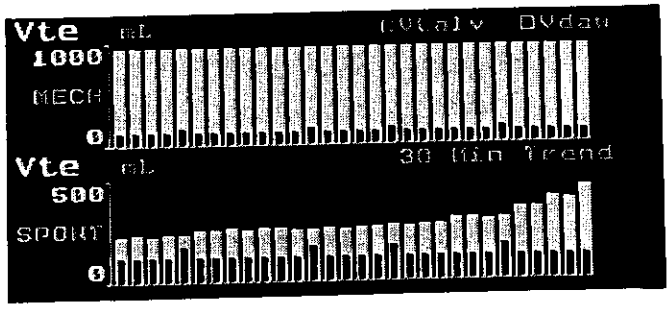
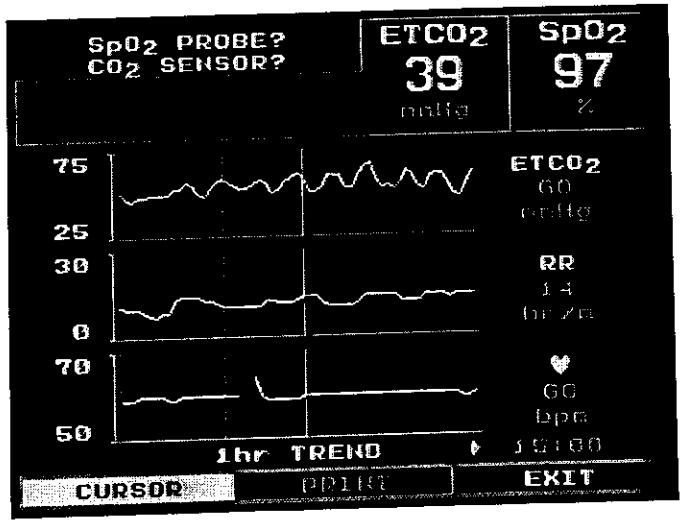
tidal volume provides information on continued success or impending failure when weaning a patient off a ventilator.



- While viewing the **Vt/Vd TREND** screen, each push of the knob will advance through the available 30 minute, and 2, 4, 8, and 12 hour trend displays.
- Data is plotted from left (oldest data) to right (newest data). Once the display is filled, data shifts left so that the oldest data point on the left is pushed out to make room for the newest point entering from the right.
- Each bar on the trend represents the average Vtalv or Vdaw value over a time period. The time periods are: 1 minute average for the 30 minute trend, 4 minute average for the 2 hour trend, 8 minutes for the 4 hour trend, 16 minutes for the 8 hour trend, and 24 minutes for the 12 hour trend.

Cardiopulmonary Trend Screen

The Cardiopulmonary **TREND** screen displays two user-selectable numeric parameters and three user-selectable trend graphs. Push then turn the **KNOB** to advance through the displays. Highlight the desired parameter, trend type or trend duration, then select by turning then pressing the **KNOB**.



- Data is plotted from left (oldest data) to right (newest data). Once the display is filled, data shifts left so that the oldest data point on the left is pushed out to make room for the newest point entering from the right.
- To move between newer and less recent trend data on the graph, press and turn the **KNOB** to highlight the **CURSOR**. Press and turn the **KNOB** again to view the desired time period. Arrows will appear below the trend graph, to signify that more data is available by turning the **KNOB**. To view the most recent data, scroll to the right using the **KNOB**, to view less recent data, scroll to the left.
- The time periods are: 1 minute average for the 1 hour trend, 2 minute average for the 2 hour trend, 4 minutes for the 4 hour trend, 8 minutes for the 8 hour trend, 12 minutes for the 12 hour trend and 24 minutes for the 24 hour trend.
- VCO_2, $ETCO_2$, RR, SpO_2, and pulse rate values will flash if an alert limit is exceeded.

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- A two-pixel wide dashed vertical line in the trend is used to denote a power-cycle where the NICO® monitor was turned off and back on or where the time and date setting was changed.
- A single pixel-wide dotted vertical line in the trend is used to mark the most recent ABG entry.
- Trend reports can be printed from the Cardiopulmonary Trend screen. See "Printing" on page 87 for details.
- The PRINT option is dimmed when HP PRINTER OUTPUT is not selected. To set the monitor to the proper interface, see "Printing" on page 87.

Tabular Data Screen

The **TABULAR DATA** screen displays the data collected for all parameters, in one-minute increments, in a table format. Cardiac output-related parameters will not be displayed and will remain dashed (--) and inactive in Respiratory Mechanics mode.

The parameter displayed in each column will vary, depending on the setting chosen by the user.

1 Highlight and select the desired column by turning then pressing the **KNOB**.

2 Turn the **KNOB** to advance through all available parameters.

3 Press the **KNOB** to accept the displayed parameter; turn to select the next column.

TIME	PIP	CO-a	SpO_2	$ETCO_2$	VCO_2
11:12	32	-.-	97	39	430
11:13	32	-.-	97	39	430
11:14	32	-.-	97	39	430
11:15	32	-.-	97	39	430
11:16	32	-.-	97	39	430
11:17	32	-.-	97	39	430
11:18	30	-.-	97	39	430

EXIT

Time Column

With the **TIME** column selected (flashing), turn the **KNOB** to display parameters collected since the beginning of the monitoring session; the most recent records are at the bottom of the table. Three arrows ↓↓↓ will display at the bottom of the column when more records are available.

Set Alerts Screen

The **SET ALERTS** screen displays the current patient values as well as the LOW and HIGH alert limit settings for various parameters. This screen also allows adjustment of alert limits, audible alert volume, and of the "No Respiration" alert. See "Alerts" on page 61 for details.

SET ALERTS	CURRENT	LOW	HIGH
VCO_2 mL/m	454	OFF	OFF
$ETCO_2$ (mmHg)	36	1	150
SpO_2 (%)	97	50	100
RR (br/m)	20	3	150
♥ (bpm)	75	31	249
AUDIO: 10		NO RESP: 20s	
AUTO LIMITS		EXIT	

The **SET ALERTS** screen can only be displayed by pressing the **MENU** key and selecting **SET ALERTS**.

- **CURRENT** - the current patient value for a parameter, shown in real time
- **LOW** and **HIGH** - the values below and above which an alert will be generated. The value will flash when a high or low alert limit is exceeded.
- 🔕 (Bell with slash) - audible alerts are disabled
- 🔔 (Bell) - audible alerts are enabled

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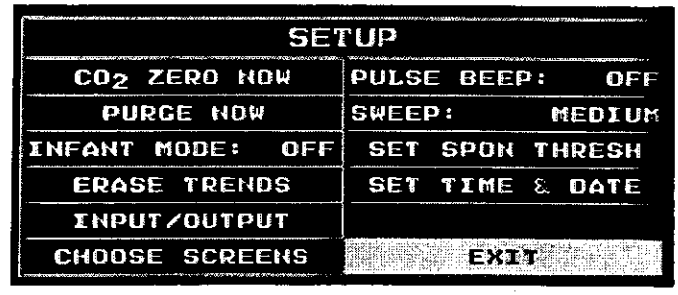
- **AUDIO** - set the audible alert volume level
- **AUTO LIMITS** - have the NICO monitor bracket alerts around current patient values
- **NO RESP:** - set the No Respiration alert delay timer

Setup Screen

The **SETUP** screen allows the user to perform certain functions, such as a CO_2 Zero, erase trend data, change items like the waveform trace sweep speed and to set the time and date. Once set, the NICO monitor will use these settings until again changed by the user.

To display the **SETUP** screen:

1. Press the **MENU** key to activate **SELECT A SCREEN.** The key's green icon illuminates.
   - Press the key again to return to the previously displayed screen.
2. Highlight and then select **SETUP** by turning and then pressing the **KNOB.**
3. The **SETUP** screen is displayed.
4. Again, turn the **KNOB** to highlight an item and push the **KNOB** to select it.



Items within the **SETUP** screen are described below:

Label	Settings/Range	Description
CO_2 ZERO NOW	Start or Cancel (default: Start)	Displays the **CO_2 ZERO NOW** screen. Place the CAPNOSTAT® CO_2 Sensor onto a clean and dry adapter. Place the adapter in room air and away from all sources of CO_2. Select **START** to begin a CO_2 Zero or **CANCEL** to exit the selection and return to the **SETUP** menu.
PURGE NOW	N/A	The system immediately purges the CO_2/Flow Sensor tubing. No messages are displayed. The Purge takes approximately 8 seconds. The flow and pressure waveform traces will return to zero during this period.
IABP Intra-Aortic Balloon Pump	ON or OFF	Displays the **SET SpO_2 IABP MODE** screen. Turn the **KNOB** to select **OFF** (default setting) or **ON** to turn off the validator algorithm so that all pulsatile data, including the normally rejected artifact generated by the IABP, are allowed to influence the SpO_2 and Pulse Rate calculations. Push the **KNOB** to accept your selection and return to the **SETUP** menu.
INFANT MODE	ON or OFF	Displays the **SET MARS INFANT MODE** screen. Infant Mode allows the NICO to accommodate neonatal and smaller patients with heart rates greater than 100 bpm. Turn the **KNOB** to select **OFF** (default setting) or **ON**. Push the **KNOB** to accept your selection and return to the **SETUP** menu.When the monitor detects a neonatal CO_2/Flow sensor, **INFANT MODE** is automatically enabled.
ERASE TRENDS	Yes or No (default: No)	Displays the **ERASE STORED TRENDS?** screen. Turn the **KNOB** to select **NO** (the default setting) or **YES**. Push the **KNOB** to accept your selection and return to the **SETUP** menu.
CHOOSE SCREENS	N/A	Displays the **CHOOSE SCREENS** menu. Turn and press the **KNOB** to select the monitoring screens you want to enable in the active screen set. Turn the **KNOB** to highlight **EXIT** and push to return to the **SETUP** menu.
INPUT/OUTPUT	ANALOG OUT 1-4 ANALOG CAL. RS232-2/RS232-3	Turn the **KNOB** to select **ANALOG OUT 1** through **ANALOG OUT 4, ANALOG CAL., RS232-2** or **RS232-3**. Push the **KNOB** to accept your selection and assign it the desired output parameter.

Label	Settings/Range	Description
PULSE BEEP	OFF and 1-10 (default: OFF)	Displays the **SET PULSE BEEP** screen. Turn the **KNOB** to select a volume (1-10 and OFF) for the audible tone to accompany each detected pulse beat. Push the **KNOB** to accept your selection and return to the **SETUP** menu.
SWEEP	Slow, Medium, Fast (default: Medium)	Displays the **SET SWEEP SPEED** screen. Turn the **KNOB** to select how quickly the CO_2, Flow and Pressure waveforms sweep across the display (Plethysmogram is unaffected). Push the **KNOB** to accept your selection and return to the **SETUP** menu.
SET SPON THRESHOLD	0-50 cmH_2O	Displays the **SET SPONTANEOUS THRESHOLD** screen. The spontaneous threshold is the airway pressure chosen to help the NICO monitor differentiate between a spontaneous breath and a mechanical breath. Turn the **KNOB** to adjust the setting indicated by a dashed line. For optimal setting of the spontaneous threshold, the dashed line should be above the peak of spontaneous breaths and below the peak of mechanical breaths. Push the **KNOB** to accept your selection and return to the **SETUP** menu.
SET TIME & DATE	hh:mm dd mmm yyyy	Displays the **SET TIME / DATE** screen. Turn the **KNOB** to highlight the portion of the time/date to change. Push the **KNOB** to select that item—it begins to flash. Turn the **KNOB** to adjust the flashing item, and when correctly set, push the **KNOB** again to accept the value. Repeat for the other time/date entries. Finally, turn the **KNOB** to highlight **EXIT** and push the **KNOB** to return to the **SETUP** menu.

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NICO®

Notes on Patient Monitoring

Automatic Purging

A double lumen connecting line (tubing) connects the NICO® Flow and CO_2/Flow sensors to the NICO monitor. The monitor includes an automatic and manual purge feature which provides a flow rate of room air to keep the sensor tubing free from water condensation and patient secretions. This feature is available for the adult, pediatric, and neonatal modes.

Adult mode

The system automatically purges the sensor tubing every 10 minutes or less, depending on system conditions. In adult mode, the system will purge both sides of the line, one at a time, during each purge cycle. The higher the pressure, the more frequent the purging. This action anticipates increased moisture migration into the sensor tubing due to the increase in circuit pressure.

Neonatal and Pediatric modes

The automatic purge cycle used in the neonatal or pediatric mode is fixed at every 3 minutes regardless of circuit pressure. Only one side of the sensor tubing will be purged during each purge cycle. The purge will only occur during the exhalation portion of the ventilator cycle, regardless of exhalation time.

Unlike the adult purge mode, the neonatal or pediatric purge mode does not use the full force of the internal pump, but rather pressurizes an internal reservoir which is used for the purge. This minimizes the pressure delivered to the ventilator circuit, but does deliver a sufficient pressure to purge the sensor tubing.

Manual Purging

Occasionally, purging may be required in between the automatic purge cycle. The manual purge may be used as often as needed, and may be used at all times **except** when a rebreathing cycle is in progress or a very low battery condition exists. During these conditions, automatic and manual purging is not allowed.

To manually purge:

1 Press the **MENU** key.

1 Turn and press the **KNOB** to select **SETUP.**

1 Turn and press the **KNOB** to select **PURGE NOW.**

2 The purge cycle will begin:

In adult mode, the system will purge both sides of the line, one at a time, during each purge cycle.

In pediatric and neonatal modes, only one side of the sensor tubing will be purged during each purge cycle. The purge is synchronized to the exhalation phase of the ventilator cycle and will not exceed exhalation time.

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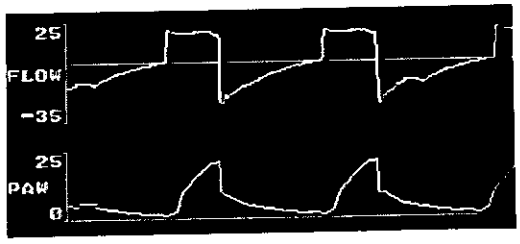
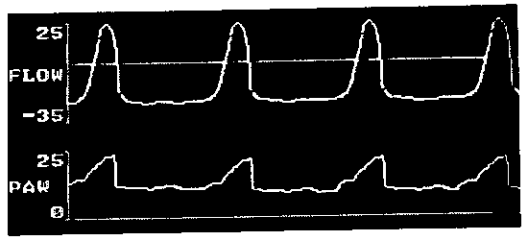
A purge can also be initiated upon request if the flow waveform appears as though the lines are partially occluded (see example below) and the purge did not initiate automatically. To initiate a purge, see Manual Purging, above.

Normal



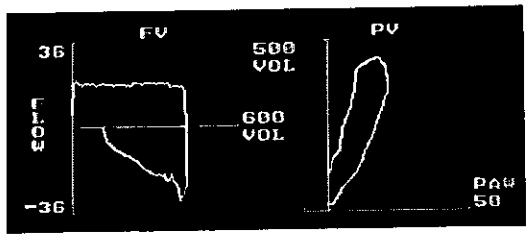
Occluded



NOTE:
If the purge does not sufficiently clear the flow tubing lines, the flow sensor should be changed.

Below is an example of a waveform that exhibits a small leak in the breathing circuit. Replace the sensor; if problem persists, refer monitor to qualified service personnel.

Small leak in flow tubing



Intra-Aortic Balloon Pump

The NICO monitor uses advanced signal processing algorithms to distinguish valid pulsatile signals from signals generated by motion or other artifact. Motion artifact, very common in all but heavily sedated patients, can swamp the true pulsatile signal or distort it enough to produce significant errors in the SpO_2 and Pulse Rate calculations. The validator algorithms reject distorted plethysmographic signals or those that lack a regular rhythmic pattern; therefore, only valid (pulsatile) signals are allowed to affect the monitor's SpO_2 and Pulse Rate calculations. Rare conditions exists where the pulsatile waveform truly is distorted and lacks a fixed rhythm, specifically during use of an Intra-Aortic Pump (IABP).

During IABP procedures the pulsatile signal can be massively distorted without affecting the patient's SpO_2. In order to accommodate these IABP procedures without compromising the monitor's superior artifact rejection algorithm, IABP MODE is available. IABP MODE allows the user to turn off the validator algorithm so that all pulsatile data are allowed to influence the SpO_2 and Pulse Rate calculations.

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NOTE

With **IABP MODE** turned ON, the clinician must exercise prudence in assessing the validity of the SpO_2 and Pulse Rate displays because any motion or other artifact—not just that associated with the IABP—can have a significant affect on the SpO_2 and Pulse Rate calculations.

While in **IABP MODE**, the displayed Pulse Rate reflects true pulsatile signal-heart rate plus the IABP ratio (e.g. #1: heart rate =120 bpm, IABP ratio = 1:1, then displayed Pulse Rate should be 120 + (120/1)=240 beats/min. e.g. #2: heart rate = 120 bpm, IABP = 1:3, then displayed Pulse Rate should be 120 + (120/3) = 180 beats/min).

If **IABP MODE** is dimmed and unavailable in the **SETUP** screen, contact your local Novametrix representative for information on how to enable this feature.

Configuration Menu

Simultaneously press and hold the **MENU** and **DATA ENTRY** keys for 3 seconds to access the Configuration Menu. Turn and press the **KNOB** to adjust and accept settings.

Parameter	Range/Units	Description	Factory Default
CO_2 UNITS	mmHg, %, kPa	Select the desired units for the capnogram, $PeCO_2$, $ETCO_2$ and $PaCO_2$ values.	mmHg
$ETCO_2$ AVG	10 sec, 20 sec, 1 Breath	Select the interval from which the displayed value of end tidal CO_2 ($ETCO_2$) is calculated.	10 sec
MARS SpO_2 AVG	0 sec, 2 sec, 4 sec, 8 sec.	Select the averaging time for the displayed value of SpO_2, using the MARS artifact rejection algorithm.	4 sec
VCO_2 AVG	10 min, 5 min, 3 min, 1 min, 8 Breath	Select the averaging time for the displayed value of CO_2 elimination (VCO_2).	1 min
ALLOW AUDIO OFF	N/A	When the ALLOW AUDIO OFF setting is set to YES, the audible alert tone may be silenced permanently by pressing and holding the SILENCE key. If the ALLOW AUDIO OFF is set to NO, the audible alert tone may not be silenced for more than 2 minutes.	Yes
LANGUAGE	N/A	Select the desired language	English
DISPLAY MODE	C.O., PCBF, CI	Select the parameter to be displayed as the large number in the upper right of the screen.	C.O.

Reference Handbooks

For a discussion on waveform interpretations, refer to the Novametrix Reference Handbooks on capnography, respiratory mechanics, and pulse oximetry. Contact Novametrix Customer Service or your local sales representative for more information.

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NICO®

Alerts

This section describes NICO® monitor alerts.

Alert Priorities

The NICO monitor prioritizes alert notifications. This prioritization allows an alert condition for which an immediate user response is required to take precedence over a lesser alert for which a less urgent response is acceptable. Alert notifications may include on-screen display messages and audible tones, and may result from violations of parameter limit settings, or from monitor or sensor related error conditions.

High Priority Alert

- Action: Immediate user response
- Audible: 3 consecutive tones, repeated every 5 seconds (if enabled)
- Visual: the **SILENCE** key indicator flashes red, and a screen message is displayed

- Example: **LOW C.O.**

Low priority Alert

- Action: User awareness
- Audible: a single tone, repeated every 15 seconds (if enabled)
- Visual: Screen message
- Example: **WAIT FOR RR<60 br/m**

Medium Priority Alert

- Action: Prompt user response
- Audible: 2 consecutive tones, repeated every 10 seconds (if enabled)
- Visual: Screen message
- Example: **HIGH RESP**

Status Messages

- Action: Informational, no urgency
- Audible: none
- Visual: Screen message
- Example: **ALERTS OFF**

Responding to Alert Audio

The **SILENCE** key is used to mute or disable audible alerts. It also visually indicates the presence of a "High Priority Alert". The Silence feature operates in two modes; a temporary "2 Minute Silence" mode and an "Audio Disabled" mode.

- 2 Minute Silence — Press and release to activate or deactivate the two minute silence. The key's icon illuminates amber when active and audible alerts will be muted for two minutes, after which the icon turns off and any active audible alert will sound.
- Audio Disabled — Press and hold for two seconds to disable audible alerts. The monitor emits two tones and the **SILENCE** key's icon illuminates amber to indicate audible alarms are disabled. Audio alerts (🔔) will be deactivated (🔕) in the **SET ALERTS** screen.
- High Priority Alerts — The **SILENCE** key's icon illuminates and flashes red to indicate High Priority Alert is active. The icon alternately flashes red and amber if the audio is silenced or disabled and a High Priority Alert is active.

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Parameter Limit Alerts

The NICO monitor allows for the establishment of high and low limit alerts for Cardiac Output (C.O., Cardiac Output mode only), CO_2 elimination (VCO_2, Respiratory Mechanics mode only, adult and pediatric only), End-Tidal Carbon Dioxide ($ETCO_2$), Oxygen Saturation (SpO_2), Respiratory Rate (RR), and Pulse Rate (♥). These alerts provide a visual (and audible, if desired) indication to the user that a parameter has violated the limit settings

Cardiac Output mode

Parameter	Range	Units
C.O.	OFF, 0.1 - 19.9	L/m
$ETCO_2$	OFF, 1 - 150 OFF, 0.1 - 19.9 OFF, 0.1 - 19.9	mmHg kPa %
SpO_2	OFF, 50 - 100	%
RR	OFF, 3 - 150	br/min
♥ (Pulse Rate)	OFF, 31 - 249	bpm

Respiratory Mechanics mode

Parameter	Range	Units
VCO_2	OFF, 20 - 999	mL/m
$ETCO_2$	OFF, 1 - 150 OFF, 0.1 - 19.9 OFF, 0.1 - 19.9	mmHg kPa %
SpO_2	OFF, 50 - 100	%
RR	OFF, 3 - 150	br/min
♥ (Pulse Rate)	OFF, 31 - 249	bpm

- All alert limit values are retained each time the monitor is turned off.
- The user can select individual limit values or have the monitor automatically assign limit values based on current patient values with the **AUTO LIMITS** feature.
- Audible alarms can be enabled or disabled.
- Limits cannot be adjusted to provide less than a 5 digit separation between the high and low limit values.

NOTE

The message **ALERTS OFF** will appear if the monitor is powered up with all alert limits set to **OFF**.

To cancel the **ALERTS OFF** message, adjust any individual limit value to activate the alert.

View Alert Settings

To view the existing alert settings:

1. Press the **MENU** key. The **SELECT A SCREEN** menu appears.
2. Highlight and then select **SET ALERTS** by turning and then pressing the knob.
3. The **SET ALERTS** screen is displayed.

Adjust Alert Limits

To adjust **LOW** or **HIGH** alert limit values:

1. Display the **SET ALERTS** screen. (Press **MENU**, then select **SET ALERTS**.)
2. Highlight and then select the **LOW** or **HIGH** limit you wish to adjust.
3. Turn the knob to adjust the limit, then press the knob to accept the displayed value.
4. If desired, enable the audio for the alerts. (See below.)

Enable/Disable Audible Alerts

To enable or disable the audible alert tone(s):

1. Display the **SET ALERTS** screen. (Press **MENU**, then select **SET ALERTS** or when the **SILENCE** key is illuminated amber, press and hold for two seconds.)
2. Highlight the bell icon.
3. Press the knob to switch between audio enabled (🔔) and disabled (🔕) settings.

To disable audible alert tones, press and hold the **SILENCE** key for two seconds.

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Adjust Alert Audio Volume

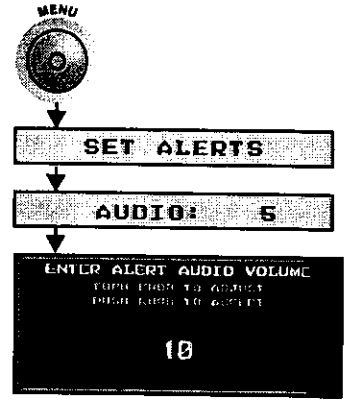
To adjust the Alert Audio Volume:

1 Display the **SET ALERTS** screen. (Press **MENU**, then select **SET ALERTS**.)

2 Highlight and then select **AUDIO** by turning and then pressing the knob.

3 Turn the knob to adjust the volume setting.
- Volume ranges from 1 to 10 (loudest).
- A representative tone sounds at each setting.

4 Press the knob to accept the displayed value.



NOTE

Make sure that the audible alert volume is not set too low to be heard over ambient noise levels.

Auto Alerts

Alert limits for **LOW** and **HIGH** C.O., VCO_2, $ETCO_2$, SpO_2, RR and Pulse rate can be set automatically for alerts which have been enabled. Alert limits are bracketed about the current patient values. Auto Alerts do not affect the status of the audible alert bell icon.

No Respiration Alert

The NICO monitor incorporates a No Respiration Alert (**NO RESP**). Once the monitor detects respiration, any loss of that signal starts the "No Resp" timer. A visual (and audible, if desired) alert occurs if the monitor does not detect a respiratory rate signal before the timer reaches its user set limit (20 seconds by default).

If a No Respiration alert occurs:

- The message **NO RESP: x:xx** is displayed (unless a higher priority alert is in progress).
- The counter shows the elapsed time (minutes:seconds) since the alert occurred.
- Press the **SILENCE** key to cancel the alert.
- The alert (message, audio and flashing **SILENCE** key) is automatically cancelled after ten minutes.

WARNING

The NICO monitor is not intended to be used as an apnea monitor.

Adjust the No Resp. Alert Limit

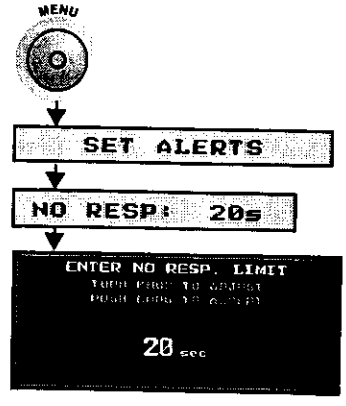
To adjust the No Respiration Alert Limit:

1 Display the **SET ALERTS** screen. (Press **MENU**, then select **SET ALERTS**.)

2 Highlight and then select **NO RESP** by turning and then pressing the knob.

3 Turn the knob to adjust the limit setting.
- The limit timer is selectable from 10-60 seconds.

4 Press the knob to accept the displayed value.



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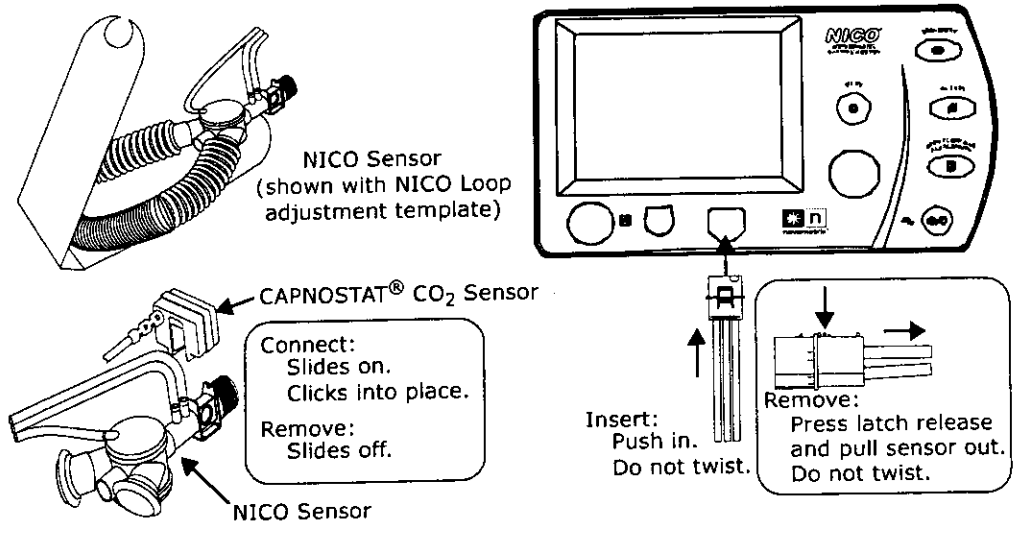
NICO Sensor

This section provides information regarding Disposable NICO Sensors and their use with the CAPNOSTAT® CO_2 Sensor and the NICO® monitor.

Disposable NICO Sensors

A NICO Sensor incorporates a rebreathing valve, NICO Loop (an adjustable rebreathing volume) and an adult CO_2/Flow Sensor. It is disposable and intended for Single Patient Use only. The NICO Sensor is not for pediatric use.

A NICO Sensor may be connected to and removed from the NICO monitor while the monitor is turned off or on.



WARNING

The Disposable NICO Sensor is intended for SINGLE PATIENT USE ONLY ②.

Re-use, including disassembly, cleaning, disinfecting, sterilizing, and other efforts made in an attempt to re-use a NICO Sensor, may compromise system performance and may cause a potential patient hazard. Performance is not guaranteed if reused.

Before use, verify the sensor is physically intact, with no broken or damaged parts. Do not use a broken or damaged sensor or one with wet, contaminated, or corroded connectors.

Do not allow the NICO Sensor to remain in the ventilator circuit when not connected to the NICO monitor. A ventilator circuit leak will occur.

CAUTION

Connect only a Novametrix NICO Sensor, Catalog Number 8950-00, 8951-00 or 8952-00 to the NICO monitor. Do not connect any other sensor in place of a NICO Sensor.

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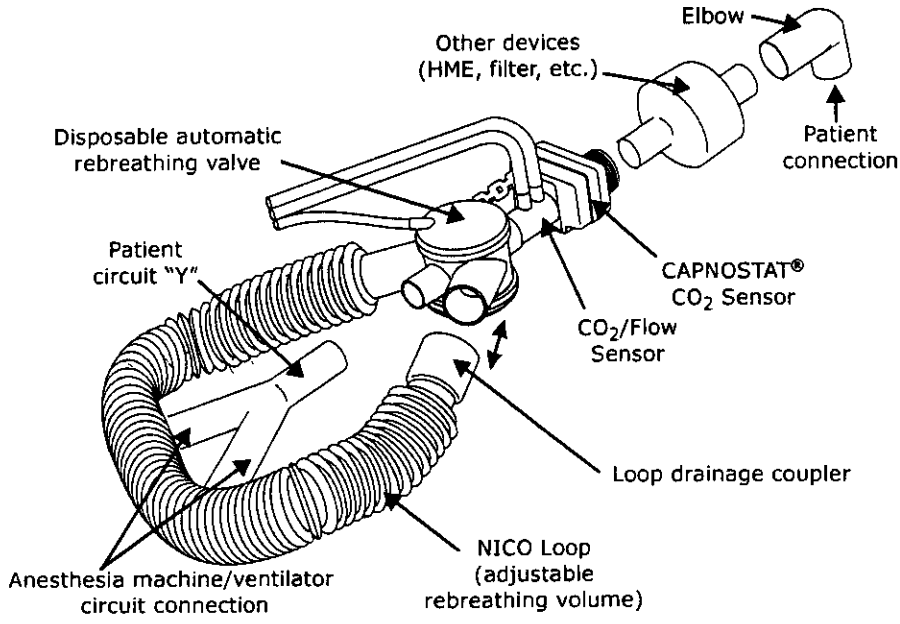
NICO Sensor and CAPNOSTAT® CO_2 Sensor



Choosing a NICO Sensor size

Choose a NICO Sensor size based on the tidal volume ranges listed below.

Sensor Size	Tidal Volume Range	Part Number
Small	For use with ventilator set tidal volumes of 200-500 ml	8950-00
Standard	For use with ventilator set tidal volumes of 400-1000 ml	8951-00
Large	For use with ventilator set tidal volumes of 750-1500 ml	8952-00

WARNING

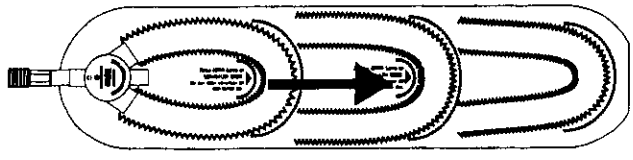
The NICO Sensor is not for pediatric use.

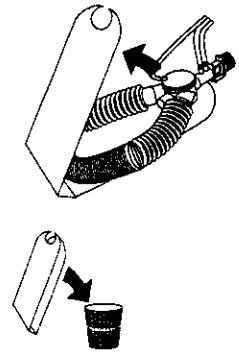
The NICO Sensor increases airway deadspace by 35 cc (minimum). At low tidal volumes, compensatory changes to ventilation protocol should be considered.

Connecting a NICO Sensor

To connect a NICO Sensor into the ventilator circuit:

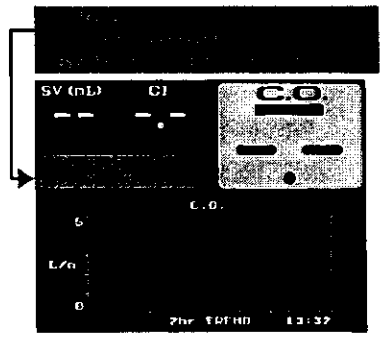
1. Remove a new NICO Sensor and loop adjustment template from its package. Open and inspect the sensor. Do not use if damaged.
2. Using the Initial Adjustment Template as a guide, adjust the NICO Loop to match the ventilator's tidal volume setting. Discard the template.





409

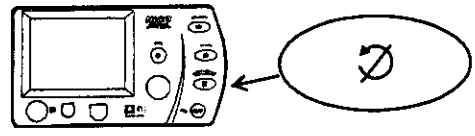
3 Insert the connector on the NICO Sensor into the monitor's front panel. Verify a **NICO SENSOR IDENTIFIED** message is briefly displayed.



4 Attach the CAPNOSTAT® CO_2 Sensor to the NICO Sensor and connect the NICO Sensor to ventilator circuit. For optimal results, place the NICO Sensor into the ventilator circuit between the endotracheal tube and the ventilator circuit wye.

- Place other devices (HME, filters, etc.) between NICO Sensor and the patient connection.
- Placement of a sidestream gas analyzer sampling port between the NICO Sensor and the patient connection may reduce accuracy at low tidal volumes.
- Sidestream or mainstream gas analyzers placed between the NICO Sensor and the patient circuit "Y" may report diluted readings during the rebreathing phase of the cycle.
- Place the sensor so that the triple lumen tubing lines exit from the top of the sensor (to help keep them clear and dry).
- Excess moisture may be removed by temporarily opening the circuit at the loop drainage coupler. Securely reconnect the coupler.

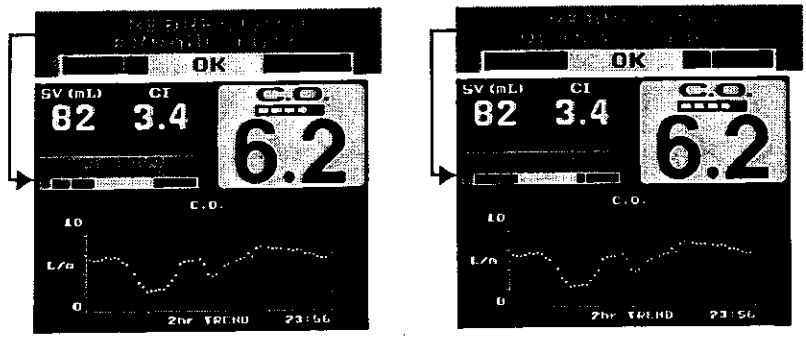
5 To begin monitoring, press the **STOP / CONTINUE REBREATHING** key.



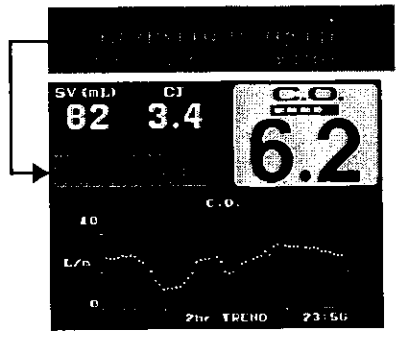
- To enhance accuracy, enter the respiratory gas composition and the arterial blood gas values whenever possible (by pressing the **DATA ENTRY** key).

Status Messages

While monitoring, if the **EXPAND** or **RETRACT LOOP** message appears, adjust the loop 3-6 inches (8-15 cm) or until the message is removed.



If the **EXPAND** or **RETRACT LOOP** message appears for more than three consecutive rebreathing cycles, and resizing the NICO Loop was not effective, the NICO monitor will suggest a different sized sensor, with a larger or smaller loop, to correct the condition.



- Small NICO Sensor: the monitor displays **CONSIDER USING A STANDARD NICO SENSOR** when ventilator set tidal volume is greater than 500 ml.
- Standard NICO Sensor: the monitor displays **CONSIDER USING A SMALL NICO SENSOR** when ventilator set tidal volume is less than 300 ml.
- Standard NICO Sensor: the monitor displays **CONSIDER USING A LARGE NICO SENSOR** when ventilator set tidal volume is greater than 1000 ml.
- Large NICO Sensor: the monitor displays **CONSIDER USING A STANDARD NICO SENSOR** when ventilator set tidal volume is less than 1000 ml.

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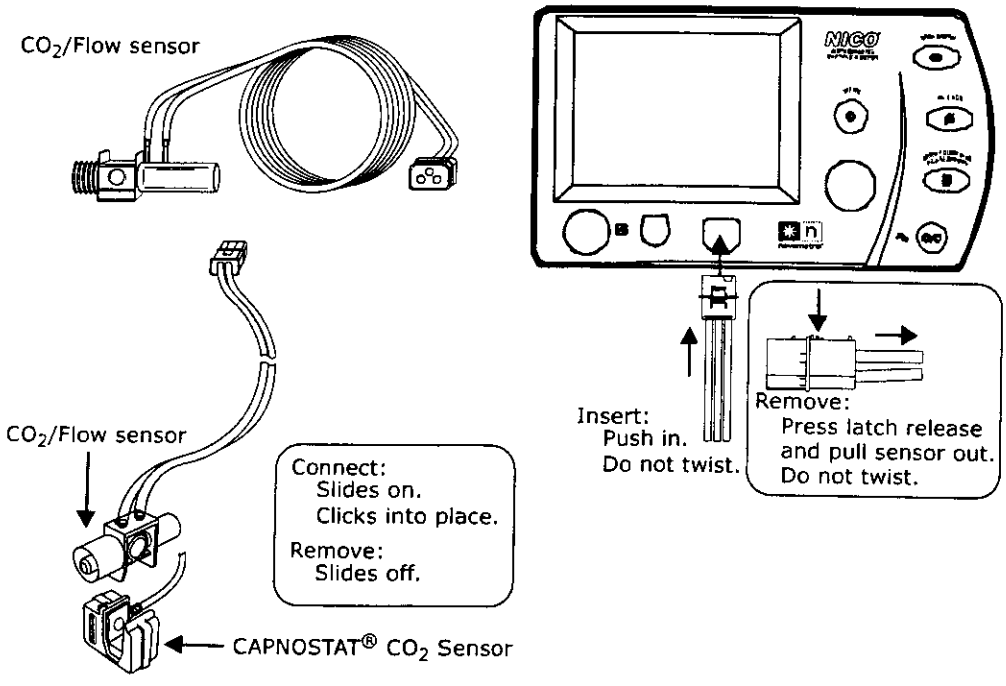
NICO®

CO_2/Flow Sensors

This section details the use of combined CO_2/Flow sensors with the NICO® monitor. This section also explains how to connect a sensor to the monitor, and how to apply the sensor to the patient. The NICO monitor automatically operates in Respiratory Mechanics mode whenever a CO_2/Flow sensor is connected to the monitor. Cardiac output and associated parameters are no longer available.

Only Novametrix NICO® CO_2/Flow sensors are compatible with the NICO monitor. Sensors may be connected and removed with the monitor off or on.



WARNING

The Disposable CO_2/Flow sensor is intended for SINGLE PATIENT USE ONLY ⊗.

Re-use, including disassembly, cleaning, disinfecting, sterilizing, and other efforts made in an attempt to re-use a CO_2/Flow sensor, may compromise system performance and may cause a potential patient hazard. Performance is not guaranteed if reused.

Before use, verify the sensor is physically intact, with no broken or damaged parts. Do not use a broken or damaged sensor or one with wet, contaminated, or corroded connectors.

Do not allow the CO_2/Flow sensor to remain in the ventilator circuit when not connected to the NICO monitor. A ventilator circuit leak will occur.

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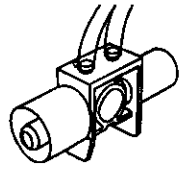
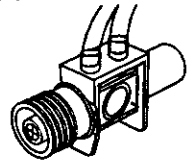
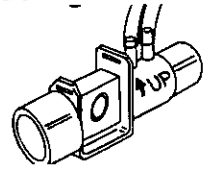
CAUTION

Connect only Novametrix NICO CO_2/Flow sensors, Catalog Number 9765-00, 9766-00, or 9767-00, to the NICO monitor. Do not connect any other sensor in place of a NICO CO_2/Flow sensor.

Choosing a CO_2/Flow Sensor

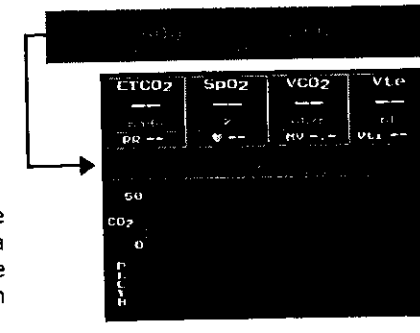
Select the appropriate combined CO_2/Flow sensor based on endotracheal tube size (ETT), volume and flow rate. Ranges for each sensor are listed in the chart below:

	Range			
Sensor	**ETT (mm)**	**Volume (ml)**	**Flow**	**Deadspace**
Neonatal  Catalog No. 9765-00	2.5-4.0	1-100	0.25-25 LPM 4-417 ml/sec	Less than 1 ml
Pediatric  Catalog No. 9766-00	3.5-6.0	30-400	0.5-100 LPM 8-1600 ml/sec	Less than 4 ml
Adult  Catalog No. 9767-00	>5.5	200-3000	2.0-180 LPM 33-3000 ml/sec	Less than 8.5 ml

Connecting a CO_2/Flow Sensor

To connect a combined CO_2/Flow sensor:

1. Remove a new CO_2/Flow sensor from its package. Open and inspect the sensor. Do not use if damaged.
2. Insert the connector on the CO_2/Flow sensor into NICO monitor's front panel. Verify a **CO2/FLOW SENSOR IDENTIFIED** message is briefly displayed.
3. Attach the CAPNOSTAT® CO_2 Sensor to the CO_2/Flow sensor. The sensor will "click" when properly seated.



When a CO_2/Flow sensor is replaced, the message **CHECK/CHANGE AIRWAY ADAPTER** may appear, this means a CO_2 zero is required to help the monitor "learn" the specific optical characteristics of the CO_2/Flow sensor in use.

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To perform an Adapter Zero:

1. Press the **MENU** key.
2. Highlight and then select **SETUP** by rotating and then pressing the knob.
3. Highlight and then select **CO_2 ZERO NOW.**
4. Place the CAPNOSTAT® CO_2 Sensor onto a clean and dry CO_2/Flow sensor (adapter) that is exposed to room air and away from all sources of CO_2. Alternatively, the CO_2 adapter provided with the CAPNOSTAT® CO_2 Sensor can be used for the zero procedure.
5. Highlight and then select **START.**
   - **ADAPTER ZERO IN PROGRESS PLEASE WAIT** is displayed during the 10 seconds needed to complete the process. Upon completion, **ADAPTER ZERO SUCCESSFUL** is briefly displayed before the monitor automatically returns to the **SETUP** screen.
6. Highlight and then select **EXIT** to return to the previous monitoring screen.

CAUTION

Position the airway adapter with its windows in a vertical and NOT a horizontal position: this helps keep patient secretions from "pooling" on the windows.

To prevent "rain-out" and moisture from draining into the airway adapter, do NOT place the airway adapter in a gravity dependent position.

Periodically check the CO_2/Flow sensor and tubing for excessive moisture or secretion build up.

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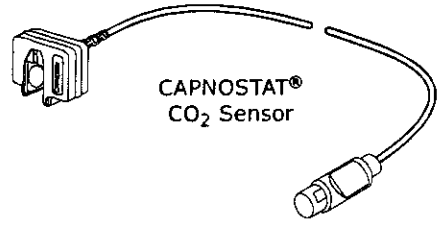
NICO®

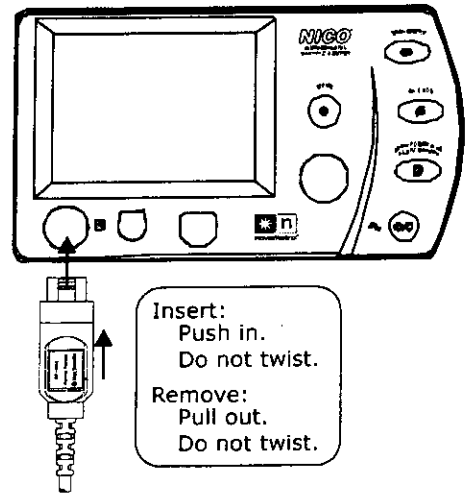
CAPNOSTAT® CO_2 Sensor

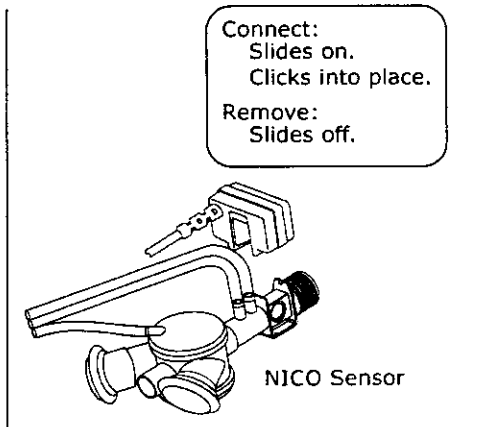
This section provides information regarding the CAPNOSTAT® CO_2 Sensor and its use with NICO Sensors and the NICO® monitor. The CAPNOSTAT® CO_2 Sensor is a rugged, solid-state, mainstream sensor. It is factory calibrated and does *not* require further calibration during use.

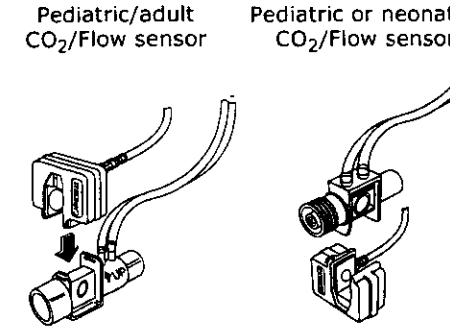
Connecting the CAPNOSTAT® CO_2 Sensor

The CAPNOSTAT® CO_2 Sensor may be connected to and removed from the NICO monitor while the monitor is turned off or on.









CAUTION

Connect only a Novametrix CAPNOSTAT® CO_2 Sensor, Catalog Number 9567-00, to the NICO monitor. Do not use other CAPNOSTAT® CO_2 Sensor types or other CO_2 sensors.

WARNING

Before use, verify the sensor is physically intact, with no broken/frayed wires or damaged parts. Do not use a broken or damaged sensor or one with wet, contaminated, or corroded connectors.

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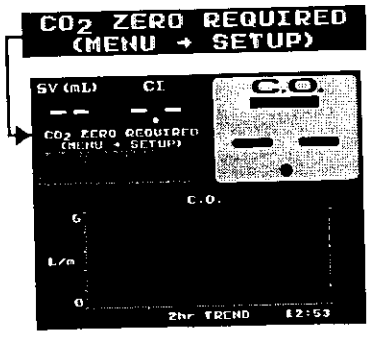
CAPNOSTAT® CO_2 Sensor Adapter Zero



An "Adapter Zero", a quick 15 second process that lets the NICO monitor "learn" the special characteristics of a particular CAPNOSTAT® CO_2 Sensor, is necessary only when the NICO monitor requests an Adapter Zero.

Such a request may occur the first time a particular CAPNOSTAT® CO_2 Sensor is connected to a particular NICO monitor—as is the case the first time you power up your NICO monitor and CAPNOSTAT® CO_2 Sensor—or if the monitor detects some change in the CAPNOSTAT® CO_2 Sensor.

Once an Adapter Zero is performed, the NICO monitor vcan be turned on and off and the CAPNOSTAT® CO_2 Sensor can be unplugged and reconnected without having to Adapter Zero the sensor. However, if a second CAPNOSTAT® CO_2 Sensor is connected in place of the first, the Adapter Zero process must be performed on the new sensor—and if at a later time, the first CAPNOSTAT® CO_2 Sensor is reconnected, it too will then have to be put through the Adapter Zero process.

Adapter Zero

To perform an Adapter Zero:

1. Press the **MENU** key.
2. Highlight and then select **SETUP** by rotating and then pressing the knob.
3. Highlight and then select **CO_2 ZERO NOW.**
4. Place the CAPNOSTAT® CO_2 Sensor onto a clean and dry NICO Sensor or CO_2/Flow sensor (adapter) that is exposed to room air and away from all sources of CO_2. Alternatively, a Single Patient Use Adult Airway Adapter (Cat. No. 6063-01) provided with the CAPNOSTAT® CO_2 Sensor can be used for the zero procedure.
5. Highlight and then select **START.**
   - **ADAPTER ZERO IN PROGRESS PLEASE WAIT** is displayed during the 10 seconds needed to complete the process. Upon completion, **ADAPTER ZERO SUCCESSFUL** is briefly displayed before the monitor automatically returns to the **SETUP** screen.

NOTE

For best results, the CAPNOSTAT® CO_2 Sensor should be connected to the NICO monitor and placed on the adapter for 2 minutes before performing the Adapter Zero procedure.

6. Highlight and then select **EXIT** to return to the previous monitoring screen.

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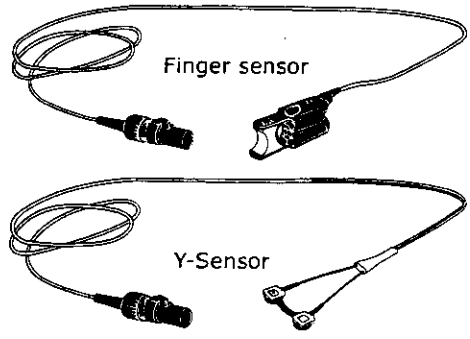
NICO®

Pulse Oximetry Sensors

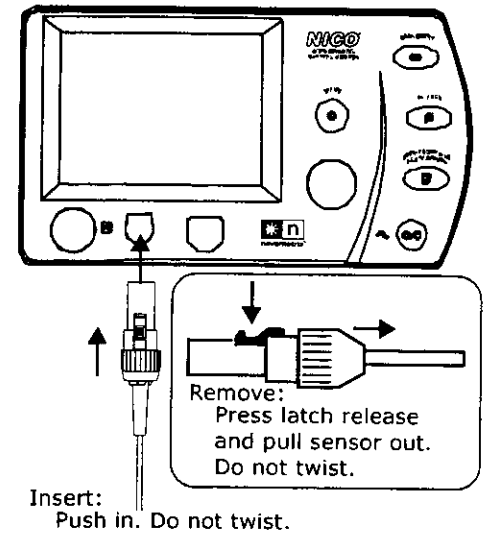
This section details the various pulse oximetry sensors and accessories that can be used with the NICO® monitor. This section also explains how to connect a sensor to the monitor, and how to apply the sensor to the patient. The NICO monitor uses the pulse oximeter portion of the monitor to enhance shunt corrections as well as to monitor patient oxygenation levels.

Oximetry Sensors

The NICO monitor is compatible with a variety of Novametrix pulse oximetry sensors including reusable Finger and Y-Sensor types and Single Patient Use sensors.



Sensors may be connected and removed with the monitor off or on.



CAUTION

Connect only Novametrix SuperBright™ SpO_2 sensors, extension cables and accessories with the NICO monitor. Do not use other SpO_2 sensors or accessories.

Overstretching the pulse oximeter finger sensor can damage the sensor and potentially affect pulse oximeter readings. Do not stretch the finger sensor open beyond the limit for which it was designed. Overstretching can be prevented: avoid opening the sensor by any means other than squeezing the grips; *DO NOT* force the sensor onto large objects such as a bedrail.

WARNING

Before applying to the patient, verify the sensor is physically intact, with no broken/frayed wires or damaged parts. Do not use a broken or damaged sensor or one with wet, contaminated, or corroded connectors.

After applying to the patient, inspect the site often for adequate circulation—at least once every four hours. Do not wrap so tightly that circulation is restricted. Note the patient's physiological condition. For example, burn patients may be more sensitive to heat and pressure and require more frequent site checks.

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Sensor Quick Check

A quick functional check of basic sensor operation.

1 With the sensor connected to the monitor but not applied to the patient, position the sensor heads so they face each other (red light shines on the detector). Is **PULSE SEARCH** displayed?

2 Apply the sensor to your finger. Are reasonable SpO_2 and pulse rate values displayed?

3 A YES to BOTH #1 and #2 indicates the sensor is operational. Apply the sensor to the patient as instructed.

- Note that the Quick Check tag on the sensor may refer to the message **Probe Off Patient.** This message does not apply to the NICO monitor—**PULSE SEARCH** does.

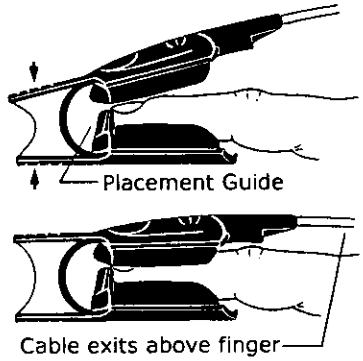
Finger Sensor

The reusable Finger Sensor is intended for adult and appropriately sized pediatric fingers and is not intended for neonatal applications.

To apply: Squeeze the grips. Position the fingertip as shown and release the grips.

To remove: Squeeze the grips. Slide the sensor from the finger and release the grips.

Caution: Overstretching can damage the sensor and affect oximetry readings. Do not force the sensor onto large objects such as bedrails.

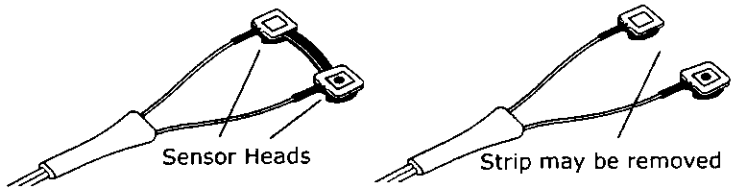


Y-Sensor

The reusable Y-Sensor is designed for use on all patients from adults to neonates.

Y-Sensor configuration

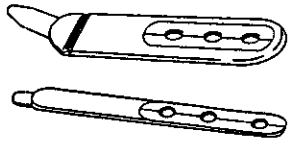
The center strip of the Y-Sensor™ may be carefully cut away if the distance between the sensor heads needs to be reduced to less than 25mm.



Y-Sensor applicators

The flexible and versatile Y-Sensor is applied to the patient using a variety of adhesive and non-adhesive applicators.

Treat applicators (except ear-clip) in accordance with hospital protocol for single-patient use. Refer to instructions packaged with the various applicators.



- 6929-00. Adhesive Foam Wraps, Large
  — Adult, pediatric or neonatal use.
- 6968-00. Adhesive Foam Wraps, Small
  — Neonatal or appropriately sized pediatric patient.

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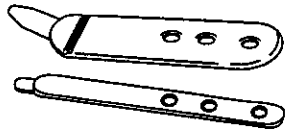
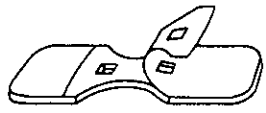
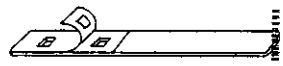


- 8836-00. Non-Adhesive Foam Wrap, Large
  — Adult, pediatric or neonatal use.
- 8943-00. Non-Adhesive Foam Wrap, Small
  — Neonatal or appropriately sized pediatric patient use.

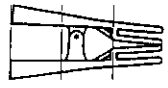


- 8831-00. 20mm Finger Style Y-Strip™ Tape (blue)
  — Appropriately sized pediatric or adult fingers.
- 8832-00. 25mm Finger Style Y-Strip™ Tape (green)
  — Adult fingers.



- 8828-00: Wrap Style Tapes 20mm (blue).
  — Neonatal foot, hand, pediatric toe, finger
- 8829-00: 25mm (green)
  — Neonatal foot, hand

Size refers to the distance between the holes in the tape.



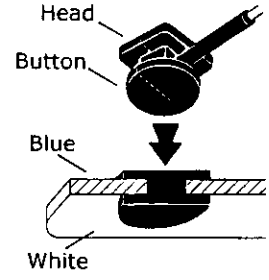
- 6131-00. Ear Clip
  — Adult or pediatric use.

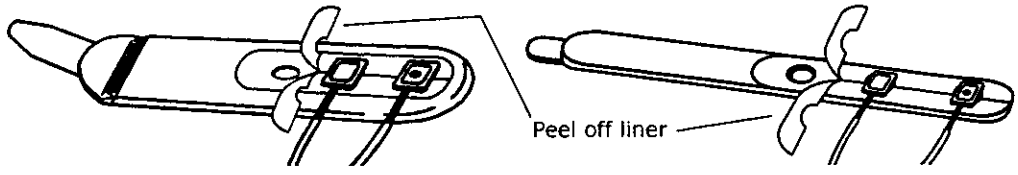
Using Foam Wraps

To use the foam wraps;

1 Press each sensor "button" through the blue side of the foam wrap.
   - Place the head with the red LED closest to the edge, and the other in either remaining hole (removing the Y-Sensor's™ center strip as required).

2 If using an adhesive foam tape, remove both sides of the paper liner.
   - You can also remove the liners prior to buttoning the sensor into the foam wrap.





3 With the blue foam towards the patient, wrap around the site. Ensure the sensor heads are opposite each other through the tissue. This prevents the sensor from being placed on a site that is too thick for proper operation.

   Position the sensor so that the tape does not extend over the space between the fingers or toes. This insures there will be no light transmission through this space.

4 Secure in place with the white plastic tab.

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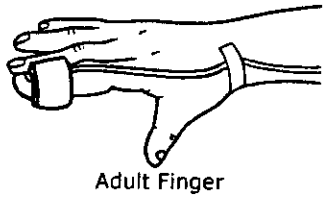
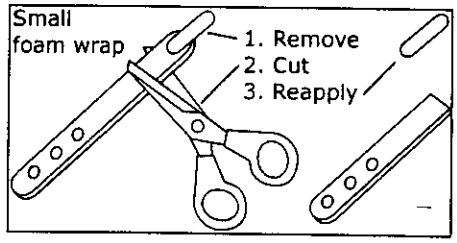
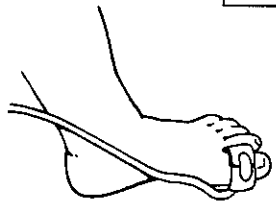
- The tab on the Small foam wrap is removable, allowing shortening for a better fit. Reapply the tab to secure the wrap in place.



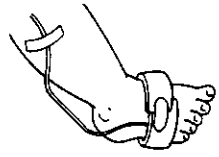
Adult Finger



Neonatal hand



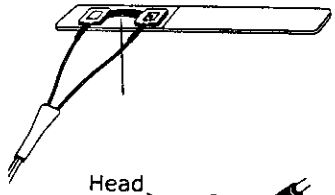
Pediatric Toe



Neonatal/pediatric foot

Using Y-Strip™ Tapes To use the Y-Strip™ Tapes;

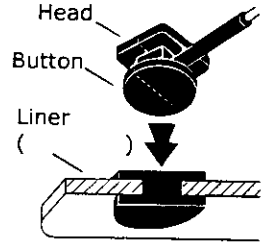
1 Remove the release liner with the holes.



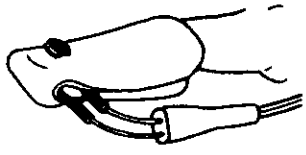
2 Press each sensor "button" through the adhesive side of the tape. (Remove the center strip of the Y-Sensor™ if required.)

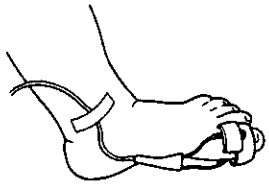
3 Remove the remaining release liner. Apply the sensor/ tape to the patient. Ensure the sensor heads are opposite each other. This prevents the sensor from being placed on a site that is too thick for proper operation.

Position the sensor so that the tape does not extend over the space between the fingers or toes. This insures there will be no light transmission through this space.

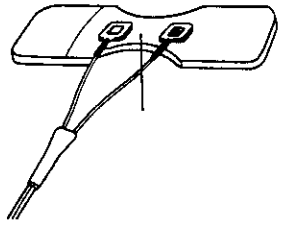


Adult/Pediatric Finger





Pediatric Toe



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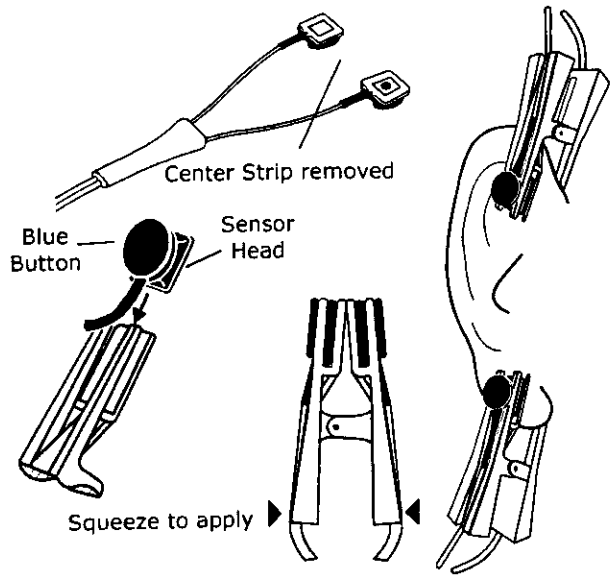
Using the Ear Clip

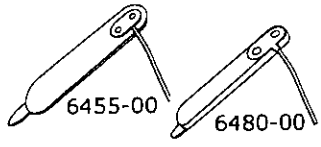
To use the ear clip;

1. Remove the center strip from the Y-Sensor.
2. Slide each Y-Sensor head into an Ear Clip receptacle with the blue button facing outwards.
3. Open the clip by squeezing its ends and apply it to the ear.
   - It may be necessary to rub the ear with your fingers in order to increase circulation prior to applying the sensor.
   - Adhesive Dots (8700-00) are included with the ear clip to help hold the clip to the ear.



Single Patient Use Sensors

These Single Patient Use Sensors are for use on appropriately sized patients.



- 6455-00. Pediatric/Adult, Foam Wrap Style
  — Adult or appropriately sized pediatric patients.
- 6480-00. Neonatal/Pediatric, Foam Wrap Style
  — Neonatal or appropriately sized pediatric patients.

CAUTION:

Single Patient Use SpO_2 sensors can be reapplied to a single patient as needed, but should not be used across multiple patients. Single Patient Use sensors should not be cleaned or disinfected. System performance may be compromised as a result. Replace sensor instead.

1. Select the appropriate size sensor based on the patient type.
2. With the blue foam towards the patient, wrap around the site. Ensure the sensor heads are opposite each other through the tissue. This prevents the sensor from being placed on a site that is too thick for proper operation.

   Position the sensor so that the tape does not extend over the space between the fingers or toes. This insures there will be no light transmission through this space.
3. Secure in place with the white plastic tab.
   - Double-sided adhesive dots, included with the sensor, can be applied over the LED and detector components to help hold the sensor to the site.

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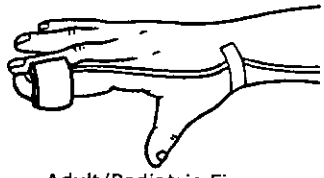
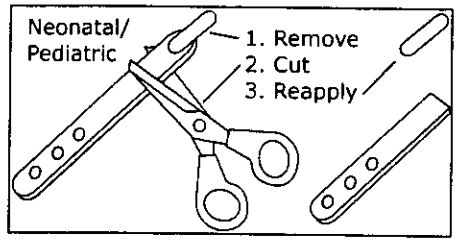
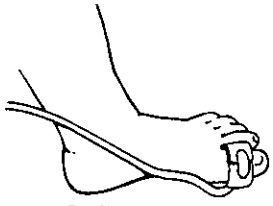
- The tab on the Neonatal/Pediatric sensor is removable, allowing shortening for a better fit. Reapply the tab to secure the sensor in place.

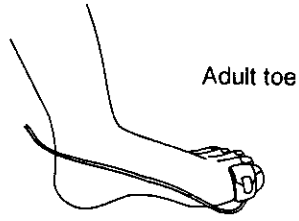


Adult/Pediatric Finger

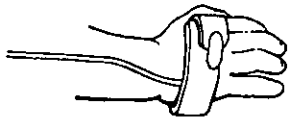




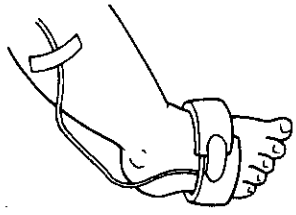
Pediatric Toe



Adult toe



Neonatal hand



Neonatal foot

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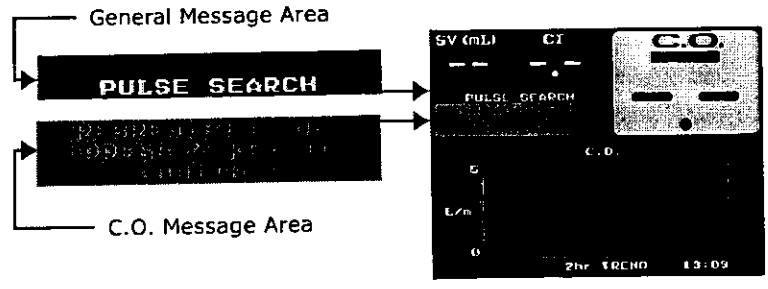
NICO®

Messages

Message Areas - Cardiac Output mode

For Respiratory Mechanics messages, see page 83.

In Cardiac Output mode, the monitor uses two screen locations, the General Message Area and the C.O. Message Area, to convey information to the user.



General Message Area

The General Message Area in Cardiac Output mode displays system status, alert, and error conditions. It may be blank or:

- contain 1 single-line message
- contain 2 single-line messages
- contain 1 multi-line message

The General Message Area messages are listed below, in alphabetical order.

(Alert Class: H-High Priority, M-Medium Priority, L-Low Priority, S-Status Message. See "Alert Priorities" on page 61 for details.)

General Message Area	Message Description	Alert Class
ALERTS OFF	Displayed as a reminder that the default for all user selectable alerts is OFF. To cancel the message, adjust any individual limit value and activate the audible alert. Both the alert limit and audible alert must be activated.	S
AMBIENT LIGHT COVER SpO_2 PROBE	The monitor detects interference on the SpO_2 sensor from ambient light. This can be corrected by covering the SpO_2 sensor, or possibly by changing the sensor site.	S
CHECK / CHANGE AIRWAY ADAPTER	A change in the CO_2 adapter portion of the NICO Sensor is detected. Possible causes: • CAPNOSTAT® CO_2 sensor off adapter • High level of moisture and/or secretions in the adapter. The moisture can be drained from the NICO Sensor and re-inserted in the circuit. Facing the pneumatic tubing upward as it exits the NICO Sensor can minimize this.	S

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General Message Area	Message Description	Alert Class
CO_2 SENSOR FAILURE REPLACE SENSOR	A problem with the CAPNOSTAT® CO_2 sensor has been identified. Replace the CAPNOSTAT® CO_2 sensor and return it to Novametrix for service.	M
CO_2 SENSOR?	The CAPNOSTAT® CO_2 sensor is not connected to the NICO® monitor.	S
CO_2 ZERO REQUIRED (MENU→SETUP)	The CAPNOSTAT® CO_2 sensor needs to be zeroed. Press the **MENU** key, then select **SETUP**, then **CO2 ZERO NOW**, and follow the instructions on the screen. NOTE: the CO_2 adapter provided with the CAPNOSTAT® CO_2 sensor can be used for the CO_2 zero procedure rather than a new NICO Sensor.	S
DEMO MODE	The monitor is in demonstration mode and is not displaying patient data (all data is simulated). To exit demo mode, turn the monitor off, then back on.	S
$ETCO_2$: XX mmHg	End tidal CO_2 is greater than 60 mmHg or exceeds the high alert limit. Appears in the general message area to supplement screens that do not display the $ETCO_2$ value.	L
HIGH C.O.	The displayed cardiac output value is above the set alert limit in the **SET ALERTS** screen (press **MENU** key, then select **SET ALERTS** to view the alert limit settings).	M
HIGH $ETCO_2$	The displayed $ETCO_2$ value is above the set alert limit in the **SET ALERTS** screen (press **MENU** key, then select **SET ALERTS** to view the alert limit settings).	H
HIGH PULSE	The displayed pulse rate value is above the set alert limit in the **SET ALERTS** screen (press **MENU** key, then select **SET ALERTS** to view the alert limit settings).	M
HIGH RESP RATE	The displayed respiration rate value is above the set alert limit in the **SET ALERTS** screen (press **MENU** key, then select **SET ALERTS** to view the alert limit settings).	M
HIGH SpO_2	The displayed SpO_2 value is above the set alert limit in the **SET ALERTS** screen (press **MENU** key, then select **SET ALERTS** to view the alert limit settings).	M
INCOMPATIBLE CO_2 SENSOR	The wrong part number CAPNOSTAT® CO_2 sensor is connected to the NICO monitor. Use only a CAPNOSTAT® CO_2 sensor with part number 9567-00 (this can be distinguished from other CAPNOSTAT® CO_2 sensor part numbers by the yellow part number label on the sensor's electrical connector).	M
INCOMPATIBLE FLOW SENSOR	The wrong flow sensor is connected to the NICO monitor. Use only a NICO Sensor, part numbers 8950-00, 8951-00 or 8952-00 (the correct flow sensor is an integral part of the NICO Sensor).	M
INFANT MODE ON	**INFANT MODE** is enabled in the **SETUP** menu to accommodate neonatal and smaller patients (press **MENU** key, then select **SETUP** to adjust the **INFANT MODE** setting).	S
INSP CO_2: xx	(where xx is a numeric value with units of mmHg, kPa, or %). At least 3 mmHg, 0.1% or 0.1 kPa of CO_2 has been detected during inspiration (other than during rebreathing) for at least ten continuous seconds.	S
LOW C.O.	The displayed cardiac output value is below the set alert limit in the **SET ALERTS** screen (press **MENU** key, then select **SET ALERTS** to view the alert limit settings).	H

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General Message Area	Message Description	Alert Class
LOW $ETCO_2$	The displayed $ETCO_2$ value is below the set alert limit in the **SET ALERTS** screen (press **MENU** key, then select **SET ALERTS** to view the alert limit settings).	M
LOW PULSE	The displayed pulse rate value is below the set alert limit in the **SET ALERTS** screen (press **MENU** key, then select **SET ALERTS** to view the alert limit settings).	H
LOW RESP RATE	The displayed respiration rate value is below the set alert limit in the **SET ALERTS** screen (press **MENU** key, then select **SET ALERTS** to view the alert limit settings).	M
LOW SpO_2	The displayed SpO_2 value is below the set alert limit in the **SET ALERTS** screen (press **MENU** key, then select **SET ALERTS** to view the alert limit settings).	H
MONITOR INOPERABLE AIRWAY ZERO ERROR	The NICO monitor detected a problem with its pneumatic flow and pressure sub-system. Contact qualified personnel for monitor repair or exchange.	L
MONITOR INOPERABLE BARO PRESS ERROR	The NICO monitor detected a problem with its internal barometric pressure sensor. Contact qualified personnel for monitor repair or exchange.	L
MONITOR INOPERABLE CLOCK FAILURE	The NICO monitor detected a problem with its internal clock. Contact qualified personnel for monitor repair or exchange.	L
MONITOR INOPERABLE EEPROM ERROR	The NICO monitor detected a problem with its internal memory. Contact qualified personnel for monitor repair or exchange.	L
MONITOR INOPERABLE FLOW ZERO ERROR	The NICO monitor detected a problem with its flow zeroing sub-system or related pneumatic components. Contact qualified personnel for monitor repair or exchange.	L
MONITOR INOPERABLE MARS HDW ERROR	The NICO monitor detected a problem with its pulse oximetry sub-system. Contact qualified personnel for monitor repair or exchange.	L
MONITOR INOPERABLE NICO VALVE ZERO ERR	The NICO monitor detected a problem with its internal rebreathing valve control circuitry or related pneumatic components. Contact qualified personnel for monitor repair or exchange.	L
MONITOR INOPERABLE SpO_2 HDW ERROR	The NICO monitor detected a problem with its pulse oximetry sub-system. Contact qualified personnel for monitor repair or exchange.	L
NO RESP: xx:xx	The time selected in the **SET ALERTS** screen for the NO RESP (no respiration) alert was exceeded since the end of the last detected breath (press **MENU** key, then select **SET ALERTS** to view the alert limit settings).	H
PULSE SEARCH	The pulse oximeter is not detecting a sufficient pulse. This could be due to: • SpO_2 sensor is off of the patient • Insufficient perfusion at the site. Reposition sensor. • Tissue at the site is too thick or too thin. Reposition sensor.	S
SpO_2?	The monitor is in N-395 interface mode, but SpO_2 data is not being received via the interface. An alarm is not generated.	S
SpO_2 PROBE FAILURE	The pulse oximeter sensor is faulty. Replace the sensor and contact qualified service personnel.	M

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General Message Area	Message Description	Alert Class
SpO_2 PROBE?	• The pulse oximeter sensor was not connected to the NICO monitor when it was powered up. • (Flashing) SpO_2 sensor was disconnected from the monitor after it was powered up. Acknowledge by pressing the Silence key.	S
WARMUP	The CAPNOSTAT® CO_2 sensor is not at proper operating temperature yet.	S

C.O. Message Area

The C.O. Message Area is dedicated to cardiac output related information and may be blank or contain a message.

The C.O. Message Area messages are listed below, in alphabetical order.

(Alert Class: H-High Priority, M-Medium Priority, L-Low Priority, S-Status Message. See "Alert Priorities" on page 61 for details.)

C.O. Message Area	Message Description	Alert Class
BLOOD GASES HAVE BEEN RESET	A NICO cycle has started after 20 minutes of a no respiration timeout. Data not available when no breaths are detected 20 minutes after the last detected breath.	S
CONSIDER USING SMALL NICO SENSOR	Resizing the NICO Loop was not effective because the ventilator set tidal volume is less than 300 ml. The NICO monitor is suggesting a different sized sensor, with smaller loop, to correct the condition.	L
CONSIDER USING STANDARD NICO SENSOR	If a small NICO Sensor is currently in use: Resizing the NICO Loop was not effective because the ventilator set tidal volume is greater than 500 ml. The NICO monitor is suggesting a different sized sensor, with a larger loop, to correct the condition. If a large NICO Sensor is currently in use: Resizing the NICO Loop was not effective because the ventilator set tidal volume is less than 1000 ml. The NICO monitor is suggesting a different sized sensor, with a smaller loop, to correct the condition.	L
CONSIDER USING LARGE NICO SENSOR	Resizing the NICO Loop was not effective because the ventilator set tidal volume is greater than 1000 ml. The NICO monitor is suggesting a different sized sensor, with a larger loop, to correct the condition.	L
EXPAND LOOP	The NICO Loop (expandable rebreathing volume on the NICO Sensor) needs to be expanded. Expand the loop by approximately 3-6 inches or until the message is removed. Note that the message is displayed only during the rebreathing phase of the NICO cycle. If the loop is not appropriately sized by the end of the rebreathing phase, the message will be removed and displayed again during the next rebreathing phase. If this message persists with maximal expansion of the NICO Loop, the tidal volume may be too large for the ventilatory conditions for the NICO monitor to report accurate results.	L

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C.O. Message Area	Message Description	Alert Class
NEXT ↻: xx:xx	There are x:xx minutes:seconds until the beginning of the next rebreathing period (provided as an indicator as to the current state of the NICO cycle).	S
NICO SENSOR?	The NICO Sensor has not been connected to the monitor since it was last turned on.	S
NOISY SIGNALS	The NICO monitor was not able to calculate an averaged cardiac output value. This can be due to: • Spontaneous breaths or efforts • Surgeon moving the lungs • Ventilator adjustments	L
↻REBREATHING	The patient is currently rebreathing a portion of his/her tidal volume in order for the NICO monitor to calculate cardiac output (provided as an indicator of the current state of the NICO cycle). The rebreathing phase of the NICO cycle lasts for 50 seconds.	S
REBREATHING OFF	Rebreathing and therefore C.O. measurements are currently disabled. The **STOP/CONTINUE REBREATHING** key is illuminated amber while rebreathing is off, and can be pressed to enable rebreathing and C.O. measurements. Rebreathing is off when: • The monitor is first turned on until the **STOP/CONTINUE REBREATHING** key is pressed • The **STOP/CONTINUE REBREATHING** key is pressed while C.O. measurements are enabled • The monitor detected a system fault or condition which warrants automatic disabling of C.O. measurements	S
REBREATHING OFF ADAPTER DISCONNECT REMOVE FROM CIRCUIT	The NICO Sensor was disconnected from the monitor after C.O. measurements had been made since the last power-up. The NICO Sensor should be removed from the breathing circuit in order to avoid leaking breathing circuit gas through the sensor connector.	S
REBREATHING OFF LARGE NICO SENSOR IDENTIFIED	A large size NICO Sensor was just connected to the NICO monitor.	S
REBREATHING OFF SMALL NICO SENSOR IDENTIFIED	A small size NICO Sensor was just connected to the NICO monitor.	S
REBREATHING OFF STANDARD NICO SENSOR IDENTIFIED	A standard size NICO Sensor was just connected to the NICO monitor.	S
REBREATHING OFF NICO SENSOR FAILURE	A problem with the NICO Sensor was detected by the monitor. Discard the sensor and replace it. If the problem persists, contact qualified service personnel.	M
REBREATHING OFF PRESS ⊘ KEY TO CONTINUE	Rebreathing and therefore C.O. measurements are currently disabled and can be enabled by pressing the **STOP / CONTINUE REBREATHING** key.	S
REBREATHING PAUSED WAITING FOR $ETCO_2$ < XX	Rebreathing and therefore C.O. measurements have been temporarily paused automatically by the monitor, and will resume automatically once the indicated parameter is within the stated range (here, XX = 85 mmHg, 11.5 kPa, 11.5 %).	L

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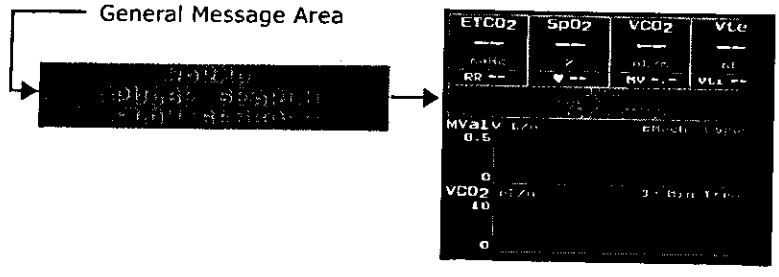
C.O. Message Area	Message Description	Alert Class
REBREATHING PAUSED WAITING FOR $ETCO_2$ > XX	Rebreathing and therefore C.O. measurements have been temporarily paused automatically by the monitor, and will resume automatically once the indicated parameter is within the stated range (here, XX = 15 mmHg, 2.0 kPa, 2.0 %).	L
REBREATHING PAUSED WAITING FOR RR < 60 br/m	Rebreathing and therefore C.O. measurements have been temporarily paused automatically by the monitor, and will resume automatically once the indicated parameter is within the stated range.	L
REBREATHING PAUSED WAITING FOR RR > 3 br/m	Rebreathing and therefore C.O. measurements have been temporarily paused automatically by the monitor, and will resume automatically once the indicated parameter is within the stated range.	L
REBREATHING PAUSED WAITING FOR VCO_2 > 20 mL/min	Rebreathing and therefore C.O. measurements have been temporarily paused automatically by the monitor, and will resume automatically once the indicated parameter is within the stated range.	L
REBREATHING PAUSED WAITING FOR Vt > 200 mL	Rebreathing and therefore C.O. measurements have been temporarily paused automatically by the monitor, and will resume automatically once the indicated parameter is within the stated range.	L
RETRACT LOOP	The NICO Loop (expandable rebreathing volume on the NICO Sensor) needs to be retracted (made smaller). Retract the loop by approximately 3-6 inches or until the message is removed. Note that the message is displayed only during the rebreathing phase of the NICO cycle. If the loop is not appropriately sized by the end of the rebreathing phase, the message will be removed and displayed again during the next rebreathing phase. If this message persists with the NICO Loop at its minimal size, the tidal volume may be too small for the ventilatory conditions for the NICO monitor to report accurate results.	L

Message Areas - Respiratory Mechanics mode

For Cardiac Output messages, see page 78.

In Respiratory Mechanics mode, the monitor uses one General Message Area to convey information to the user.



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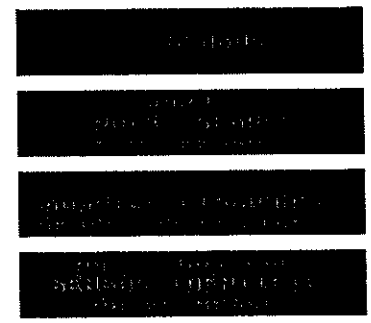
General Message Area

The General Message Area in Respiratory Mechanics mode displays all messages, including system status, alert, and error conditions. It may be blank or:

- contain 1, 2 or 3 single-line messages
- contain 1 multi-line message
- contain 1 multi-line message and 1 single-line message



The General Message Area messages are listed below, in alphabetical order.

(Alert Class: H-High Priority, M-Medium Priority, L-Low Priority, S-Status Message. See "Alert Priorities" on page 61 for details.

General Message Area	Message Description	Alert Class
ADAPTER DISCONNECT REMOVE FROM CIRCUIT	The CO_2/Flow sensor is not connected to the NICO monitor. The CO_2/Flow sensor should be removed from the breathing circuit in order to avoid leaking breathing circuit gas through the sensor's connector. NOTE: If a two-line message will not fit in the General Message Area because other higher priority messages are present, the message "FLOW SENSOR?" will be used for the same condition.	S
ADULT CO_2/FLOW SENSOR IDENTIFIED	An adult size CO_2/Flow sensor was just connected to the NICO monitor.	S
ALERTS OFF	Displayed as a reminder that the default for all user selectable alerts is OFF. To cancel the message, adjust any individual limit value and activate the audible alert. Both the alert limit and audible alert must be activated.	S
AMBIENT LIGHT COVER SpO_2 PROBE	The monitor detects interference on the SpO_2 sensor from ambient light. This can be corrected by covering the SpO_2 sensor, or possibly by changing the sensor site.	S
CHECK / CHANGE AIRWAY ADAPTER	A change in the CO_2 adapter portion of the CO_2/Flow sensor is detected. Possible causes: • CAPNOSTAT® CO_2 sensor off adapter • High level of moisture and/or secretions in the adapter. Replace if needed.	S
CO_2 SENSOR FAILURE REPLACE SENSOR	A problem with the CAPNOSTAT® CO_2 sensor has been identified. Replace the CAPNOSTAT® CO_2 sensor and return it to Novametrix for exchange or repair.	M
CO_2 SENSOR?	The CAPNOSTAT® CO_2 sensor is not connected to the NICO monitor.	S
CO_2 ZERO REQUIRED (MENU→SETUP)	The CAPNOSTAT® CO_2 sensor needs to be zeroed. Press the **MENU** key, then select **SETUP**, then **CO2 ZERO NOW**, and follow the instructions on the screen. NOTE: the CO_2 adapter provided with the CAPNOSTAT® CO_2 sensor can be used for the CO_2 zero procedure rather than a new sensor.	S
DEMO MODE	The monitor is in demonstration mode and is not displaying patient data (all data is simulated). To exit demo mode, turn the monitor off, then back on.	S

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General Message Area	Message Description	Alert Class
$ETCO_2$ > XX mmHg	End tidal CO_2 is greater than 60 mmHg or exceeds the high alert limit. Appears in the general message area to supplement screens that do not display the $ETCO_2$ value.	L
FLOW SENSOR?	The CO_2/Flow sensor is disconnected. NOTE: This message may also be used in place of ADAPTER DISCONNECT REMOVE FROM CIRCUIT, when a two-line message will not fit in the General Message Area.	S
HIGH $ETCO_2$	The displayed $ETCO_2$ value is above the set alert limit in the **SET ALERTS** screen (press **MENU** key, then select **SET ALERTS** to view the alert limit settings).	H
HIGH PULSE	The displayed pulse rate value is above the set alert limit in the **SET ALERTS** screen (press **MENU** key, then select **SET ALERTS** to view the alert limit settings).	M
HIGH RESP RATE	The displayed respiration rate value is above the set alert limit in the **SET ALERTS** screen (press **MENU** key, then select **SET ALERTS** to view the alert limit settings).	M
HIGH SpO_2	The displayed SpO_2 value is above the set alert limit in the **SET ALERTS** screen (press **MENU** key, then select **SET ALERTS** to view the alert limit settings).	M
HIGH VCO_2	The displayed VCO_2 value is above the set alert limit in the **SET ALERTS** screen (press **MENU** key, then select **SET ALERTS** to view the alert limit settings).	M
INCOMPATIBLE CO_2 SENSOR	The wrong part number CAPNOSTAT® CO_2 sensor is connected to the NICO monitor. Use only a CAPNOSTAT® CO_2 sensor with part number 9567-00 (this can be distinguished from other CAPNOSTAT® CO_2 sensor part numbers by the yellow part number label on the sensor's electrical connector).	M
INCOMPATIBLE FLOW SENSOR	The wrong flow sensor is connected to the NICO monitor. Use only a NICO CO_2/Flow sensor part number 9765-00, 9766-00, or 9767-00. If message persists, a hardware error is may exist. Contact qualified personnel for monitor repair or exchange.	M
INFANT MODE ON	**INFANT MODE** is enabled in the **SETUP** menu to accommodate neonatal and smaller patients (press **MENU** key, then select **SETUP** to adjust the **INFANT MODE** setting).	S
INSP CO_2: xx	(where xx is a numeric value with units of mmHg, kPa, or %). At least 3 mmHg, 0.1% or 0.1 kPa of CO_2 has been detected during inspiration (other than during rebreathing) for at least ten continuous seconds.	S
LOW $ETCO_2$	The displayed $ETCO_2$ value is below the set alert limit in the **SET ALERTS** screen (press **MENU** key, then select **SET ALERTS** to view the alert limit settings).	M
LOW PULSE	The displayed pulse rate value is below the set alert limit in the **SET ALERTS** screen (press **MENU** key, then select **SET ALERTS** to view the alert limit settings).	H
LOW RESP RATE	The displayed respiration rate value is below the set alert limit in the **SET ALERTS** screen (press **MENU** key, then select **SET ALERTS** to view the alert limit settings).	M
LOW SpO_2	The displayed SpO_2 value is below the set alert limit in the **SET ALERTS** screen (press **MENU** key, then select **SET ALERTS** to view the alert limit settings).	H

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General Message Area	Message Description	Alert Class
LOW VCO_2	The displayed VCO_2 value is below the set alert limit in the **SET ALERTS** screen (press **MENU** key, then select **SET ALERTS** to view the alert limit settings).	M
MONITOR INOPERABLE AIRWAY ZERO ERROR	The NICO monitor detected a problem with its pneumatic flow and pressure sub-system. Contact qualified personnel for monitor repair or exchange.	L
MONITOR INOPERABLE BARO PRESS ERROR	The NICO monitor detected a problem with its internal barometric pressure sensor. Contact qualified personnel for monitor repair or exchange.	L
MONITOR INOPERABLE CLOCK FAILURE	The NICO monitor detected a problem with its internal clock. Contact qualified personnel for monitor repair or exchange.	L
MONITOR INOPERABLE EEPROM ERROR	The NICO monitor detected a problem with its internal memory. Contact qualified personnel for monitor repair or exchange.	L
MONITOR INOPERABLE FLOW ZERO ERROR	The NICO monitor detected a problem with its flow zeroing sub-system or related pneumatic components. Contact qualified personnel for monitor repair or exchange.	L
MONITOR INOPERABLE MARS HDW ERROR	The NICO monitor detected a problem with its pulse oximetry sub-system. Contact qualified personnel for monitor repair or exchange.	L
MONITOR INOPERABLE SpO_2 HDW ERROR	The NICO monitor detected a problem with its pulse oximetry sub-system. Contact qualified personnel for monitor repair or exchange.	L
NEONATAL CO_2/FLOW SENSOR IDENTIFIED	A neonatal size CO_2/Flow sensor was just connected to the NICO monitor.	S
NO RESP: xx:xx	The time selected in the **SET ALERTS** screen for the NO RESP (no respiration) alert was exceeded since the end of the last detected breath (press **MENU** key, then select **SET ALERTS** to view the alert limit settings).	H
PEDIATRIC CO_2/FLOW SENSOR IDENTIFIED	A pediatric size CO_2/Flow sensor was just connected to the NICO monitor.	S
PULSE SEARCH	The pulse oximeter is not detecting a sufficient pulse. This could be due to: • SpO_2 sensor is off of the patient • Insufficient perfusion at the site • Tissue at the site is too thick or too thin	S
SpO_2?	The monitor is in N-395 interface mode, but SpO_2 data is not being received via the interface. An alarm is not generated.	S
SpO_2 PROBE FAILURE	The pulse oximeter sensor is faulty. Replace the sensor and contact qualified service personnel.	M
SpO_2 PROBE?	• The pulse oximeter sensor was not connected to the NICO monitor when it was powered up. • (Flashing) SpO_2 sensor was disconnected from the monitor after it was powered up. Acknowledge by pressing the Silence key.	S
WARMUP	The CAPNOSTAT® CO_2 sensor is not at proper operating temperature yet.	S

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External Devices

The NICO monitor provides both analog and digital means of communicating with external devices. The monitor must be set to the appropriate interface.

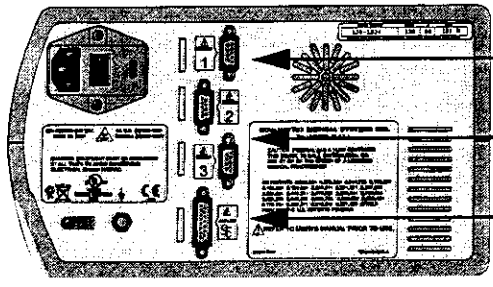
1 Press the **MENU** key to activate **SELECT A SCREEN**. The key's green icon illuminates.
   - Press the key again to return to the previously displayed screen.

2 Highlight and then select **SETUP** by turning and then pressing the **KNOB**.

3 The **SETUP** screen is displayed.

4 Turn and press the **KNOB** to select **INPUT/OUTPUT**.

All interfaces, printers and external devices are selected from the **INPUT/OUTPUT** screen. All devices are connected to a rear panel connector using an appropriate cable.



Printing

The NICO monitor provides an HP (Hewlett-Packard) compatible printer interface. When activated, printing is available from the Cardiopulmonary **TREND** screen.Refer to "Cardiopulmonary Trend Screen" on page 46. The **PRINT** selection is dimmed until the NICO monitor is set to the **HP PRINTER OUTPUT** interface in the **RS232-2** or **RS232-3** screen.

Setup

From the **INPUT/OUTPUT** screen:

1 Turn and press the **KNOB** to select **RS232-2** or **RS232-3**.

2 Turn and press the **KNOB** to select **HP PRINTER OUTPUT**.

3 Connect the printer to the appropriate rear panel connector. A serial cable and a serial to parallel converter is required. Contact Novametrix Service for converter recommendations.

4 Configure your serial to parallel converter to 19200 bps, no parity, 8 data bits, 1 stop bit, XON/XOFF handshaking.

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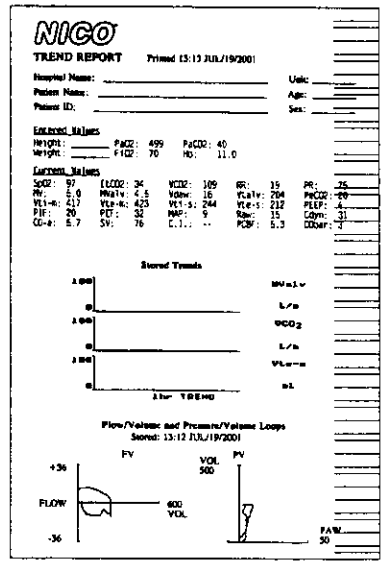
Output

Output to the printer includes entered values, current values, stored flow/volume and pressure/volume loops and stored trends. To change the trend selection, see "Cardiopulmonary Trend Screen" on page 46. To store FV/PV loops, see "Flow Volume and Pressure Volume Loops" on page 44.

Space is provided at the top of the printout for hospital and patient information.



ASCII Output

The NICO monitor must be set to the appropriate interface for output to a serial printer or data collection using a PC. From the **INPUT/OUTPUT** screen:

1. Turn and press the **KNOB** to select **RS232-2** or **RS232-3**.
2. Turn and press the **KNOB** to select:
   - **ASCII OUTPUT 1** to a serial printer
   - **ASCII OUTPUT 2** for data collection using a PC
3. Connect the device to the appropriate rear panel connector.

Output to a Serial Printer

For output to a serial printer such a strip chart recorder or the Seiko DPU-414 printer, configure your serial printer to 9600 bps, no parity, 8 data bits, 1 stop bit.

An output sample is shown at right:

JUL 6, 2000		9:47:14		
C.O.	C.I.	S.V.	C.O.-f	PCBF
5.2	2.8	69	5.2	4.9
VCO2	MV	Mvalv	Vti	Vte
0	0.0	0.0	0	0
PIP	MAP	PEEP	Cdyn	Raw
23	9	4	27	15
ETCO2	RR	SpO2	PR	
33.9	15	97	75	

Output files for use on a PC

When configured to **ASCII OUTPUT 2**, the NICO monitor will output a text string that can be imported into a spreadsheet program. Configure your serial device to 19200 bps, no parity, 8 data bits, 1 stop bit.

Data is output once every breath. An output sample is shown below:

10:40:04, PR=75, SPO2=97, RR=20, C.O.=0.0, C.O.-f=0.0, CI=0.0, SV=0, VCO2=429, ETCO2=39, PECO2=32, MV=12.2, MVALV=11.0, Vti=916, Vte=907, Vtalv=546, VdAW=63, PIP=45, MAP=22, PEEP=9, Cdyn=27, Raw=13

Analog Output

The NICO monitor directly supports interface to analog devices such as strip chart recorders, etc. Set the monitor to the appropriate interface from the **INPUT/OUTPUT** screen:

Setup

1. Turn and press the **KNOB** to select **ANALOG OUT 1-4**.
2. Turn and press the **KNOB** to select the parameters you want from **ANALOG OUT 1-4** (maximum of 1 per), to be transmitted to an analog device.

   CO, CI, SV, PCBF, $ETCO_2$, SpO_2, resp rate, and pulse rate value outputs are available, as well as CO_2, plethysmogram, flow, and airway pressure waveform data.
3. Calibrate the recorder to the correct voltage levels using the **ANALOG CAL.** setting. Press

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ZERO, **HALF** and **FULL** to set the analog outputs.

- **ZERO** — 0 volts
- **HALF** — 0.50 volts
- **FULL** — 1.00 volts

Agilent Technologies VueLink Interface

The NICO monitor interface to the Agilent Technologies[1] VueLink module provides a pathway for data from the monitor to be viewed on the Agilent Technologies Patient Monitoring System. Data from the NICO monitor is available for display in conjunction with the other parameters configured for display on the Agilent Technologies Patient Monitor.

Setup

To setup and connect the NICO monitor to the Agilent VueLink module, you will need the following:

- NICO monitor with software revision 3.1 or greater.
- Agilent Patient Monitor with software revision C (9.xx) or higher.
- Agilent VueLink module, Auxiliary Plus B with Open Interface (product number M1032 option A05).
- Agilent 4-meter VueLink Interface Cable (part number K6B)
- 25-pin female to 9-pin male null modem (crossover) cable

NOTE: The Agilent Patient Monitor, VueLink Module and Agilent interface cable are supplied by Agilent.

The NICO monitor must be set to the appropriate interface for output to the VueLink module. From the **INPUT/OUTPUT** screen:

1. Turn and press the **KNOB** to select **RS232-2** or **RS232-3**.
2. Turn and press the **KNOB** to select **VUELINK**.
3. Connect the VueLink Interface Cable to the null modem cable, then connect the null modem cable to the rear panel of the NICO monitor (RS232-2 or RS232-3). Tighten screws.
4. Connect the VueLink cable to the VueLink module.
5. Refer to the operator's manuals for the Agilent VueLink Module and the Agilent Patient Monitor prior to use.

Alerts and Messages

Alarms and messages are not transmitted from the NICO monitor to the Agilent VueLink module. All alarms and messages should be viewed directly from the NICO monitor.

Transmitted Parameters

The parameter selection varies depending upon whether you are in Cardiac Output mode or Respiratory Mechanics mode.

Label	Parameter	Units
AWRR	Respiratory Rate	rpm
Cdyn	Dynamic Compliance	ml/cmH_2O
RAW e	Expired Airway Resistance (Dynamic)	cmH_2O/L/S
PIP	Peak Inspiratory Pressure	cmH_2O
PEEP	Positive End Expiratory Pressure	cmH_2O
Pmean	Mean Airway Pressure	cmH_2O
Pulse	Pulse Rate	bpm
SpO_2	SpO_2	%

1.Agilent Technologies was formerly Hewlett-Packard. The information above also applies to existing HP products.

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Label	Parameter	Units
$ETCO_2$	$ETCO_2$	*mmHg, %, kPa
$PECO_2$	Mixed Expired CO_2	*mmHg, %, kPa
PEF	Peak Expiratory Flow	L/min
TVin	Inspired Tidal Volume	ml
TVex	Expired Tidal Volume	ml
MV t	Total Minute Volume	L
MV s	Spontaneous Minute Volume	L
MV m	Mechanical Minute Volume	L
VCO_2	CO_2 Elimination	ml/min
VD aw	Airway Deadspace	ml
Respiratory Mechanics Mode only:		
RAW i	Inspired Airway Resistance (Dynamic)	$cmH_2O/L/S$
VT alv t	Total Alveolar Tidal Volume	ml
VT alv s	Spontaneous Alveolar Tidal Volume	ml
VT alv m	Mechanical Alveolar Tidal Volume	ml
MV alv	Alveolar Minute Volume (Total)	L
VdVtPh	Physiologic deadspace to tidal volume ratio	
Cardiac Output Mode only:		
CO-a	Average Cardiac Output	L/min
CO-f	Fast-mode Cardiac Output	L/min
CI	Cardiac Index	$L/min/m^2$
PCBF	Pulmonary Capillary Blood Flow	L/min
SV	Stroke Volume	ml
SVR	Systemic Vascular Resistance	dynes sec/cm^5

*CO_2 parameters are reported in either mmHg, kPa, or %, depending upon the CO_2 units currently selected for the NICO monitor.

Transmitted Waveforms

A total of five waveform are transmitted to the Agilent Patient Monitor; a maximum of two may viewed at one time.

Label	Waveform	Units
AWF	Airway Flow	L
AWP	Airway Pressure	cmH_2O
CO_2	CO_2 Capnogram	mmHg, %, kPa
PLETH	Plethysmogram	N/A
AWV	Volume	ml

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GE Medical Systems Solar® Interface

The NICO monitor connects to the Solar® monitor from GE Medical Systems Information Technologies (GEMS-IT), via an Octanet and a DIDCA™ interface adapter, both available from GEMS-IT. Solar® interface software is compatible with NICO monitor software release 3.1 or above. [1]

Transmitted Parameters

The following parameters are transmitted from the NICO monitor to the Solar® monitor.

- The CO, CI, SV, CO confidence level and PCBF values will be displayed in the parameter block for the NICO monitor.
- Four of the following sub parameters can be displayed in the RM parameter block: PEF, MV, MVs, MVm, TV, TVs, TVm, PIP, MAWP, PEEP, RR, RRs, RRm, I:E, CYDN, RAWe.
- The CO_2 inspired, CO_2 expired, and respiration rate (RR) values will be displayed in the CO_2 parameter block.
- The SPO_2 value and pulse rate (RATE) value will be displayed in the SPO_2 parameter block.

Setup

To setup and connect the NICO monitor to the GEMS-IT Solar® monitor, you will need the following:

- NICO monitor with software revision 3.1 or greater
- GEMS-IT Solar® monitor, Model 7000, or 8000 with software version V6A or higher, or GEMS-IT Solar® monitor, Model 8000M with software version V1A or higher
- GEMS-IT Octanet module, (PN: OCTANET=A)
- DIDCA™ interface adapter, (PN: 420915-058)
- GEMS-IT Octanet cable (PN: 418335-00x). Cables come in various lengths and are available from GEMS-IT.
- GEMS-IT Solar® monitor cable (PN: 409752-00x or 700520-00x)
- Optional: GEMS-IT TRAM-Net Hub (PN: 410217-001) and TRAM-Net cable (PN: 409752-00x). Instructions for use of the TRAM-Net are detailed within Octanet and other service documents provided by GEMS-IT.

  NOTE: All GEMS-IT parts are supplied by GEMS-IT.

1. Connect the DIDCA™ interface adapter to the connector labeled RS232-1 on the back of the NICO monitor. The interface adapter is programmed specifically to work with a NICO monitor.
2. Connect the Octanet cable between the interface adapter and one of the eight Octanet serial ports.
3. Connect the Solar monitor cable (PN: 409752-00x for Models 7000 and 8000, PN: 700752-00x for model 8000M) from the Octanet to the Solar® monitor
4. Complete the communication cabling by referring to the instructions found in the Octanet Connectivity Device Service Manual (PN: 418264-003).
5. Ensure Octanet serial port LED is steady green.

Alerts and Messages

Most alarms and messages are not transmitted from the NICO monitor to the GEMS-IT Solar® monitor. All alarms and messages should be viewed directly from the NICO monitor.

Nellcor Model N-395 Interface

The N-395 Interface provides a pathway for pulse rate and oxygen saturation data from the Nellcor Model N-395 Pulse Oximeter to be viewed on the NICO monitor. When the interface is selected, pulse rate data from the N-395 is used by the NICO monitor for stroke volume (SV)

1.If the software in your NICO monitor is updated, please complete and fax the software notification found in the GEMS-IT service manual, so GEMS-IT can confirm continued compatibility.

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and stroke volume index (SVI) calculations; SpO_2 measurements are used for intrapulmonary shunt calculations.

The units interact in several ways:

- Numeric data for SpO_2 and pulse rate is obtained from the N-395 and displayed on the NICO monitor.
- A Pleth/SpO_2 waveform appears on the N-395 only. The message "Pleth Not Available" appears on the NICO monitor in the waveform plot area.
- SpO_2 and pulse rate alerts and alarms on the NICO monitor are derived from the data obtained by the N-395.
- If the NICO monitor is not receiving data from the N-395, the message "SpO_2?" is displayed.
- If the N-395 interface is selected and both Novametrix and Nellcor oximetry sensors are connected, the Novametrix readings will override the N-395 readings on the NICO monitor. Disconnecting the Novametrix oximetry sensor will allow the N-395 data to be transmitted.

Setup

To set up and connect the Nellcor N-395 pulse oximeter to the NICO monitor, you will need the following:

- NICO monitor with software revision 4.5 or greater
- Nellcor Pulse Oximeter, Model N-395
- 15-pin to 9-pin interface cable (supplied by Nellcor)

The NICO monitor must be set to the appropriate interface for output to the Nellcor N-395 pulse oximeter. From the **INPUT/OUTPUT** screen:

1. Turn and press the **KNOB** to select **RS232-2** or **RS232-3**.
2. Turn and press the **KNOB** to select **N-395**.
3. Be sure a Novametrix oximetry sensor is NOT connected to the NICO monitor.
4. Connect the interface cable to the N-395 monitor, then to the rear panel of the NICO monitor. Tighten screws.
5. Refer to the Nellcor N-395 operator's manual.

SpaceLabs Medical Flexport System

The NICO monitor transmits data to SpaceLabs Medical Ultraview Care Network monitors using the SpaceLabs Flexport system.

Setup

To set up and connect the NICO monitor to the Flexport, you will need the following:

- NICO monitor with software revision 5.0 or greater
- Spacelabs Medical Flexport system
- Interface cable (supplied by Spacelabs Medical)

The NICO monitor must be set to the appropriate interface for output to the Flexport. From the **INPUT/OUTPUT** screen:

1. Turn and press the **KNOB** to select **RS232-2** or **RS232-3**.
2. Turn and press the **KNOB** to select **FLEXPORT**.
3. Connect the Flexport interface cable to the rear panel of the NICO monitor. Tighten screws.
4. Refer to the Flexport System Interface document from Spacelabs Medical.

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Alerts and Messages

With NICO software revision level 5.0 and above, alarms and messages are transmitted from the NICO monitor through the Flexport to the UltraView Care system. All alarms and messages can be viewed from either the NICO monitor or the Flexport.

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NICO®

Maintenance

This section details routine maintenance procedures for the NICO® monitor, its sensors and accessories.

Cleaning and Sterilization

To clean and/or sterilize the monitor and its accessories:

Single Patient Use NICO Sensor

- Treat the NICO Sensor in accordance with hospital protocol for single-patient use items.

CO_2/Flow Sensors

- Treat CO_2/Flow sensors in accordance with hospital protocol for single-patient use items.

CAPNOSTAT® CO_2 Sensor

- Do not immerse the sensor. Do not sterilize the sensor.
- The sensor can be cleaned and disinfected by wiping with solutions such as a 70% isopropyl alcohol, 2% gluteraldehyde, or 10% bleach solution. Then wipe down with a water dampened clean cloth to rinse. Dry before use.
- Make certain that the sensor windows are clean and dry before reuse.

NICO Monitor

- Do not immerse the monitor. Do not sterilize the monitor.
- Turn the monitor off and unplug from the AC power source before cleaning.
- The monitor can be cleaned and disinfected by wiping with solutions such as a 70% isopropyl alcohol, 2% gluteraldehyde, or 10% bleach solution. Then wipe down with a water dampened clean cloth to rinse. Dry before use.

SpO_2 Finger Sensor

- Do not immerse the finger sensor. Do not sterilize the finger sensor.
- The sensor can be cleaned and disinfected by wiping with solutions such as a 70% isopropyl alcohol, 2% gluteraldehyde, or 10% bleach solution. Then wipe down with a water dampened clean cloth to rinse. Dry before use.
- Make certain that the finger sensor windows are clean and dry before reuse.
- After cleaning the finger sensor, perform a Quick Check to verify the sensor is functional (See "Sensor Quick Check" on page 73).

SpO_2 Y-Sensor

- The Y-Sensor may be immersed up to—but not including—the connector, in a 2% gluteraldehyde solution, or 10% bleach solution. Refer to manufacturer's instructions and standard hospital protocols to determine recommended times for disinfection and sterilization.
- Rinse thoroughly with water and dry before use. (Do not rinse the connector).
- After cleaning or sterilizing the Y-Sensor, perform a Quick Check to verify the sensor is functional (See "Sensor Quick Check" on page 73).

SpO_2 Tapes and Foam Wraps

- Treat tapes and foam wraps in accordance with hospital protocol for single-patient use items.

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Ear Clip

- Clean with a cloth dampened with 70% isopropyl alcohol. After cleaning, thoroughly wipe the ear clip with a clean, water dampened cloth.

Monitor Maintenance Schedules

The NICO monitor performs a diagnostic self-test at powerup that checks the internal electronics. If this self test fails, the normal monitoring display will not appear. Remove the NICO monitor from use and contact qualified service personnel.

The NICO monitor should undergo inspection and safety checks on a regular basis or according to institutional protocol. A Service Manual (Catalog No. 9226-90) containing information to assist qualified service personnel is available.

Battery Maintenance

The monitor may not power up on battery power if the battery is not sufficiently charged. If the NICO monitor has not been used or powered by the AC Mains for an extended time—3 months or more—allow the battery to charge for 12 hours before use. (The internal battery may slowly discharge over long periods of non-use.)

To charge the battery, connect the line cord to an AC source and set the rear panel power switch ON (|). Check that the AC Mains Power Indicator on the front panel is illuminated (green). Allow the battery to charge for 12 hours. (Refer battery replacement to qualified service personnel.)

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NICO®

Specifications

General

Specifications for the Novametrix NICO® Monitor, Model 7300, are listed for informational purposes only and are subject to change without notice.

Cardiac Output

- Measurement Frequency: Rebreathing cardiac output measurement made every three minutes, rebreathing period is 35 seconds.
- Cardiac Output Range: 0.5-19.9 liters/minute
- Cardiac Output Resolution: 0.1 liters/minute
- Pulmonary Capillary Blood Flow (PCBF) Range: 0.5-19.9 L/min, Resolution: 0.1 L/min
- Cardiac Index Range: 0-9.9 L/min/meter^2, Resolution: 0.1 L/min/meter^2
- Stroke Volume Range: 0-250 ml, Resolution: 1 ml
- Rebreathing Valve/sensor:
  - Valve type: dual diaphragm, pneumatically controlled
  - Return spring: automatically returns valve to normal position
  - Resistance: 3 cmH_2O/L/min maximum
  - Rebreathed volume: normal position 35 ml; rebreathing position 150-450 ml (std.)
  - CO_2/flow sensor: integrated into valve assembly
- Parameter limits for NICO measurements:
  - VCO_2: >20 ml/min
  - RR: >3, <60
  - Vt: >200 (small and standard), >400 (large)
  - $ETCO_2$: >15, <85 mmHg (<100 mmHg during rebreathing)
    >2.0, <11.5 kPa or % (<13.5 kPa or % during rebreathing)

CO_2

- Principle of Operation: Non-Dispersive Infrared (NDIR) absorption, dual wavelength ratiometric-single beam optics, mainstream sensor.
- Response Time: Less than 60 ms
- Gas composition effects: O_2, N_2O (operator selectable)
- CAPNOSTAT® CO_2 Sensor:
  - Weight: Less than 18 g without cable
  - Sensor Size: 1.3 x 1.67 x .85 inches (3.3 x 4.2 x 2.2 cm), 8 foot cable (2.44 m)
  - Construction: Durable high performance plastic, ultra-flexible cable. Shock Resistant: Sensor will withstand a 6 foot drop to a tile floor.
- End Tidal CO_2:
  - Range: 0-150 mmHg, 0-20 kPa or % at Pb 760 mmHg
  - Accuracy: ± 2 mmHg for 0-40 mmHg, ± 5% of reading for 41-70 mmHg, ± 8% of reading for 71-150 mmHg
- Respiratory Rate:
  - Range: 2-150 breaths/min
  - Accuracy: ± 1 breath/min

Flow

- Flow Range (L/min) at Pb 760 mmHg, room air, 35°C
  - Adult: 2 to 180
  - Pediatric: .5 to 100
  - Neonatal: .25 to 25
- Flow Accuracy: Greater of ± 3% reading or:
  - Adult: .5 L/min
  - Pediatric: .25 L/min
  - Neonatal: .125 L/min
- Tidal Volume Range (ml)
  - Adult: 200 to 3000
  - Pediatric: 30-400

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- Neonatal: 1-100
- Airway Pressure Range (cmH_2O): ± 120
  - Accuracy: greater of 0.5 cmH_2O or ± 2% reading
- Gas composition effects: O_2, anaesthetic agent, CO_2, N_2O, N_2, He (operator selectable)

SpO_2

- Oxygen Saturation
  - Range: 0-100%
  - Accuracy: ± 2% for 70 -100% for 1 standard deviation, unspecified for 0-69%
  - Averaging Time: 2 seconds, or selectable, none, 2, 4, or 8 seconds (MARS Mode only).
  - Display Resolution: 1%
  - Settling Time: Display settles to within 1% of the final reading less than 15 seconds after the sensor is properly applied.
- Pulse Rate:
  - Range: 30-250 beats per minute
  - Accuracy: ± 1% of full scale (for 1 standard deviation or approximately 68% of readings)
  - Averaging Time: 8 seconds, or selectable 0, 2, 4, or 8 seconds, based on SpO_2 setting (MARS Mode only).
  - Display Resolution: 1 bpm
  - Settling Time: Display settles to within 1% of the final reading less than 15 seconds after the sensor is properly applied.

Monitor Specifications

- Classification (IEC601-1): Class I/internal power source, type BF, continuous operating mode, enclosure protection rating IPX0.
- Operating Environment: 50-104° F (10-40° C), 10-90% relative humidity (non-condensing)
- Size: Height 6.5 in., Width 10.75 in., Depth 9.5 in.
- Weight: 9 lbs, 6 oz.
- Power: 100-240 VAC, 50-60 Hz, 70VA
- Fuse Rating: 100-120 VAC, 1.0 A/250 V Slo-Blo (x2); 200-240 VAC, T 500 mA/250 V (x2)
- Battery: Internal, Sealed lead-acid gel-cell, 45 minute life on full charge (on-screen life indicator), 12 hours recharge time.
- Display: 4.625 x 3.5 inch EL, 320 x 240 pixels
- Electromagnetic Emissions: Conforms to EMC Directive 93/42/EEC, CISPR Class A. Tested to EN55011 (1998) and CISPR11 (1999).
- Electromagnetic Immunity: Conforms to EMC Directive 93/42/EEC. Tested to IEC60601-1-2 (2001), IEC61000-4-2 (2001) ESD, IEC61000-4-3 (2002) RF, IEC61000-4-4 (1995) EFT, IEC61000-4-5 (2001) Surge, IEC61000-4-6 (2001) Conducted RF, IEC61000-4-8 (2001) Magnetic Fields, IEC61000-4-11 (2001) Voltage Dips, Interruptions and Variations, IEC61000-3-2 (2001) Harmonic Distortion, IEC61000-3-3 (2002) Voltage Fluctuations and Flicker.

RS232 Communications

- RS232 Communications Ports:

Pin #	RS232-1	RS232-2	RS232-3
2	Rx	Rx	Rx
3	Tx	Tx	Tx
5	Ground	Ground	Ground
7	n/a	RTSB	n/a
8	n/a	CTSB	n/a
9	n/a	Power	n/a

Analog Specifications

- Analog Input/Output Port (selectable, 0 to 1 volt range):
  - C.O. - Cardiac Output, 0-20 L/m, 50mV/L/m
  - CI - Cardiac Index, 0-20 L/m, 50mV/L/m
  - SV - Stroke Volume, 0-20 L/m, 50mV/L/m
  - PCBF - 0-20 L/m, 50 mV/L/m
  - $ETCO_2$ - 0-150 mmHg, 0-20 kPa or %, 6.67mV/mmHg
  - SpO_2 - 0-100%, 10mV/%
  - Resp Rate - 0-150 br/min, 6.67mV/br/min

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- Pulse Rate - 0-250 bpm, 4mV/bpm
- CO_2 Waveform - 0-150 mmHg, 0-20 kPa or %, 6.67mV/mmHg
- Pleth Waveform - auto scaled
- Flow Waveform - -125 to +125 L/m, 4mV/L/m
- Airway Pressure Waveform - -20 to +105 cmH_2O, 8mV/cmH_2O

Pin#	Description	Pin #	Description
1	Ground	9	Ground
2	Channel 1 - input (not enabled)	10	Ground
3	Channel 2 - input (not enabled)	11	Channel 1 - output
4	Channel 3 - input (not enabled)	12	Channel 2 - output
5	Channel 4 - input (not enabled)	13	Channel 3 - output
6	Ground	14	Channel 4 - output
7	Ground	15	Input/Output Sense
8	Ground		

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NICO®

Accessories

Catalog No.	Description
9226-00	***NICO*® Cardiopulmonary Management System**, Model 7300 Includes: Monitor, *CAPNOSTAT*® CO_2 Sensor, SpO_2 Sensor, Power Cord and User's Manual. Warranty for *NICO* Monitor and *CAPNOSTAT*® CO_2 Sensor is 2 years.
8950-00	***NICO* Sensor** (10 per box) **Small size (for tidal volumes of 200 - 500 mL)**
8951-00	***NICO* Sensor** (10 per box) **Standard size (for tidal volumes of 400 - 1000 mL)**
8952-00	***NICO* Sensor** (10 per box) **Large size (for tidal volumes of 750 - 1500 mL)**
9567-00	***CAPNOSTAT*® CO_2 Sensor - NICO**
6934-00	**Cable Management Straps** for use with the *CAPNOSTAT*® CO_2 Sensor. Organizes and holds multiple cables and tubings (package of 5)
8751-00	***CAPNOSTAT*® CO_2 Sensor Cable Holding Clips** (50 per box)
8776-00	***SuperBright*™ Finger Sensor** (10 ft. sensor cable) 1 yr. warranty
8791-00	***SuperBright*™ Y-Sensor** (10 ft. sensor cable) 90 day warranty
9765-00	***NICO* CO_2/Flow Sensors** (10 per box) **Neonatal size**
9766-00	***NICO* CO_2/Flow Sensors** (10 per box) **Pediatric size**
9767-00	***NICO* CO_2/Flow Sensors** (10 per box) **Adult size**
6063-01	**Single Patient Use Airway Adapter** - (1 piece) Adult size
6455-00	**Single Patient Use SpO_2 Sensor (10 per box) Pediatric/Adult**
6455-25	**Single Patient Use SpO_2 Sensor (25 per box) Pediatric/Adult**
6480-00	**Single Patient Use SpO_2 Sensor (10 per box) Neonatal/Pediatric**
6480-25	**Single Patient Use SpO_2 Sensor (25 per box) Neonatal/Pediatric**
4941-00	**Saturation Sensor Extension Cable** (4 feet)
4942-00	**Saturation Sensor Extension Cable** (6 feet)
4943-00	**Saturation Sensor Extension Cable** (10 feet)
5266-00	**Saturation Sensor Extension Cable** (25 feet)
6147-00	**Saturation Sensor Extension Cable** (50 feet)
8828-00	**20mm Wrap Style Y-Strip Taping System** (100 per box) Neonatal foot and hand, pediatric toe or finger, color coded blue
8829-00	**25mm Wrap Style Y-Strip Taping System** (100 per box) Neonatal foot and hand, color coded green
8831-00	**20mm Finger Style Taping System** (100 per box) Use on pediatric finger or on small adult finger, color coded blue
8832-00	**25mm Finger Style Taping System** (100 per box) Use on adult finger, color coded green
6929-00	**Adhesive Foam Wraps**, Large (25 per box)
6968-00	**Adhesive Foam Wraps**, Small (25 per box)
8836-00	**Non-Adhesive Foam Wraps**, Large (25 per box)
8943-00	**Non-Adhesive Foam Wraps**, Small (25 per box)
6131-50	**Ear Clips** (5 per box)
6131-25	**Ear Clips** (25 per box)
8700-00	**Adhesive Dots** (200 per box)

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Catalog No.	Description
9861-00	**Flow Connector Cap**, 3 port (25 per bag)
601012	***NICO Monitor*** 9-pin to 9-pin null modem (crossover) cable
600026	**Power Cord** (included with monitor)
9226-23	***NICO Monitor*** User Manual
9226-90	***NICO Monitor*** Service Manual
9960PED-00	***CAPNO$_2$mask***™ - Pediatric O_2 Delivery/CO_2 Mainstream Monitoring Mask (10 per bag)
9960STD-00	***CAPNO$_2$mask***™ - Adult Standard O_2 Delivery/CO_2 Mainstream Monitoring Mask (10 per bag)
9960LGE-00	***CAPNO$_2$mask***™ - Adult Large O_2 Delivery/CO_2 Mainstream Monitoring Mask (10 per bag)

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NICO®

Warranty

Equipment manufactured or distributed by Respironics Novametrix Inc., is fully guaranteed, covering materials and workmanship, for a period of one year from the date of shipment, except for certain disposable products and products with stated guarantees other than one year. Respironics Novametrix reserves the right to perform guarantee service(s) at its factory, at an authorized repair station, or at the customer's installation.

Respironics Novametrix' obligations under this guarantee are limited to repairs, or at Novametrix' option, replacement of any defective parts of our equipment, except fuses, batteries, and calibration gasses, without charge, if said defects occur during normal service.

Claims for damages during shipment must be filed promptly with the transportation company. All correspondence concerning the equipment must specify both the model name and number, and the serial number as it appears on the equipment.

Improper use, mishandling, tampering with, or operation of the equipment without following specific operating instructions will void this guarantee and release Respironics Novametrix from any further guarantee obligations.

Respironics, Inc.
Customer Service & Product Support:

USA and Canada
Phone 1-800-345-6443
Customer Service Fax 1-800-886-0245
Product Support Fax 1-724-387-5236

International
Phone 724-387-4000
Fax 724-387-5012

service@respironics.com
clinical@respironics.com

Caution: Federal (U.S.A.) law restricts this device to sale, distribution, or use by or on the order of a licensed medical practitioner.

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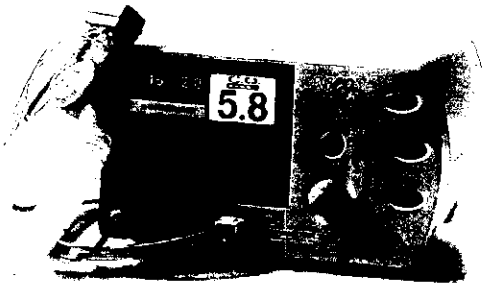
NICO 5.0 with MarSpO2
DRAFT COPY

RESPIRONICS
www.respironics.com



NICO

NICO® Revision 5.0 Firmware

What is in this release?

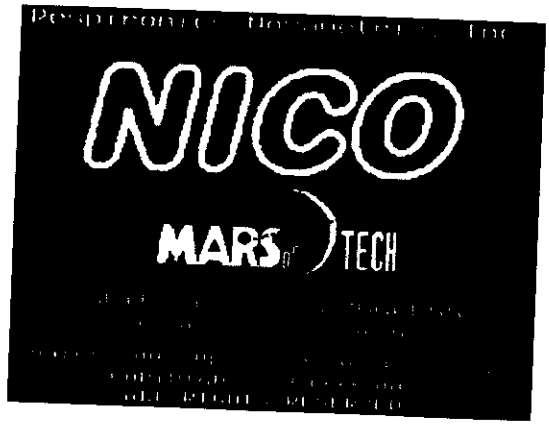
Respironics Hospital Division is pleased to announce the release of NICO version 5.0 firmware. This version of the NICO Cardiopulmonary Management System firmware offers improvements and new features, designed to simplify the use of the monitor for patient monitoring.

NEW FEATURES

NICO is now MARSpO2™ Upgradeable!

MARS TECH

The NICO 5.0 firmware supports MARS™ (Motion Artifact Rejection System) pulse oximetry technology. MARS technology uses advanced digital signal processing to provide good clinical performance during challenging conditions including motion and low perfusion. NICO 5.0 firmware automatically determines if the NICO monitor is equipped with the MARSpO2™ hardware. If the MARSpO2 hardware is not detected the NICO monitor reverts back to standard pulse oximetry.



NICO Start-Up Screen when MARSpO2 hardware is detected.

RESPIRONICS®
www.respironics.com

Customer Service: 1-800-345-6443 or 724-387-4000
Respironics Europe: +33-(0)1-55-60-19-80
Respironics Asia Pacific: +852-234-342-18

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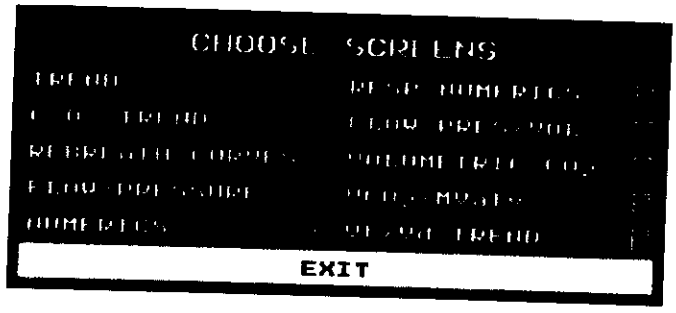
PEOPLE. PRODUCTS. PROGRAMS.℠

CHOOSE SCREENS MENU



The **CHOOSE SCREENS** menu allows the user to customize the active screen set accessible by turning the KNOB for monitoring in the Cardiac Output or Respiratory Mechanics modes. In Respiratory Mechanics mode, **C.O.TREND**, **REBREATH CURVES** and **RESP NUMERICS** are unavailable (dimmed). **CO_2/SpO_2** is the base screen and is always available.

Enabling Screens

To enable or disable specific screens, press the MENU key to display **SELECT A SCREEN**. Turn the KNOB to highlight **SETUP** and push the KNOB. From the **SETUP** screen, select **CHOOSE SCREENS** and push the KNOB.

In the **CHOOSE SCREENS** menu, turn and push the KNOB to add or remove each monitoring screen from the active screen set. When a screen is enabled, a check is in the checkbox. In monitoring mode, enabled screens will appear with successive turns of the KNOB. If a screen is unchecked, it will not appear when the KNOB is turned, but can be accessed directly from **SELECT A SCREEN** or **SELECT RESPIRATORY SCREENS**.

SET ALERTS SCREEN

The **SET ALERTS** screen displays the current patient values as well as the LOW and HIGH alert limit settings for various parameters. This screen also allows adjustment of alert limits, audible alert volume, and of the "No Respiration" alert.

The **SET ALERTS** screen can only be displayed by pressing the MENU key and selecting **SET ALERTS**.

- **CURRENT** - the current patient value for a parameter, shown in real time.
- **LOW** and **HIGH** - the values below and above which an alert will be generated. NOTE: The value will flash when a high or low alert limit is exceeded.
- (Bell with slash) - audible alerts are disabled
- (Bell) - audible alerts are enabled
- **AUDIO** - set the audible alert volume level

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- **AUTO LIMITS** - have the NICO monitor bracket alerts around current patient values
- **NO RESP:** - set the No Respiration alert delay timer

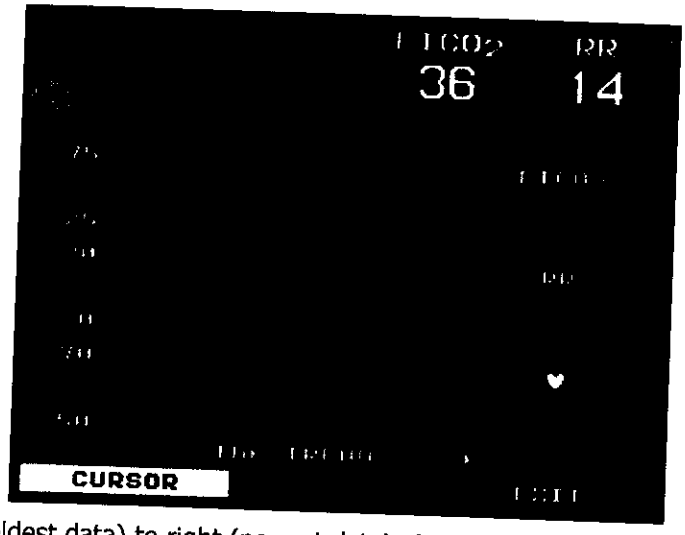
DISPLAY HOLD

In all cardiac output modes, when rebreathing is turned off and eight minutes has elapsed, the NICO will dim and hold the large-digit reading for C.O., PCBF or C.I. The CObar™ or text for **FAST MODE** or **MANUAL MODE** is replaced with the time the last cycle was completed.

If the user modifies the monitor settings between C.O., PCBF and C.I., the time stamp will not change and the display will remain dimmed. After 12 hours, the large number display will turn to dashes (--) and the time stamp will be removed.

CURSOR – IN THE CARDIOPULMONARY TREND SCREEN

The Cardiopulmonary **TREND** screen displays two user-selectable numeric parameters and three user-selectable trend graphs. Push then turn the KNOB to advance through the displays. Highlight the desired parameter, trend type or trend duration, then select by turning then pressing the KNOB.



- Data is plotted from left (oldest data) to right (newest data). Once the display is filled, data shifts left so that the oldest data point on the left is pushed out to make room for the newest point entering from the right.
- To move between newer and less recent trend data on the graph, press and turn the KNOB to highlight the **CURSOR**. Press and turn the KNOB again to view the desired time period. An arrow will point to the time stamp when less recent data is viewed. To view the most recent data, scroll to the right using the KNOB.
- The time periods are: 1 minute average for the 1 hour trend, 2 minute average for the 2 hour trend, 4 minutes for the 4 hour trend, 8 minutes for the 8 hour trend, 12 minutes for the 12 hour trend and 24 minutes for the 24 hour trend.

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- C.O., VCO_2, $ETCO_2$, RR, SpO_2 and pulse rate values will flash if an alert limit is exceeded.
- A two-pixel wide dashed vertical line in the trend is used to denote a power-cycle where the NICO® monitor was turned off and back on or where the time and date setting was changed.
- A single pixel-wide dotted vertical line in the trend is used to mark the most recent ABG entry.
- Trend reports can be printed from the Cardiopulmonary Trend screen. See "Printing" in the Users Manual for details.
- The PRINT option is dimmed when HP PRINTER OUTPUT is not selected. To set the monitor to the proper interface, see "Printing" in the Users Manual.

For additional information refer to NICO User's Manual, Rev. 10, Catalog No. 9226-23-10

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TEAR OPEN AT PERFORATION

NICO®

CARDIOPULMONARY MANAGEMENT SYSTEM

$NICO_2$ SENSOR

SMALL SIZE

For set Tidal Volumes (Vt) of 200-500 mL

REF 8950-00

FOR SINGLE PATIENT USE ONLY

WARNING: Not for pediatric use.

WARNING: NICO Sensor increases airway deadspace by 35cc (minimum). At low tidal volumes, compensatory changes to ventilation protocol should be considered.

Reuse may pose a patient hazard.
Performance is not guaranteed if reused.
Do not disassemble, clean, disinfect or sterilize.

Refer to User's Manual prior to use.

novametrix™

NOVAMETRIX MEDICAL SYSTEMS INC.
WALLINGFORD, CT 06492 U.S.A.
1-800-243-3444 203-265-7701
http://www.novametrix.com

450

LOT

CE 0086

TEAR OPEN AT PERFORATION

NICO®

CARDIOPULMONARY MANAGEMENT SYSTEM

$NICO_2$ SENSOR

STANDARD SIZE

For set Tidal Volumes (Vt) of 400-1000 mL

REF 8951-00

FOR SINGLE PATIENT USE ONLY

WARNING: Not for pediatric use.

WARNING: NICO Sensor increases airway deadspace by 35cc (minimum). At low tidal volumes, compensatory changes to ventilation protocol should be considered.

Reuse may pose a patient hazard.

Performance is not guaranteed if reused.

Do not disassemble, clean, disinfect or sterilize.

Refer to User's Manual prior to use.

novametrix™

NOVAMETRIX MEDICAL SYSTEMS INC.
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LOT

CE 0086

457

9385-02-03

TEAR OPEN AT PERFORATION

NICO®

CARDIOPULMONARY MANAGEMENT SYSTEM

$NICO_2$ SENSOR

LARGE SIZE

For set Tidal Volumes (Vt) of 750-1500 mL

REF 8952-00

FOR SINGLE PATIENT USE ONLY

WARNING: Not for pediatric use.

WARNING: NICO Sensor increases airway deadspace by 35cc (minimum). At low tidal volumes, compensatory changes to ventilation protocol should be considered.

Reuse may pose a patient hazard.

Performance is not guaranteed if reused.

Do not disassemble, clean, disinfect or sterilize.

Refer to User's Manual prior to use.

novametrix™

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WALLINGFORD, CT 06492 U.S.A.
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LOT

452

CE 0086

9385B-02-03

TEAR OPEN AT PERFORATION

NICO®
CARDIOPULMONARY MANAGEMENT SYSTEM

CO_2/Flow Sensor
ADULT

For use with NICO® model 7300 when monitoring patients with endotracheal tube sizes 5.5mm or greater or non-intubated patients.

REF 9767

FOR SINGLE PATIENT USE ONLY

Reuse may pose a patient hazard.
Performance is not guaranteed if reused.
Do not disassemble, clean, disinfect or sterilize.

Refer to User's Manual prior to use.

novametrix™
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LOT

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TEAR OPEN AT PERFORATION

NICO®
CARDIOPULMONARY MANAGEMENT SYSTEM

CO_2/Flow Sensor
PEDIATRIC

For use with NICO model 7300 when monitoring patient with endotracheal tube sizes 3.5mm to 6.0mm.

REF 9766

FOR SINGLE PATIENT USE ONLY

Reuse may pose a patient hazard.
Performance is not guaranteed if reused.
Do not disassemble, clean, disinfect or sterilize.

Refer to User's Manual prior to use.

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WALLINGFORD, CT 06492 U.S.A.
1-800-243-3444 203-265-7701
http://www.novametrix.com

454

LOT

CE 0086

US PATENTS: 6,099,481 5,793,044 5,789,660 5,693,944 5,616,923 5,535,633 5,379,650 5,369,277 5,347,843 5,251,121 5,153,436 5,146,092 4,958,075 4,859,859 4,859,858; other foreign and US patents pending.

TEAR OPEN AT PERFORATION

NICO®
CARDIOPULMONARY MANAGEMENT SYSTEM

CO_2/Flow Sensor
NEONATAL

For use with NICO model 7300 when monitoring patient with endotracheal tube sizes 2.5mm to 4.0mm.

REF 9765

FOR SINGLE PATIENT USE ONLY

Reuse may pose a patient hazard.
Performance is not guaranteed if reused.
Do not disassemble, clean, disinfect or sterilize.

Refer to User's Manual prior to use.

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http://www.novametrix.com

455

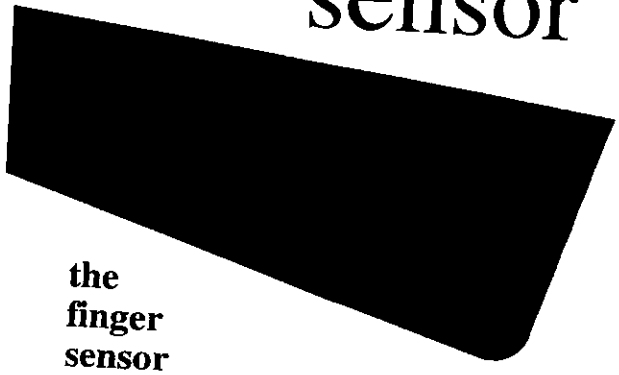
LOT

CE 0086

US PATENTS: 6,099,481 5,793,044 5,789,660 5,693,944 5,616,923 5,535,633 5,379,650 5,369,277 5,347,843 5,251,121 5,153,436 5,146,092 4,958,075 4,859,859 4,859,858 other foreign and US patents pending.

SuperBright™

finger sensor



the finger sensor

is intended for use on Adult Fingers. Sensor is not intended for neonatal applications.

Refer to Oximeter User's Manual prior to use.

For use only with Novametrix Pulse Oximeters configured for SuperBright™ Sensors.

Cat. No. 8776 Qty. 1

NOVAMETRIX
MEDICAL SYSTEMS INC.
WALLINGFORD, CONNECTICUT U.S.A. 06492

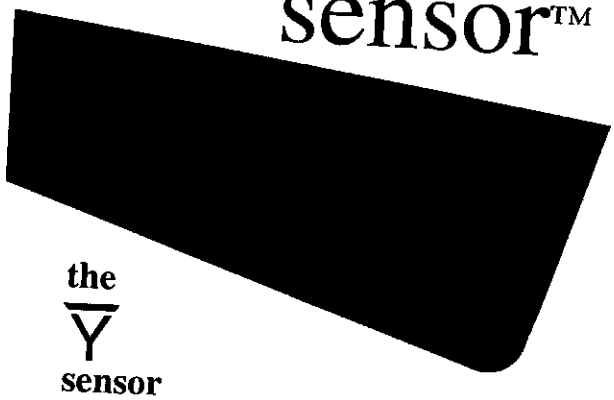
CE 0086

8786-02-02

Novametrix PN: 8786-02-02
Artwork, Label, Finger Sensor (composite)
Used with PN: 8776

456

SuperBright™ Y sensor™



the Y sensor

is reusable and sterilizable. Refer to package insert for details.

Refer to Oximeter User's Manual prior to use.

For use only with Pulse Oximeters configured for SuperBright™ Sensors.

Cat. No. 8791 Qty. 1

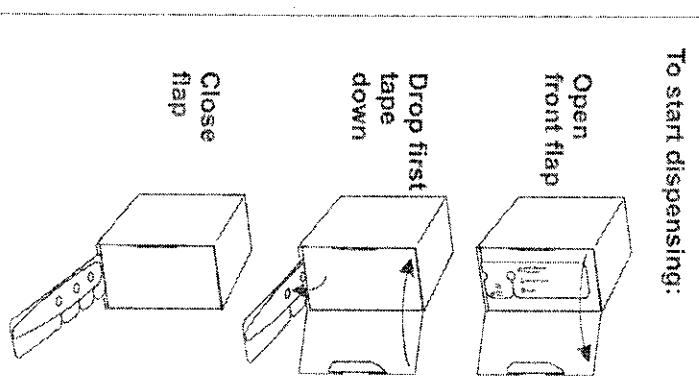
NOVAMETRIX
MEDICAL SYSTEMS INC.
WALLINGFORD, CONNECTICUT U.S.A. 06492
U.S. PATENTS 5,170,786

CE 0086

5412-02-03

Novametrix PN: 5412-02-03
Artwork, Label, "Y" Sensor Composite
Used with PN: 8791

457



Neonatal/Pediatric
Y-Strip™ Tape
REF 8828-00

QTY: 100

PULL HERE

novametrix™

⚠ Refer to User's Manual prior to use

WARNING: Do not wrap around the limb so tightly that circulation is restricted. Inspect the site often, at least once every four hours, for adequate circulation.

Treat wrap in accordance with hospital protocol for *single patient use*.

This product is latex free.

CAUTION: Federal (U.S.A.) Law restricts this device to sale by or on the order of a licensed medical practitioner.

novametrix™
Novametrix Medical Systems Inc.
Wallingford CT U.S.A. 06492
www.novametrix.com

CE 0086

Patent Pending

5461-02-04

novametrix™ sensor.

The sensor cable can be taped to the patient limb to further secure the

Neonatal/Pediatric Y-Strip™ Tape REF 8828-00

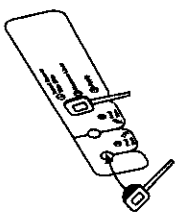
For use when applying the Novametrix Y-Sensor™ to a neonatal foot or hand, or pediatric finger, toe or foot.

Sensor Application

Easy as 1 - 2 - 3

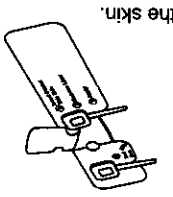
1 Insert sensor

With instructions facing up, press blue sensor buttons through holes in liner. The spacing of the holes allows customization to different sized sites; first and second for pediatric toes or fingers, first and third for neonatal feet, hands and pediatric feet.



2 Remove liner

Peel tabs as indicated to remove liner and expose adhesive.



3 Apply

Wrap the tape around the site with adhesive facing the skin.

Novametrix PN: 5461-02-04 composite

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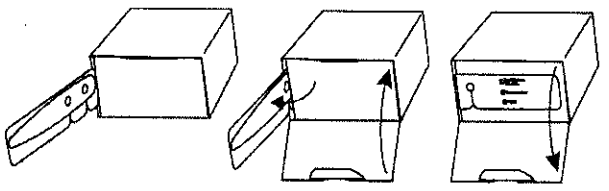
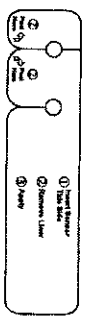
To start dispensing:



Adult Y-Strip™ Tape

REF 8829-00



QTY: 100

PULL HERE

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Wallingford CT U.S.A. 06492
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Patent Pending

CE 0086

⚠ Refer to User's Manual prior to use.

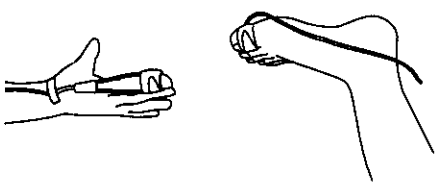
WARNING: Do not wrap around the limb so tightly that circulation is restricted. Inspect the site often, at least once every four hours, for adequate circulation.

Treat wrap in accordance with hospital protocol for *single patient use*.

This product is latex free.

CAUTION: Federal (U.S.A.) Law restricts this device to sale by or on the order of a licensed medical practitioner.

5459-02-03



The sensor cable can be taped to the patient limb to further secure the sensor.

Adult Y-Strip™ Tape **REF 8829-00**

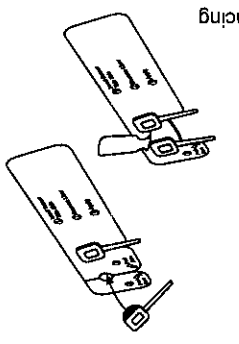
For use when applying the Novametrix Y-Sensor™ to an adult finger or toe.

Sensor Application
Easy as 1 - 2 - 3

❶ Insert sensor
With instructions facing up, press blue sensor buttons through holes in liner.

❷ Remove liner
Peel tabs as indicated to remove liner and expose adhesive.

❸ Apply
Wrap the tape around the site with adhesive facing the skin.



Novametrix PN: 5459-02-03

① Insert Sensor This Side

② Remove Liner

③ Apply

② Peel Here

② Peel Here

Novametrix PN: 8828-02-01

460

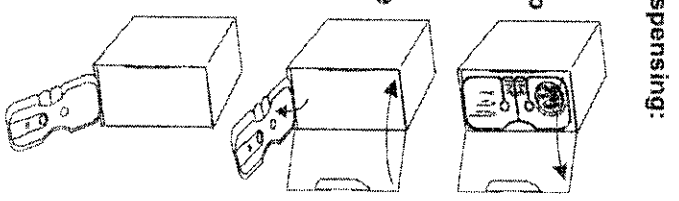
194

To start dispensing:

Open front flap

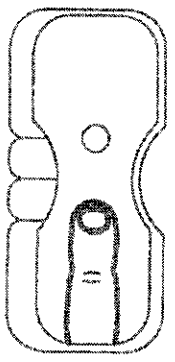
Drop first tape down

Close flap



Pediatric Butterfly Wrap

REF 8831-00



QTY: 100

PULL HERE

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CE 0086

⚠ Refer to User's Manual prior to use.

WARNING: Do not wrap around the limb so tightly that circulation is restricted. Inspect the site often, at least once every four hours, for adequate circulation.

Exercise caution when giving "Special Patient Sticker" to patients. Potential choking hazard.

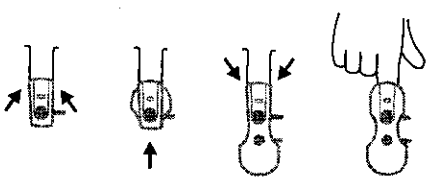
Treat wrap in accordance with hospital protocol for *single patient use*.

This product is latex free.

CAUTION: Federal (U.S.A.) Law restricts this device to sale by or on the order of a licensed medical practitioner.

6133-02-06

novametrix™



Align the finger illustration on the tape over the patient's finger. Adhere the wings on the top side around the finger. Fold remaining wrap over finger tip. Adhere wrap to bottom of finger, fold wings up around finger to secure.

The sensor cable can be taped to the patient limb to further secure the sensor.

Pediatric Butterfly Wrap REF 8831-00

For use when applying the Novametrix Y-Sensor™ to pediatric fingers.

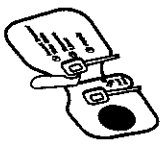
Sensor Application
Easy as 1 - 2 - 3

1. Insert sensor

With instructions facing up, press blue sensor buttons through holes in liner.

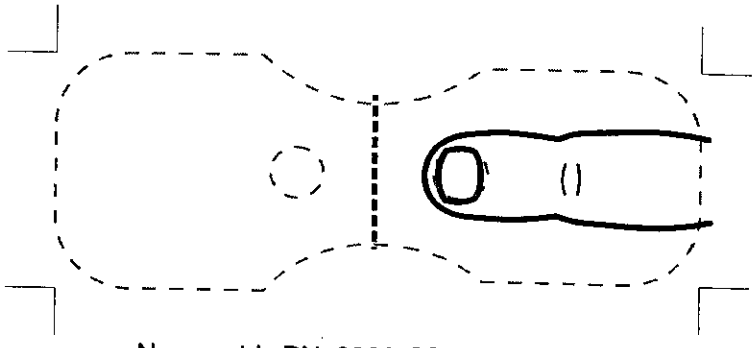
2. Remove liner

Peel tabs as indicated to remove liner and expose adhesive. Special Patient Sticker can be peeled off liner and given to patient if appropriate.



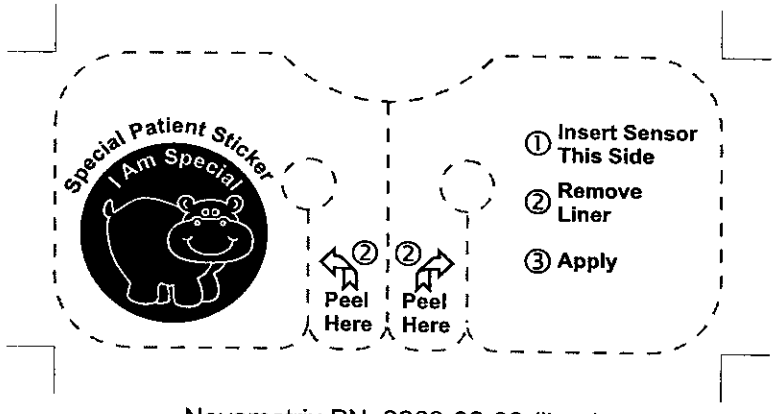
3. Apply

Novametrix PN: 6133-02-06
Black & Pantone 2562



Novametrix PN: 9968-02-00 (applicator)

462



Novametrix PN: 9969-02-00 (liner)

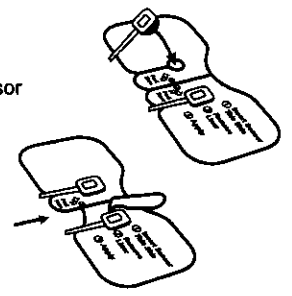
463

Adult Butterfly Wrap

REF 8832-00

For use when applying the Novametrix Y-Sensor™ to adult fingers.

Sensor Application
Easy as 1 - 2 - 3



❶ Insert sensor

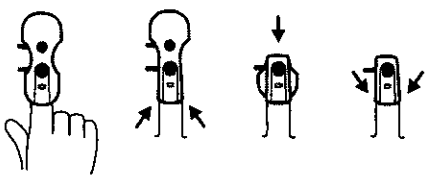
With instructions facing up, press blue sensor buttons through holes in liner.

❷ Remove liner

Peel tabs as indicated to remove liner and expose adhesive.

❸ Apply

Align the finger illustration on the tape over the patient's finger. Adhere the wings on the top side around the finger. Fold remaining wrap over finger tip. Adhere wrap to bottom of finger, fold wings up around finger to secure.
The sensor cable can be taped to the patient limb to further secure the sensor.



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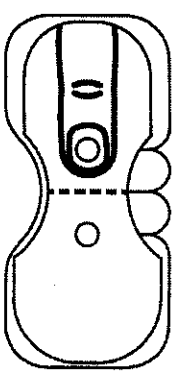
Novametrix PN: 5460-02-06
Black & Pantone 2583

Adult Butterfly Wrap
REF 8832-00



QTY: 100

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Wallingford CT U.S.A. 06492
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Patent Pending

0086

5460-02-06

CAUTION: Federal (U.S.A.) Law restricts this device to sale by or on the order of a licensed medical practitioner.

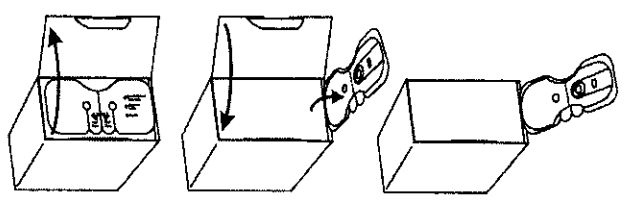
This product is latex free.

Treat wrap in accordance with hospital protocol for *single patient use*.

WARNING: Do not wrap around the limb so tightly that circulation is restricted. Inspect the site often, at least once every four hours, for adequate circulation.

⚠ Refer to User's Manual prior to use.

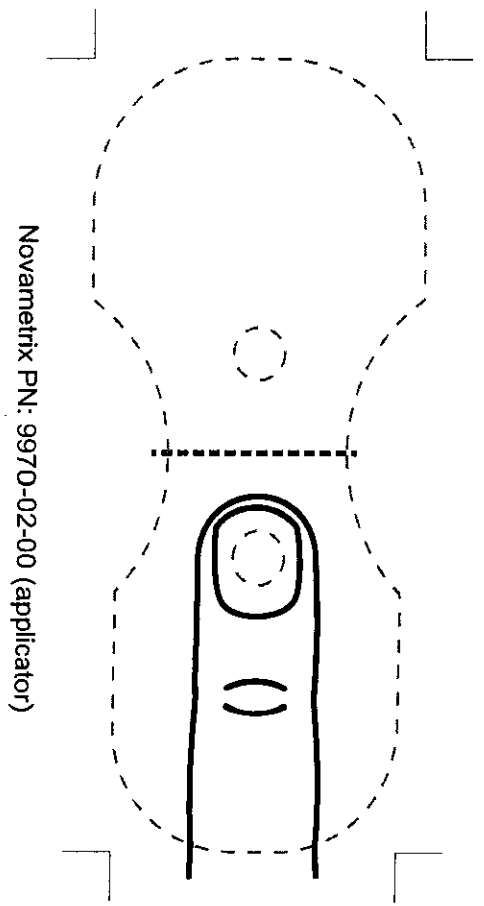
To start dispensing:



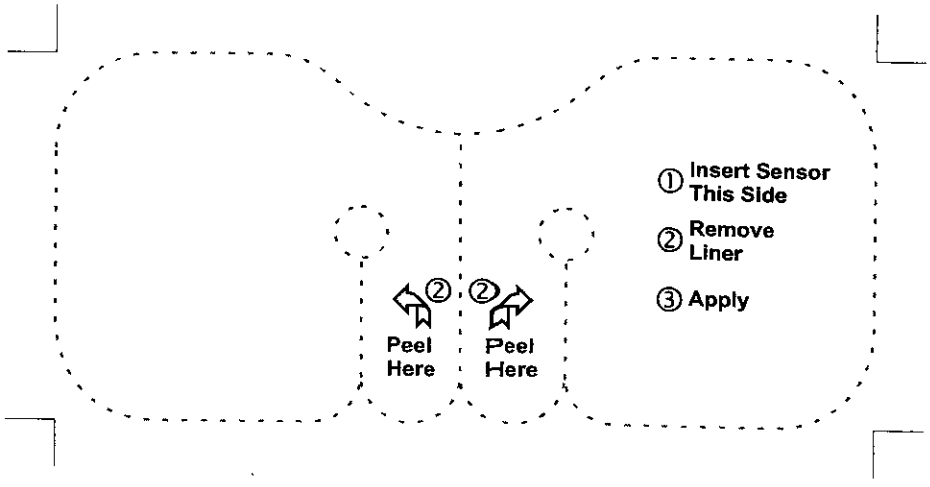
Open front flap

Drop first tape down

Close flap



465



Novametrix PN: 9971-02-00 (liner)

466

Large Non-Adhesive Foam Wrap

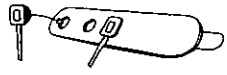
REF 8836

For use when applying the Novametrix Y-Sensor™ to adult, pediatric or neonatal patients.

Sensor Application Easy as 1 - 2 - 3

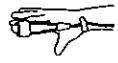
❶ Insert sensor

Press buttons through blue side of the foam wrap.



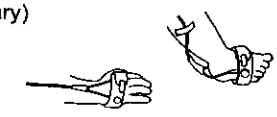
❷ Apply

Wrap around the site with blue side facing the skin.



❸ Secure

Cut excess foam (if necessary) and secure with tab



⚠ Refer to User's Manual prior to use.

WARNING: Do not wrap around the limb so tightly that circulation is restricted. Inspect the site often, at least once every four hours, for adequate circulation.

Treat foam wrap in accordance with hospital protocol for *single patient use.*

This product is latex free.

novametrix™

QTY: 25

CE 0086

8836-02-02

Novametrix Medical Systems Inc.
Wallingford CT U.S.A. 06492
www.novametrix.com

Novametrix PN: 8836-02-02

467

Small Non-Adhesive Foam Wrap

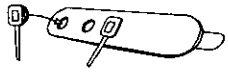
REF 8943

For use when applying the Novametrix Y-Sensor™ to neonatal or pediatric patients.

Sensor Application Easy as 1 - 2 - 3

❶ Insert sensor

Press buttons through blue side of the foam wrap.

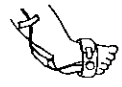


❷ Apply

Wrap around the site with blue side facing the skin.

❸ Secure

Cut excess foam (if necessary) and secure with tab



⚠ Refer to User's Manual prior to use.

WARNING: Do not wrap around the limb so tightly that circulation is restricted. Inspect the site often, at least once every four hours, for adequate circulation.

Treat foam wrap in accordance with hospital protocol for *single patient use*.

This product is latex free.

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QTY: 25

CE 0086

8943-02-02

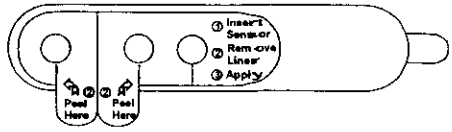
Novametrix Medical Systems Inc.
Wallingford CT U.S.A. 06492
www.novametrix.com

Novametrix PN: 8943-02-02

468

Large Adhesive Foam Wrap

REF 6929



For use when applying the Novametrix Y-Sensor™ to adult, pediatric or neonatal patients.

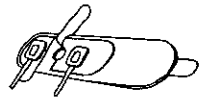
Sensor Application Easy as 1 - 2 - 3

Insert sensor

Press buttons through blue side of the foam wrap.

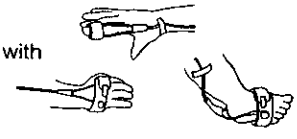
Remove liner

Pull tabs as indicated to remove liner and expose adhesive.



Apply

Wrap around the site with blue side (adhesive) facing the skin and secure with tab.



⚠ Refer to User's Manual prior to use.

WARNING: Do not wrap around the limb so tightly that circulation is restricted. Inspect the site often, at least once every four hours, for adequate circulation.

Treat foam wrap in accordance with hospital protocol for *single patient use*.

This product is latex free.

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QTY: 25

CE 0086

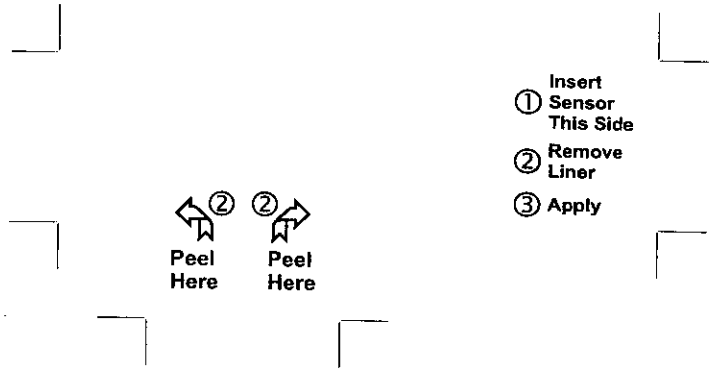
6929-02-03

Novametrix Medical Systems Inc.
Wallingford CT U.S.A. 06492
www.novametrix.com

U.S. Patent No. 5,999,834

Novametrix PN: 6929-02-03

469

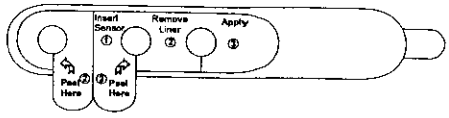


Novametrix PN: 9953-02-01

470

Small Adhesive Foam Wrap

REF 6968



For use when applying the Novametrix Y-Sensor™ to neonatal or pediatric patients.

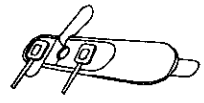
Sensor Application Easy as 1 - 2 - 3

Insert sensor

Press buttons through blue side of the foam wrap.

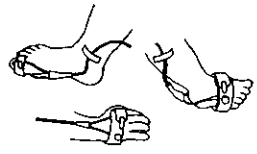
Remove liner

Pull tabs as indicated to remove liner and expose adhesive.



Apply

Wrap around the site with blue side (adhesive) facing the skin (cut excess foam if necessary) and secure with tab.



⚠ Refer to User's Manual prior to use.

WARNING: Do not wrap around the limb so tightly that circulation is restricted. Inspect the site often, at least once every four hours, for adequate circulation.

Treat foam wrap in accordance with hospital protocol for *single patient use*.

This product is latex free.

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QTY: 25

CE 0086

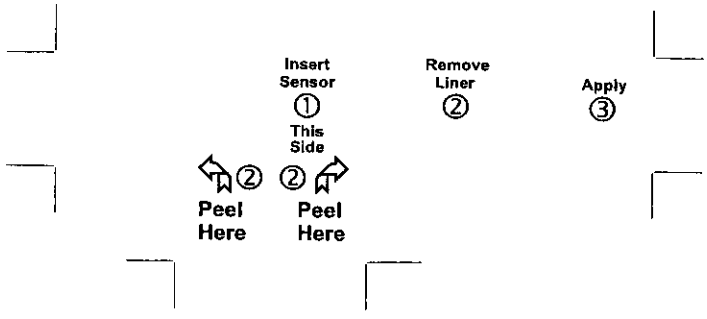
Novametrix Medical Systems Inc.
Wallingford CT U.S.A. 06492
www.novametrix.com

U.S. Patent No. 5,999,834

6968-02-02

Novametrix PN: 6968-02-02

471



Novametrix PN: 9952-02-01

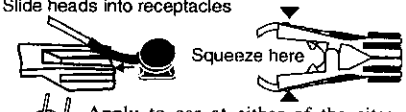
472

Ear Clip

For use with SuperBright™ Y-Sensor™

Sensor Application:

Slide heads into receptacles



Apply to ear at either of the sites shown (if satisfactory reading cannot be obtained, gently rub site and/or use adhesive dots for better response). The adhesive dots (reorder No. 8700-00) included in the package may also be used to assist in holding the ear clip in place.

This accessory provides an alternative site for using the Y-Sensor. If a reading cannot be obtained, a different site should be selected.

The ear clip is reusable and can be wiped with alcohol between patients. Refer to Oximeter User's Manual prior to use.

Caution: Federal (USA) law restricts this device to sale, distribution or use by or on the order of a licensed medical practitioner.

CE 0086

Cat. No: **6131**

Qty:

Lot:

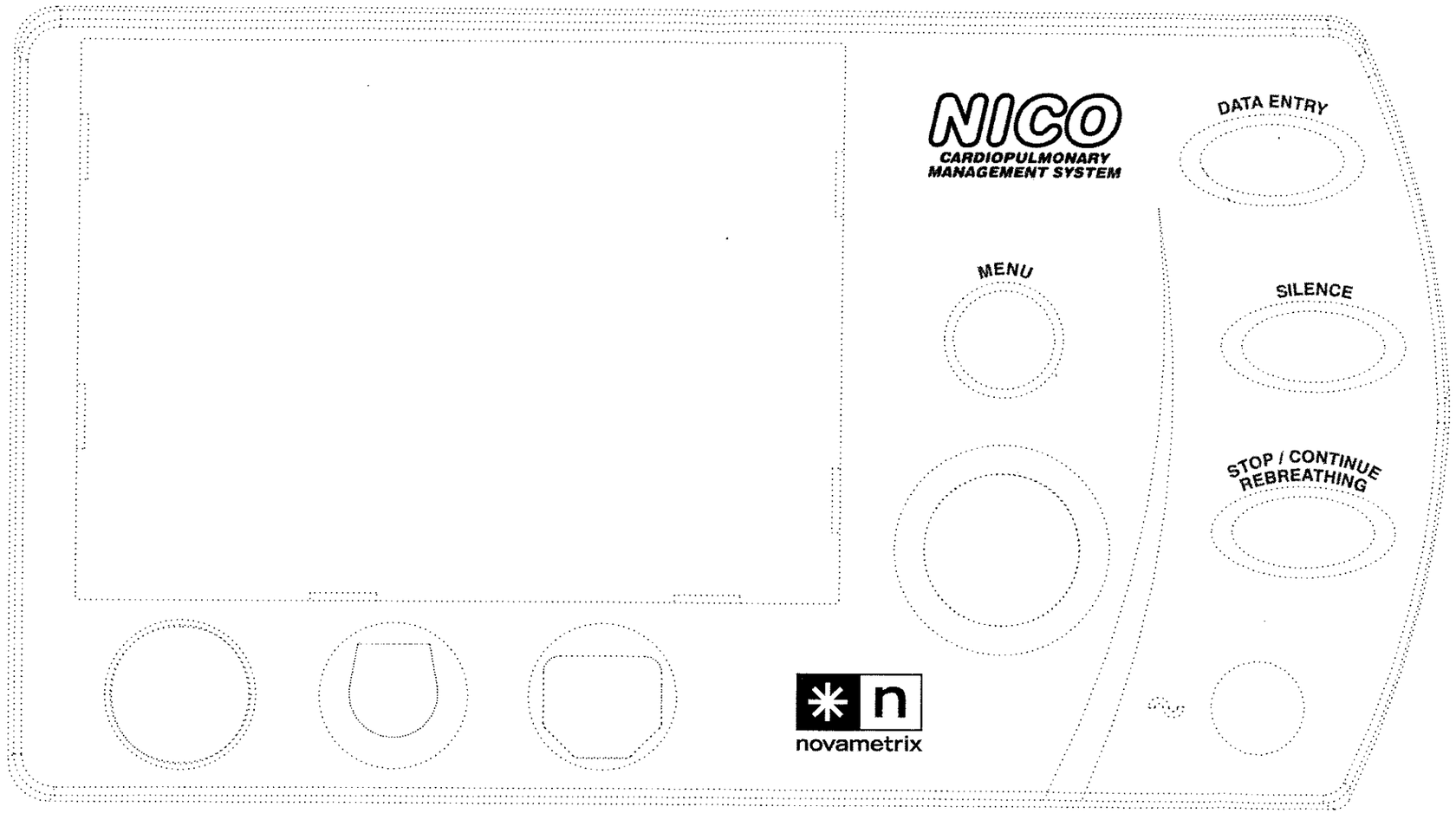
8928-02-02

novametrix™

NOVAMETRIX MEDICAL SYSTEMS INC.
WALLINGFORD, CONNECTICUT U.S.A. 06492

Novametrix PN: 8928-02-02
Artwork, Label, Ear Clips
Used with PN: 6131

473



Novametrix PN:9501-02-01, Artwork, Model 7300 front panel

474

NICO®

CARDIOPULMONARY MANAGEMENT SYSTEM

novametrix™

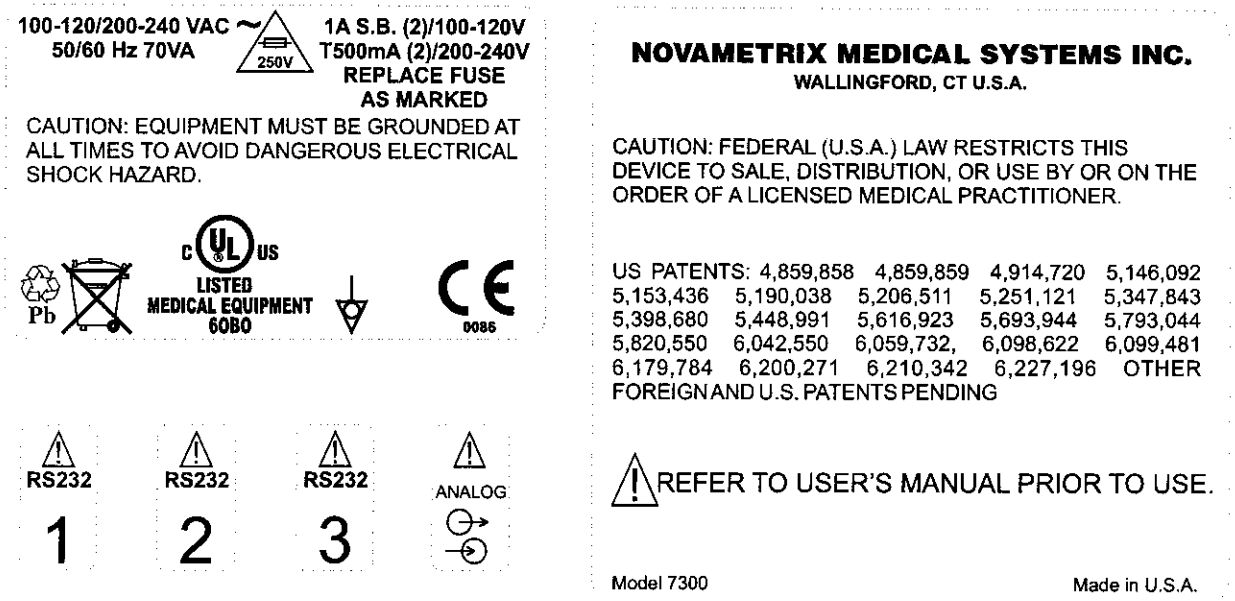
DANGER - EXPLOSION HAZARD. DO NOT USE IN PRESENCE OF FLAMMABLE ANESTHETICS.

DANGER - RISQUE D'EXPLOSION. NE PAS EMPLOYER EN PRÉSENCE D'ANESTHÉSIQUES INFLAMMABLES.

CAUTION - ELECTRIC SHOCK HAZARD. DO NOT REMOVE COVERS OR PANELS. REFER SERVICING TO QUALIFIED SERVICE PERSONNEL.

ATTENTION - RISQUE DE DÉCHARGES ÉLECTRIQUES. NE PAS ENLEVER LES COUVERCLES OU LES PANNEAUX. SE RÉFÉRER POUR L'ENTRETIEN À UN PERSONNEL QUALIFÉ.

Novametrix PN: 9487-02-02 Artwork, top cover label, Model 7300



Novametrix PN: 9486-02-03 Artwork, rear panel Model 7300

APPENDIX 2: PREDICATE DEVICES INFORMATION

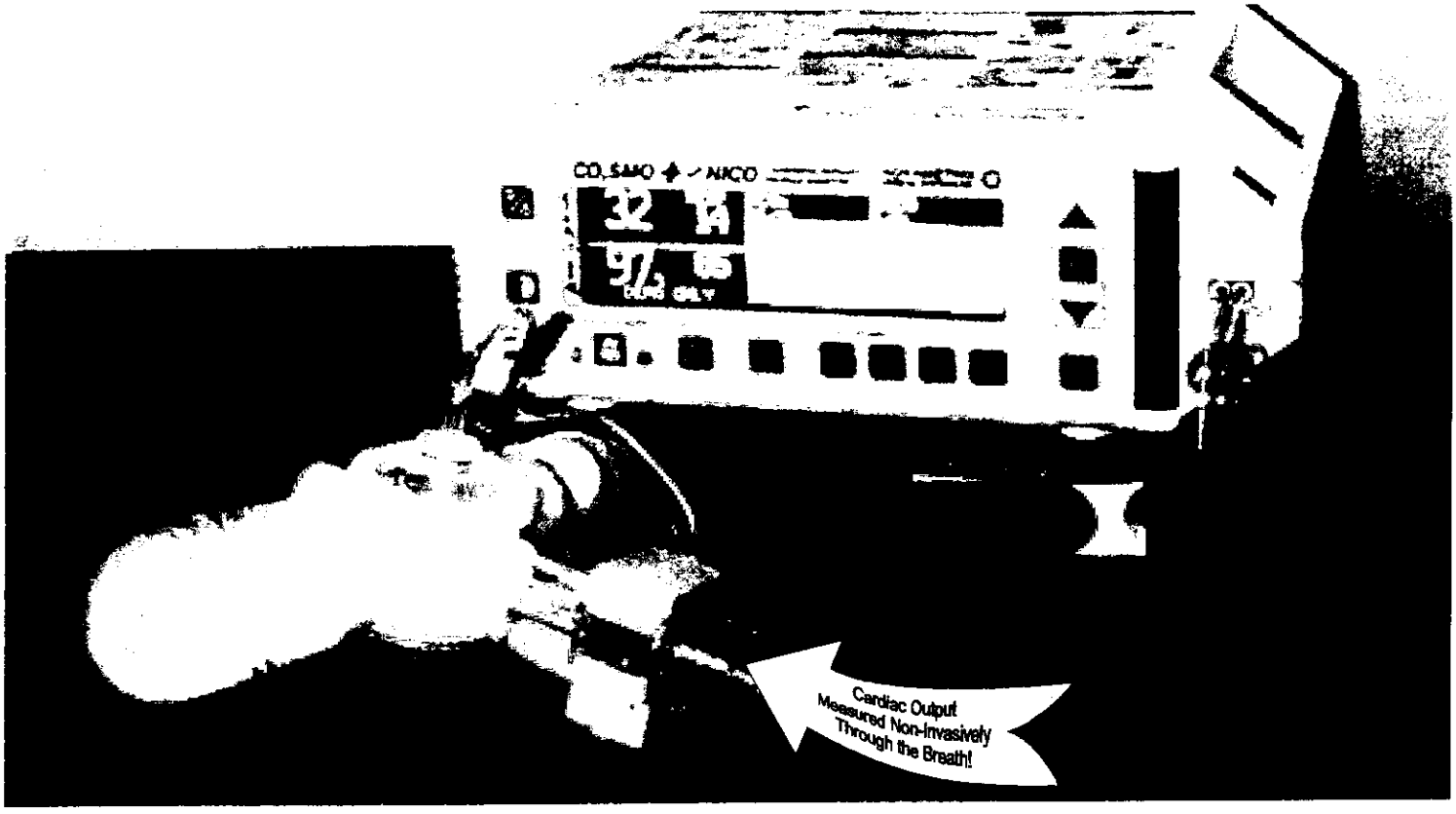
The predicate devices product literature listed in the table below for the Respironics Novametrix *NICO with MARS* are included in this appendix.

Device Name	510(k) Number (if applicable)	Manufacturer	Comments
CO_2SMO Plus! with NICO, Model 8200/ NICO Model 7300	K982499	Respironics Novametrix, Inc.	Respiratory Profile Monitor that includes partial rebreathing cardiac output
MARSpO_2 , Model 2001	K993979 K000794	Respironics Novametrix, Inc.	Stand-alone Pulse Oximeter

477

CO_2SMO PLUS! with NICO

CARDIOPULMONARY PROFILE MONITOR



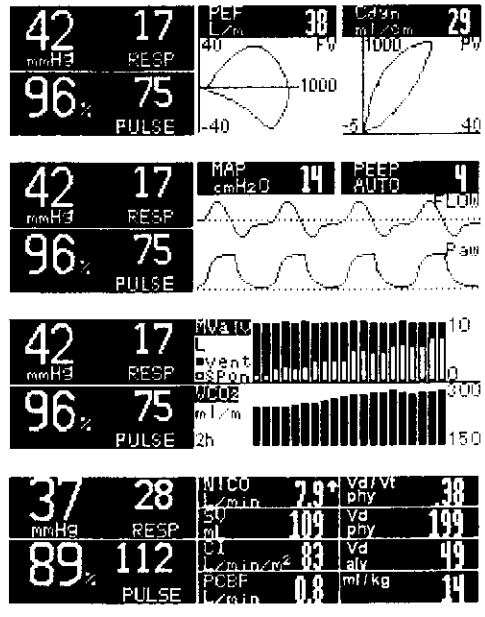
NEW FEATURE! Noninvasive Cardiac Output...

The CO_2SMO Plus! now has noninvasive cardiac output measurements for adult and larger pediatric patients on mechanical ventilation. Cardiac output measurements are made through the breath based on the Fick principle, using the partial CO_2 rebreathing technique. Stroke volume, cardiac index and pulmonary capillary blood flow can also be displayed.

FEATURES

- ***Efficient patient management*** - Provides a continuous cardiopulmonary profile, including cardiac output, CO_2 production and deadspace measurements*.
- ***True determination of patient status*** - Critical flow, pressure and volume measurements are made at the patient's airway rather than inside the ventilator.
- ***Versatility*** - Works with any ventilator and can be used during intra-hospital transport**.
- ***Enhanced graphics*** - Can be connected to a personal computer for enhanced graphics and trending.
- ***Safety*** - Capnography, pulse oximetry and respiratory mechanics are combined into one easy to use monitor.
- ***Standard two year warranty*** - On the *CO_2SMO Plus! with NICO* and CAPNOSTAT® mainstream CO_2 sensor.

PLUS! DISPLAY FORMATS



* See reverse for parameter list.

** NICO measurements for patients on mechanical ventilation only.

PRELIMINARY
Pending 510(k)
Clearance

NOVAMETRIX
MEDICAL SYSTEMS INC.

4/28

Technical Specifications for CO_2SMO Plus with NICO

PRELIMINARY
Pending 510(k) Clearance

CAPNOGRAPH

PRINCIPLE OF OPERATION
Single beam, non-dispersive infrared absorption, solid state.

INITIALIZATION TIME
Capnogram within 15 sec., full specifications within 60 sec.

CALIBRATION
Routine calibration not required. Adapter zero performed when changing to different style of adapter. Verifier on sensor cable.

CAPNOSTAT® MAINSTREAM CO_2 SENSOR

Size:	1.30" x 1.67" x .85" (3.30 x 4.24 x 2.16 cm)
Weight:	.64 oz. (18 grams) - cable excluded
Durability:	Withstands repeated 6 foot drops.

AIRWAY ADAPTERS
Adult/pediatric and neonatal single patient use CO_2 adapters available separately or combined with flow sensor. Reusable CO_2 adapters also available.

CO_2 (CARBON DIOXIDE)

Range:	0 - 100 mmHg
Accuracy:	±2 mmHg (for 0 - 40 mmHg)
	±5% of reading (for 41 - 70 mmHg)
	±8% of reading (for 71 - 100 mmHg)
Resolution:	1 mmHg
Response Time:	60 ms

RESPIRATORY RATE

Range:	0 - 150 br/min
Accuracy:	±1 br/min
Resolution:	1 br/min

FLOW SENSOR

PRINCIPLE OF OPERATION
Fixed orifice, differential pressure (pediatric/adult and neonatal).

FLOW

Range:	0.25 - 35 L/min (neo.), 2 - 180 L/min (ped./adult)
Accuracy:	Greater of ±3% of reading or
	.125 L/min (neonatal), .5 L/min (ped./adult)

OTHER (RANGE)

Minute Volume:	0.1 - 15 L/min (neo.), 2 - 60 L/min (ped./adult)
Tidal Volume:	1 - 500 ml (neo.), 100 - 3000 ml (ped./adult)
Airway Presure:	-120 to +120 cmH_2O

PULSE OXIMETER

SpO_2 (OXYGEN SATURATION)

Range:	0 - 100%
Accuracy:	±2% SpO_2 (for 80 - 100% SpO_2)
	(1 SD, or 68% of readings within claim)
	Unspecified (for 0 - 79% SpO_2)
Resolution:	1%

PULSE RATE

Range:	30 - 250 bpm
Accuracy:	±1% of full scale
Resolution:	1 bpm
Averaging:	8 seconds

SENSORS
Reusable Finger & Y-Sensors™. Single patient use sensors.

CARDIAC OUTPUT NICO

PRINCIPLE OF OPERATION
Partial CO_2 rebreathing differential Fick, non-invasive.

MEASUREMENT FREQUENCY
Rebreathing measurement made every three minutes for 50 seconds, displayed value updated every breath based on VCO_2.

DATA ENTRY SCREEN
Provides a simple means to enter patient data†.

REBREATHING VALVE / SENSOR

Valve Type:	Dual diaphragm, pneumatically controlled.
Return Spring:	Automatically returns valve to normal position.
Resistance:	3 cmH_20/L/min maximum
Rebreathed Vol.:	Normal position: 35 ml
	Rebreathing position: 100-275 ml (small)
	150-400 ml (large)
Sensor:	CO_2 / Flow sensor integrated into valve assy.

† Entering gas composition and blood gas values can enhance NICO accuracy.

GENERAL

PARAMETERS MEASURED
Parameters include $ETCO_2$, SpO_2, VCO_2, mixed expired CO_2, MV, V_T, compliance, resistance, PIP, MAP, PEEP (also identifies auto PEEP), PIF, PEF, I:E, t_i, t_e, rapid-shallow breathing index, and deadspace-related calculations: airway deadspace, alveolar minute ventilation, alveolar tidal volume, and with user entry of $PaCO_2$: physiologic deadspace, alveolar deadspace, physiologic V_D/V_T. NICO parameters: cardiac output, stroke volume, cardiac index, and pulmonary capillary blood flow (PCBF).

TREND MEMORY
Select parameters trended for 8 hours, battery backed, available through RS-232. VCO_2, MV alv, NICO and PCBF trends on-screen.

DOT MATRIX COLD CATHODE DISPLAY (CCD)
Size: 5" W x 1.5" H (12.7 x 3.08 cm)

ALERTS
Adjustable limits: $ETCO_2$, SpO_2, RR, PR, No Respiration, NICO
Audio: Adjustable volume, 2 min. silence or OFF (LED indicators)
Visual: On-screen indicator and red "Alert Bar"

RS232 COMMUNICATION OUTPUT
Connects to a PC for printing, enhanced graphics and trending

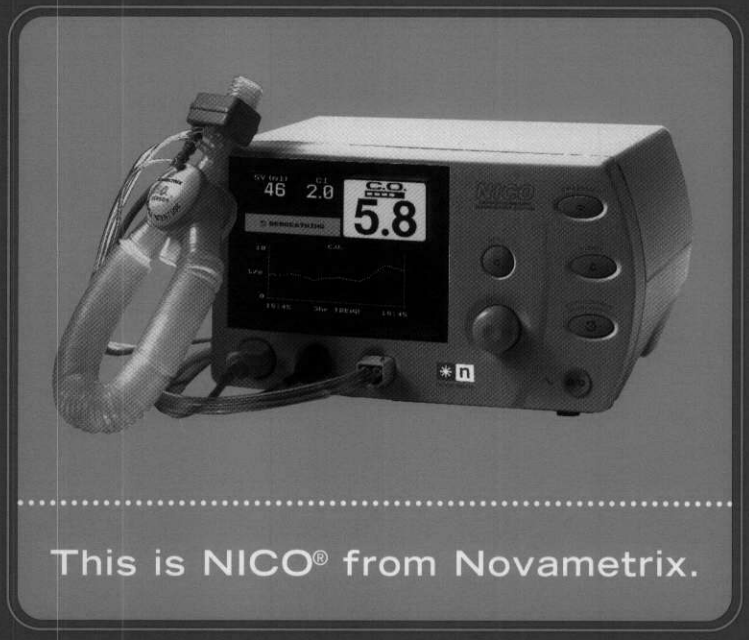
PHYSICAL
Size: 3.3" H, 9.0" W, 8.0" D (8.38 x 22.86 x 20.32 cm)
Weight: 8 lb (3.63 kg)

ELECTRICAL
Power requirements: 100 - 120/200 - 240 VAC, 50 - 60 Hz, 30 VA
Battery: Sealed lead acid gel cell, 1 hr. life, 12 hr. recharge

ENVIRONMENTAL
Operating temperature: 50 - 104°F (10 - 40°C)
Operating humidity: 0 - 90% relative (non-condensing)

NOVAMETRIX
MEDICAL SYSTEMS INC.
... simply, the leading edge

5 Technology Drive
P.O. Box 690
Wallingford, CT, USA 06492
800-243-3444 or (203) 265-7701
Fax (203) 284-0753
http://www.novametrix.com



This is NICO® from Novametrix.

The world's only integrated, non-invasive

CARDIOPULMONARY MANAGEMENT SYSTEM.

Soon to be the **standard of care** in

ORs and ICUs **around the world.**

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Photo: Courtesy of Hartford Hospital.

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Integrated cardiopulmonary management.

The heart and the lungs are designed to work together. And yet, a system that measures what the heart and lungs do together has never been developed.

UNTIL NOW.

Now, there's NICO from Novametrix – the world's only integrated and non-invasive cardiopulmonary management system.

- **With NICO, you can take the guesswork out of fluid management by accurate measurement of cardiac output.**
- **With NICO, you can optimize ventilation without compromising cardiac performance.**
- **With NICO, you can quickly identify when a patient is retaining CO_2 through breath-by-breath volumetric CO_2 measurement.**
- **With NICO, you can monitor effective cardiopulmonary performance.**

NICO from Novametrix.

Soon to be the standard of care in ORs and ICUs around the world.

Now you can take the guesswork out of ventilation management.

Why do ICU professionals need NICO? Because true ventilation management is about patient response to ventilator settings.

Many ventilators monitor the machine side of the breathing circuit. We give you the patient side.

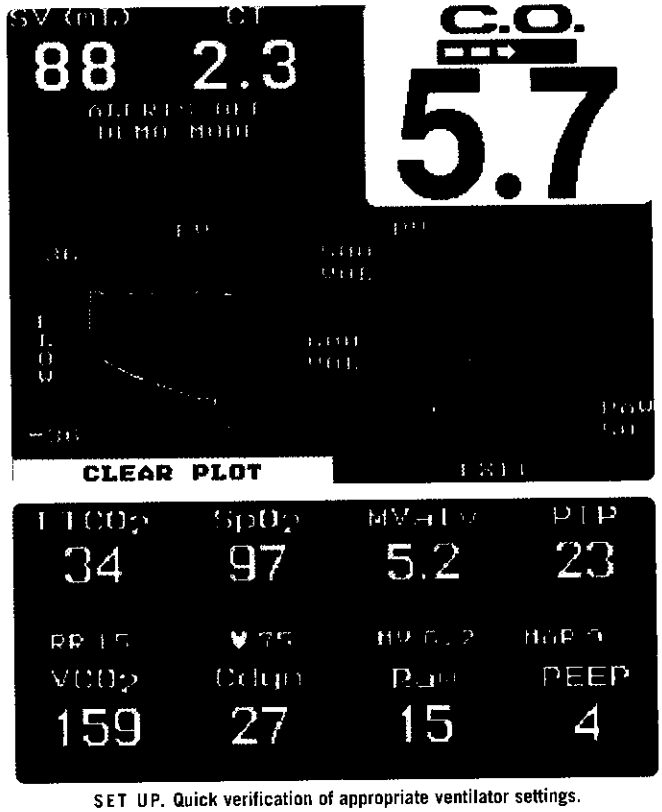
FROM SET UP TO WEANING.

NICO is a valuable tool during the entire ventilation process: set up, monitoring and weaning.

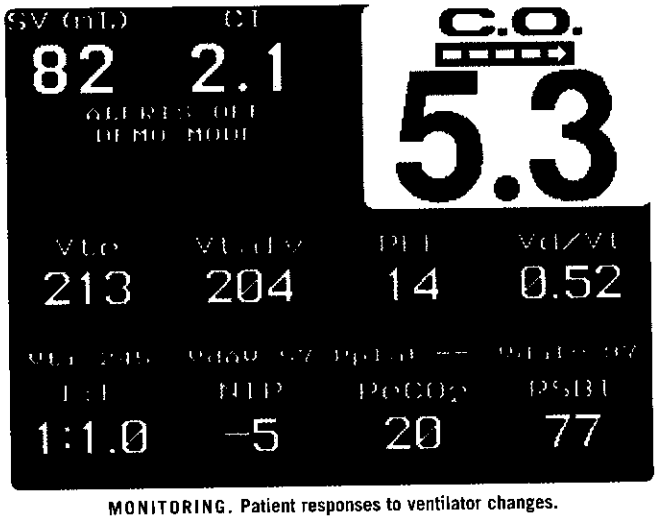
BREATH-BY-BREATH VOLUMETRIC CO2: A REVOLUTIONARY BREAKTHROUGH IN VENTILATOR MANAGEMENT.

NICO goes beyond conventional capnography to measure breath-by-breath volumetric CO_2 – a unique feature from Novametrix.

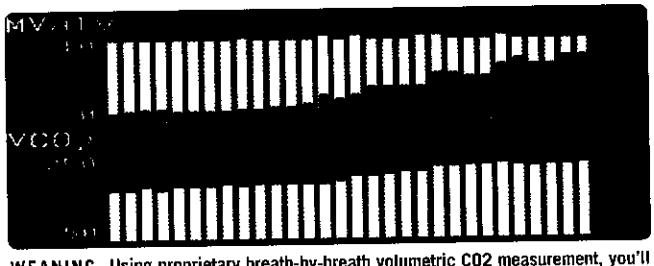
Breath-by-breath volumetric CO_2 is a revolutionary breakthrough in ventilator management. It provides you with faster patient feedback when it really counts. And it's the only patient variable that can provide early warning of CO_2 retention.



SET UP. Quick verification of appropriate ventilator settings.



MONITORING. Patient responses to ventilator changes.



WEANING. Using proprietary breath-by-breath volumetric CO2 measurement, you'll know if your patient is weaning successfully. Only NICO provides you with early warning of weaning failure.

UNTIL NOW, VENTILATION MANAGEMENT HAS BEEN EDUCATED GUESSWORK.

Now, NICO offers a different approach: data. For instance, NICO:

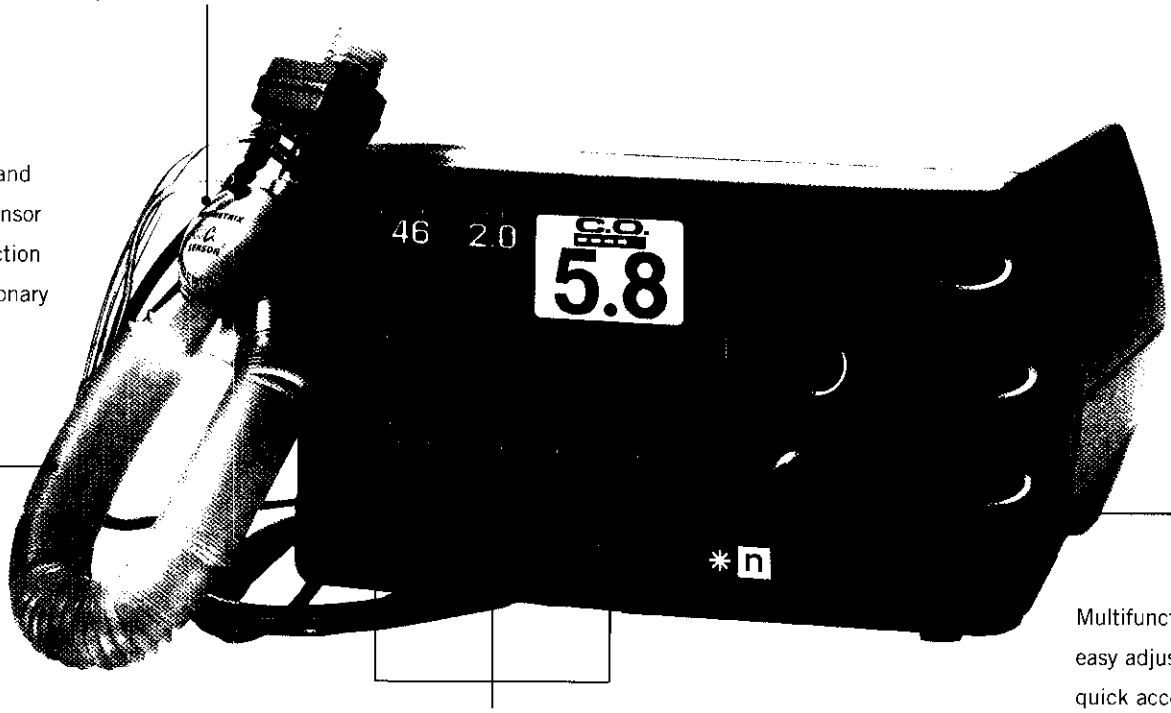
- > Allows quick ventilator set up.
- > Provides quickly identified patient responses to ventilator changes.
- > Helps optimize ventilator settings to accelerate the weaning process and reduce hospital costs.

With NICO, guesswork, extra costs, and patient risk are all reduced. That's why NICO is fast becoming the standard of care in the ICU today.

VENTILATION WITHOUT COMPROMISING CARDIAC PERFORMANCE.

Mechanical ventilation can compromise cardiac performance by increasing intrathoracic pressure. The NICO cardiopulmonary management system calculates cardiac output, allowing ICU professionals to know when a patient's heart is under stress.

With NICO, you can optimize ventilation without compromising cardiac performance.



Soon to be the standard of care in the OR for virtually every procedure.

Why do OR professionals need NICO? Because the NICO cardiopulmonary management system is an invaluable tool in the OR for virtually all procedures – from a simple appendectomy to the most complex heart transplant.

With NICO, you can monitor over forty variables for cardiopulmonary assessment, including:

> Cardiac output.

> Cardiac index.

> Stroke volume.

> Pulmonary capillary blood flow (PCBF).

Until now, you've been unable to measure cardiac performance in most of your surgical patients because of the hazards and risks of PA catheters.

Since NICO is non-invasive and easy to use, you can monitor cardiac performance and diagnose hemodynamic instability in all your patients.

NICO AND THE FICK PRINCIPLE.

NICO uses partial CO_2 rebreathing, based on the well-known and accepted Fick Principle.

With this method, the cardiac output is based on breath-by-breath measurements of CO_2 elimination by our proprietary NICO Sensor.

BY MEASURING PCBF, NICO IS THE ONLY MONITOR THAT MEASURES "EFFECTIVE CARDIAC OUTPUT."

By monitoring PCBF through respiratory gas analysis, NICO measures how effectively the heart and lungs are functioning together.

This measurement can be considered "effective cardiac output" and it can be a valuable asset in the OR.

YOU DON'T HAVE TO FLY BLIND MANAGING REFRACTORY HYPOTENSION.

How do you differentiate loss of vascular tone from volume depletion when diagnosing hypotension? Are you flying blind deciding between vasoconstrictors and volume replacement to treat hypotension?

Making the wrong choice can have serious consequences. But now you don't have to guess. Now, thanks to NICO, you have the hard data you need to make the right decision.

The more you know the flow, the more peace of mind you'll have.

WANT MORE INFORMATION?

NICO is a revolutionary product that replaces guesswork with comprehensive and accurate information about a patient's cardiopulmonary condition.

If you want more information, please call us at **1-800-345-6443** or **724-387-4000** or visit our website at **www.novametrix.com**.

NICO from Novametrix. Soon to be the standard of care in ORs and ICUs around the world.

Courtesy of Hartford Hospital.

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NOVAMETRIX NICO®
Cardiopulmonary Management System

NICO® SPECIFICATIONS

Ventilation Mode

Patients on controlled mechanical ventilation or patients breathing spontaneously with ventilation support.

Principle of Operation

Partial CO_2 rebreathing differential Fick, non-invasive.

Measurement Frequency

Rebreathing measurement made every three minutes for 35 seconds.

NICO Sensor

Valve Type: Dual diaphragm, pneumatically controlled.

Return Spring: Automatically returns valve to normal position.

Rebreathed Volume: Normal position: 35 ml.
Rebreathing Position:
125-285 ml (small)
150-450 ml (standard)
200-835 ml (large)

CO_2/Flow Sensor: Integrated into NICO Sensor.

Alerts

Adjustable limits: C.O., $ETCO_2$, SpO_2, RR, ♥, No Respiration.

Audio: Adjustable volume, 2 min. silence or OFF (LED indicator).

Visual: On-screen indication and red LED for high-priority alerts.

Internal Battery

Life: 45 minutes.

Recharge Time: 12 hours.

Type: Lead acid gel cell.

Parameters Measured	Label
Cardiac Output	CO
Cardiac Index	CI
Stroke Volume	SV
Stroke Volume Index	SVI
Pulmonary Capillary Blood Flow	PCBF
End Tidal Carbon Dioxide	$ETCO_2$
Inspired Carbon Dioxide	Insp CO_2
Mixed Expired CO_2	$PeCO_2$
Respiration Rate	RR
Oxygen Saturation	SpO_2
Pulse Rate	♥
CO_2 Elimination	VCO_2
Positive End Expiratory Pressure	PEEP
Mean Airway Pressure	MAP
Peak Inspiratory Pressure	PIP
Peak Inspiratory Flow	PIF
Peak Expiratory Flow	PEF
Systematic Vascular Resistance	SVR
Airway Deadspace	VdAw
Deadspace to Tidal Volume Ratio	Vd/Vt
Rapid Shallow Breathing Index	RSBI
Minute Volume	MV
Alveolar Minute Volume	MV_{alv}
Inspired Tidal Volume	Vti
Expired Tidal Volume	Vte
Dynamic Compliance	C_{dyn}
Airway Resistance	R_{aw}

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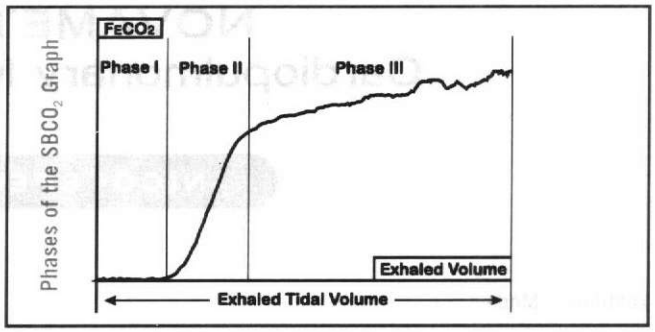
VOLUMETRIC CO_2 MEASUREMENT

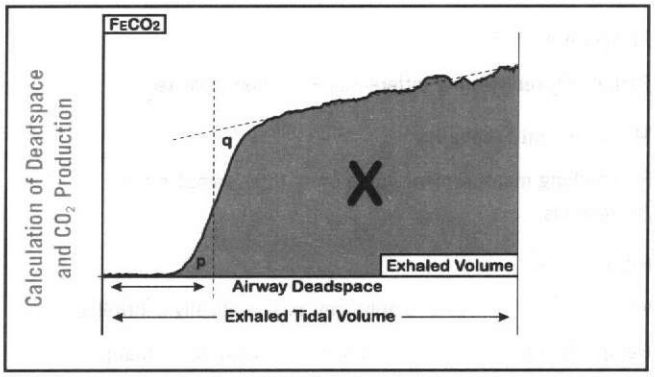
Phases of the $SBCO_2$ Graph

- Phase I represents airway deadspace. It is the CO_2-free portion of the exhaled breath from the conducting airways.
- Phase II represents the mixing of airway deadspace gas with alveolar gas and is characterized by a significant rise in CO_2.
- Phase III represents alveolar volume. The plateau reflects the level of effective ventilation in the alveoli.



Calculation of Deadspace and CO_2 Production

- Two lines (shown dotted) are constructed on the graph: one on the slope of Phase III and the other such that areas p and q are equal.
- Airway deadspace (Vd airway) is measured from the start of expiration to the point where the vertical line crosses the exhaled volume axis.
- The volume of CO_2 in the breath is equal to area X, the total area under the curve. Adding individual breath volumes allows CO_2 production to be calculated (in ml/min).

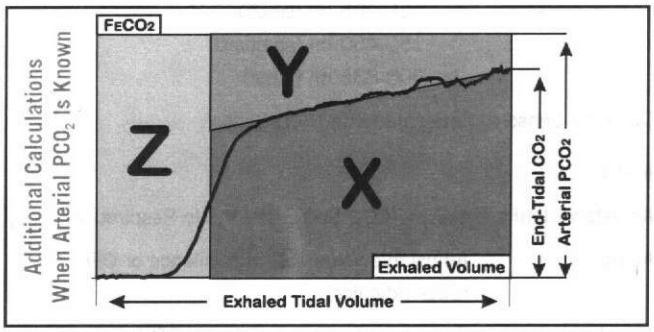


Additional Calculations when Arterial PCO_2 is Known

- Physiologic Vd/Vt as well as physiologic and alveolar deadspace can also be calculated if arterial PCO_2 is known. A line representing the arterial PCO_2 value is constructed parallel to the exhaled volume axis creating areas Y and Z. Area X represents the volume of CO_2 in the exhaled tidal volume. Areas Y and Z represent wasted ventilation due to alveolar and airway deadspace respectively.

Calculations:

- Physiologic Vd/Vt = (Y+Z) / (X+Y+Z)
- Physiologic Deadspace (Vd phys) = (Vd/Vt phys) (Vt)
- Alveolar Deadspace (Vd alv) = Vd phys - Vd airway



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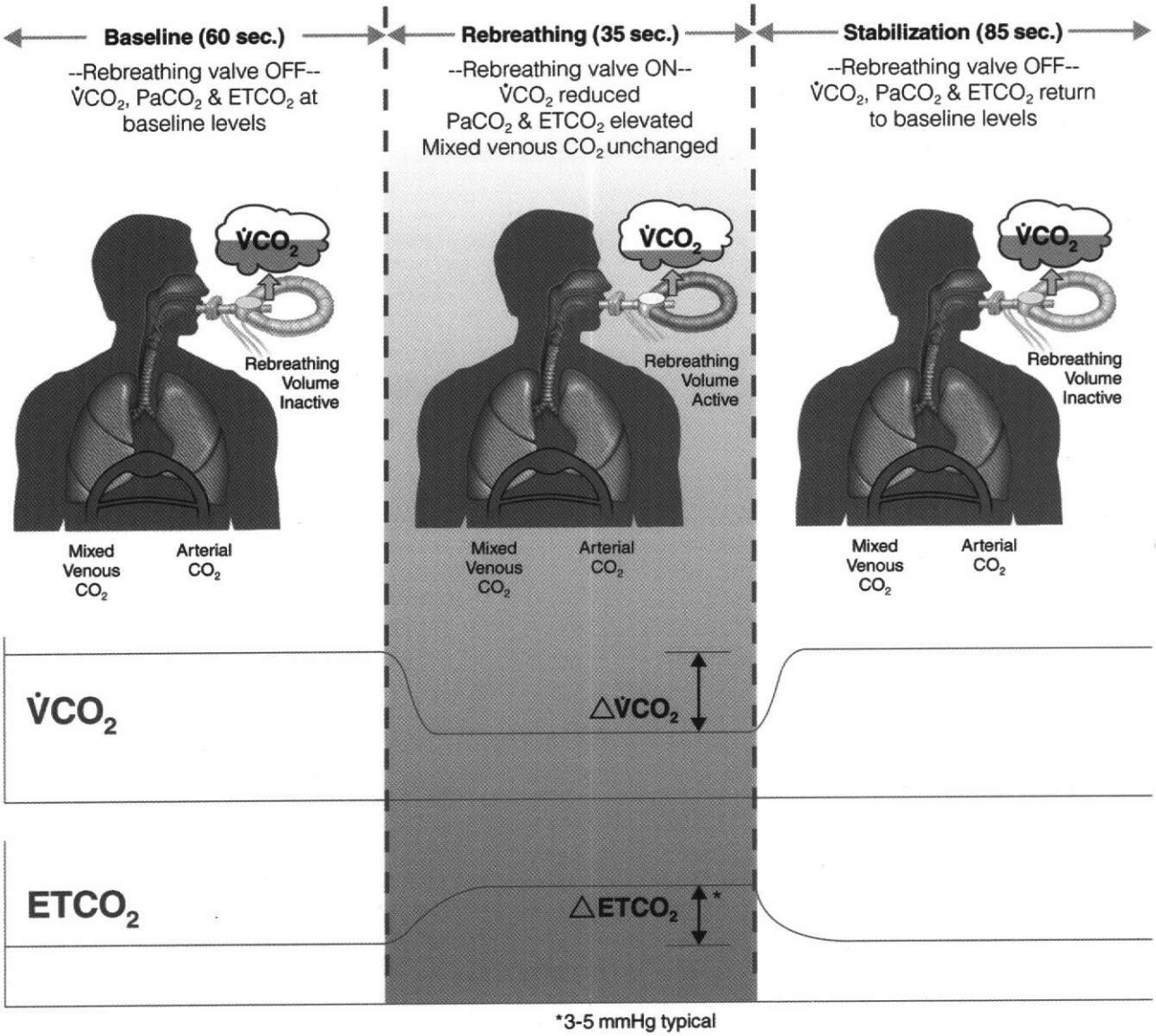
NOVAMETRIX NICO®
Cardiopulmonary Management System

MEASURING CARDIAC OUTPUT BY FICK CO_2

The NICO® system provides continual non-invasive cardiac output monitoring. It uses a method known as partial CO_2 rebreathing, which is based on the well-accepted Fick principle. With this method, the cardiac output is proportional to the change in CO_2 elimination divided by the change in end tidal CO_2 resulting from a brief rebreathing period. These changes are accomplished and measured by the proprietary NICO Sensor, which periodically adds a rebreathing volume into the breathing circuit.

NICO TIMING DIAGRAM (3-MINUTE CYCLE)



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PARTIAL CO_2 REBREATHING DIFFERENTIAL FICK EQUATION

CO_2 Fick Equation: C.O. = $\dfrac{\dot{V}CO_2}{C_{\bar{v}}CO_2 - C_aCO_2}$

Applied with and without rebreathing:

$$\text{C.O.} = \frac{\dot{V}CO_{2N}}{C_{\bar{v}}CO_{2N} - C_aCO_{2N}} = \frac{\dot{V}CO_{2R}}{C_{\bar{v}}CO_{2R} - C_aCO_{2R}}$$

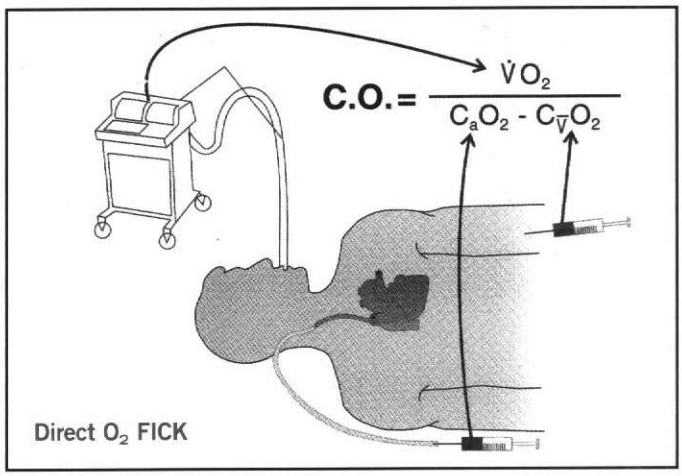
Combining to form the differential Fick equation (based on the Law of Ratios):

$$\left(\frac{A}{B} = \frac{C}{D} = \frac{A\text{-}C}{B\text{-}D} = X\right)$$

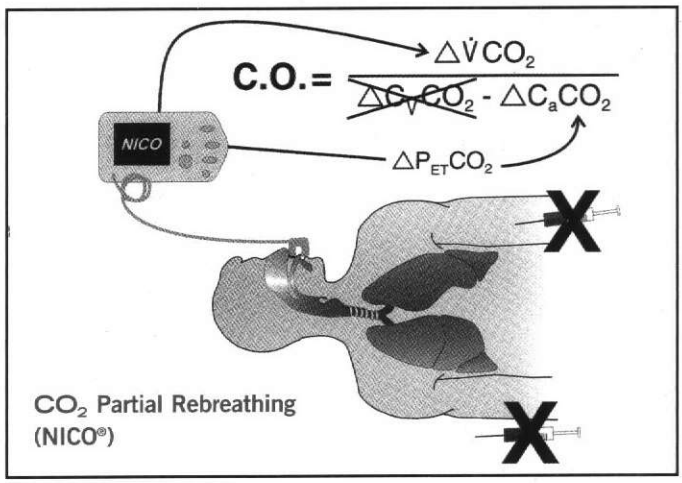
$$\text{C.O.} = \frac{\dot{V}CO_{2N} - \dot{V}CO_{2R}}{(C_{\bar{v}}CO_{2N} - C_aCO_{2N}) - (C_{\bar{v}}CO_{2R} - C_aCO_{2R})}$$

$$= \frac{\Delta\dot{V}CO_2}{\Delta C_aCO_2} = \frac{\Delta\dot{V}CO_2}{S\Delta ETCO_2}$$

Where	Assumptions
• C.O. = cardiac output. • R = rebreathing, N = normal breathing. • $C\bar{v}CO_2$ = mixed venous CO_2 content. • C_aCO_2 = arterial CO_2 content. • $\dot{V}CO_2$ = CO_2 elimination rate • S = slope of CO_2 dissociation curve.	• $C\bar{v}CO_2$ and V_D/V_T are constant during the measurement period. • A shunt correction is added to the final equation, based on FiO_2 and SpO_2.



- $\dot{V}O_2$ measured by metabolic cart.
- C_aO_2 calculated from arterial blood gas analysis.
- $C_{\bar{v}}O_2$ calculated from mixed venous blood gas analysis.
- Intrapulmonary shunt included in the measurement.



- Change in $\dot{V}CO_2$ measured by CO_2/Flow sensor.
- Change in C_aO_2 measured by mainstream CO_2 sensor (reflected as change in $ETCO_2$).
- Use of partial rebreathing method eliminates need for $C_{\bar{v}}O_2$.
- Corrected for intrapulmonary shunt.

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SLEEP MANAGEMENT℠ | CHRONIC RESPIRATORY MANAGEMENT℠ | CARDIORESPIRATORY CARE℠ | ASTHMA, ALLERGY & SINUSITIS MANAGEMENT℠ | NEONATAL & INFANT CARE℠

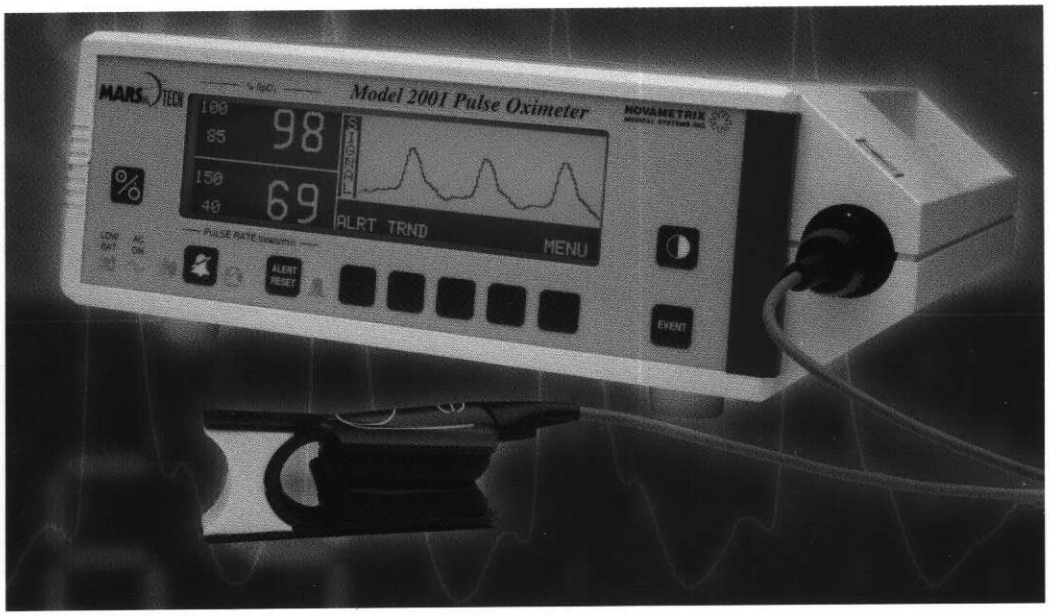
Since 1978, Novametrix has been at the forefront of designing, developing, and manufacturing leading-edge electronic instruments and sensors for the medical profession. | Our unique and proprietary products in cardiopulmonary management, pulse oximetry, capnography, transcutaneous monitoring and developmental care have been widely recognized for their quality and technical superiority. | The versatility of our products extends to the operating room, emergency room, intensive care unit, neonatal intensive care unit, respiratory care department and patient transport.

Customer Service: 1-800-345-6443 or 724-387-4000

MONITORS

Model 2001 Pulse Oximeter

The Next Generation in Pulse Oximetry.



Exceptional: Leading-edge technology at half the price of other systems.

Informative: More data when you need it most.

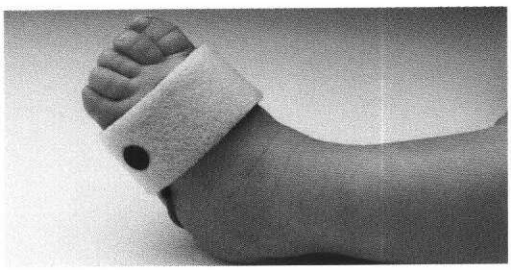
Reliable: Even under the most challenging clinical conditions.

The technology engineered for clinicians

The Novametrix Model 2001 MARSpO2™ Pulse Oximeter is the next generation in pulse oximetry technology. As a clinician, you know that reliable readings are critical. Novametrix's remarkable Motion Artifact Rejection System (MARS) takes advantage of new technological breakthroughs in signal processing to provide improved analysis of the patient signal. The result is more reliable SpO2 readings, a reduction in false alarms, and less monitoring interruptions.

Grace under pressure

Two problems have traditionally plagued pulse oximeters: obtaining readings under adverse conditions, and unnecessary, false alarms. Poor-quality signals cause traditional pulse oximeters to blank the display, set off alarms, or display erratic values while it searches for a high-quality signal. Novametrix's state-of-the-art MARS technology enables the pulse oximeter to provide reliable readings, even in the presence of excessive motion or low perfusion. The result is superior performance during the most challenging clinical conditions, guaranteeing enhanced clinical management at a lower cost than traditional technologies.



The Y-Sensor™ attaches quickly and easily with a wide variety of applicators.

User friendly

As with all Novametrix monitors, the Model 2001 MARS Pulse Oximeter includes a multitude of features selected by clinicians to make it easier and more convenient to use. A variety of user-selected functions are available, along with analog and serial data output options.

MARS pO2 TECH

Novametrix's MARS (Motion Artifact Rejection System) is pulse oximetry monitoring technology that significantly reduces false alarms.

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The Novametrix Model 2001 Pulse Oximeter offers a wide selection of sensors and applicators.

Non-adhesive Foam Wrap
Large 8836-00
Small 8943-00

Adhesive Foam Wrap
Large 6929-00
Small 6968-00

Tape Strips
20mm 8828-00
25mm 8829-00

Butterfly Style Wraps
20mm 8831-00
25mm 8832-00

Ear Clips
6131-50
6131-25

Finger Sensor
8776-00
8744-00

Y-Sensor
8791-00
8793-00

Novametrix
Medical Systems Inc.
5 Technology Drive,
Wallingford, CT 06492
(800) 243-3444
(203) 265-7701
www.novametrix.com

CE
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An intelligent investment

As with all Novametrix pulse oximeters, the Model 2001 MARS Pulse Oximeter uniquely combines state-of-the-art technology with our innovative reusable sensor program. Sized to accommodate every patient, the sensors are designed to provide the ultimate in patient comfort and durability. Simple to clean and easy to reuse, Novametrix reusable sensors can be applied over and over again at just half the cost of disposable sensors.

Technical Specifications

Principle of Operation
- Red/Infrared Absorption

Oxygen Saturation (SpO_2)
- *Range:* 0-100%
- *Accuracy:* 70-100% ±2% (1 standard deviation); 0-69% unspecified (Approximately 68% of the observations are within the accuracy claims)
- *Resolution:* 1%
- *Averaging:* 8 seconds
- *Audible SpO_2 Trend Feature:* Pitch of Pulse Rate tracks the SpO_2 value (i.e. decreasing SpO_2 values are signaled by lower pitched beeps)

Pulse Rate
- *Range:* 30-250 beats per minute (bpm)
- *Accuracy:* ±1% of full scale
- *Resolution:* 1 bpm
- *Averaging:* 8 seconds

Sensors
- Reusable Y-Sensor™ (can be sterilized and used on all patient populations) and reusable adult finger sensor

Plethysmogram
- Pulsatile waveform with autogain (autogain in menu selectable on/off)

General Specifications

Alerts
- *Limits:* Automatic and adjustable limits for SpO_2 and pulse rate
- *Audio:* Adjustable volume, 2 min. silence or OFF (LED indicators)
- *Visual:* Flashing numerics upon violated limit(s) & red "Alert Bar"
- *Messages:* Sensor disconnect, sensor off patient, low signal, insufficient light, high ambient light, pulse out of range, sensor faulty, monitor faulty

Display
- *Type:* Dot matrix, Cold Cathode Display (CCD)
- *Size:* 5" W x 1.5" H (12.7 x 3.08 cm)

Graphic Trend/Histogram
- *Memory:* 24 hrs, battery backed
- *Format:* On-screen in 30 minutes, 2, 8 or 12 hour segments, printed up to 24 hours

Communication Output:
- *Digital:* RS232 (NovaCARD™ software, computer interface, Seiko DPU 414 thermal printer)
- *Analog:* Optional module, 0-1 VDC (numerics and waveform)

Physical:
- *Size:* 3.3" H x 9.0" W x 8.0" D (8.38 x 22.86 x 20.32 cm)
- *Weight:* 7 lbs, 5 oz. (3.32 kg)

Electrical:
- *Power Requirements:* 100-120/200-240 VAC, 50-60 Hz, 30 VA
- *Battery:* Sealed lead acid gel cell, 3 hr. life, 12 hour recharge

Environmental:
- *Operating Temperature:* 50-104° F (10-40°C)
- *Operating Humidity:* 0-90% relative (non-condensing)

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NOVAMETRIX MEDICAL SYSTEMS INC.

APPENDIX 3: SUBSTANTIAL EQUIVALENCE COMPARISON CHARTS

Overview

The *NICO Model 7300 with MARS* and all of its sensors are similar to the 510(k) cleared CO_2SMO Plus! with NICO and its sensors or the MARSpO2 Model 2001 and its sensors. The functions, calculated parameters, device technologies, specifications, design, materials, features, ranges and accuracies of flow, volume and pressure, sampling rate and other pertinent aspects of both of these devices are compared.

Table A3-1 – Respiratory Profile Monitor Predicate Device

Manufacturer	510(k) #	Product Name	Device Type
Novametrix	K982499	CO_2SMO Plus! with NICO	standalone respiratory mechanics monitor with partial rebreathing cardiac output
Novametrix	K993979 K000794	MARSpO_2	Standalone pulse oximeter

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TABLES OF COMPARISON TO LEGALLY MARKETED DEVICES

The following tables compare the intended uses, specifications and parameters measured of the modified device, the NICO with MARS monitor to the predicate devices.

Table A3- 2 - List of Comparison Tables for Predicate Devices

Table	Table Name	Purpose
A3-3	Intended Uses	Lists the intended uses of the NICO with MARS and CO_2SMO Plus! with NICO
A3-4	Adult/Pediatric/Neonatal Flow Specifications – CO2/Flow Sensor	Lists the specifications of the flow sensors
A3-5	CO_2 Specifications	Lists the specifications relating to CO_2.
A3-6	SpO_2 Specifications	Lists the specifications relating to SpO_2
A3-7	Miscellaneous Specification	Lists other specification not provided in Tables A3- 4-7.
A3-8	Parameters	Lists the calculated parameters of the NICO with MARS and CO_2SMO Plus! with NICO
A3-9	Predicate Devices -Valve	Compares the rebreathing value of the NICO with MARS and CO_2SMO Plus! with NICO.
A3-10	Partial Rebreathing Algorithm	Compares the cardiac output algorithm of the NICO with MARS and CO_2SMO Plus! with NICO.

Table A3-3 - Intended Uses CO_2SMO Plus! with NICO and Predicate Devices

Intended Use(s)	New-Modified Device NICO with MARS	Predicate Device(s) CO_2SMO Plus! with NICO
ICU, ventilator management - pediatric/ adults	√[a]	√[a]
ICU, ventilator management - neonates	√[a]	√[a]
ED	√[a]	√[a]
OR – ventilator management	√[a]	√[a]
ICU – cardiac output monitoring	√[a]	√[a]
OR – cardiac output monitoring	√[a]	√[a]

a. Separate sensors but same system for adult, pediatric and neonatal.

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Table A3-4 - Adult/Pediatric/Neonatal Flow Specifications – CO2/Flow Sensor - NICO with MARS and CO_2SMO Plus! with NICO

Specification	Adult Flow/CO_2 Sensor		Neonatal Flow/CO_2 Sensor		Pediatric Flow/CO_2 Sensor	
	NICO with MARS	CO2SMO Plus! with NICO	NICO with MARS	CO2SMO Plus! with NICO	NICO with MARS	CO2SMO Plus! with NICO
Flow Range (LPM)	2 - 180	same	0.25 - 25	same	0.5 - 100	N/A
Flow Accuracy	greater of 0.5 LPM or ± 3% of reading	same	greater of 0.125 LPM or ± 3% of reading	same	greater of 0.25 LPM or ± 3% of reading	N/A
Tidal Volume Range (mL)	100 - 3000	same	2 - 100	same	30 - 400	N/A
Volume Accuracy	greater of ± 10 mL or ± 3% of reading	same	greater of ± 1.0 mL or ± 3% of reading	same	greater of ± 3.0 mL or ± 3% of reading	N/A
Respiratory Rate Range (br/min)	2 - 120	same	10 - 150	same	5 - 120	N/A
Respiratory Rate Accuracy	± 1 breath/min	same	± 1 breath/min	same	± 1 breath/min	N/A
Airway Pressure Range (cmH_2O)	± 120 cmH_2O	same	± 120 cmH_2O	same	± 120 cmH_2O	N/A
Airway Pressure Accuracy	greater of 0.5 cmH_2O or ± 2%	same	greater of 0.5 cmH_2O or ± 2%	same	greater of 0.5 cmH_2O or ± 2%	N/A
Pressure Drop	2.1 cmH_2O at 60 LPM	same	3.1 cmH_2O at 60 LPM	same	2.1 cmH_2O at 30 LPM	N/A
Frequency Response	greater than 12 Hz	same	greater than 12 Hz	same	greater than 12 Hz	N/A
Deadspace	< 8.5 cc installed	same	< 1 cc installed	same	< 4 cc installed	N/A
Weight of the Sensor body (gm)	9.8	same	9.6	same	10.5	N/A
ETT sizes (mm) (recommended)	5.5 mm or greater	same	4.0 mm or smaller	same	3.5 mm to 6.0 mm	N/A
Other Parameter Specifications						
Respiratory Rate - Max (breaths/min)	120	same	150	same	120	N/A
Airway Pressure Range (cm H_2O)	± 120	same	± 120	same	± 120	N/A
Airway Pressure Accuracy	greater of ±2% or 0.5 cm H_2O	same	greater of ±2% or 0.5 cm H_2O	same	greater of ±2% or 0.5 cm H_2O	N/A
Signal Processing-front end	Single gain stage with 20 bit A/D	4 gain stage with 12 bit A/D	Single gain stage with 20 bit A/D	4 gain stage with 12 bit A/D	Single gain stage with 20 bit A/D	N/A
Connector to monitor	3 port	2 port	3 port	2 port	3 port	N/A

Table A3-5 - CO_2 Specifications

Item to be Compared	NICO Model 7300	CO_2SMO Plus! with NICO
CO_2 Specifications		
Measurement Technology	mainstream/sidestream non-dispersive IR absorption	Same
Calibration Required?	routine calibration not required	Same
Range (mmHg) Resolution (mmHg)	0-150 1	0-100 1
etCO_2 Accuracy (%)	±2mmHg (0-40) ±5% of reading (41-70) ±8% of reading (71-100) Unspecified (100-150)	Same for 0-100
Compensation for N_2O / O_2	Yes, user activated	Same
Response Time (msec) (10-90% of step change)	60 ms	Same
Other Parameter Specifications		
Respiratory Rate - Accuracy (bpm)	±1	Same
Resolution (b/min) - Range (breaths/min)	1 0-150	Same
Algorithm	8 breath average	Same

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Table A3-6 – SpO_2 Specifications

Item to be Compared	NICO Model 7300	CO_2SMO Plus! with NICO	MARSpO2 Model 2001
Pulse Oximeter Specifications			
Principle of Operation	Red/Infrared absorption	Same	Same
SpO_2 - Accuracy	±2% (70-100%) Unspecified for 0-69%	±2% (80-100%) Unspecified for 0-79%	±2% (70-100%) Unspecified for 0-69%
Resolution -Range -Averaging	1% 0-100% none, 2,4 or 8 sec	1% 0-100% 2,4 or 8 sec	1% 0-100% 8 sec
Pulse Rate -Accuracy	±1% of full scale	Same	Same
Resolution (bpm) -Range (bpm) -Averaging	1 30-250 8 sec	Same	Same
Algorithm	MARS	VENUS**	MARS
Sensor	Reusable Y-Sensor or adult finger sensor, disposable adult or neonatal	Same	Same
Y-Applicators	Butterfly wrap with release liner, tape strip with release liner, adhesive and no-adhesive foam wraps	Butterfly wrap, tape Strip, adhesive and no-adhesive foam wraps	Butterfly wrap, tape Strip, adhesive and no-adhesive foam wraps

** The VENUS algorithm is the algorithm in use in all Novametrix pulse oximeters prior to the introduction of the MARSpO2 monitor. It features a robust artifact detection algorithm.

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Table A3-7 - Miscellaneous Specifications

Item to be Compared	NICO Model 7300	CO_2SMO Plus! with NICO	MARSpO2 Model 2001
Miscellaneous Features			
Board configuration	4 boards – power, digital, analog board, MARS DSP board	Single board	Main board and MARS DSP board
RS232 Output	Yes, user selectable	Yes, user selectable	Yes, user selectable
AC Power	Internal	same	same
Battery Power Type	Yes sealed lead acid gel cell	same	same
Indicators	• AC Power/Charging • Active Alert • Battery status • N_2O and O_2 Compensation • System errors • Alert audio status • Alarms- hi/lo SpO_2 and pulse rate; automatic detection of probe/patient related errors	• Same	• AC Power/Charging • Active Alert • Battery status • System errors Alert audio status • Alarms- hi/lo SpO_2 and pulse rate; automatic detection of probe/patient related errors
Memory	24 hr trend	8 hr trend	24 hr SpO_2 and pulse rate stored with 8 second resolution
EMC Safety	EN 60601-1-2 (2001) IEC 601-1, UL 544	IEC 1000-3-2, 1000-3-3, 1000-4-2, 1000-4-3, IEC 601-1, UL 544	CISPR 11 class A, IEC 801-2-3-4; IEC 601-1, CSA C22,2 No 125, UL 544
Display (size in inches, type)	EL, 5.8Wx4.1H	Dot matrix CCD 5Wx1.5H	Dot matrix CCD 5Wx1.5H
Mechanical			
Dimensions (inches)	7Hx11Wx11D	3.3Hx9Wx8D	3.3Hx9Wx8D
Weight (lbs)	9 lbs 7 oz.	8 lbs	7 lbs 5oz

Notes: CCD= cold cathode display, EL= electro-luminescent display

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Table A3-8 - Adult/Neonatal Parameters – NICO with MARS and CO_2SMO Plus! with NICO

Parameter	Units	NICO Model 7300	CO_2SMO Plus! with NICO
Minute Ventilation	LPM	√	same
Frequency	breaths/min	√	same
VT - inspired	ml	√	same
VT - expired	ml	√	same
Resistance (exp, dyn)	cm H_2O/L/sec	√	same
Compliance (dyn)	L/cm H_2O	√	same
Peak Inspiratory Pressure	cm H_2O	√	same
Peak Inspiratory Flow	LPM	√	same
Peak Expiratory Flow	LPM	√	same
Mean airway pressure	cm H_2O	√	same
PEEP	cm H_2O	√	same
RSBI (f/VT)	Breaths/min/L	√	same
Other			
Mech vs Spont discrimination	-	√	same
Parameters			
Minute Ventilation- Alv (MV alv)	LPM	√	same
V_T - effective	ml	√	same
V_D - airway	ml	√	same
VCO_2	ml/min	√	same
V_D/V_T phys	-	√	same
Mixed Exp CO_2	% or mmHg	√	same
End Tidal CO_2	% or mmHg	√	same
Inspired CO_2	% or mmHg	√	same
SpO_2	%	√	same
Pulse Rate	beats/min	√	same
Cardiac Output Parameters			
Cardiac Output	LPM	√	same
Pulmonary Capillary Blood Flow	LPM	√	same
Stroke Volume	ml	√	same
Stroke Volume Index**	ml/m^2	√	-
Systemic Vascular Resistance***	Dynes-sec/cm^5	√	-
Cardiac Index	LPM/m^2	√	same

** Stroke volume divided by body surface area (estimated from height and weight via DuBois equation)
*** Pressures are user entered.

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Table A3-9 - Predicate Devices – Valve

	NICO with MARS	CO2SMO Plus! with NICO
510(k)	K982499	K993979 K000794
Primary application	Rebreathing for cardiac output	Same
Size (valve only)	68 x 50 x 76 mm	Same
Disposable/ Single Patient Use?	Yes	Same
Actuation/Control	Pneumatically actuated double diaphragm	Same
Construction/Materials	Injection molded (body, 2 caps and 2 diaphragms, connecting rod and spring)	Same
Valve Deadspace (ml) (normal mode)	25 cc	Same
Configuration of loop ports	Y configuration	T configuration

Table A3-10 - Partial Rebreathing Algorithm

	NICO with MARS	CO2SMO Plus! with NICO
Deadspace added	35-70% of tidal volume	20-75% of tidal volume
Duration of rebreathing (secs)	Up to 35 seconds**	Up to 50 seconds
Algorithm	Regression	Bi-directional
Frequency (typical)	Once every 3 minutes Manual Mode***	Once every 3 minutes
How estimated?	Differential Fick uses *all* breath estimates of $PetCO_2$ and VCO_2 with regression approach. Content estimated from $PetCO_2$ (with various corrections)	Differential Fick requires two estimates of $PetCO_2$ and VCO_2 – one during the baseline and one during the rebreathing. Content estimated from $PetCO_2$ (with various corrections)

** see report in Appendix 4E.

*** Manual mode is an on-demand that performs 3 cycles of 3 min with 35 seconds rebreathing and stops.

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APPENDIX 4: PERFORMANCE DATA

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Appendix 4A - Performance Validation - Specification Tests

Test	Objective
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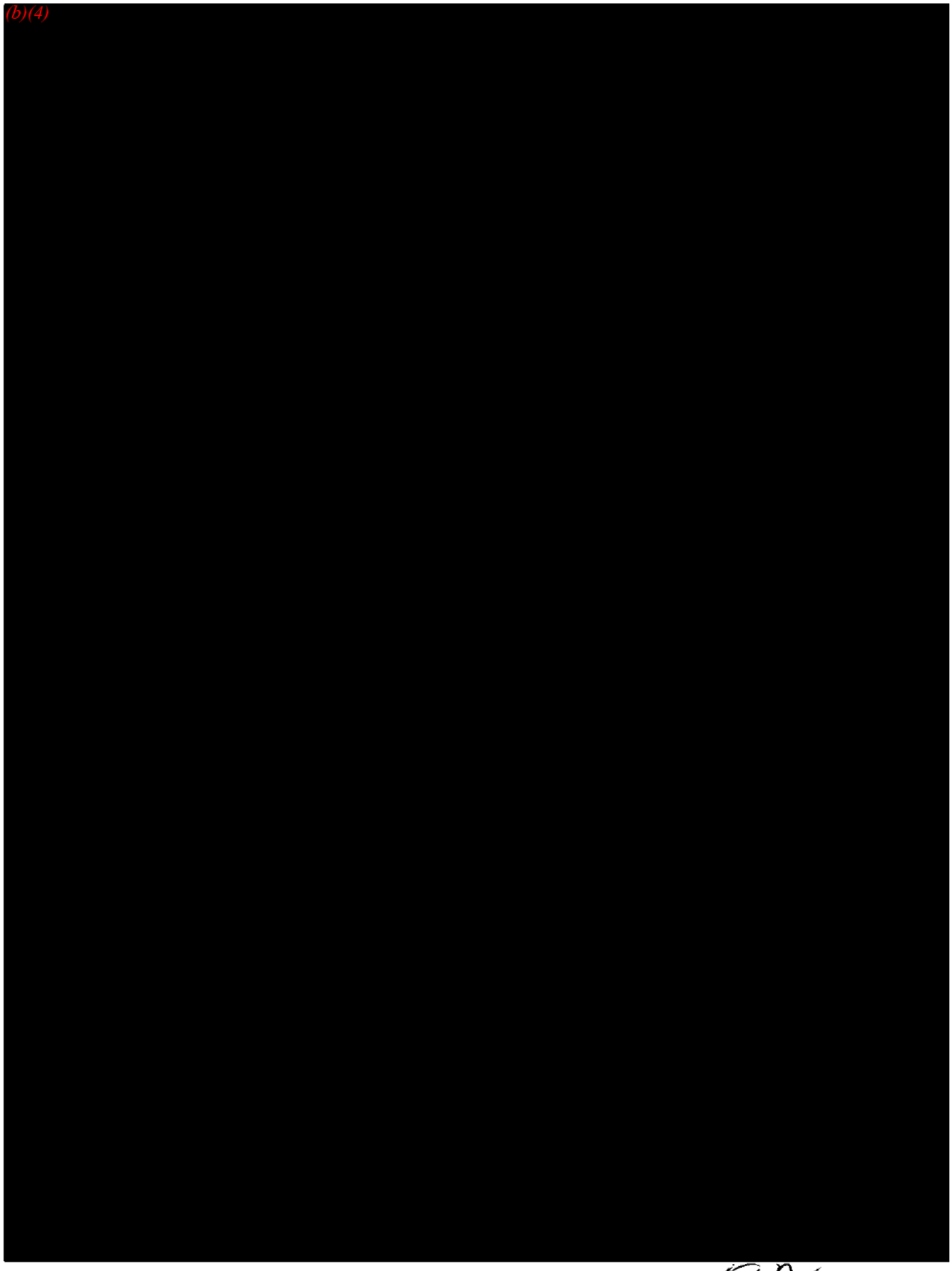

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APPENDIX 4B: PERFORMANCE DATA- INTER-DEVICE COMPARISONS

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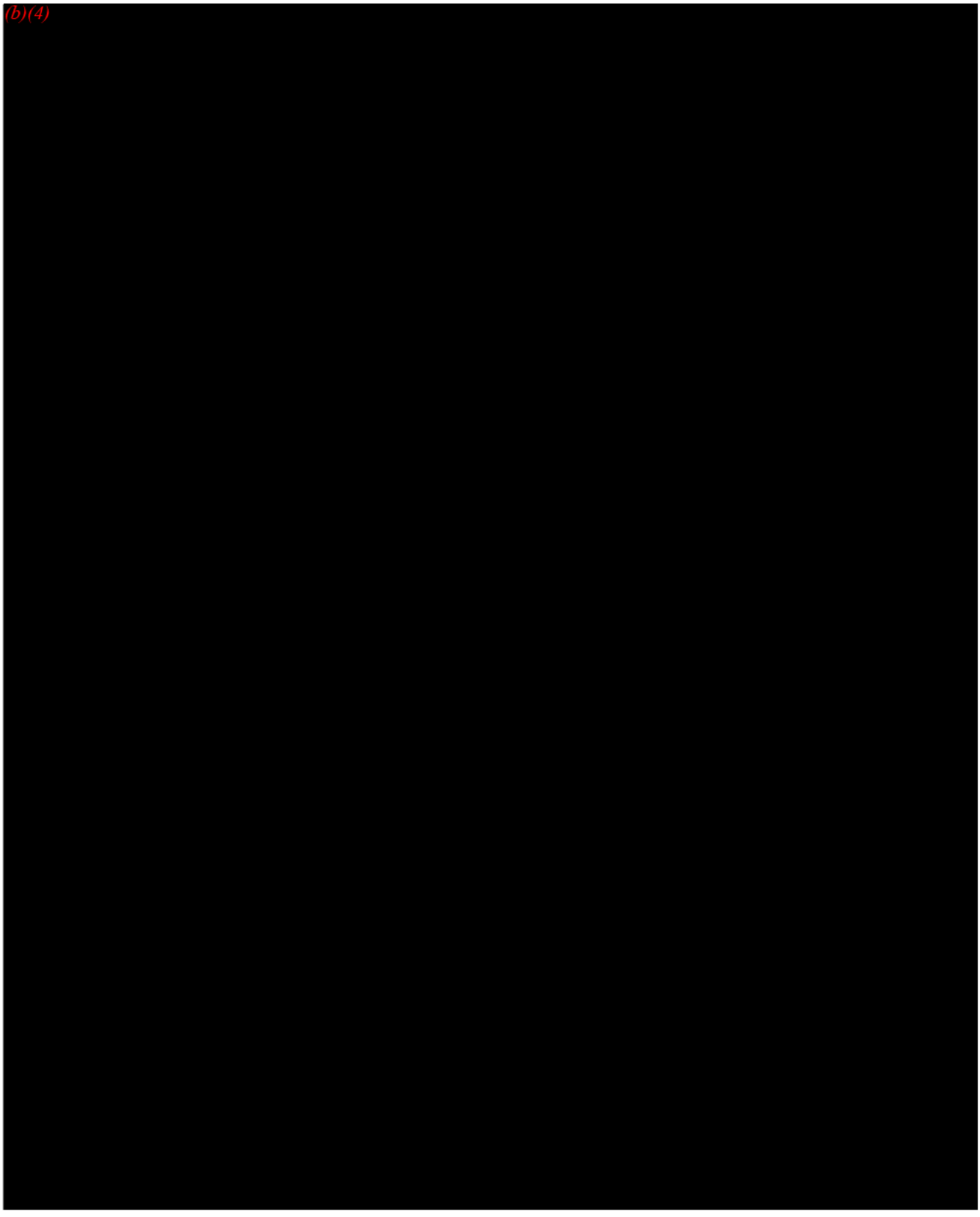

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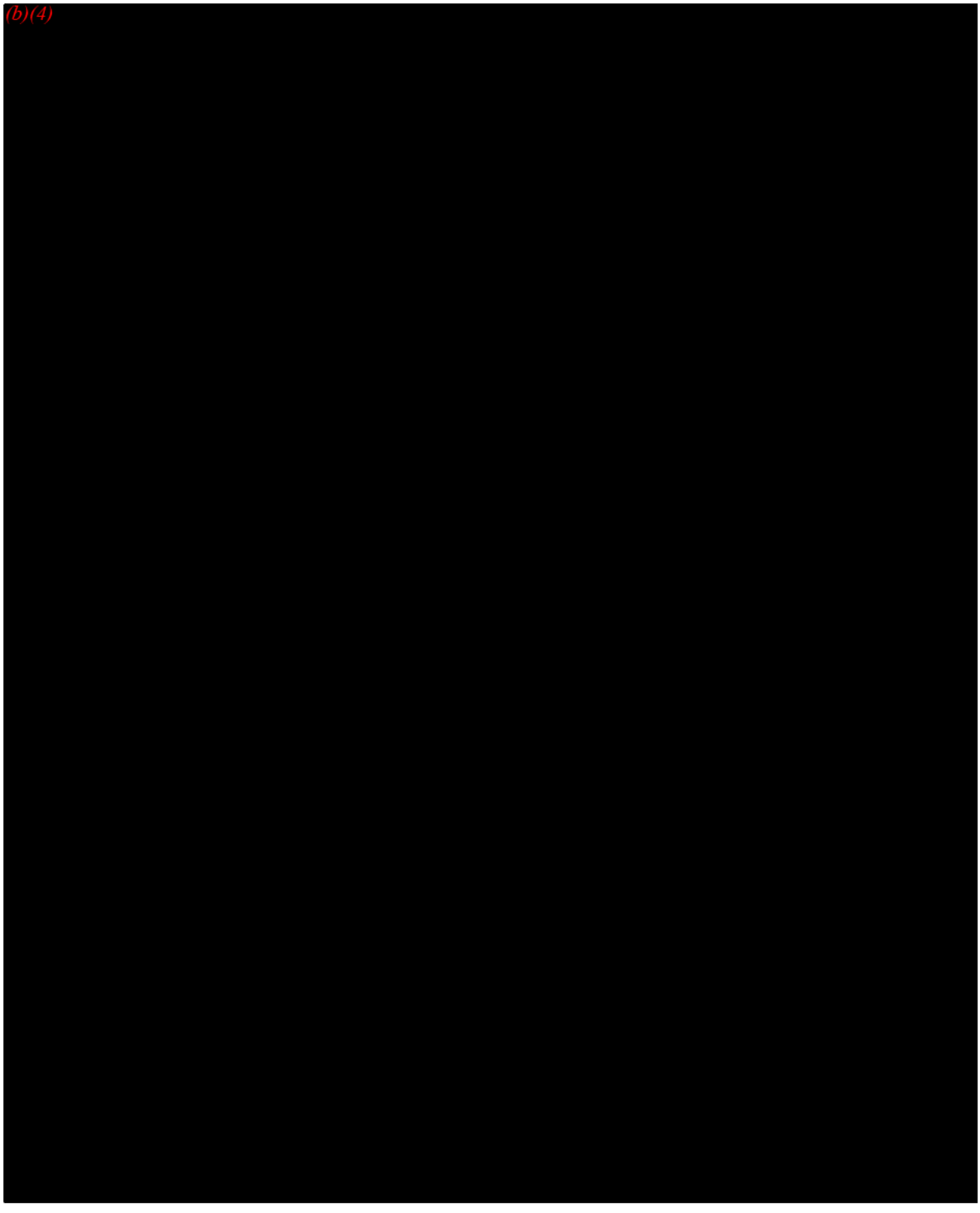

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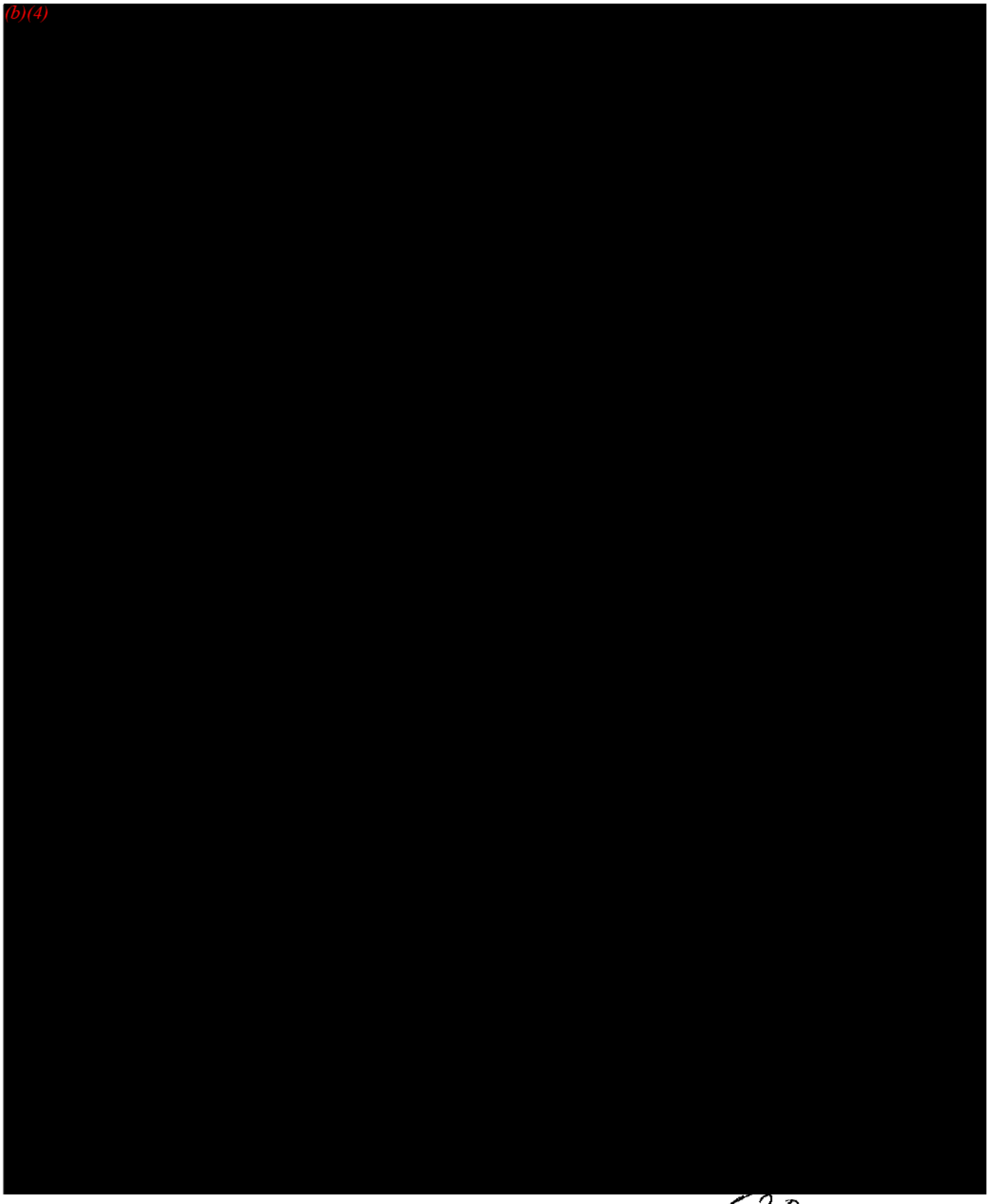

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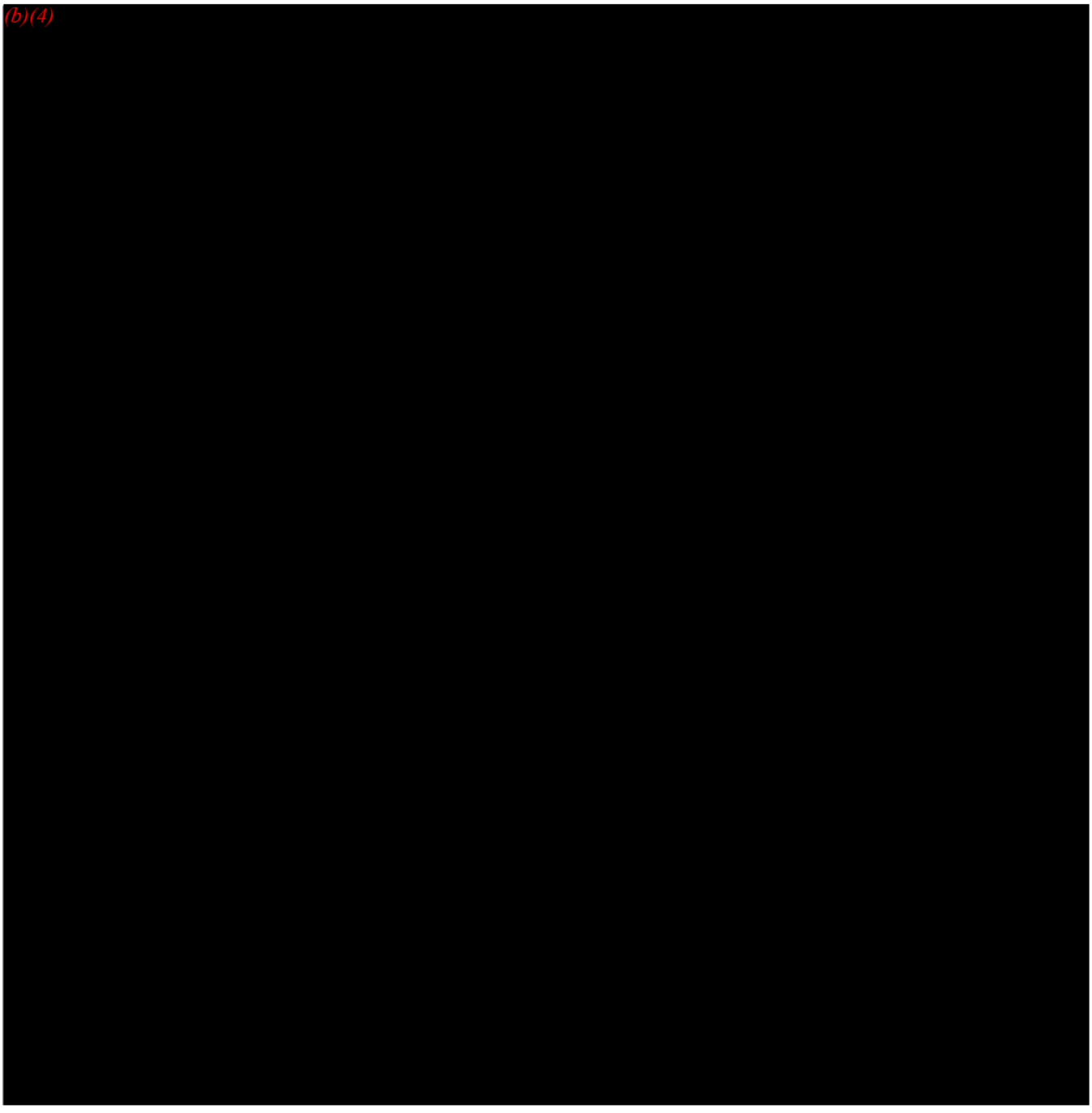

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APPENDIX 4C: PERFORMANCE DATA - ENVIRONMENTAL TESTING

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Performance Requirements- Mechanical and Environmental

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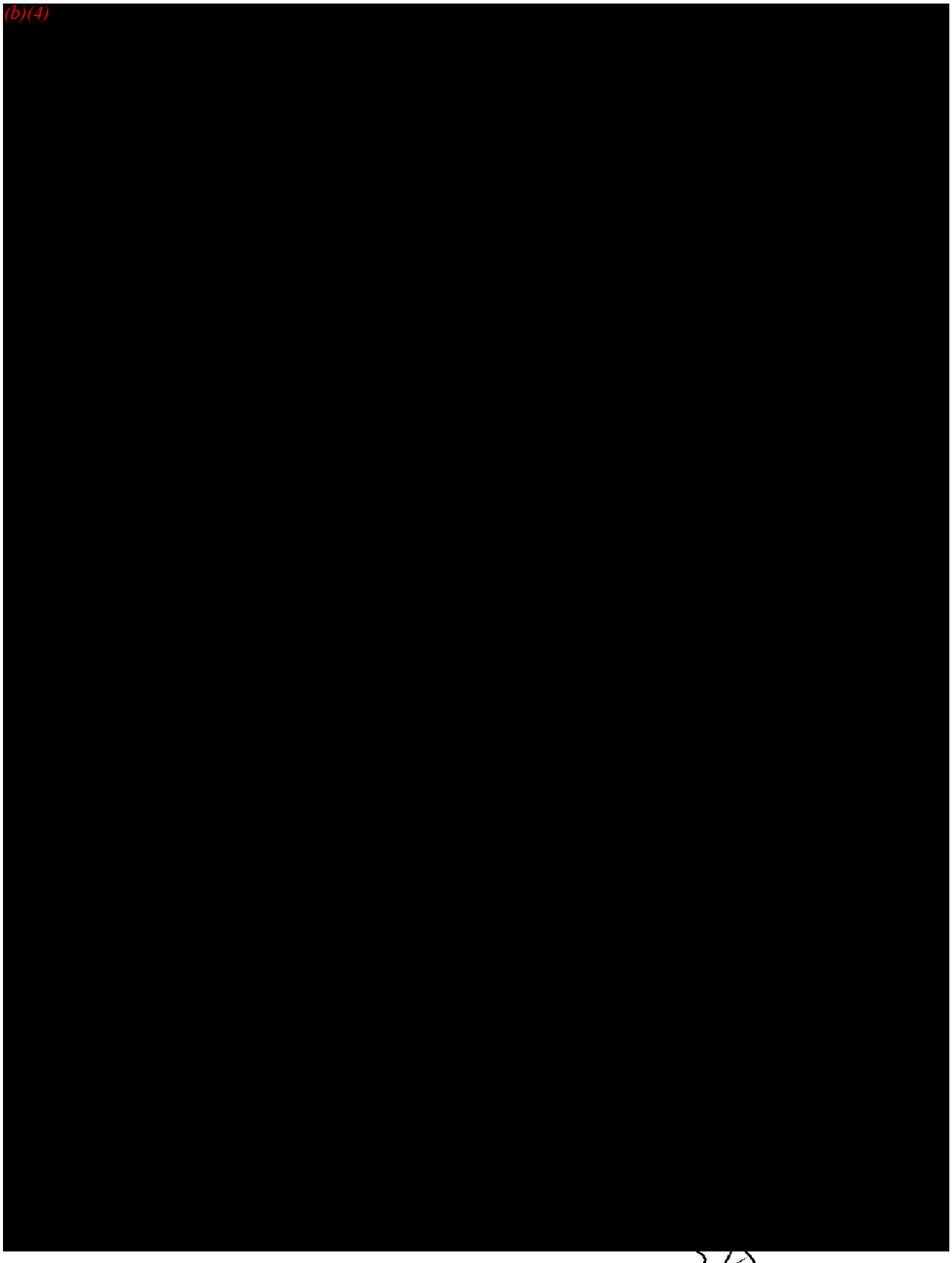

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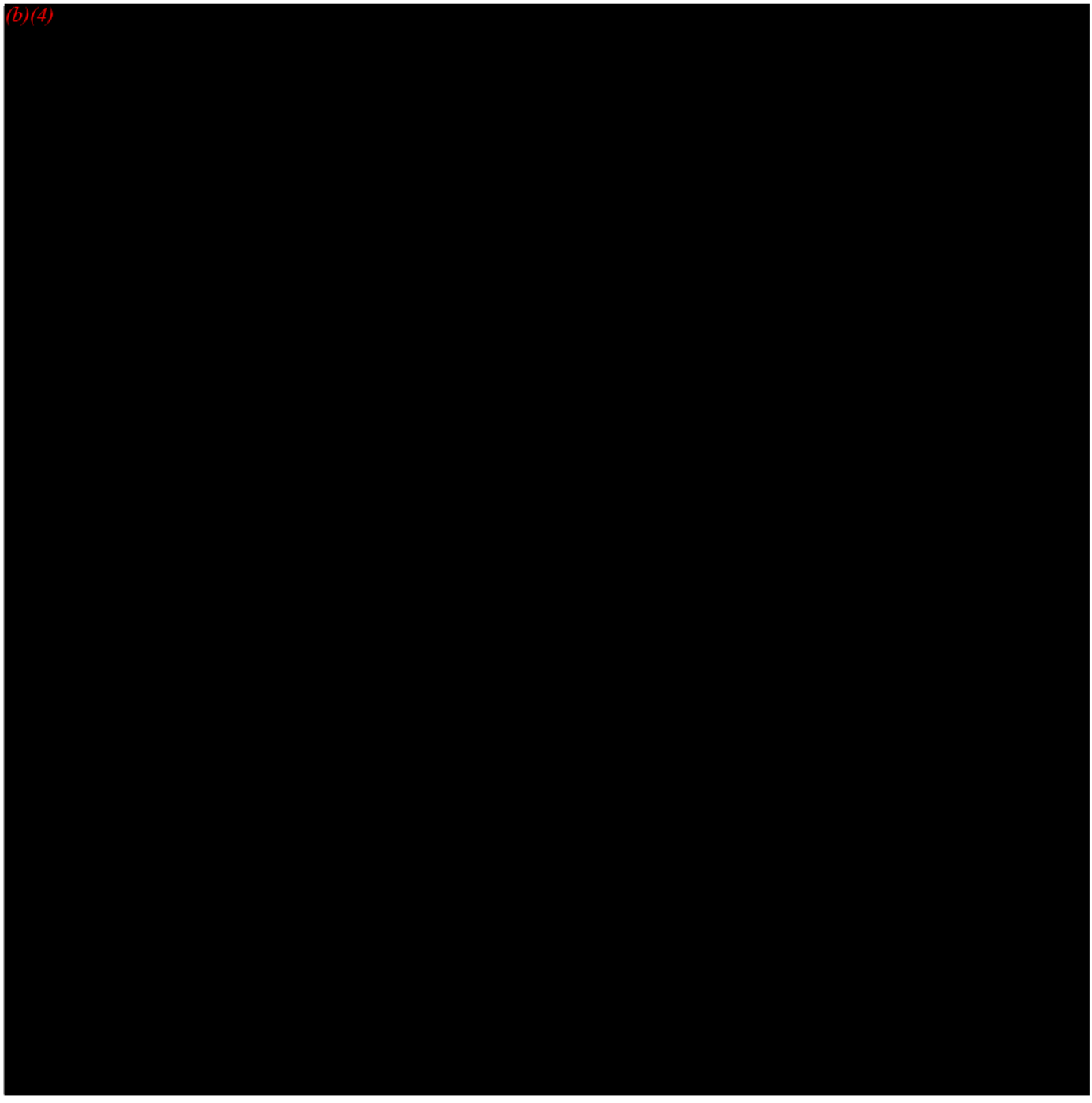

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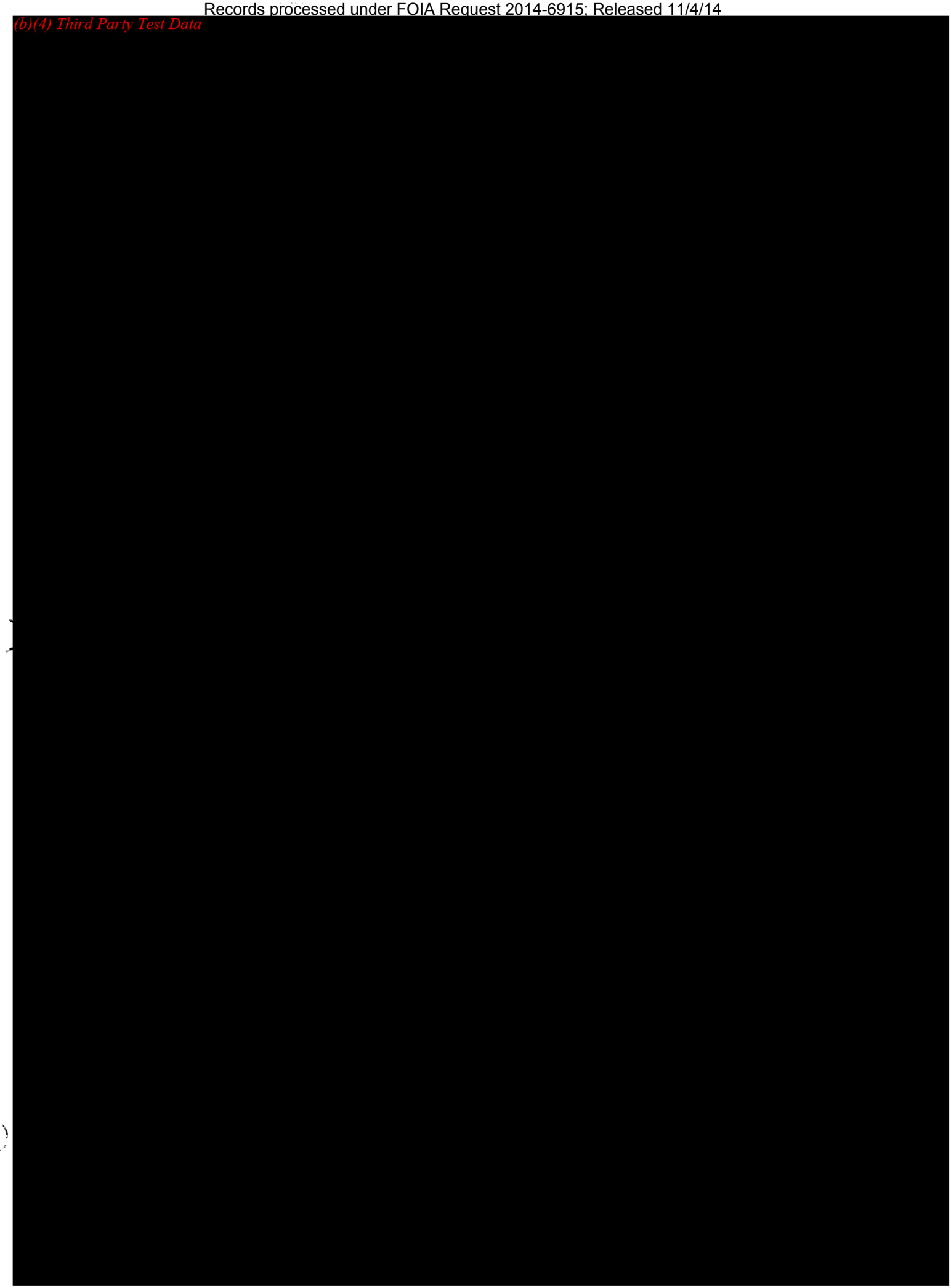

PV 138-D9226-00
System Validation Summary for NICO/MARS

Top level P/N: (b) (4)

Main Assembly P/N:

Digital PCB P/N:
Power PCB P/N:
Analog PCB P/N:

Authors: Eric Wigforss and Rich Daniels

Approvals:

Engineering: (b) (6)

Project Manager — Date 17 Mar 03

Quality Engineering — Date 17-Mar-03

Hardware Design Mana — Date 17 MAR 03

Director of Engineering — Date 17-Mar-03

Regulatory:

RA/QA — Date 17/March/03

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1.0 Introduction

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2.0 Verification and Validation Summary

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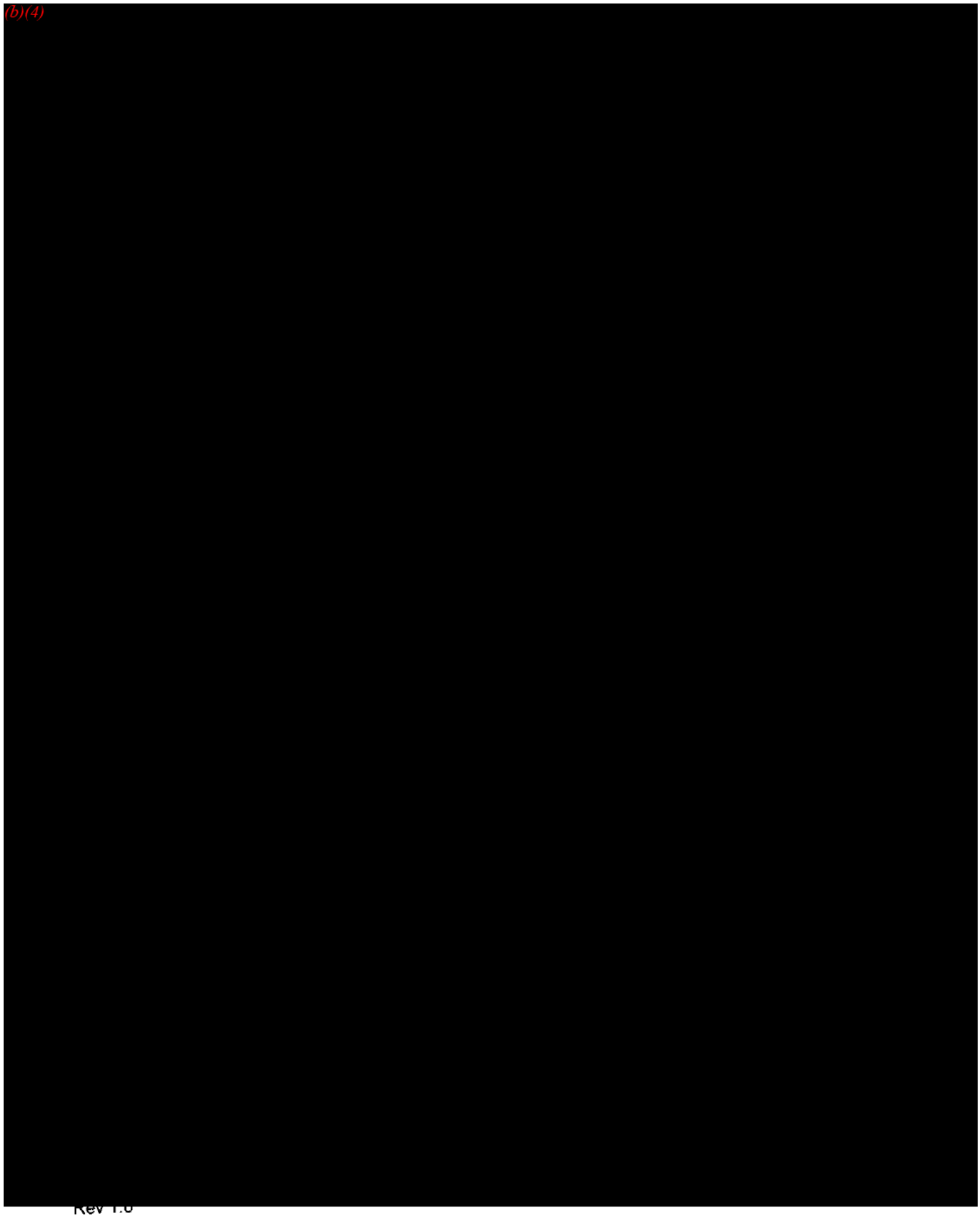

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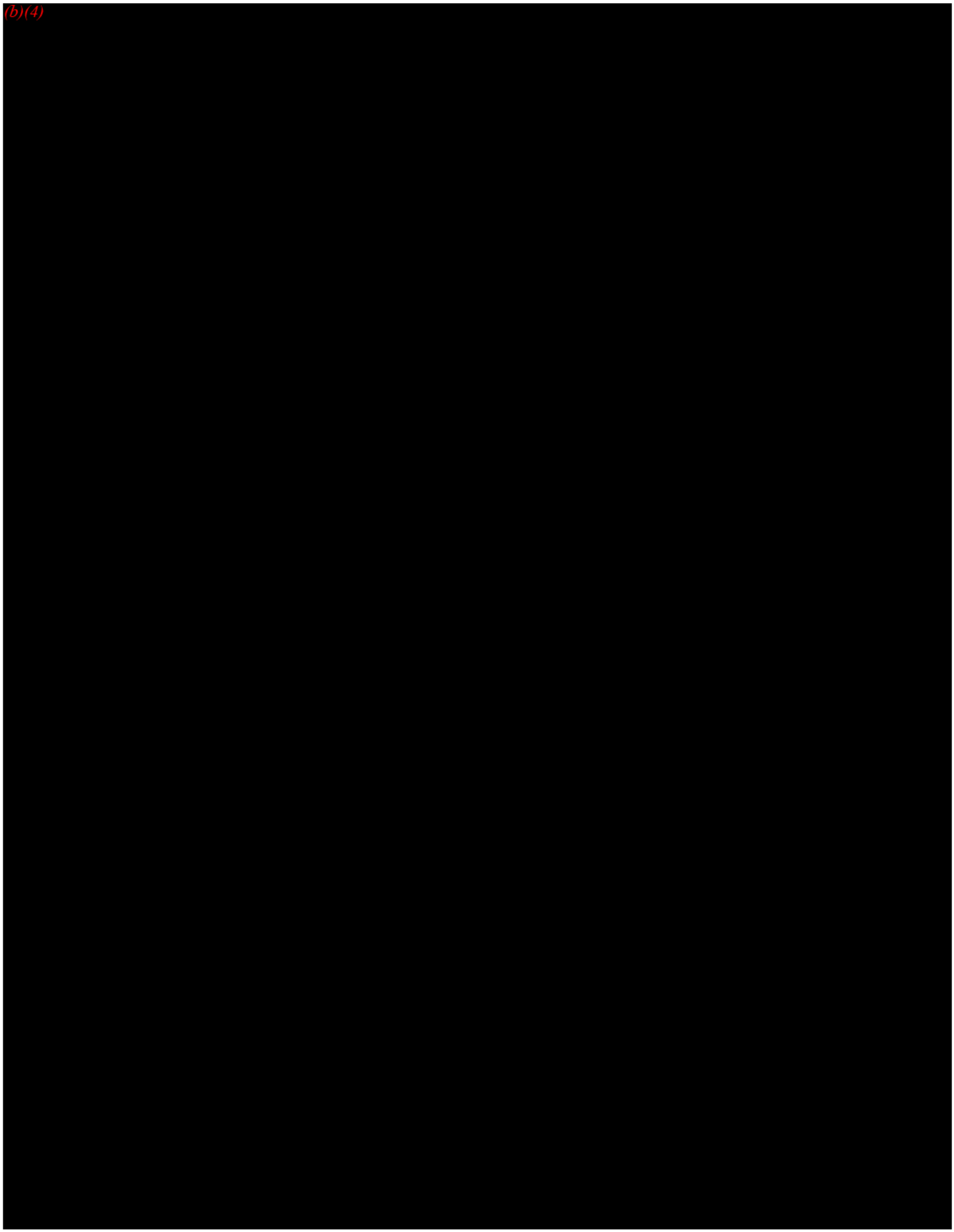

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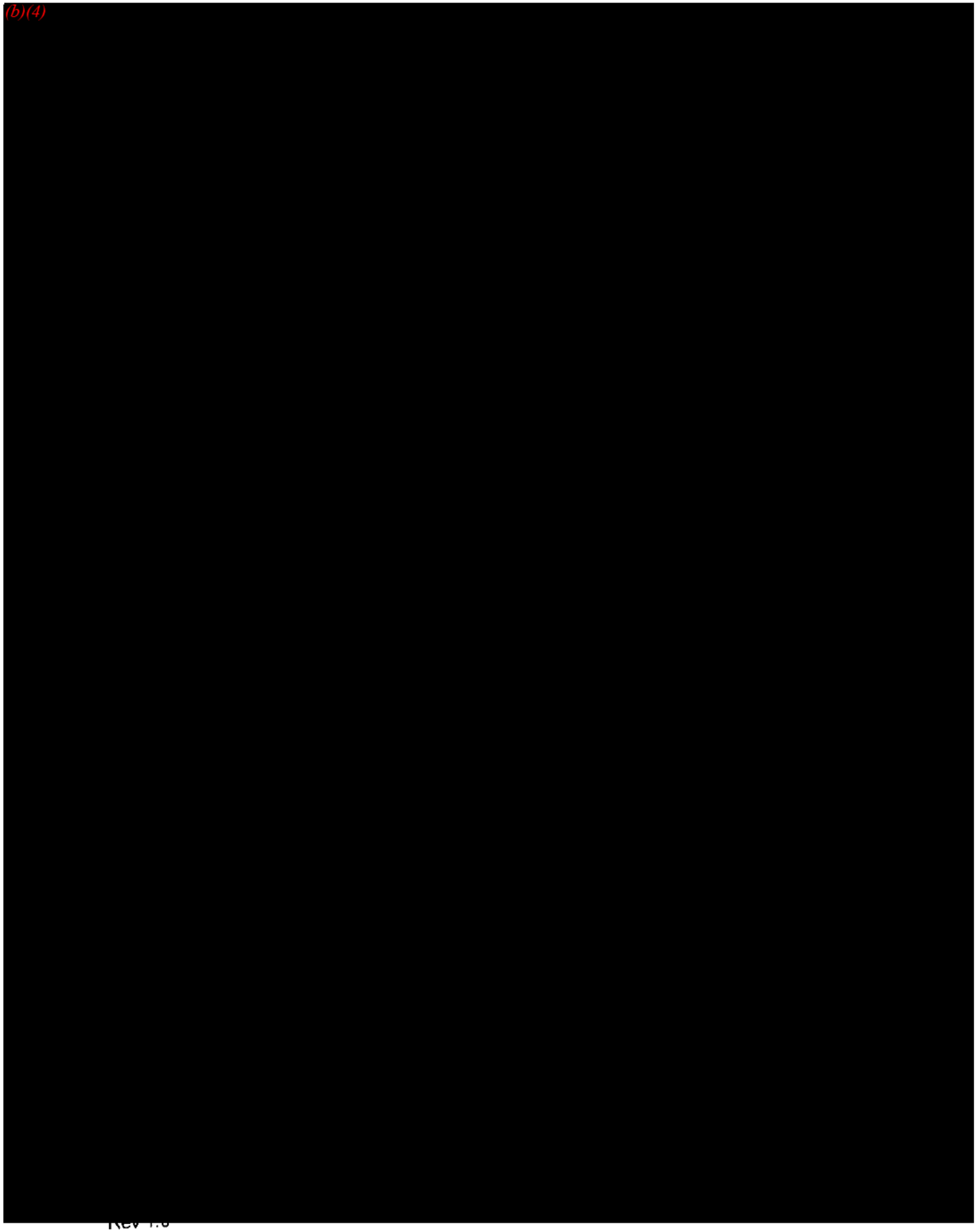

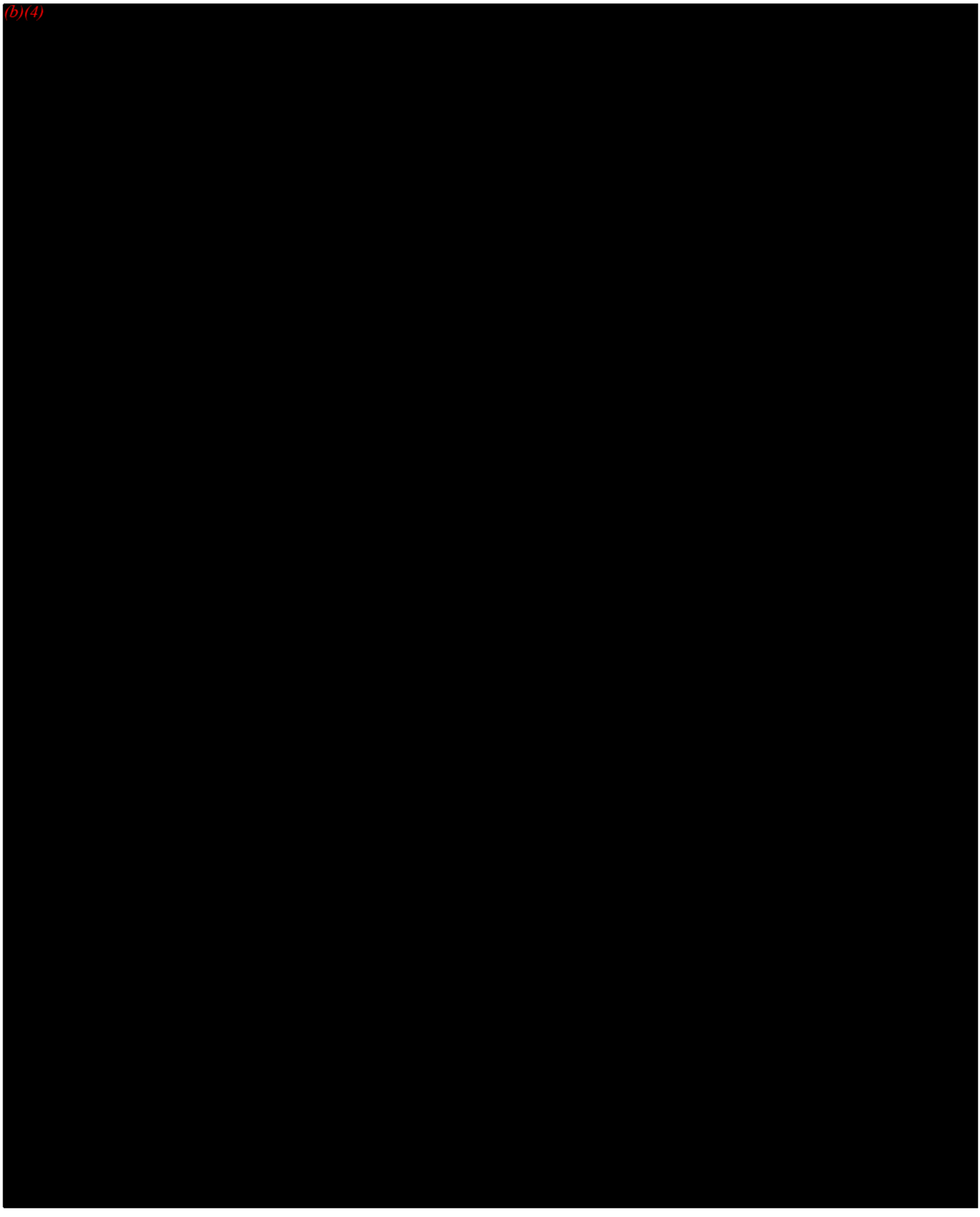

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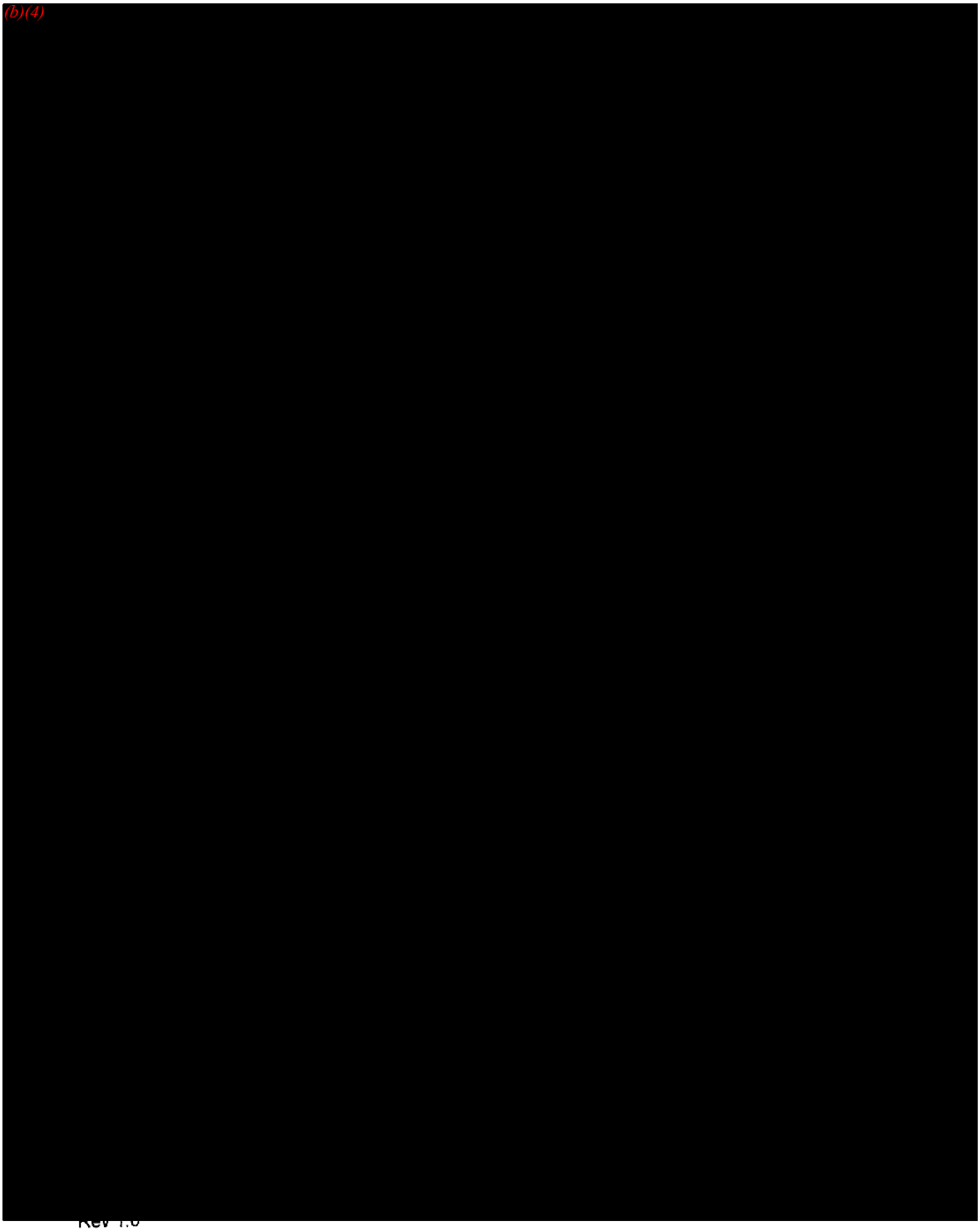

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3.0 System Assessment

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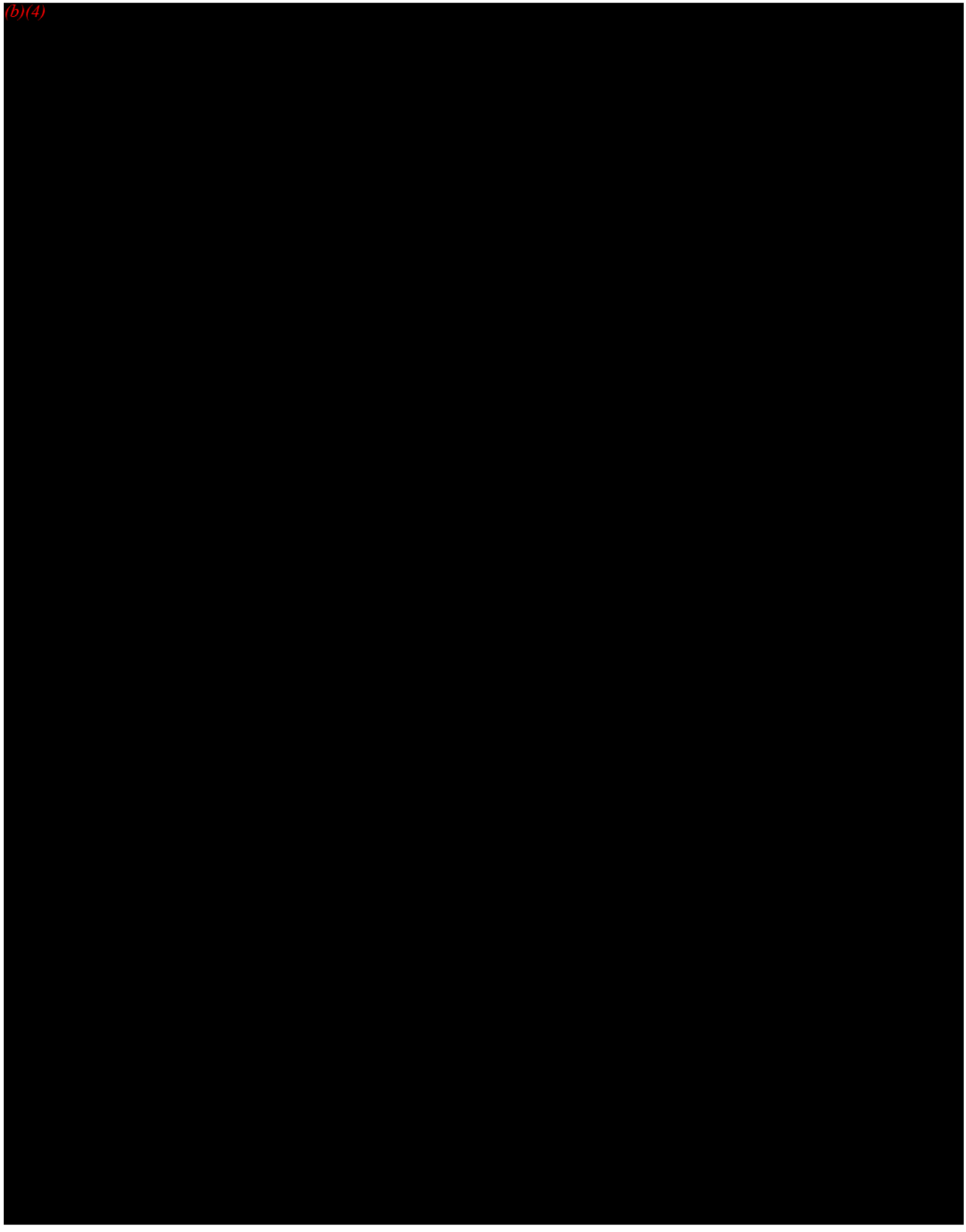

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APPENDIX 4D: PERFORMANCE DATA - BIOCOMPATABILITY TESTING

(b)(4)

[redacted]

615

(b)(4)

[redacted]

616

(b)(4)

[redacted]

617

(b)(4)

[redacted]

618

(b)(4)

[redacted]

619

(b) (4)

(b) (4)

(b) (4)

TEST REPORT

(b) (4)

[redacted]

TEST REPORT

(b) (4)

[redacted]

624

ATTACHMENT I

Erythema and Eschar Formation	Value
No erythema	0
Very slight erythema (barely perceptible)	1
Well defined erythema	2
Moderate to severe erythema	3
Severe erythema (beet redness) to slight eschar formation (injuries in depth)	4
Edema Formation	
No Edema	0
Very slight edema (barely perceptible)	1
Slight edema (edges of area well defined by definite raising)	2
Moderate to severe edema (raised approximately 1 mm)	3
Severe edema (raised more than 1 mm and extending beyond the area of exposure)	4

(b) (4)

TEST REPORT
SAMPLE #95-0021
(cont'd.)

Conclusion:

The sample evaluated does meet the requirements of the Guinea Pig Maximization Test.

Analyst: (b) (4) [redacted]

Certified by: [redacted]

627

TEST REPORT

(b) (4)

[redacted]

** Refer to the Numerical Value Explanation for any scores

)

628

TEST REPORT

(b) (4)

[redacted]

629

(b) (4)

TEST REPORT

(b) (4)

[redacted]

TEST REPORT

(b) (4)

[redacted]

Note - Scores are recorded as left side, right side.
[1]er = erythema, ed = edema
[2]Avg. Score is sum of 24, 28 & 72 hour scores ÷ 6
[3]PIS = "Primary Irritation Score which is test average score minus control average score.
[4]Total PIS is PIS added for all three animals.
[5]Primary Irritation Index: Total PIS ÷ 3 animals

632

SCORING CRITERIA

Erythema and Eschar Formation	Value
No erythema	0
Very slight erythema (barely perceptible)	1
Well defined erythema (pale red color)	2
Moderate to severe erythema (red and area well defined)	3
Severe erythema (beet redness) to slight eschar formation (injuries in depth)	4

Edema Formation	Value
No edema	0
Very slight edema (barely perceptible)	1
Slight edema (edges of area well defined by definite raising)	2
Moderate to severe edema (raised approximately 1 mm and extending beyond the area of exposure)	4

Primary Irritation Response Categories

Response Category	Mean Score (PII)
Negligible	0.0 to 0.4
Slight	0.5 to 1.9
Moderate	2.0 to 4.9
Severe	5.0 to 8.0

(b) (4)

(b) (4)

TEST REPORT

(b) (4)

[redacted]

636

MTL Sample No. 98-4176

GUINEA PIG MAXIMIZATION TEST
EVALUATION OF SKIN REACTIONS*

(b) (4)

[redacted]

637

NUMERICAL VALUE EXPLANATION

(b) (4)

[redacted]

(b) (4)

(b) (4)

TEST REPORT

(b) (4)

[redacted]

641

TEST REPORT

(b) (4)

[redacted]

642

SCORING CRITERIA

Erythema and Eschar Formation	Value
No erythema	0
Very slight erythema (barely perceptible)	1
Well defined erythema (pale red color)	2
Moderate to severe erythema (red and area well defined)	3
Severe erythema (beet redness) to slight eschar formation (injuries in depth)	4

Edema Formation	Value
No edema	0
Very slight edema (barely perceptible)	1
Slight edema (edges of area well defined by definite raising)	2
Moderate to severe edema (raised approximately 1 mm and extending beyond the area of exposure)	4

Primary Irritation Response Categories

Response Category	Mean Score (PII)
Negligible	0.0 to 0.4
Slight	0.5 to 1.9
Moderate	2.0 to 4.9
Severe	5.0 to 8.0

643

(b) (4)

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TEST REPORT

(b) (4)

[redacted]

TEST REPORT

(b) (4)

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TEST REPORT

(b) (4)

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TEST REPORT

(b) (4)

[redacted]

649

(b) (4)

TEST REPORT

(b) (4)

[redacted]

651

TEST REPORT

(b) (4)

[redacted]

652

(b) (4)

[redacted]

(b) (4)

[redacted]

CYRO Industries 25 Executive Blvd., P.O. Box 550, Orange, CT 06477-0550 Ph: (203) 795-6081 Fax: (203) 795-5800

October 5, 2001

Mr. John Triunfo
Novametrix Medical Systems, Inc.
5 Technology Drive
Wallingford, CT 06492

Dear Mr. Triunfo:

I would like to answer your recent request for information on some short term in vitro and in vivo biological testing of some specific grades and colors of our products following tripartite protocols. ACRYLITE® L40 (L40-002-000), ACRYLITE® H-15 (H15-012-000), acrylic resins; XT® Polymer 250 (250-000-301), CYROLITE® G 20 (G20-100-001), CYROLITE® G 20 HIFLO (G20-300-001), CYROLITE® G 20 color 8038 (G20-100-8038), CYROLITE® GS 90 (G90-200-001), CYROLITE® CG 97 (G97-100-001), CYROLITE® Med (EXT-125-001) acrylic multipolymers; CYREX® 200-8005 (REX-200-8005) and CYREX® 201-5096 (REX-201-5096), acrylic-polycarbonate alloy, have all been found to be non-hemolytic, non-cytotoxic, non-pyrogenic, non-sensitizing and non-mutagenic by these tests. In addition, these products meet the requirements for a USP Class VI (24 hours, 70 C, 4g/20ml extraction) material.

Many other CYRO products and grades also have been tested and found to meet the USP Class VI requirements and most grades including all that are specifically mentioned above meet the appropriate FDA food contact use regulations. (21 CFR177.1010, 21CFR180.22 and 21CFR177.1580 as applicable to the specific product.) The summaries describing the tripartite and USP testing of the above products are available. If you have already requested the summary data on one or more of these products, it is attached. Thank you for your inquiry and interest in CYRO products.

655

If you need further information, please contact me or a Technical Service Engineer here at the CYRO Technical Center. Douglas H. Haff is your CYRO Representative who can be reached through our Regional Sales Office in Rockaway, NJ (973)442-6123. Doug would always be pleased to help in any way possible especially in assisting you to place an order and providing pricing, delivery or other sales information.

Sincerely yours,

Francis J. Hewitt

Francis J. Hewitt
Senior Chemist, Product Compliance

Attachments:
Tripartite/USP Data - G20-300-001

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CYRO INDUSTRIES 25 Executive Boulevard, Orange, Connecticut 06477 (203) 795-6081 Fax (203) 795-5800

TRIPARTITE TEST RESULT SUMMARY

NAME OF MATERIAL: CYROLITE®G20-300-001 MOLDING COMPOUND

PROJECT NUMBER: (b) (4)

TEST MATERIAL IDENTIFICATION
Test Code Name: CT-522-92C
Appearance: Granules/Plaque
Laboratory Notebook #: (b) (4)
Lot Number: 8H2-6571
1993

LABORATORY IDENTIFICATION
Name: (b) (4)

Study Date: April 19 and 26,

RESULTS

All studies were conducted in compliance with FDA Good Laboratory Practices.

Hemolysis Test - In Vitro - A ratio of 6g/10ml

(b) (4)

TRIPARTITE TEST RESULT SUMMARY CON'T

(b) (4)

[redacted]

TRIPARTITE TEST RESULT SUMMARY CON'T

(b) (4)

[redacted]

TRIPARTITE TEST RESULT SUMMARY CON'T

(b) (4)

[redacted]

NAmSA®
World Leader in Testing Services for the Medical Device Industry

2261 Tracy Road
Northwood, OH 43619
Phone 419•666•9455
FAX 419•666•2954

LAB NO. 93T 02041 00
P.O. NO. Patty Vernon

ID NO. Lot 8H2-6571

CYTEC INDUSTRIES
FIVE GARRET MOUNTAIN PLAZA
WEST PATERSON, NJ 07424
ATTN: PATRICIA A. VERNON

CERTIFICATE OF COMPLIANCE
USP BIOLOGICAL TESTS
CLASSIFICATION VI

Test Article: CT-522-92C
CYROLITE® G-20-300-001

ACUTE SYSTEMIC TOXICITY (USP): The saline, alcohol in saline, polyethylene glycol 400 and cottonseed oil extracts of the test article injected into mice did not produce a significantly greater systemic reaction than the blank extractant.

INTRACUTANEOUS TOXICITY (USP): The saline, alcohol in saline, polyethylene glycol 400 and cottonseed oil extracts of the test article injected intracutaneously in rabbits did not produce a significantly greater tissue reaction than the blank extractant.

IMPLANTATION TEST (USP): The macroscopic reaction of the test article implanted 7 days was not significant as compared to the USP negative control plastic.

The sample of test article extracted at a ratio of 4 g/20 ml and at a temperature of 70°C for 24 hour(s) met the requirements of a USP Class VI Plastic.

Kirk D. Dammeyer, BS
Study Director, Toxicology

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lmg Completed: 4-92 Approved: [illegible]

Material Safety Data Sheet

May be used to comply with OSHA's Hazard Communication Standard, 29 CFR 1910.1200. Standard must be consulted for specific requirements.

U.S. Department of Labor
Occupational Safety and Health Administration
(Non-Mandatory Form)
Form Approved
OMB No. 1218-0072

IDENTITY (As Used on Label and List)
Uniform S82B Polyurethane Foam

Notes: Blank spaces are not permitted. If any item is not applicable, or no information is available, the space must be marked to indicate that.

Section I

Manufacturer's Name Wm. T. Burnett & Co., Inc.	Emergency Telephone Number (410) 799-1788
Address (Number, Street, City, State, and ZIP Code) 2112 Montevideo Road Jessup, MD 20794	Telephone Number for Information Same Date Prepared 2-4-97 Signature of Preparer (optional)

Section II — Hazardous Ingredients/Identity Information

Hazardous Components (Specific Chemical Identity; Common Name(s))	OSHA PEL	ACGIH TLV	Other Limits Recommended	% (optional)
The foam material contains tertiary amine and organo-silicone ingredients which are present at less than 1% of the composition and therefore, in accordance with 29 CFR 1910.1200, Section (g) are not subject to listing as health hazards.				

Section III — Physical/Chemical Characteristics

Boiling Point	N.A.	Specific Gravity (H_2O = 1)	N.A.
Vapor Pressure (mm Hg.)	N.A.	Melting Point	Approx. 500-530°F.
Vapor Density (AIR = 1)	N.A.	Evaporation Rate (Butyl Acetate = 1)	N.A.

Solubility in Water
Insoluble

Appearance and Odor
Foam material is a flexible, resilient solid, essentially odorless.

Section IV — Fire and Explosion Hazard Data

Flash Point (Method Used) ASTM-D-1929 Self-Ignition Temperature 800°-850° F	Flammable Limits N.A.	LEL N.A.	UEL N.A.

Extinguishing Media
Water, Carbon Dioxide, Dry Powder

Special Fire Fighting Procedures
Use of self-contained breathing equipment is recommended.

Unusual Fire and Explosion Hazards
Combustion of foam can produce hazardous gases.

(Reproduce locally)

OSHA 174, Sept. 1985

662

Section V — Reactivity Data

Stability	Unstable		Conditions to Avoid: Strong acids and alkalis will deteriorate foam material properties.
	Stable	X	

Incompatibility (Materials to Avoid): Strong oxidizing agents.

Hazardous Decomposition or Byproducts: Combustion of foam material may produce carbon monoxide, oxides of nitrogen, and traces of isocyanates and hydrogen cyanide.

Hazardous Polymerization	May Occur		Conditions to Avoid
	Will Not Occur	X	

Section VI — Health Hazard Data

Route(s) of Entry: Inhalation? N.A. Skin? N.A. Ingestion?

Health Hazards (Acute and Chronic): Foam material is essentially nontoxic and nonallergenic in normal usage.

Carcinogenicity: NTP? IARC Monographs? OSHA Regulated?
Foam material is not known to be carcinogenic.

Signs and Symptoms of Exposure: N.A.

Medical Conditions Generally Aggravated by Exposure

Emergency and First Aid Procedures: N.A.

Section VII — Precautions for Safe Handling and Use

Steps to Be Taken in Case Material Is Released or Spilled: N.A.

Waste Disposal Method: Sanitary Landfills, Commercial Incineration

Precautions to Be Taken in Handling and Storing: Foam material is flammable by definition in OSHA 29 CFR Hazard Communication, Part-1910.1200, when tested by method described in 16 CFR 1500.44.

Other Precautions: Foam material should be stored and handled away from open flames or abnormally high temperatures.

Section VIII — Control Measures

Respiratory Protection (Specify Type): N.A.

Ventilation	Local Exhaust: Required if foam material is processed under melting or flaming conditions.	Special
	Mechanical (General)	Other
Protective Gloves		Eye Protection: N.A.
Protective Clothing or Equipment		
Hygienic Practices: N.A.		

Style 3900

Milco Industries Inc.

Material Safety Data Sheet

Section I

Date: 5/26/99
Telephone #570-784-0400
MSDS #5431-99

Product Name or Style Number: Style 5431

Manufacturer: Milco Industries Inc.
550 E. Fifth St.
Bloomsburg PA 17815

Description: Nylon Velcro Compatible Fabric

Section II: Hazardous Ingredients

Component	Percent
Nylon	99.1 - 92.65% *
Nonionic Softener	0.85%
Anionic Antistat	0.20%
Acid Dyestuffs	05 5.5% *

* Percentages of nylon fiber and acid dyestuff are dependent on the depth of shade
This fabric is not treated with any formaldehyde resins.

Section III Physical Data

Boiling Point (F)	N/A	Specific Gravity (H2O=1)	N/A
Vapor Pressure (mm Hg.)	N/A	Percent volatile by volume (%)	N/A
Vapor Density (AIR=1)	N/A	Evaporation Rate (Butyl Acetate=1)	N/A
Solubility in Water	N/A	Appearance and odor of fabric	No odor

Section IV Fire Explosion Hazard Data

This product is an ordinary combustible. Use water, fog, dry chemical, dry powder, or Halon fire extinguisher to extinguish fire. Use a self-contained breathing apparatus with full face piece operated in positive pressure mode.

CORPORATE HEADQUARTERS

MILCO INDUSTRIES INC. • 550 E. Fifth St. • Bloomsburg PA 17815 • (570) 784-0400

Section V Health Hazard Data

Acute Toxicity: None

Chronic Toxicity: None

Threshold Limit Value (TLV) and Permissible Exposure Limit (PEL) are not limited

Medical conditions generally aggravated by exposure: None

First Aid:

Eyes: No protection needed

Skin: If dermatitis occurs, thin protective gloves may be worn

Inhalation: No protection needed.

Section VI Reactivity Data

Stability: Stable
Conditions To Avoid: None
Incompatibility (Materials to Avoid): None
Hazardous Decomposit on Products: Carbon Dioxide, Carbon Monoxide and Hydrocarbons
Hazardous Polymerization: None
Conditions to Avoid: None

Section VII Spill or Leak Procedures

Waste Disposal: Land disposal in accordance with local, state and federal regulations

Handling and Storage Procedures: Store in dry area

Section VIII Special Protection Information

None

Prepared by Wallace Wechter

665

[redacted]

Scapa

TECHNICAL DATA

Bioflex®
RX746P

PRELIMINARY PERFORMANCE VALUES

(b) (4)

[redacted]

Bioflex is a trademark of Scapa Tapes, North America.

305-98(ESB)

666

(800)801-0323 ➤ www.scapana.com ➤ appsupport@scapana.com

[redacted]

Scapa

TECHNICAL DATA

	ITEM NO.	REVISION LEVEL
	(b) (4) [redacted]	C
MATERIAL DESCRIPTION	White elastic woven fabric, coated on one side with a latex free medical grade rubber adhesive, supplied on 60# liner.	PAGE: 1 of 1

GENERAL MATERIAL INFORMATION

1.0. MATERIAL DESCRIPTION:

(b) (4) [redacted]

www.scapana.com ➤ TIB# 0398006 appsupport@scapana.com

Medical Specialties
3M Health Care

3M Company
St. Paul, Minnesota 55144-1000

3M

June 29, 2001

Brian Fudge
Novametrix

Dear Mr. Fudge:

Your request regarding the status of Medical Specialties Product # 1776, 3M Nonwoven Medical Tape, 1527L, 3M Plastic Medical Tape, and 1512, 3M Double Coated Medical Tape, in reference to latex content has been forwarded to me.

Product # 1776, contains neither natural rubber latex nor dry natural rubber as a component in the product or in packaging as we supply it.

Product # 1527L, contains neither natural rubber latex nor dry natural rubber as a component in the product or in packaging as we supply it.

Product # 1512, contains neither natural rubber latex nor dry natural rubber as a component in the product or in packaging as we supply it.

If you have further questions regarding this or other products, please feel free to contact me, Marcia Smith, at 651/737-1277.

We appreciate your continued support of 3M Medical Specialties products.

Best Regards,

Marcia Smith
Clinical Research
Medical Specialties
3M Center
260-3A-04
St. Paul, MN 55144-1000

C: P. Ignelzi
H. Kaur

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Medical Specialties
3M Health Care

3M Center
St. Paul, MN 55144-1000
651 733 1110

3M

PRODUCT CLINICAL DATA SUMMARY
NO. 1776
3M Nonwoven Medical Tape
Effective: January 1996

The adhesive as a component used in No. 1776 3M Nonwoven Medical Tape has been subjected to the following safety evaluations:

In Vitro Cytotoxicity (Agar Overlay)
Protocol reference: Guess, W. L. et al; "Agar Diffusion Method for Toxicity Screening of Plastics on Cultured Cell Monolayers" J. Pharm. Sci. 54:1545-1547 (1965).
Results: 1.0/0.25

Acute Primary Skin Irritation in Albino Rabbits
Protocol reference: Draize: Appraisal of the Safety of Chemicals in Food, Drugs and Cosmetics (1965). Published by the Editorial Committee of the Association of Food and Drug Officials of the United States.
Results: 0.4/8.0

3M No. 1776 has been subjected to the following safety evaluations:

Repeated Insult Patch Test (Draize) in Humans
Protocol reference: Draize: Appraisal of the Safety of Chemicals in Food, Drugs and Cosmetics (1965). Published by the Editorial Committee of the Association of Food and Drug Officials of the United States.
Results: No evidence of induced contact sensitization.

21-day Cumulative Irritation in Humans
Protocol reference: Draize: Appraisal of the Safety of Chemicals in Food, Drugs and Cosmetics (1965). Published by the Editorial Committee of the Association of Food and Drug Officials of the United States.
Results: Consistent with responses characteristic of adhesive materials; within historically acceptable levels for surgical tapes.

These tests are in accordance with the ISO 10993 Part-1 "Biological Evaluation of Medical Devices", as put forth by the FDA. The adhesive used in No. 1776 has satisfied the requirements for devices in contact with intact skin for short term application (up to 29 days). All laboratory testing was conducted in accordance with the FDA Good Laboratory Practices Regulation of 1978.

It is the responsibility of our customers to determine the final suitability of our products for their application.

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Medical Specialties
3M Health Care

3M Center
St. Paul, MN 55144-1000
651 733 1110

3M

PRODUCT CLINICAL DATA SUMMARY
NO. 1527-L
3M Plastic Medical Tape
Effective: January 1996

No. 1527-L 3M Plastic Medical Tape has been subjected to the following safety evaluations:

In Vitro Cytotoxicity (Agar Overlay)
Protocol reference: Guess, W. L. et al; "Agar Diffusion Method for Toxicity Screening of Plastics on Cultured Cell Monolayers" J. Pharm. Sci. 54:1545-1547 (1965).
Results: 1.0/0.75

Acute Primary Skin Irritation in Albino Rabbits
Protocol reference: Draize: Appraisal of the Safety of Chemicals in Food, Drugs and Cosmetics (1965). Published by the Editorial Committee of the Association of Food and Drug Officials of the United States.
Results: 0.9/8.0

Repeated Insult Patch Test (Draize) in Humans
Protocol reference: Draize: Appraisal of the Safety of Chemicals in Food, Drugs and Cosmetics (1965). Published by the Editorial Committee of the Association of Food and Drug Officials of the United States.
Results: No evidence of induced contact sensitization.

21-day Cumulative Irritation in Humans
Protocol reference: Draize: Appraisal of the Safety of Chemicals in Food, Drugs and Cosmetics (1965). Published by the Editorial Committee of the Association of Food and Drug Officials of the United States.
Results: Consistent with responses characteristic of adhesive materials; within historically acceptable levels for surgical tapes.

These tests are in accordance with the ISO 10993 Part-1 "Biological Evaluation of Medical Devices", as put forth by the FDA. No. 1527-L has satisfied the requirements for devices in contact with intact skin for short term application (up to 29 days). All laboratory testing was conducted in accordance with the FDA Good Laboratory Practices Regulation of 1978.

The use of the term "hypoallergenic" has come to indicate a product which is non-sensitizing to the general public. The hypoallergenic claim for this product is supported by clinical evaluation using the repeated insult patch test in humans, commonly known as the Draize test. This protocol involves repeated application of samples on 200 healthy volunteers for a 2- to 3-week induction period, followed by a 2-week rest period and a challenge application. To be termed hypoallergenic, 3M Medical Specialties products are required to show no evidence of sensitization potential under these test conditions.

It is the responsibility of our customers to determine the final suitability of our products for their application.

670

(b) (4)

TEST REPORT

(b) (4)

[redacted]

TEST REPORT

(b) (4)

[redacted]

TEST REPORT

(b) (4)

[redacted]

674

ATTACHMENT I

Erythema and Eschar Formation	Value
No erythema	0
Very slight erythema (barely perceptible)	1
Well defined erythema	2
Moderate to severe erythema	3
Severe erythema (beet redness) to slight eschar formation (injuries in depth)	4
Edema Formation	
No Edema	0
Very slight edema (barely perceptible)	1
Slight edema (edges of area well defined by definite raising)	2
Moderate to severe edema (raised approximately 1 mm)	3
Severe edema (raised more than 1 mm and extending beyond the area of exposure)	4

(b) (4)

(b) (4)

TEST REPORT

(b) (4)

[redacted]

TEST REPORT

(b) (4)

[redacted]

TEST REPORT

(b) (4)

[redacted]

(b) (4)

TEST REPORT

(b) (4)

[redacted]

682

TEST REPORT

(b) (4)

[redacted]

TEST REPORT

(b) (4)

[redacted]

PII = Primary Irritation Index

684

ATTACHMENT I

Erythema and Eschar Formation	Value
No erythema	0
Very slight erythema (barely perceptible)	1
Well defined erythema	2
Moderate to severe erythema	3
Severe erythema (beet redness) to slight eschar formation (injuries in depth)	4
Edema Formation	
No Edema	0
Very slight edema (barely perceptible)	1
Slight edema (edges of area well defined by definite raising)	2
Moderate to severe edema (raised approximately 1 mm)	3
Severe edema (raised more than 1 mm and extending beyond the area of exposure)	4

(b) (4)

TEST REPORT

(b) (4)

[redacted]

687

TEST REPORT

(b) (4)

[redacted]

TEST REPORT

(b) (4) [redacted]

(cont'd.)

NUMERICAL VALUE EXPLANATION

ATTACHMENT I

Erythema and Eschar Formation	Valu
No erythema	
Very slight erythema (barely perceptible)	
Well defined erythema	
Moderate to severe erythema	
Severe erythema (beet redness) to slight eschar formation (injuries in depth)	
Edema Formation	
No Edema	
Very slight edema (barely perceptible)	
Slight edema (edges of area well defined by definite raising)	
Moderate to severe edema (raised approximately 1 mm)	
Severe edema (raised more than 1 mm and extending beyond the area of exposure)	

All Results Reported As: Erythema and Eschar Formation Value
Edema Formation Value

(b) (4) [redacted]

689

(b) (4)

(b) (4)

APPENDIX 4E : PERFORMANCE VALIDATION - CLINICAL TESTING

(b)(4)

[redacted]

692

PV 138-D9226-00
Clinical Evaluation Report – NICO with [redacted]

Author: James Bement

Approvals:

[redacted]

Clinical:

Peer Review Date 3/12/03

Director of Clinical Researc Date 3/13/03

Engineering:

Project Manager Date 3/12/03

Dir of Engineering Date 3/12/03

Regulatory:

RA/QA Manager Date 3/12/03

Marketing:

Product Manager Date 3/12/03

Revision Record

Revision	Date	Prepared By
[redacted]		

643

1.0 Purpose

(b)(4) [redacted]

2.0 Scope

(b)(4) [redacted]

3.0 Study Details

(b)(4) [redacted]

te

n

(b)(4)

[redacted]

4.0 Data Collection

(b)(4)

[redacted]

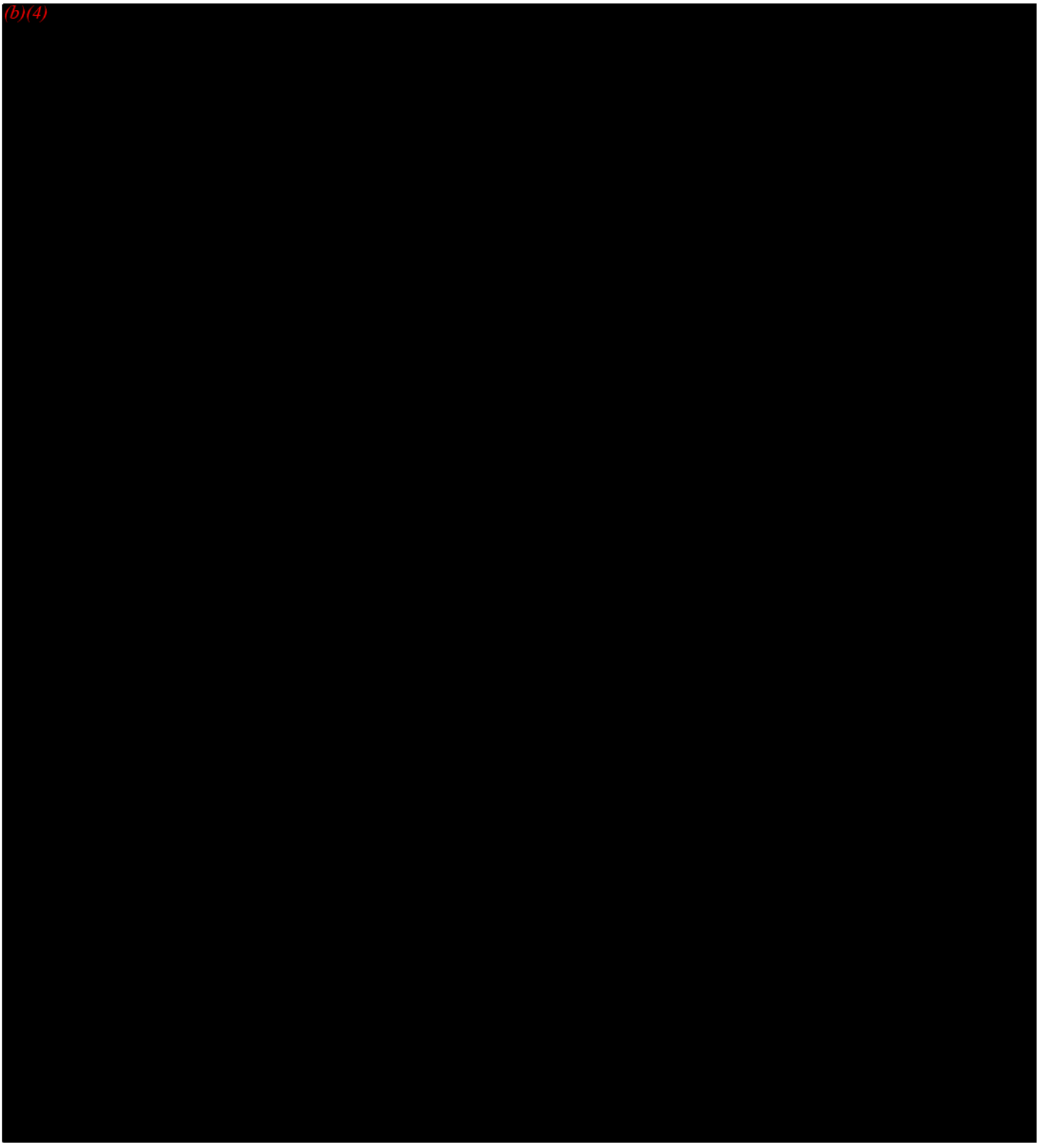
695

5.0 Results of Cardiac Output Comparison: Data Analysis

(b) (4)

[redacted]

(b)(4)



(b)(4)

[redacted]

6.0 Summary

(b)(4)

[redacted]

698

Revision Record

(b)(4)

[redacted]

699

PV 138-D9226-00
Summary of "NICO with (b)(4) [redacted]

Author: David Rich

Approvals: (b) (6) [redacted]

Engineering:		
Project Manager		Date 10 Mar 03
Clinical Manager		Date 10-MAR 03
Dir of Engineering		Date 10-MAR-03
Marketing:		
Product Manager		Date 3/10/03
Regulatory:		
RA/QA		Date 3/11/03

Revision Record

Revision	Date	Prepared By
(b) (6), (b) (4) [redacted]		

700

1.0 Introduction

(b)(4)

[redacted]

2.0 Summary of Test Results

(b)(4)

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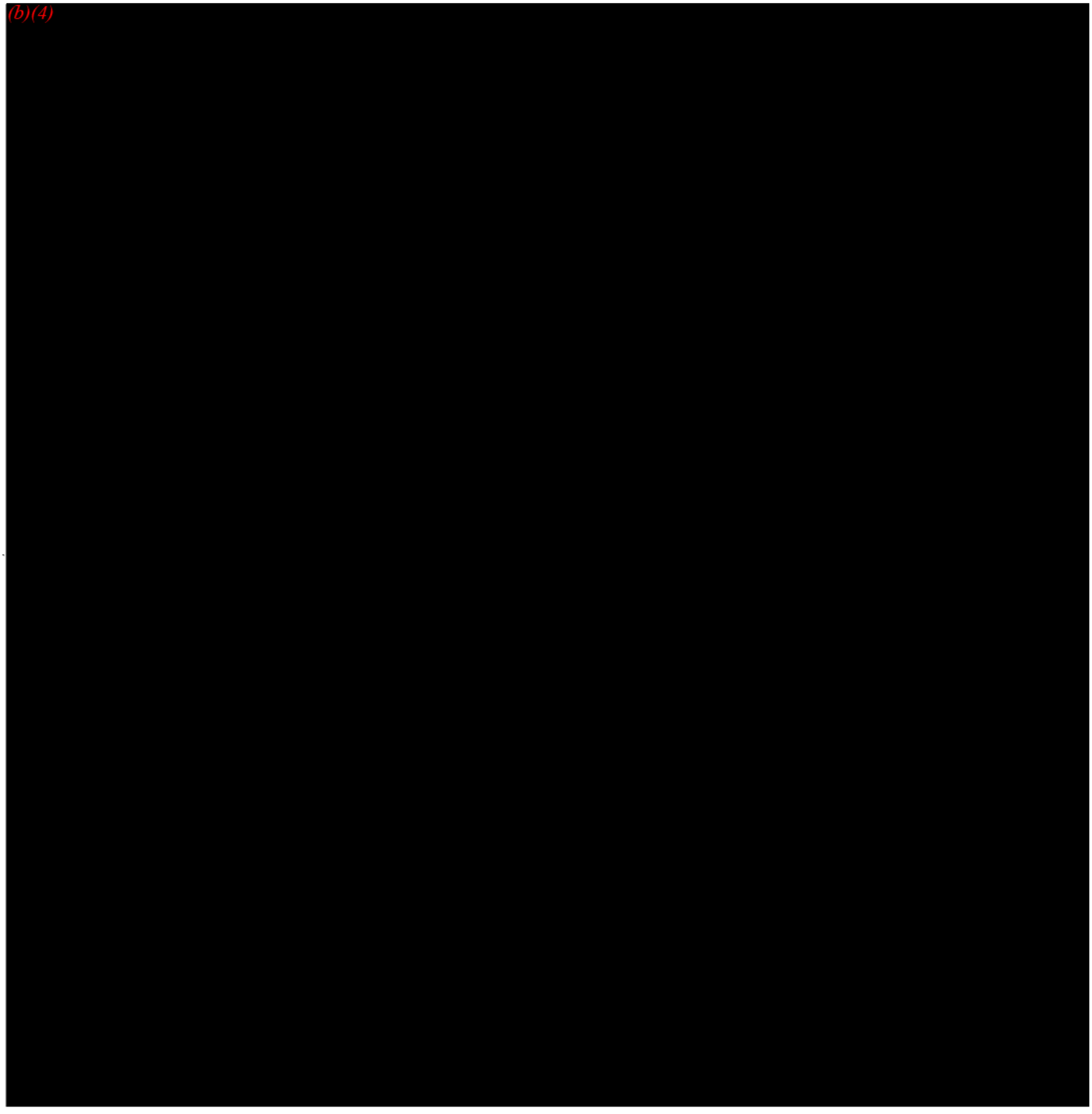

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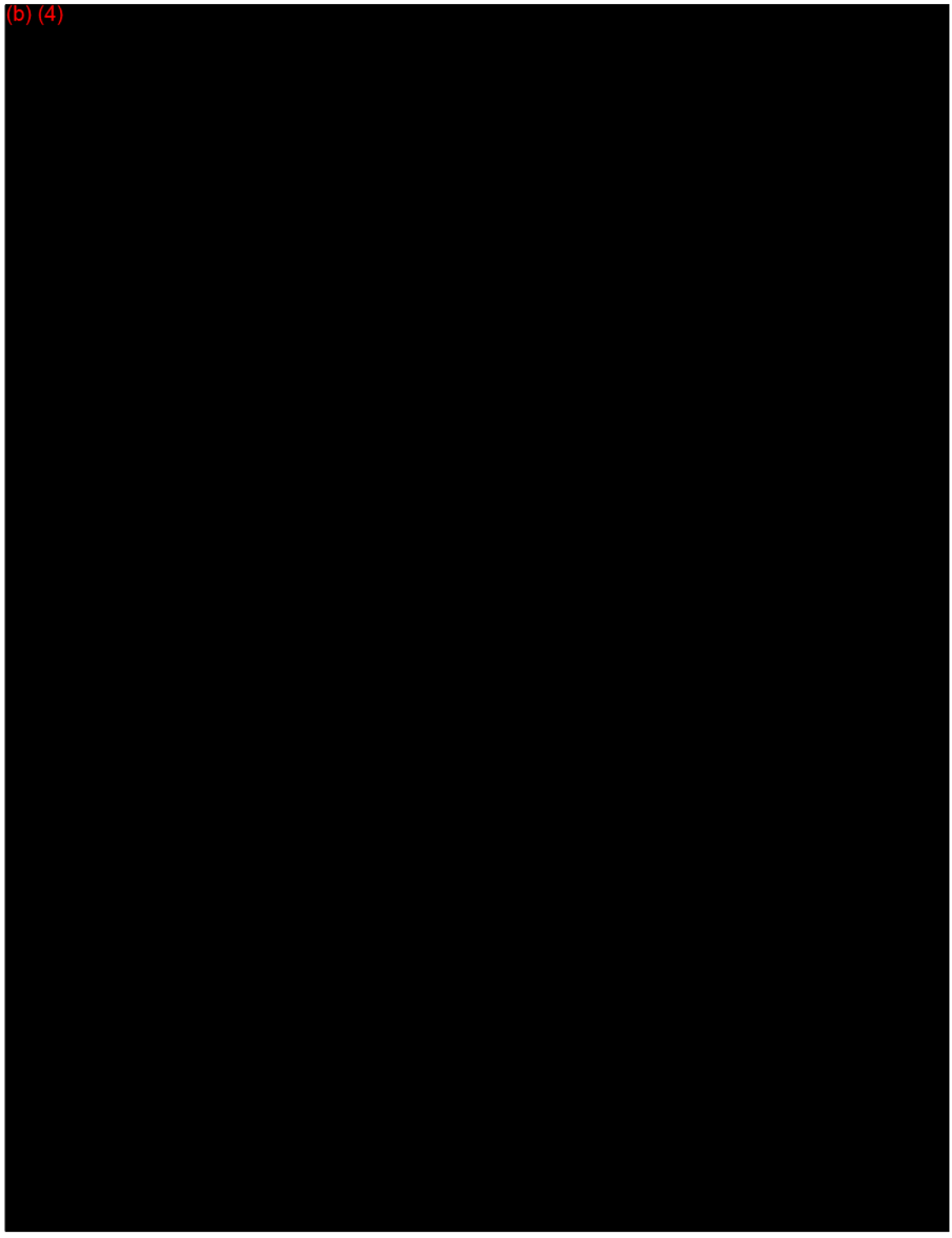

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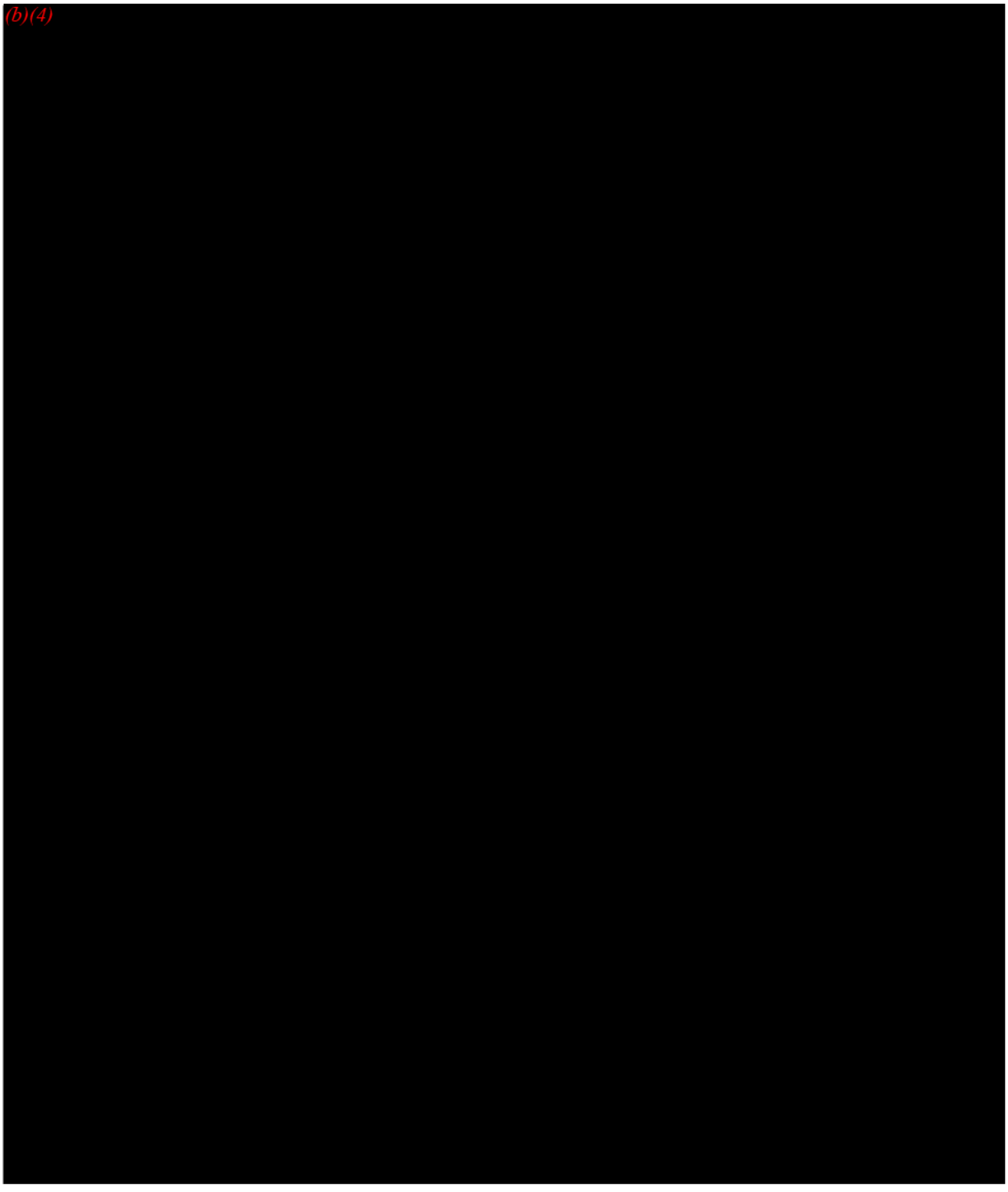

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Clinical Evaluation Summary

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Cardiac Output Estimation Performance of the

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2. MATERIAL AND METHODS

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3. RESULTS

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(NICO 3min/50sec) [L/min]

Novametrix Medical Systems Inc.

Clinical Evaluation Protocol

$NICO_2$® *Non-Invasive Cardiac Output/Respiratory Profile Monitor*

Author: James Bement

(b) (6)

Approvals:

Regulatory — Date: 12/19/00

Engineering — Date: 20-Dec-2000

Clinical — Date: 19-DEC-00

Marketing — Date: 12/19/00

Revision	Date	Prepared By
(b) (6), (b) (4)		

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2.0 PURPOSE

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3.0 SCOPE

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4.0 RISK ASSESSMENT

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5.0 EQUIPMENT

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6.0 CONFIDENTIAL DISCLOSURE AGREEMENT

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7.0 HARDWARE AND SOFTWARE CHANGE DESCRIPTION

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8.0 PATIENT SELECTION AND STUDY METHODOLOGY

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9.0 OPERATION VERIFICATION PROCEDURE

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10.0 DOCUMENTATION AND RECORD KEEPING

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11.0 MONITORING PROCEDURES

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12.0 ADVERSE REACTION REPORT

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13.0 CLINICAL TRIAL SUMMARY QUESTIONNAIRE

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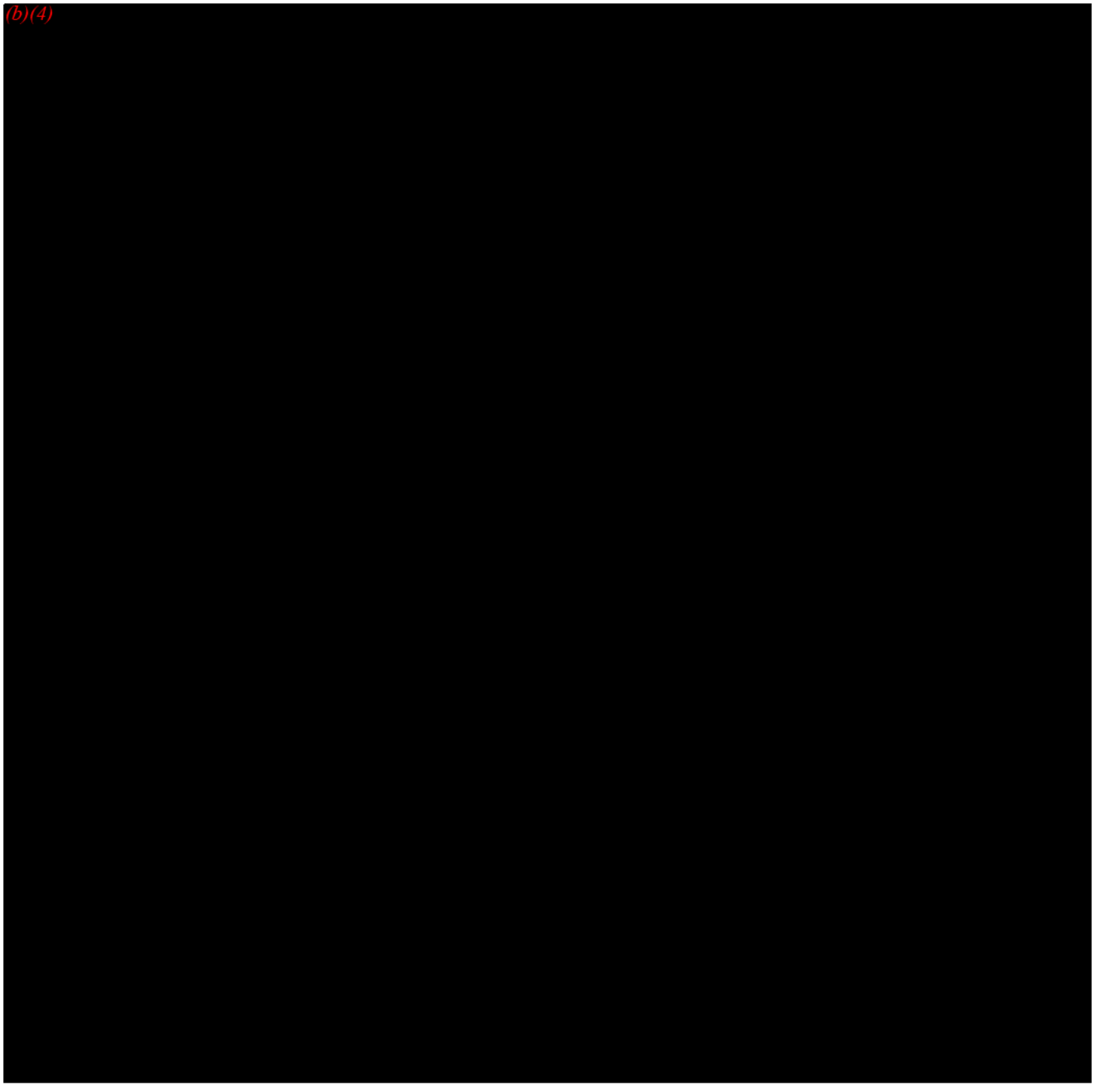

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EPD99107
Generic Protocol for De-saturation Studies using Novametrix Pulse Oximetry Systems

Author: (b) (6)
Editor: (b) (6)

Approvals:

Regulatory		Date: 9/19/01
Engineering		Date: 19 SEP 01
Clinical		Date: 9/19/2001
Marketing		Date: 9/19/01

Revision Record

Revision	Date	Prepared By
(b) (4), (b) (6)		

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(b)(4) Trial Protocol

1.0 Note of Confidentiality

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2.0 Scope

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3.0 Purpose

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4.0 Risk Assessment

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5.0 Equipment

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6.0 Patient Population

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7.0 Clinical Trial Procedure

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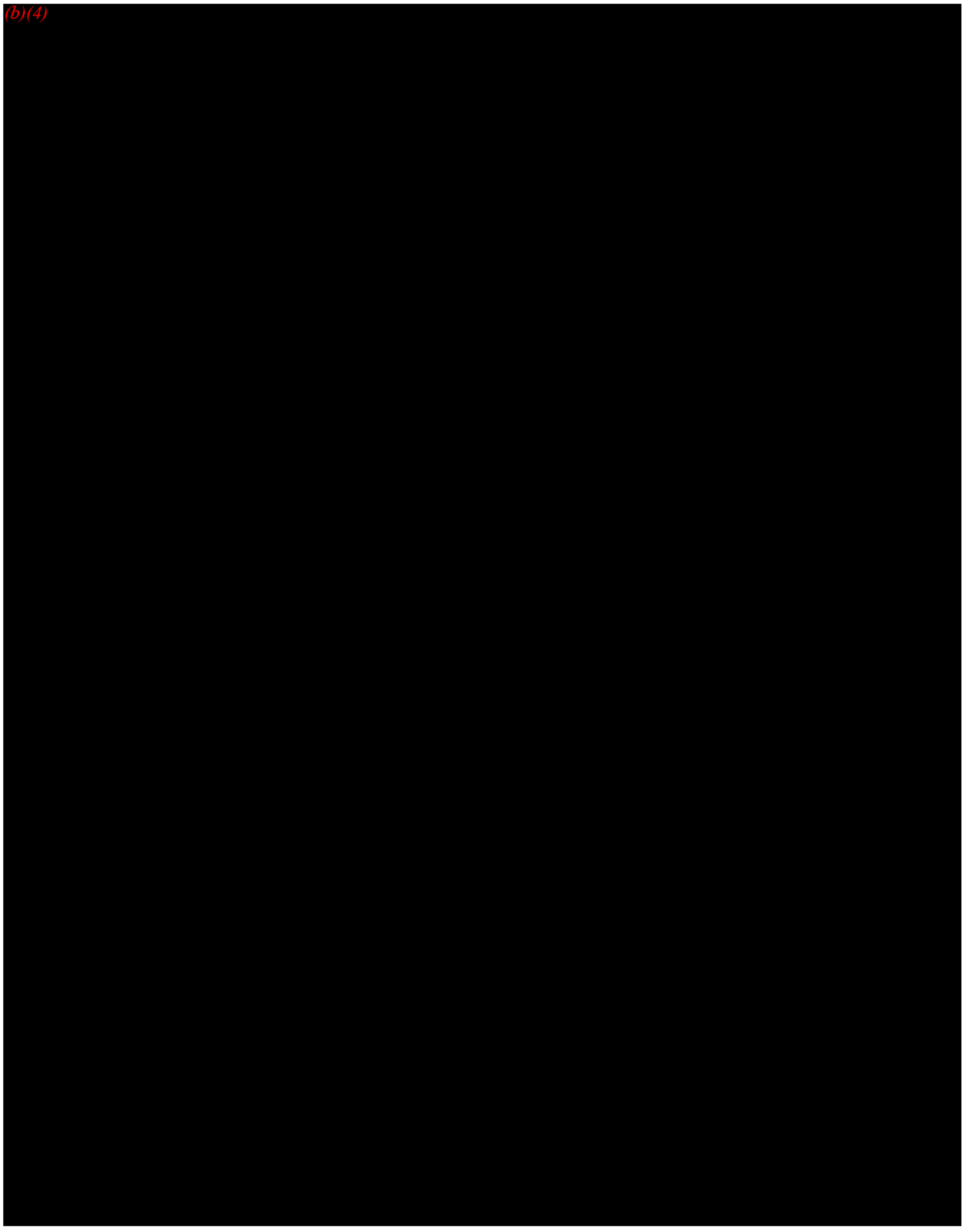

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Sample Co-oximeter Worksheet

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Sensor Location Work Sheet

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Revision Record

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APPENDIX 5: SOFTWARE VALIDATION AND VERIFICATION

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A. Software Development for the *NICO with* (b)(4)

Development Process

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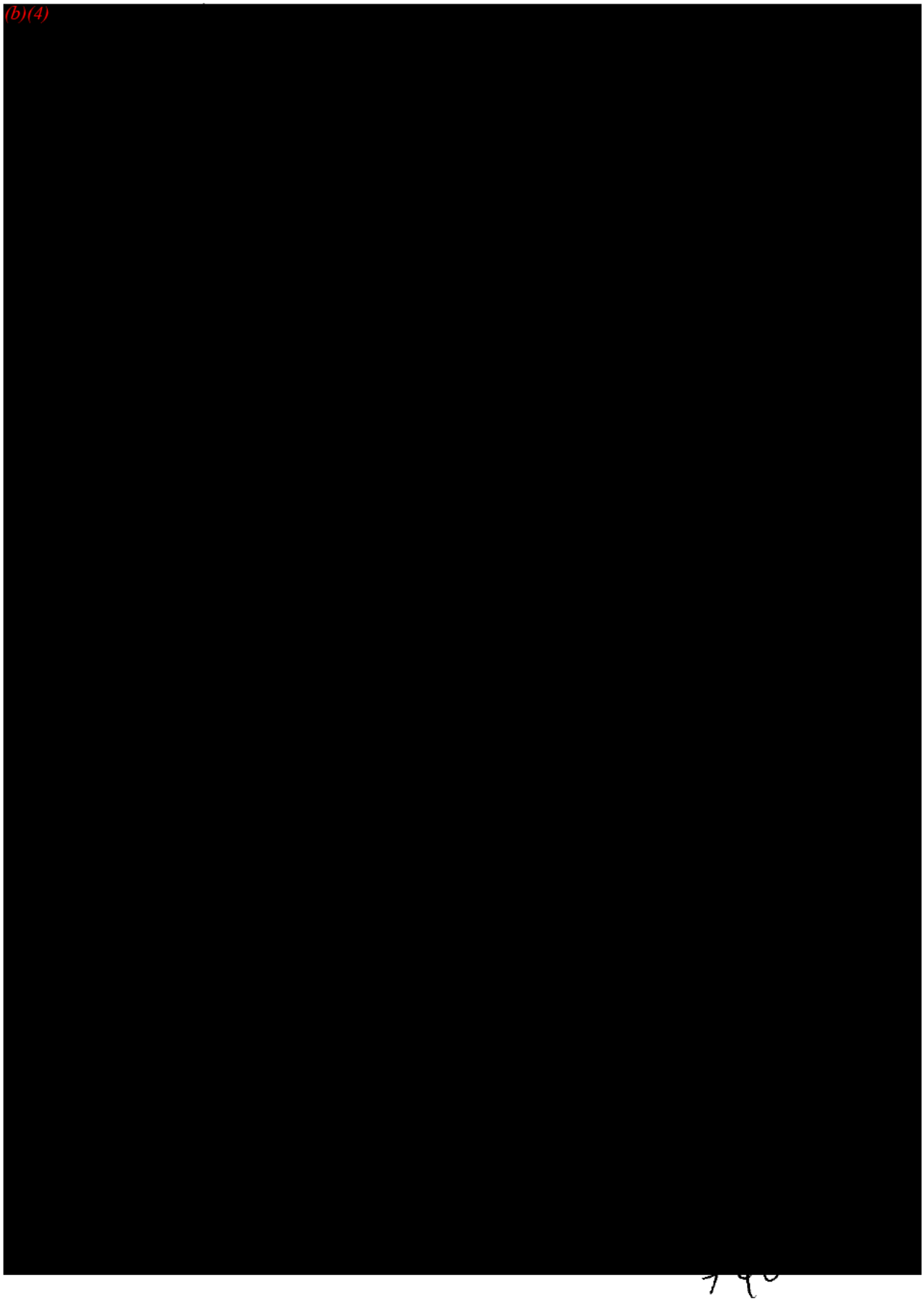

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EPD98138
Software Requirements Specification for NICO Model 7300

Author: (b) (6)
Contributing Authors:

Approvals:

Engineering:

Project Manager (b) (6) Date 3-Mar-03

Software Coordinator Date 7 MAR 03

Director of Engineering Date 10-MAR-03

Marketing

Product Manager Date 3/10/03

Revision Record

Revision	Date	Prepared By
(b) (6), (b) (4)		

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1.3 Definitions, Acronyms, and Abbreviations

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1.5 Overview

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2. Overall Description

2.1 Product Perspective

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2.2 Product Functions

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2.3 User Characteristics

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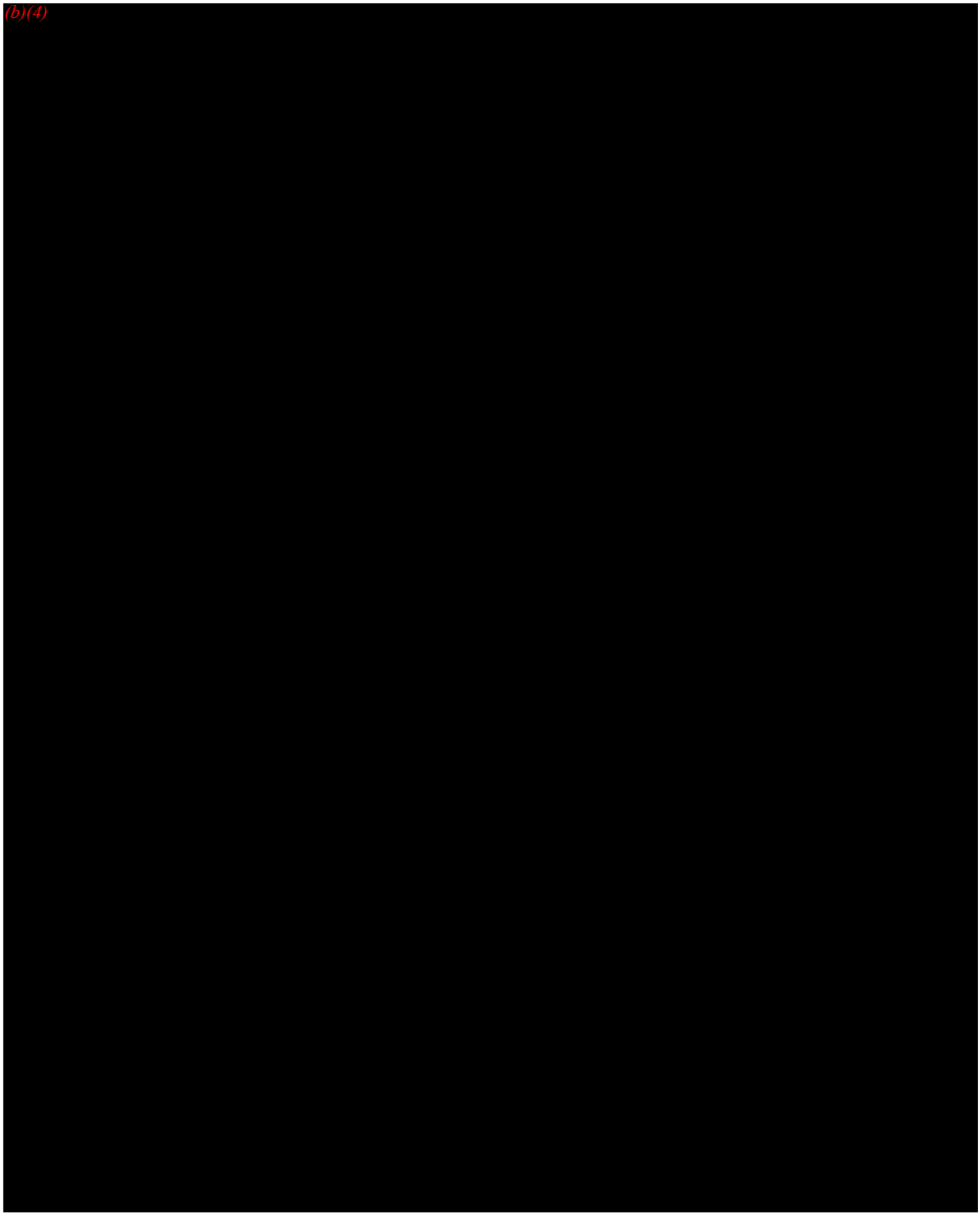

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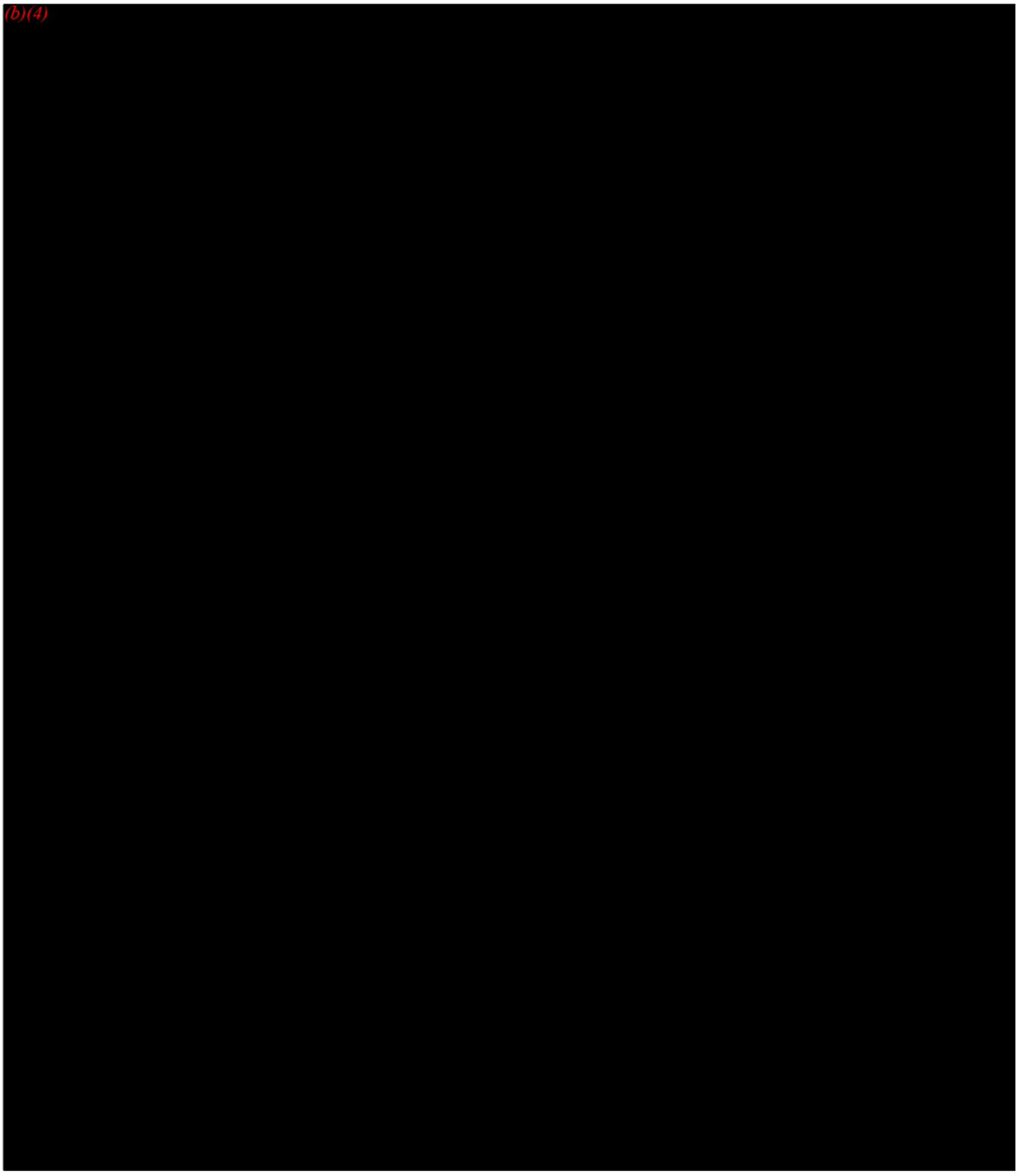

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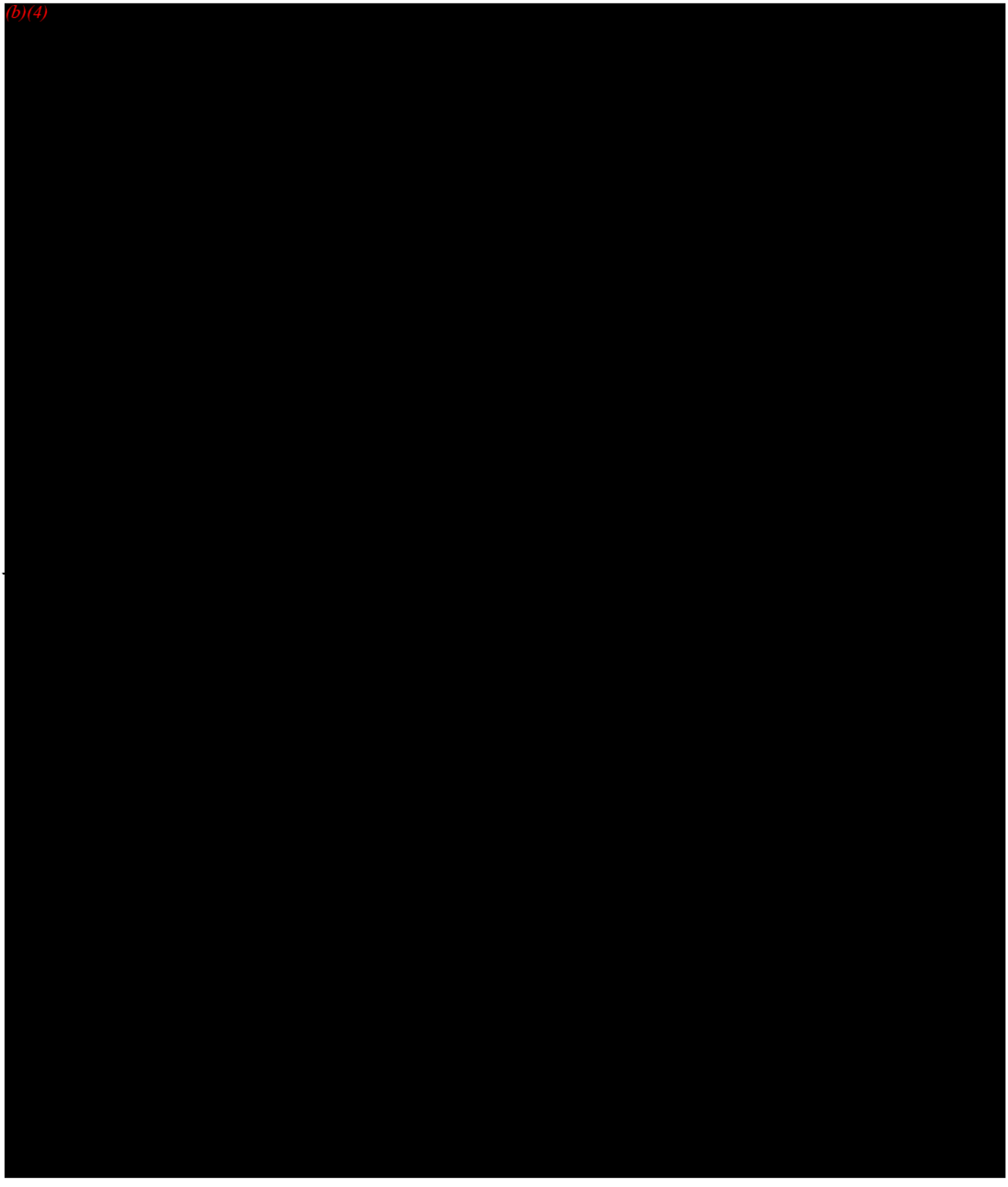

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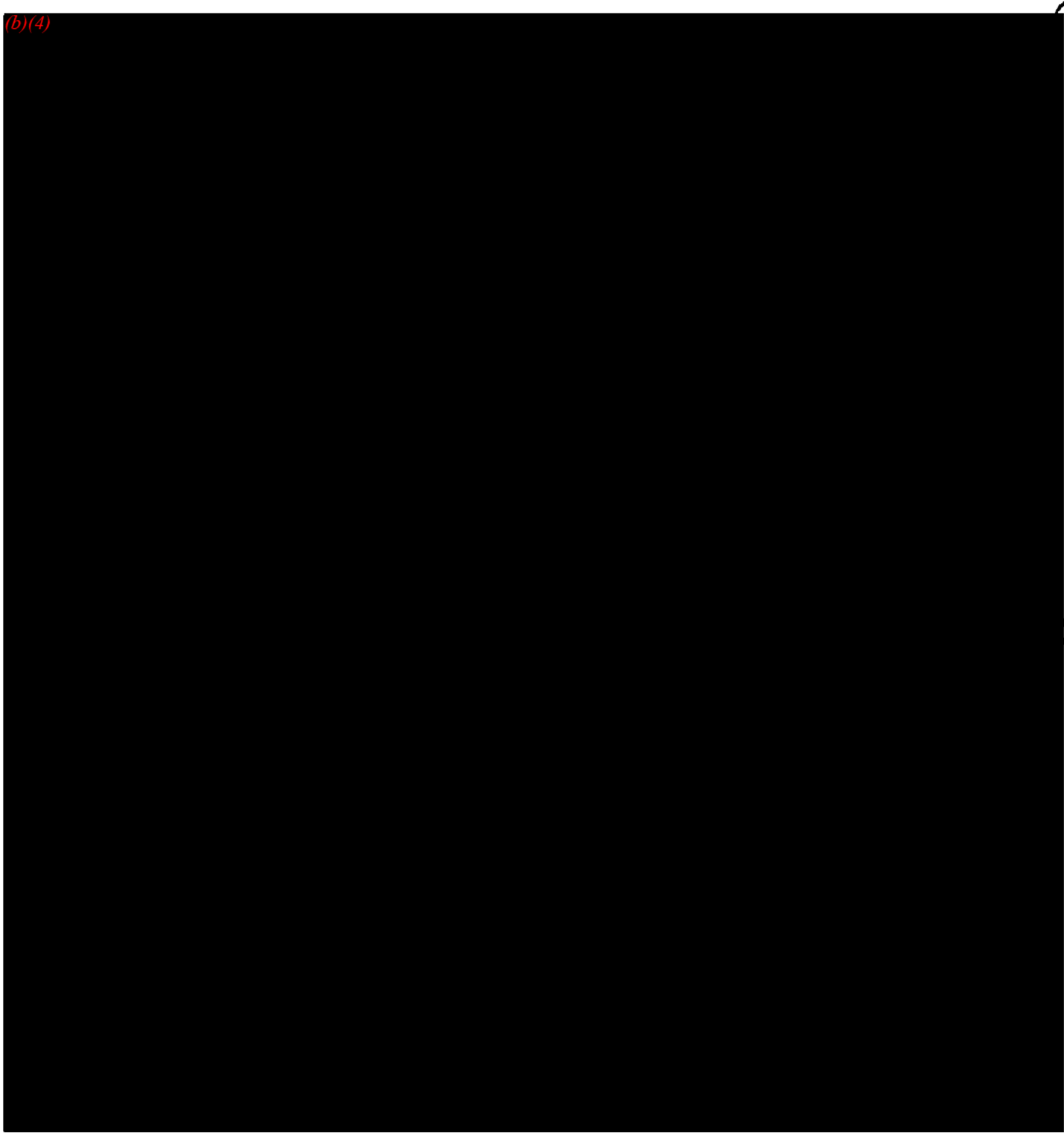

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5. Performance Requirements

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Appendix A

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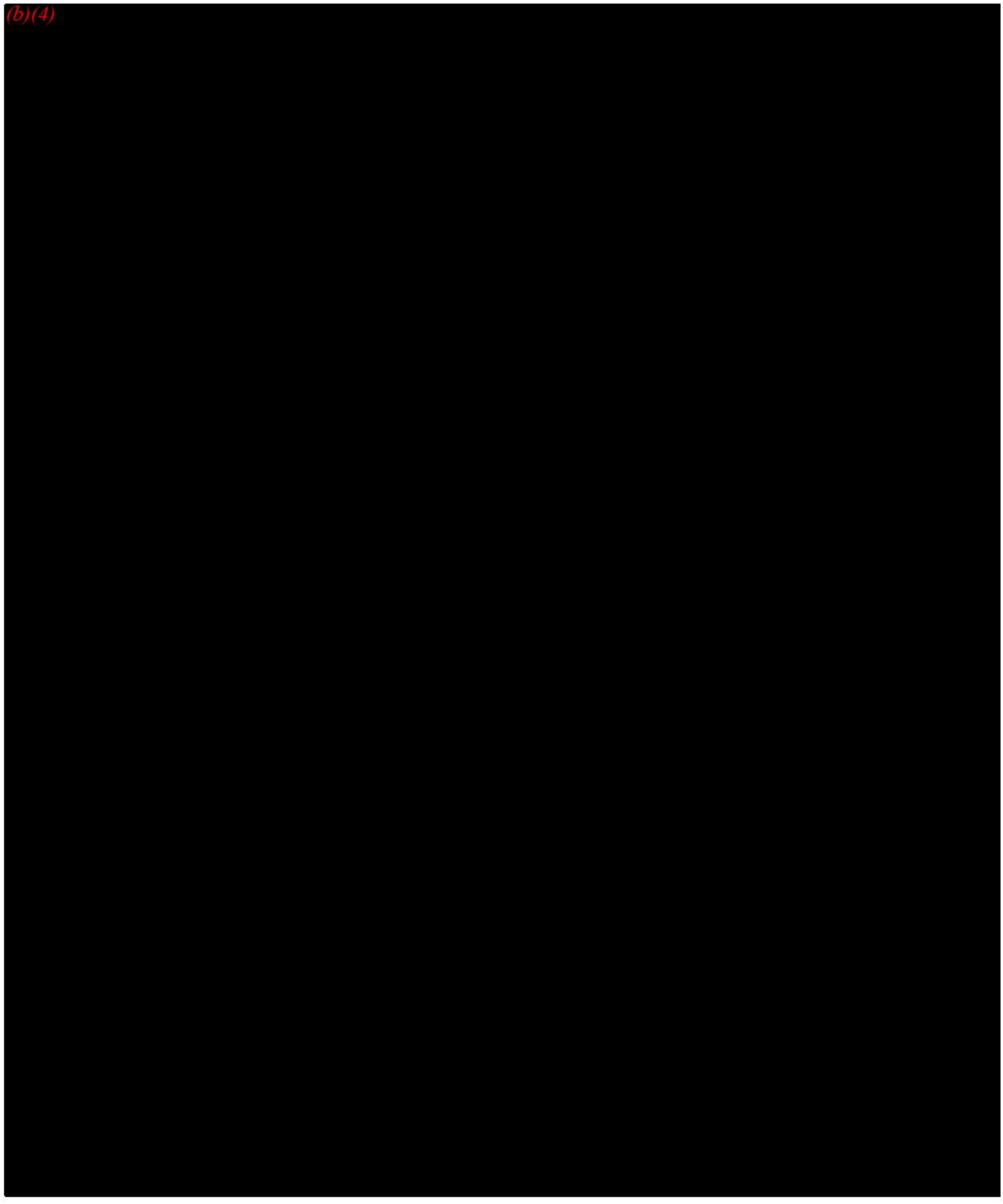

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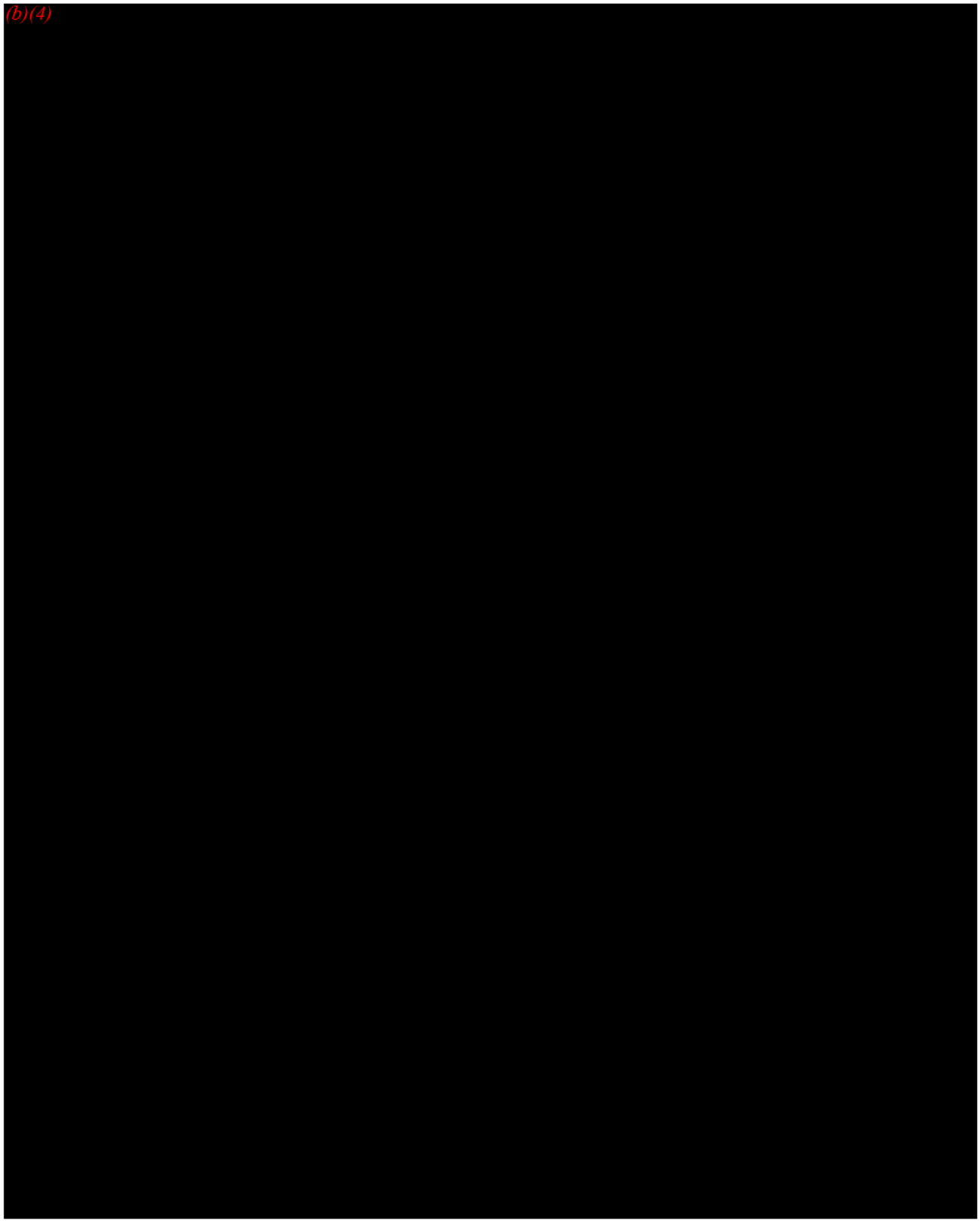

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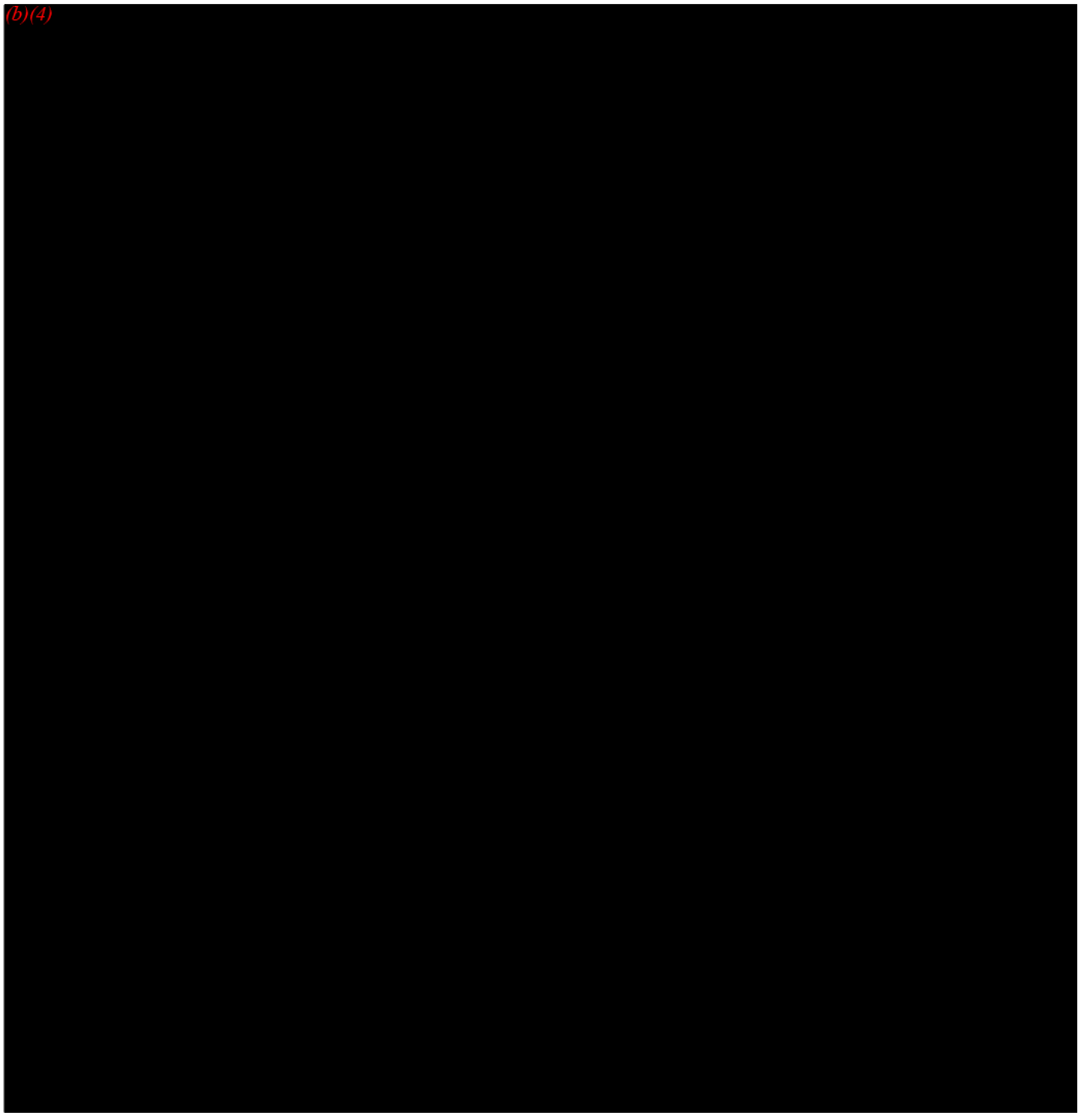

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EPD98139
Software Design Description for *NICO Model* 7300

Author (b) (6) [redacted]
Contrib

Approvals:

(b) (6) [redacted]

Engineering:

Project Manager _____ Date 28 Feb 03

Software Coordinator _____ Date 7 MAR 2003

Peer Review _____ Date 28 Feb 2003

Revision History

Revision	Date	Changed by	Reason For Change
(b) (6), (b) (4) [redacted]			

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1.3 Definitions, Acronyms, and Abbreviations

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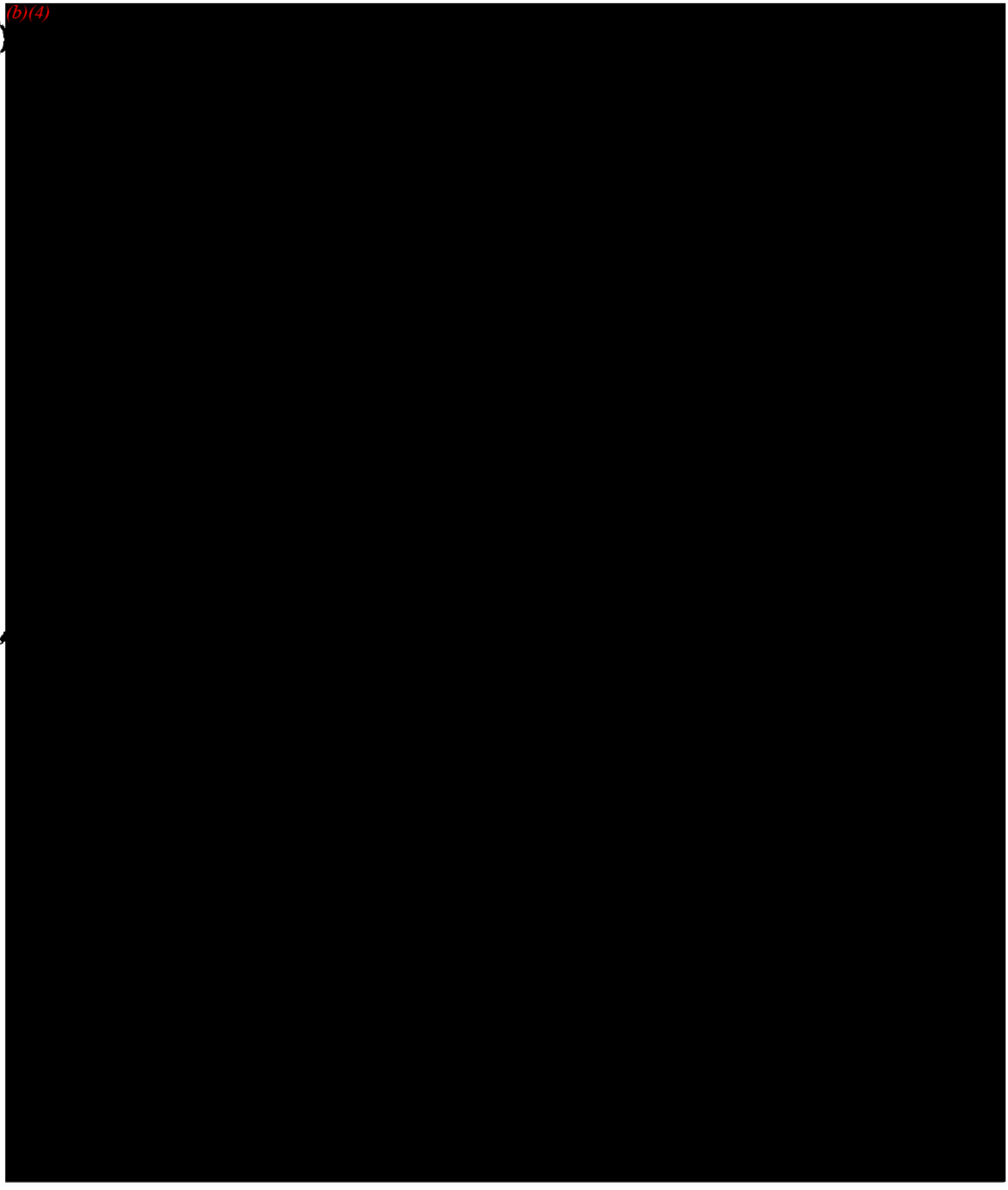

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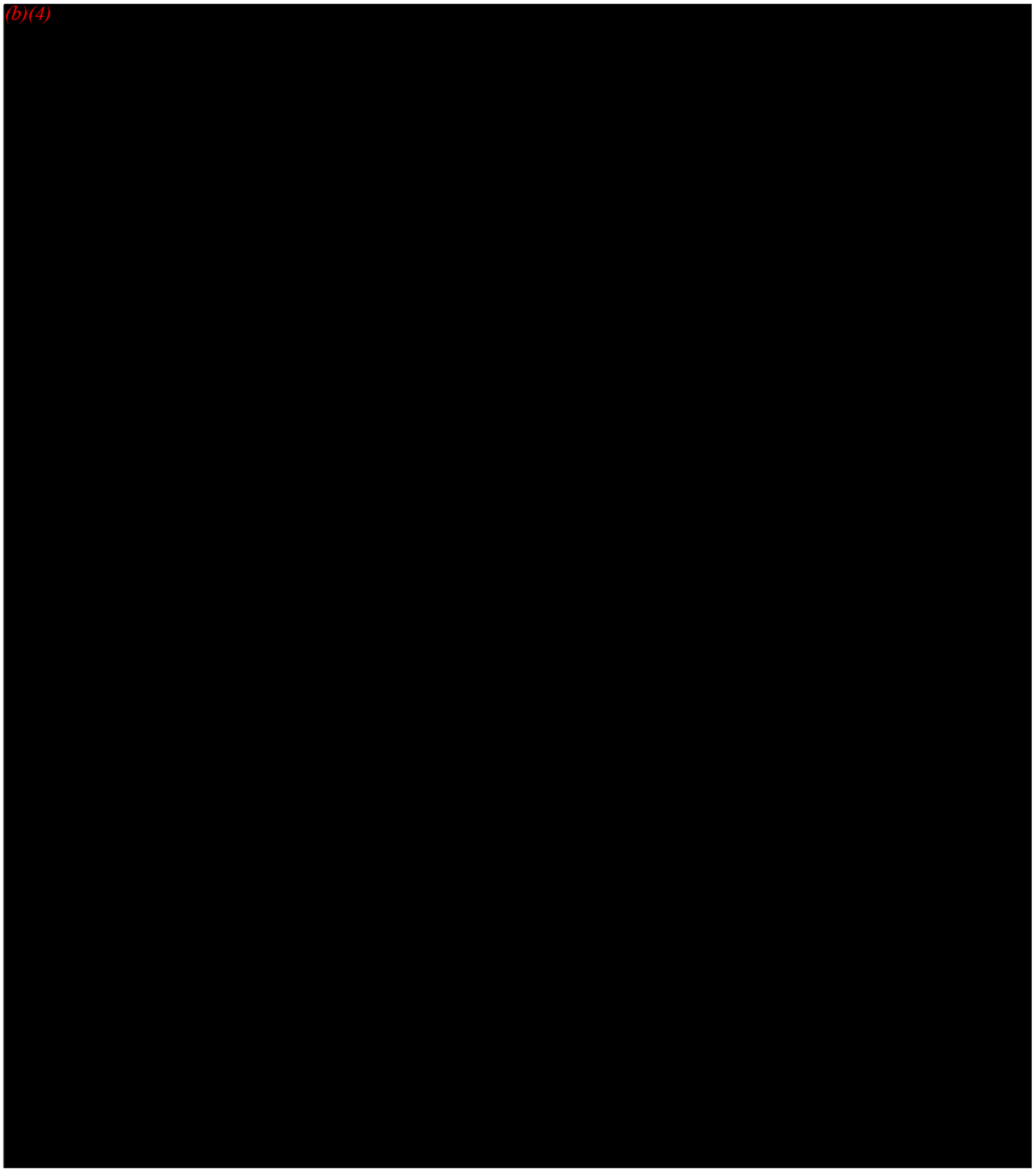

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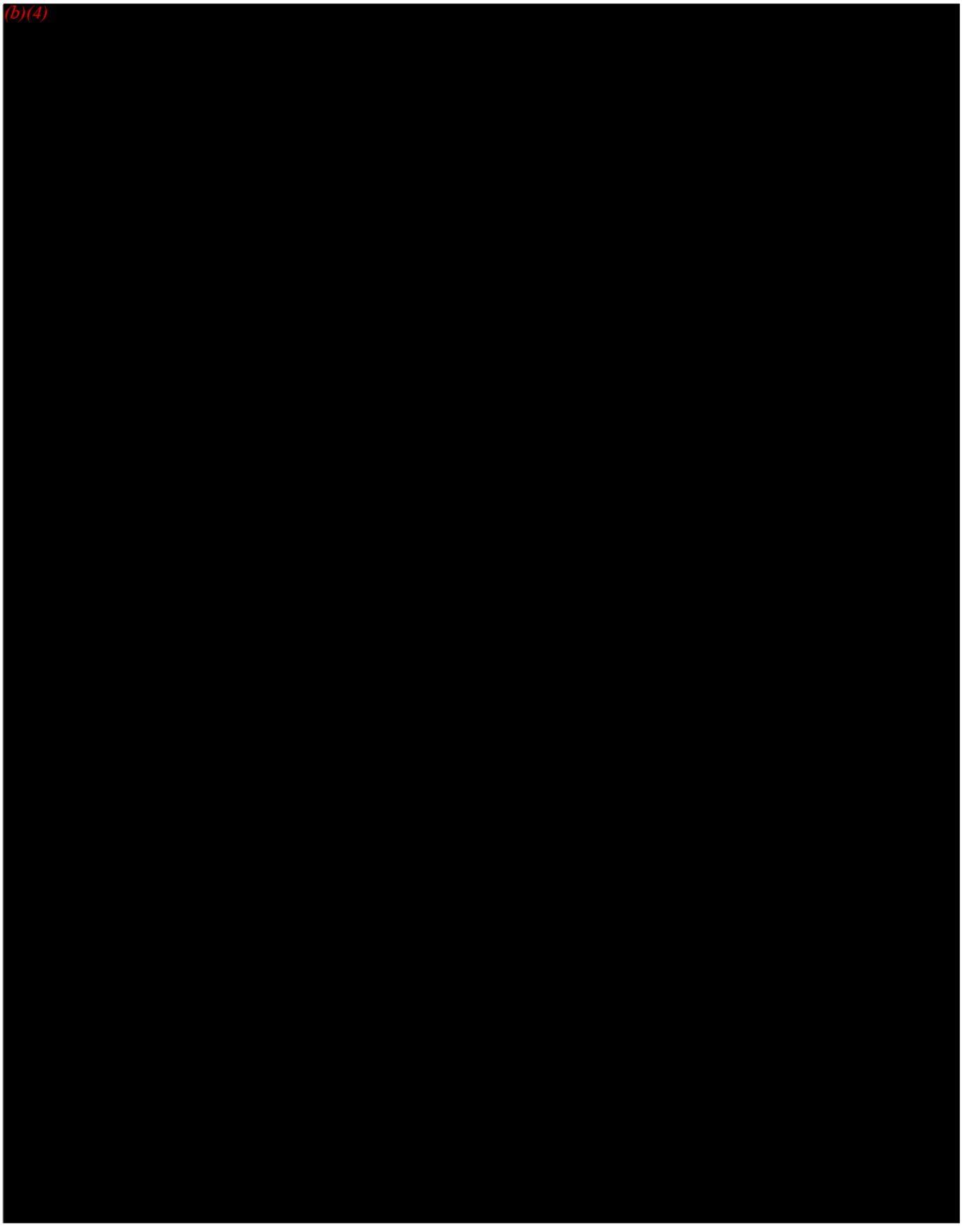

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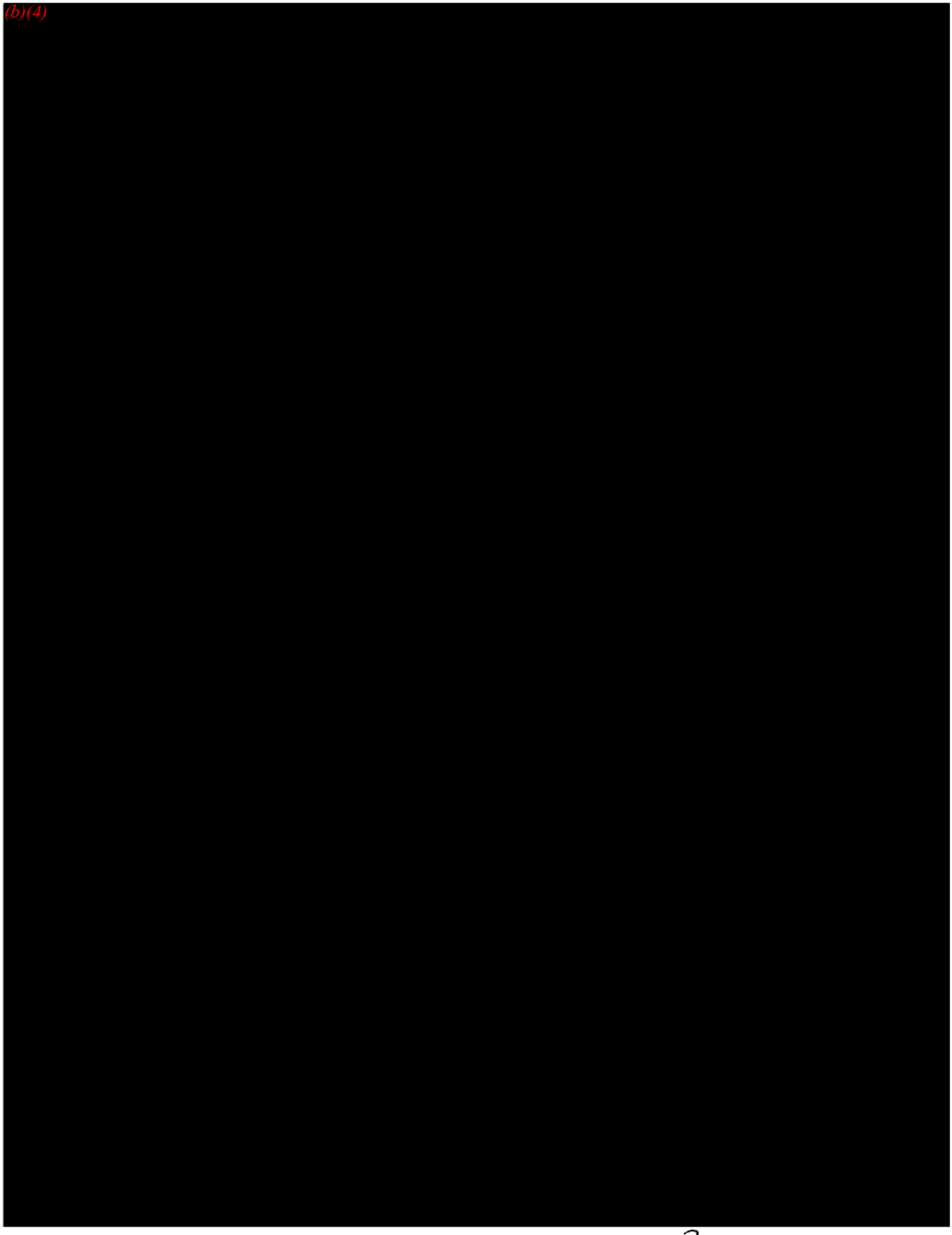

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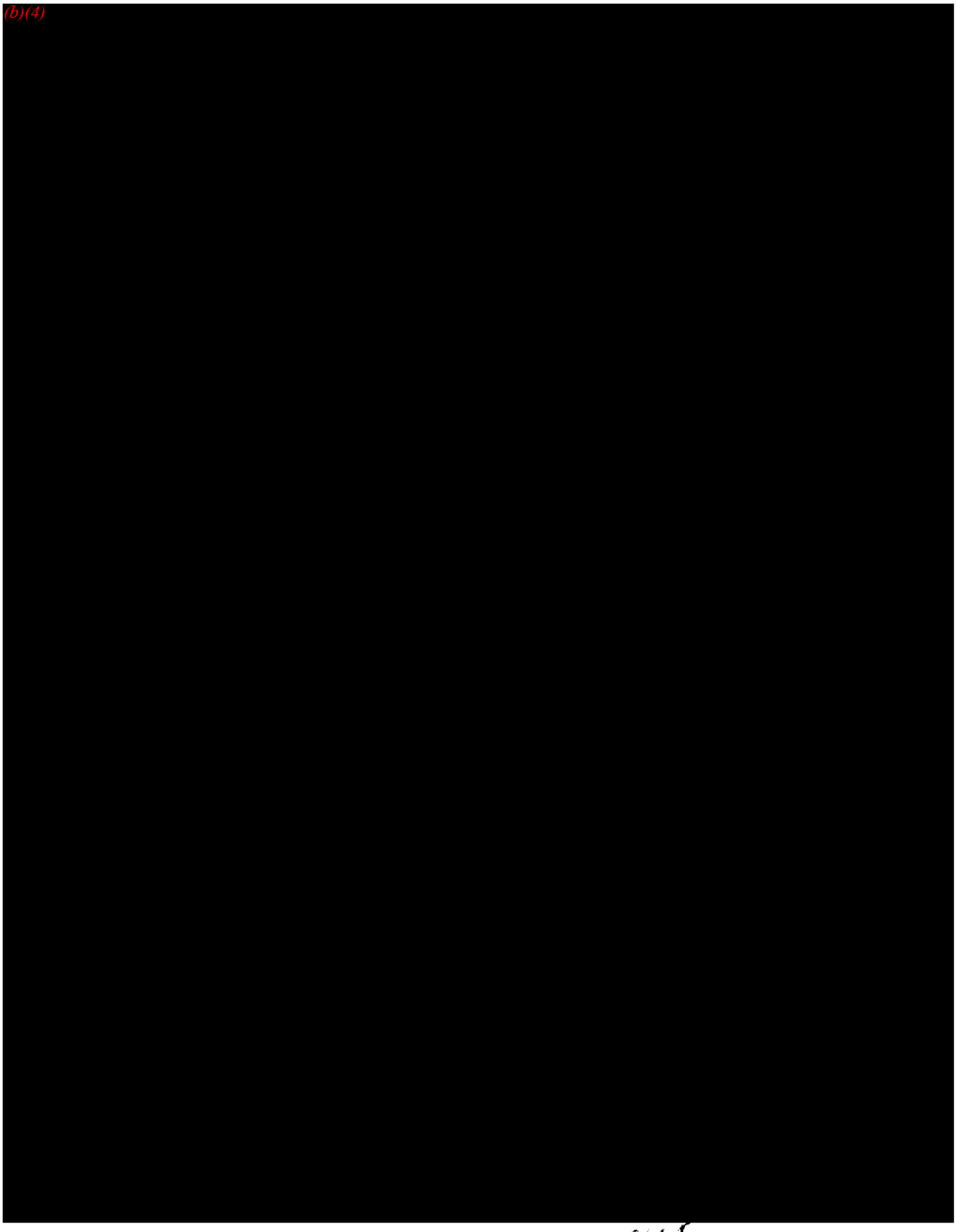

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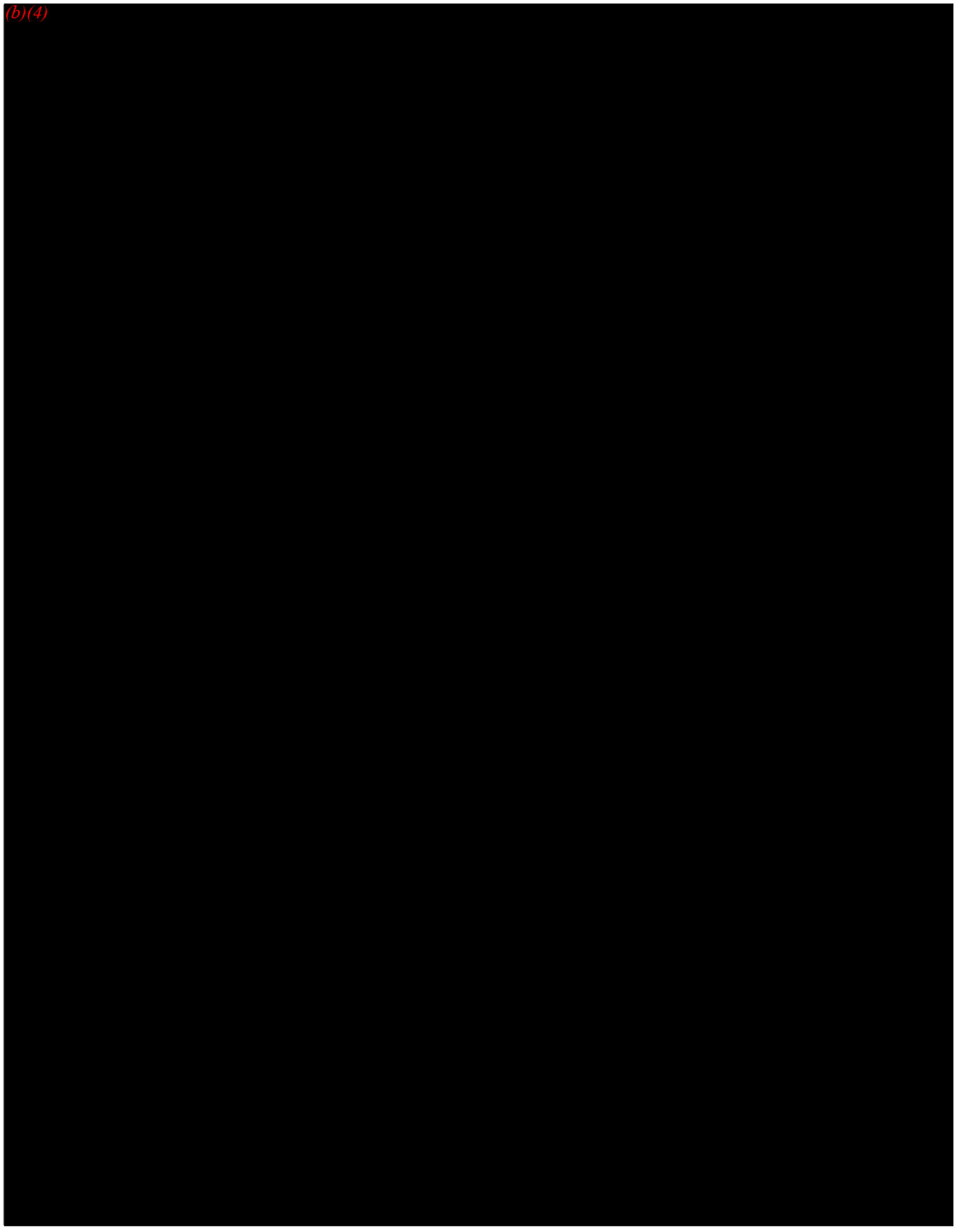

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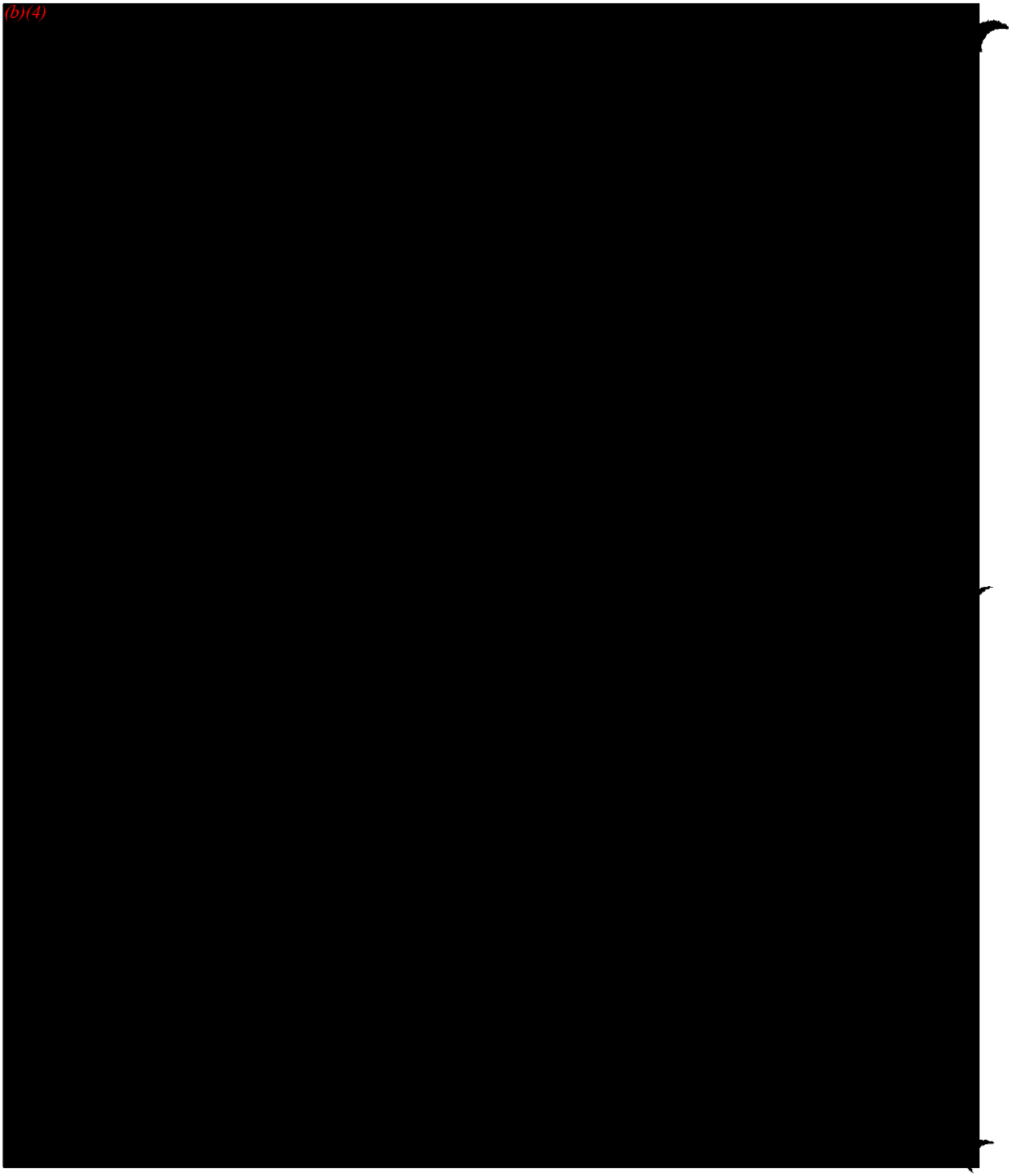

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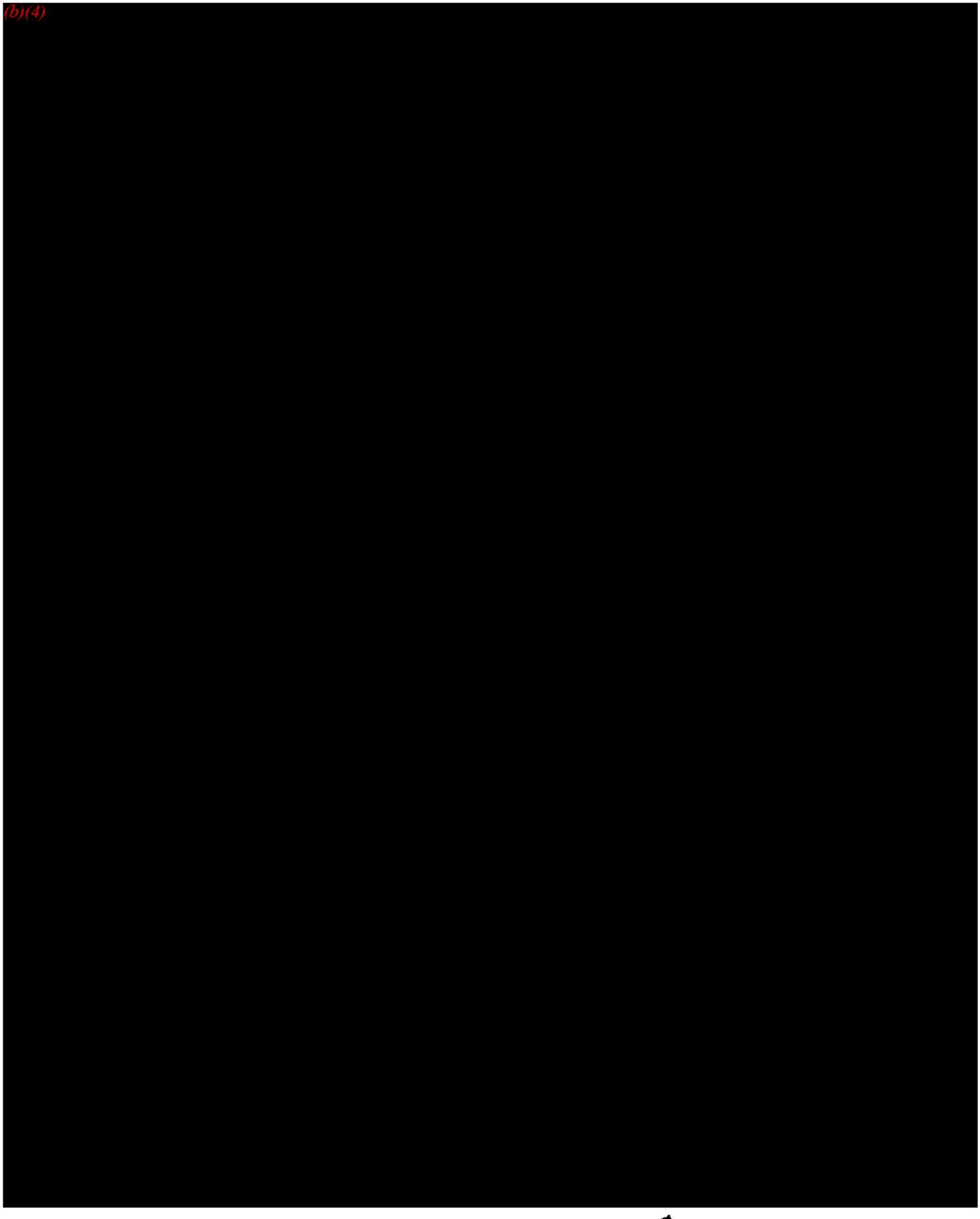

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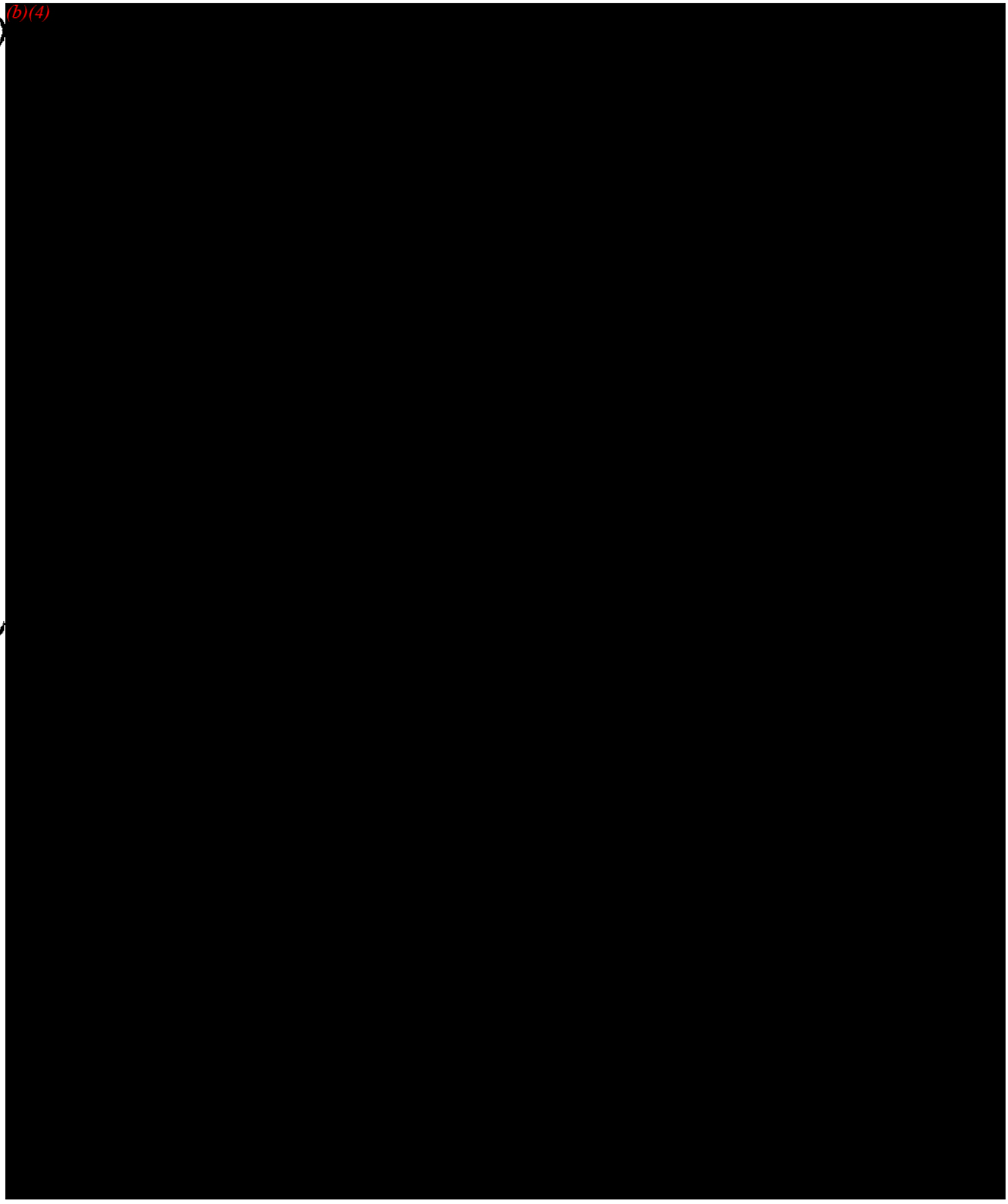

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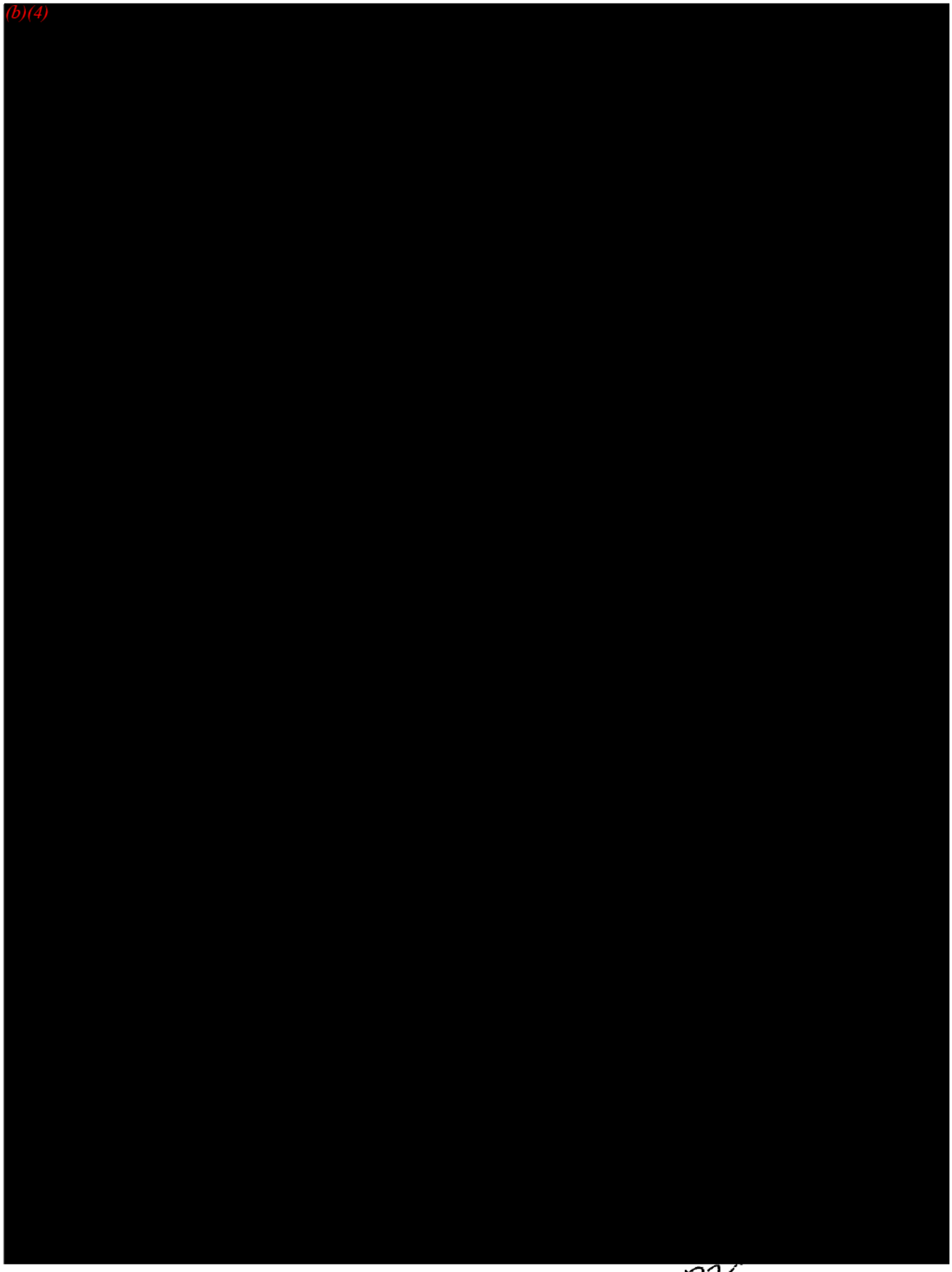

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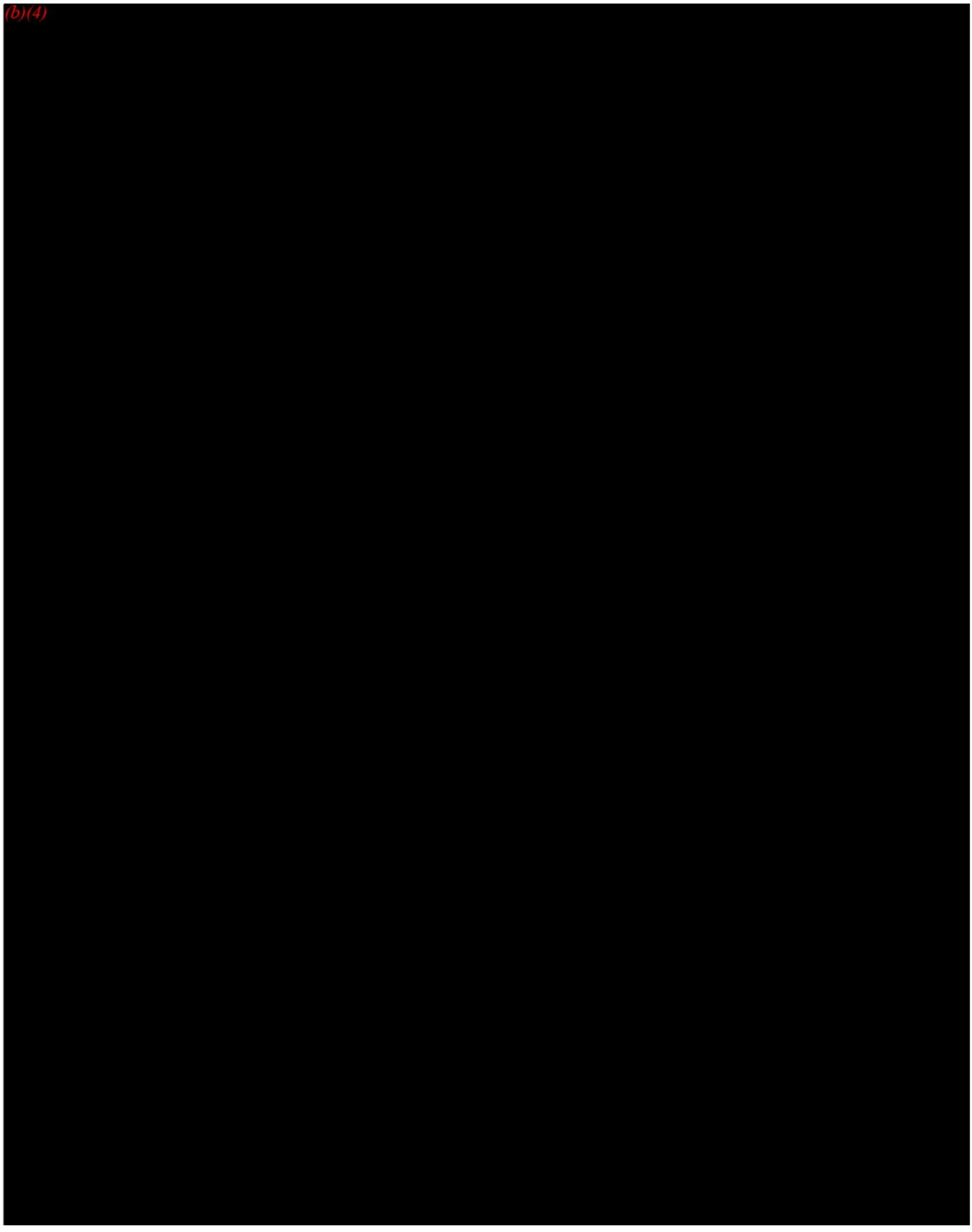

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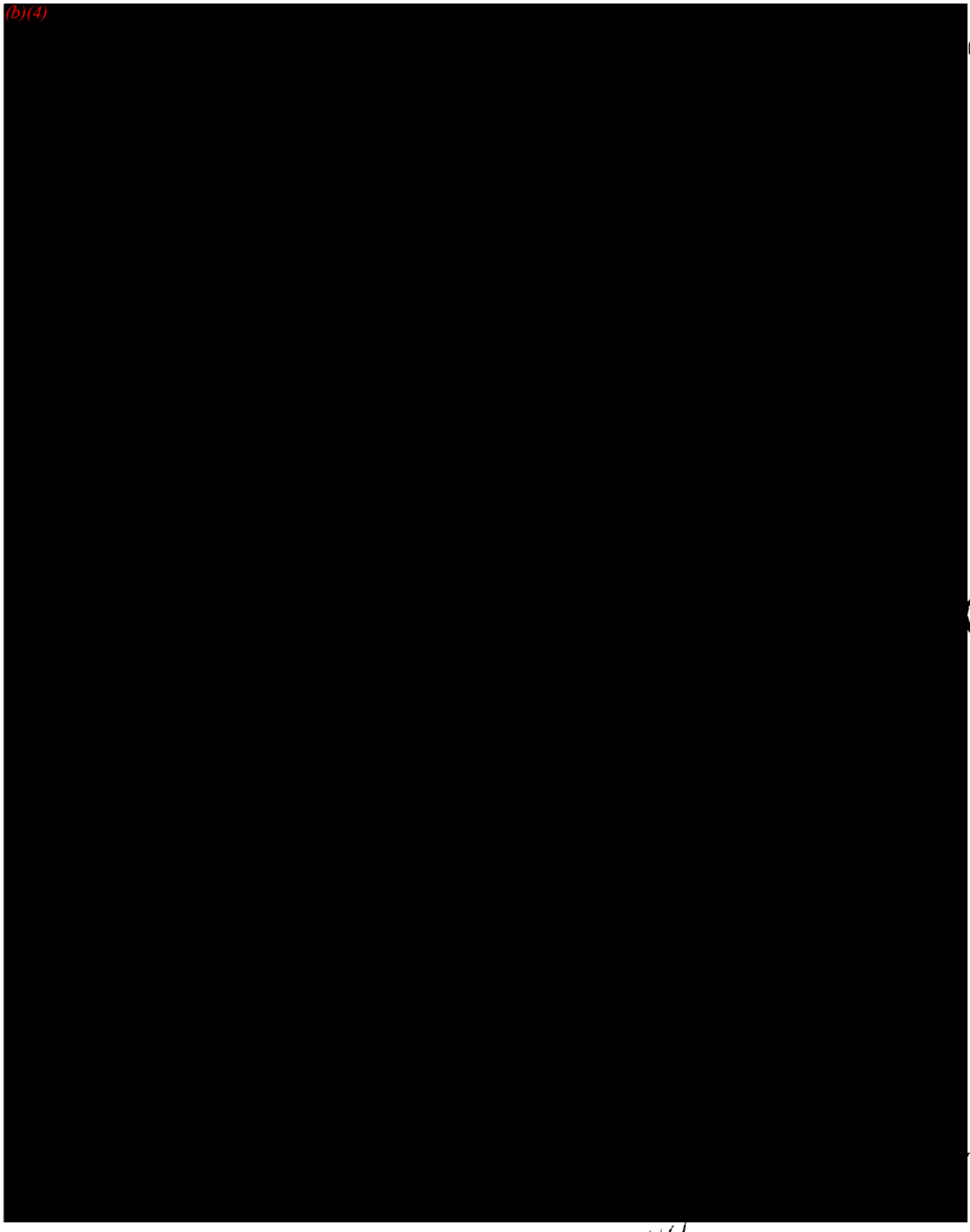

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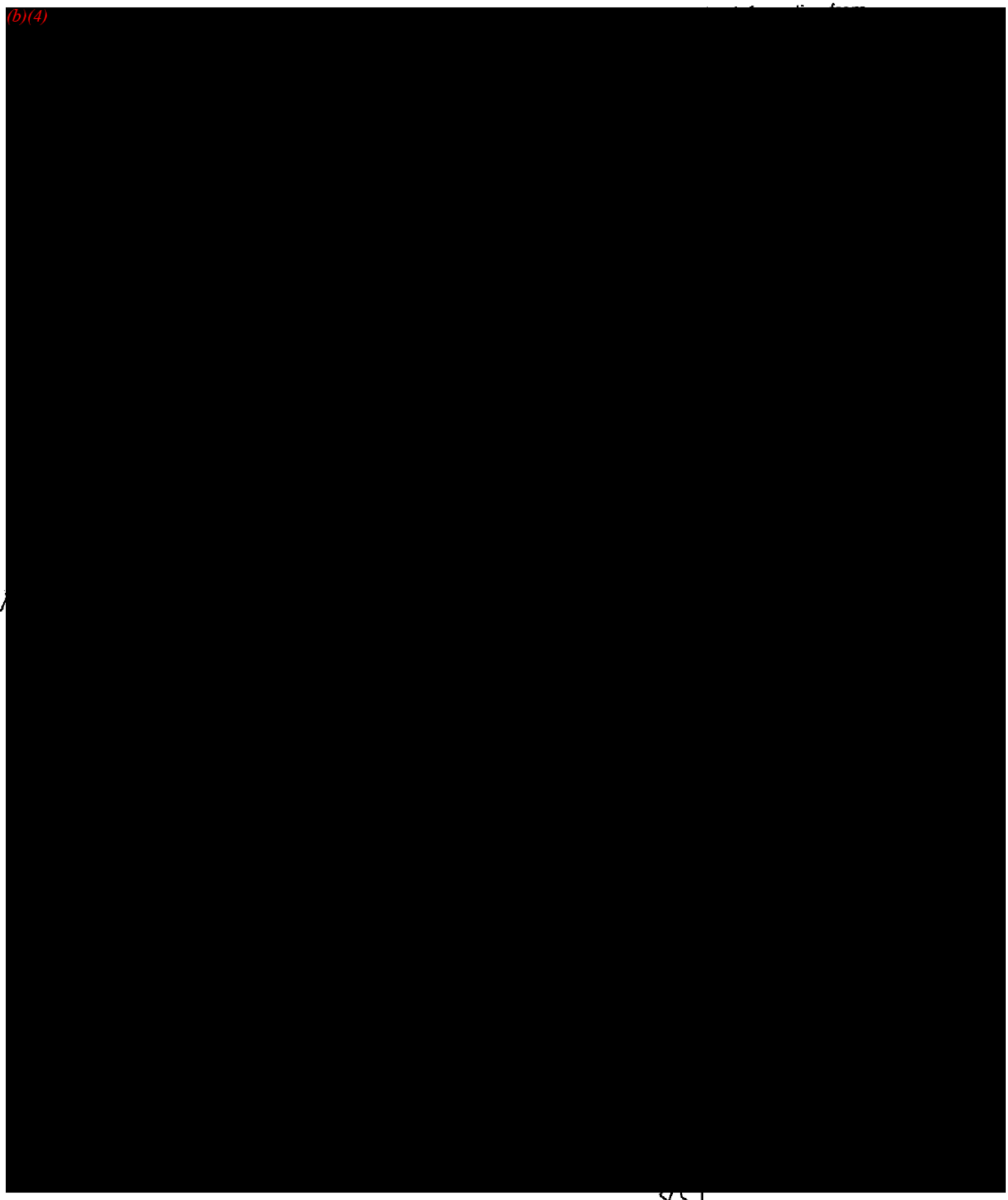

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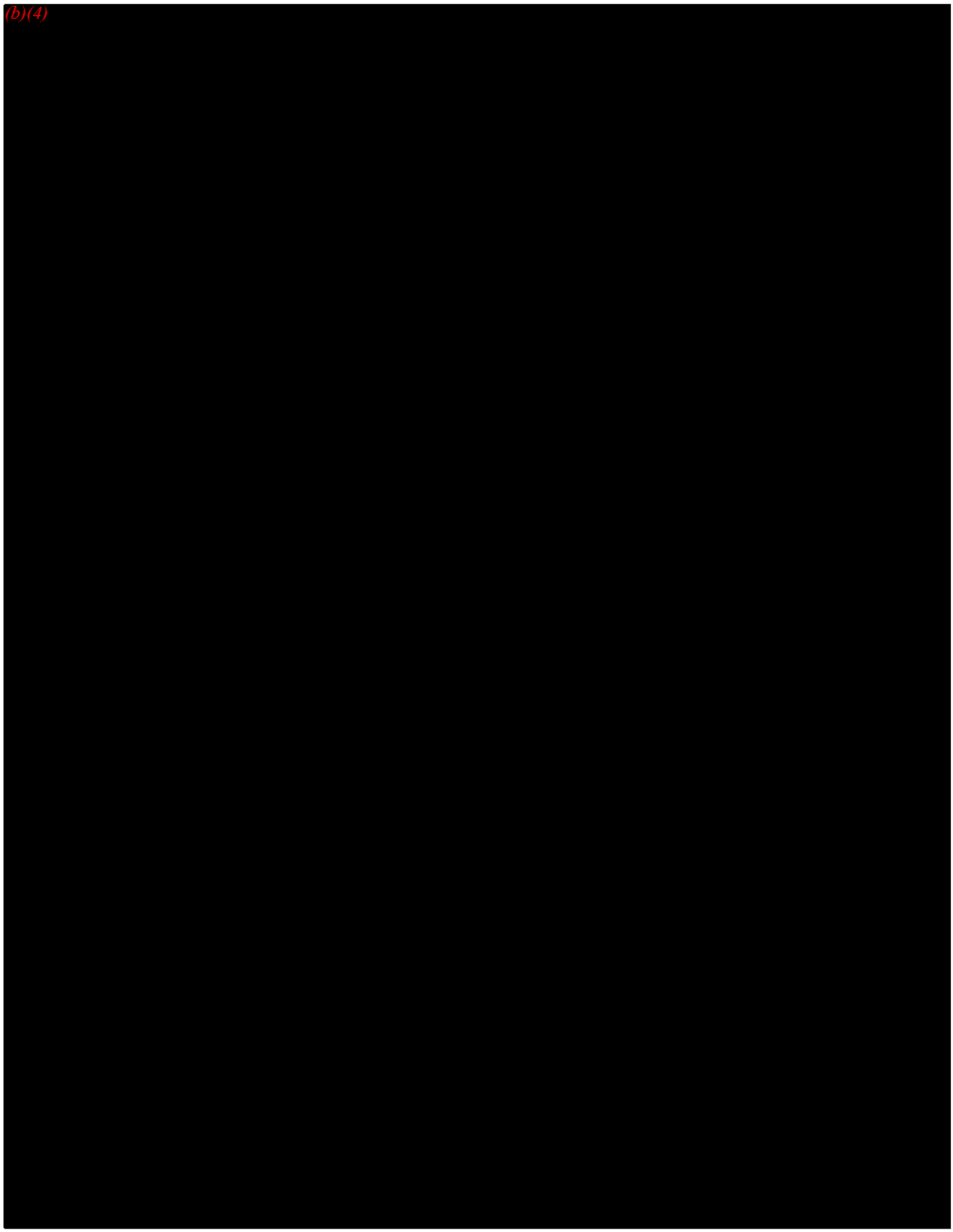

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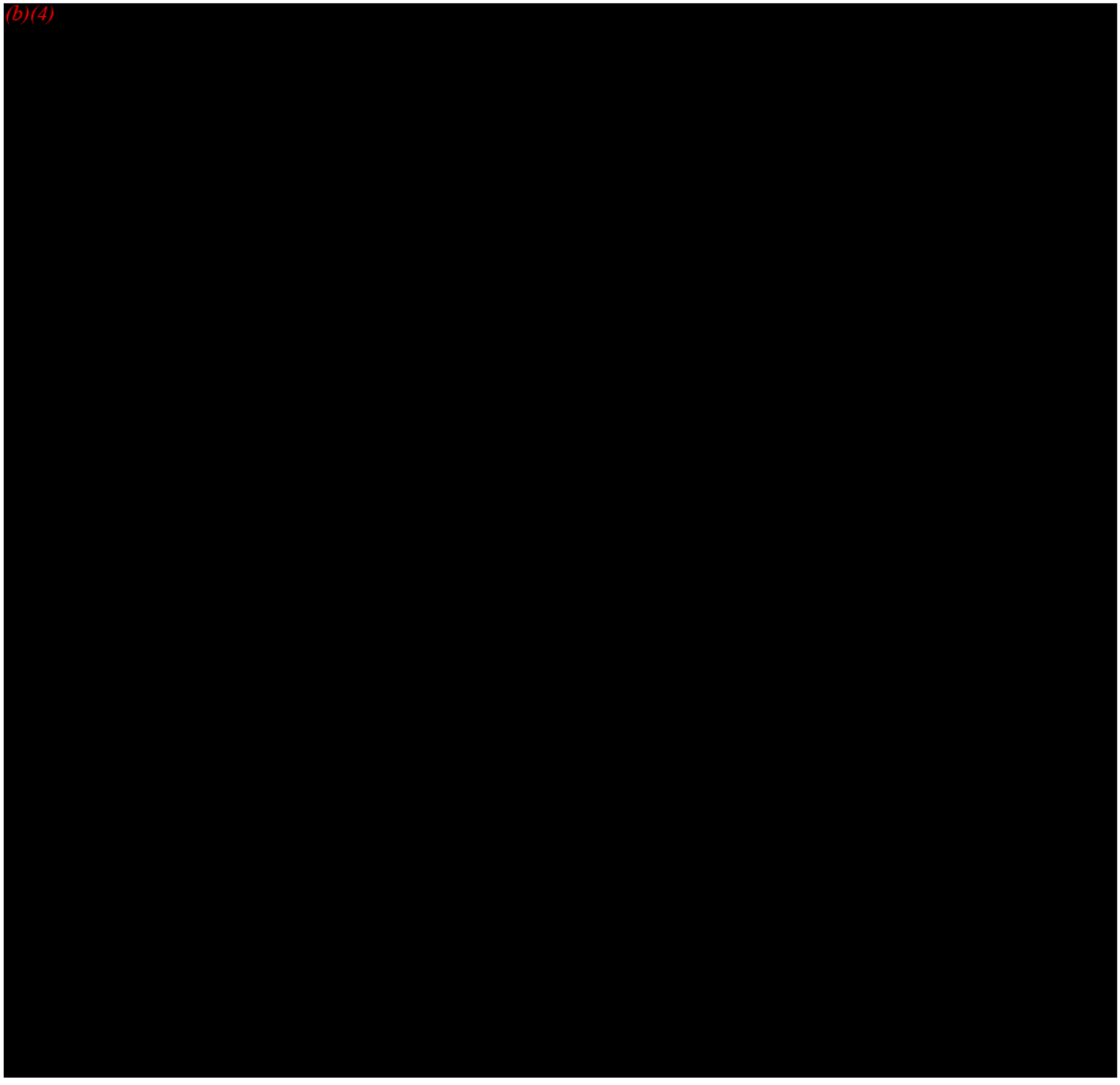

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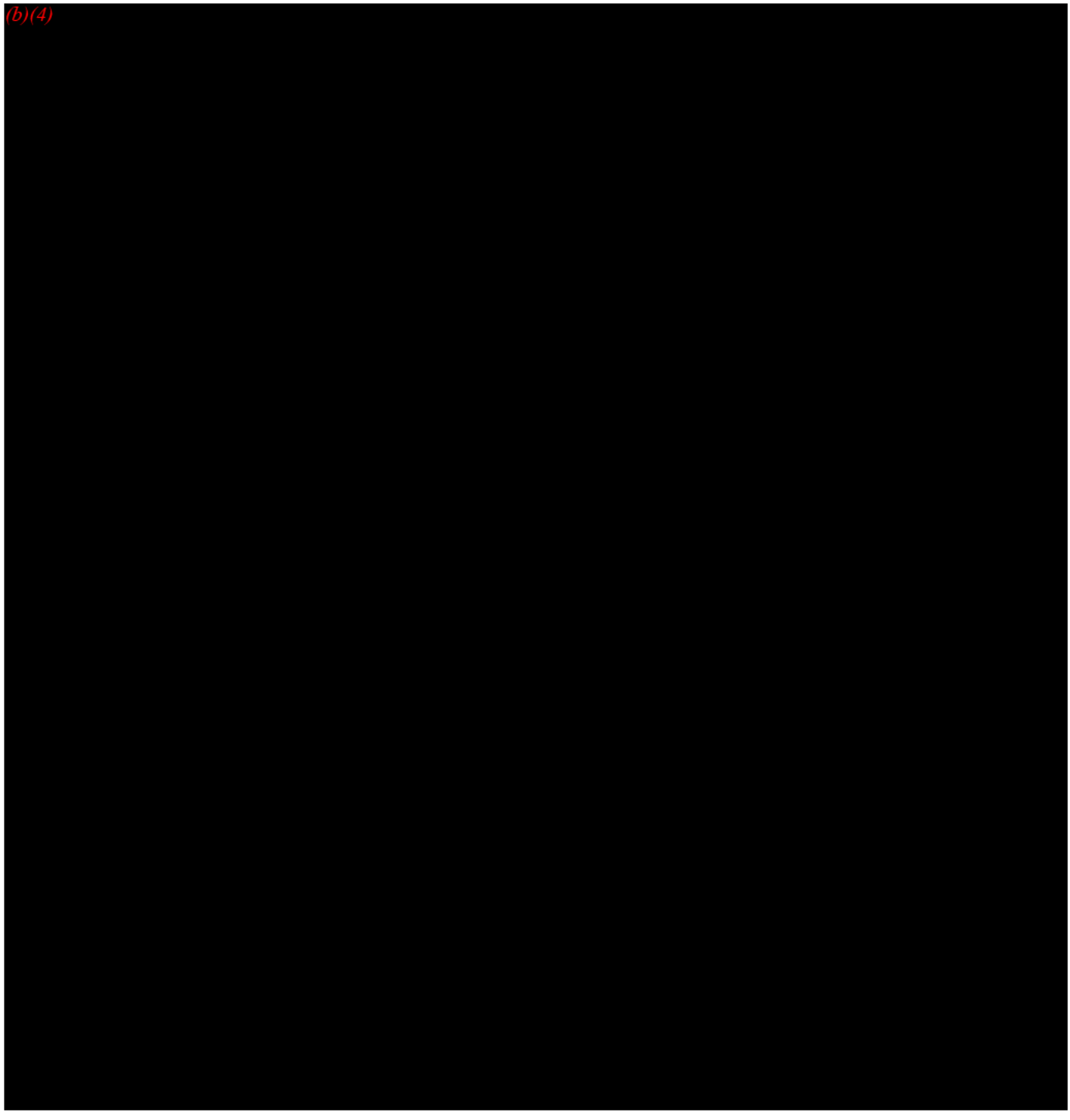

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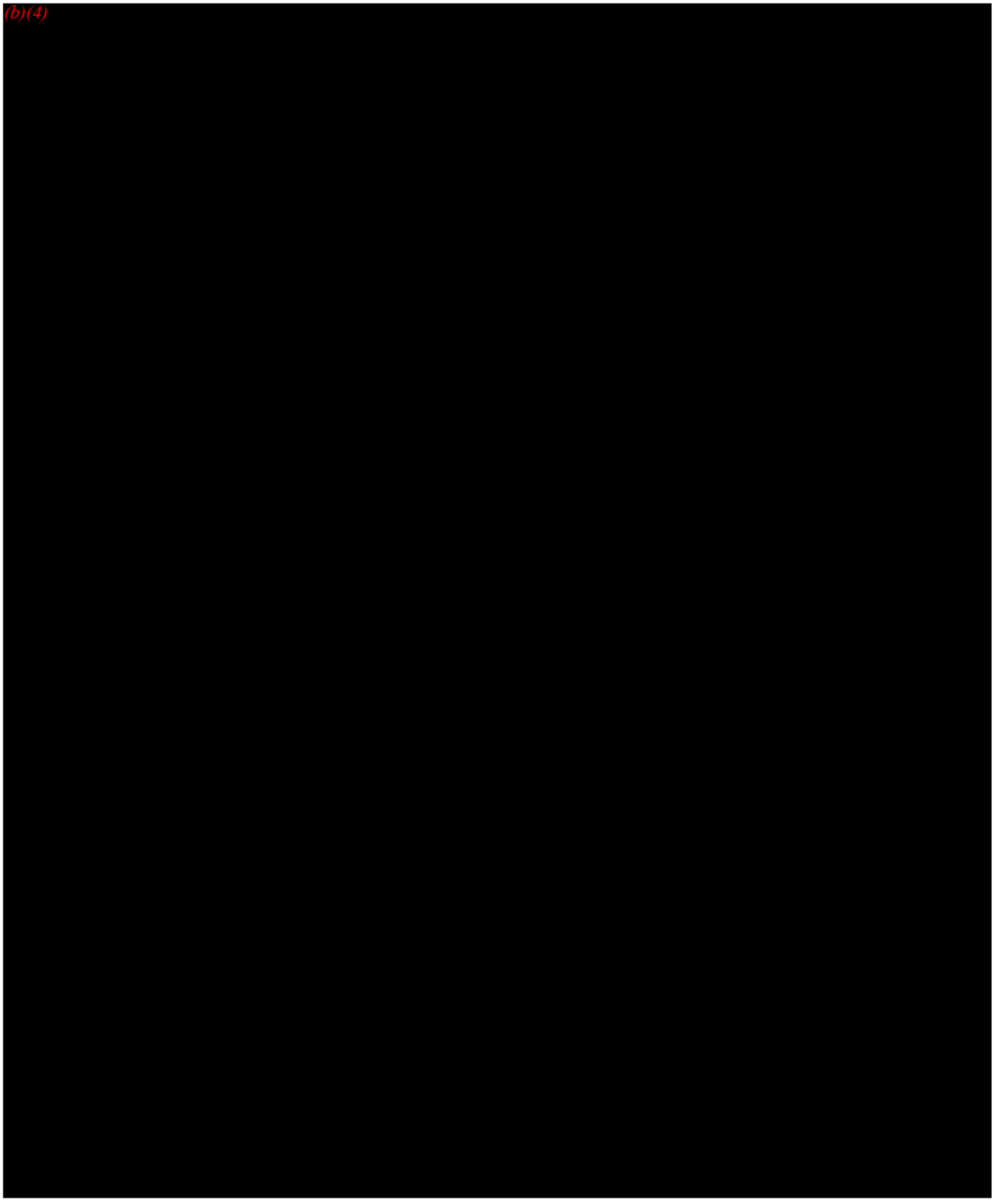

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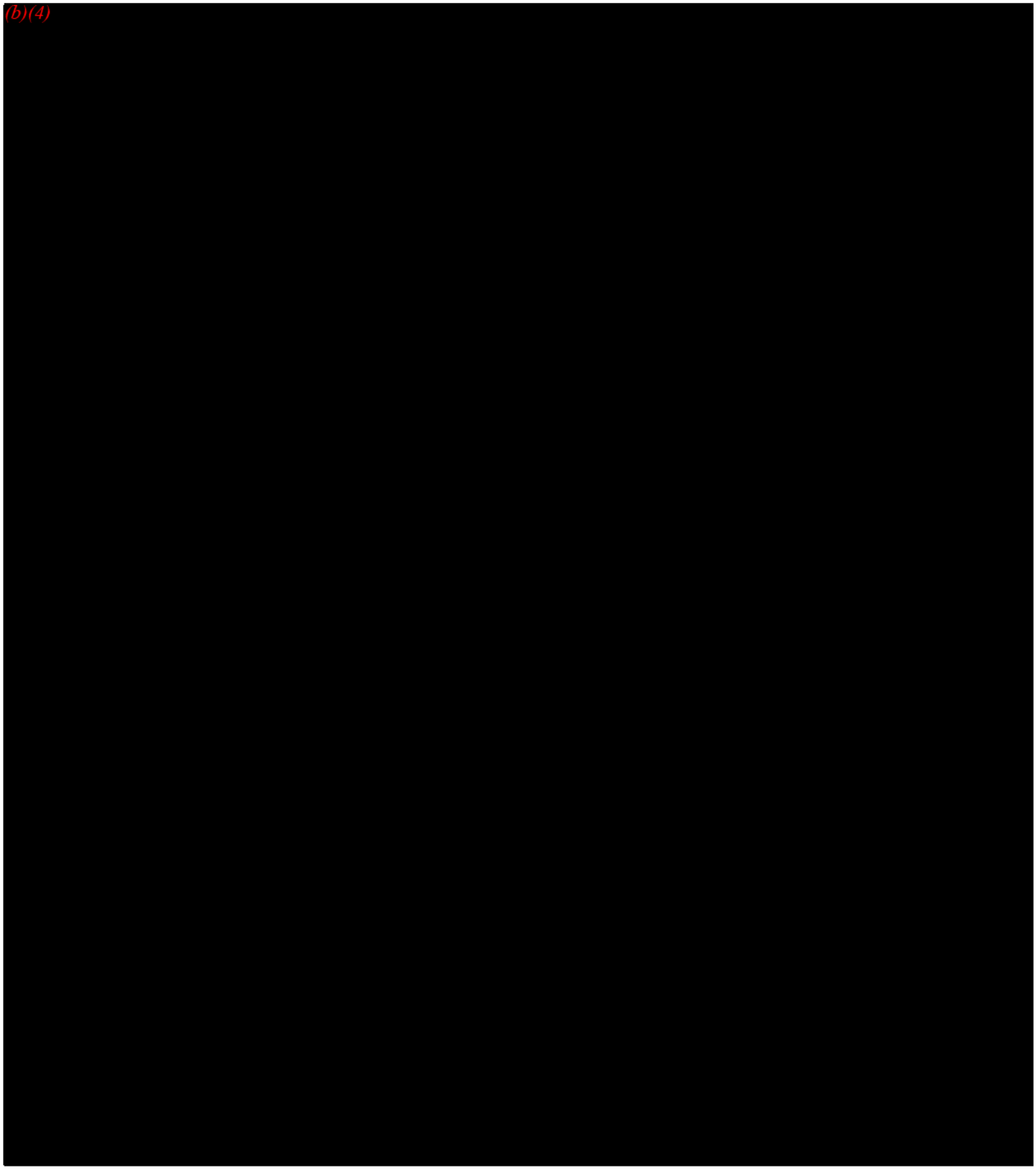

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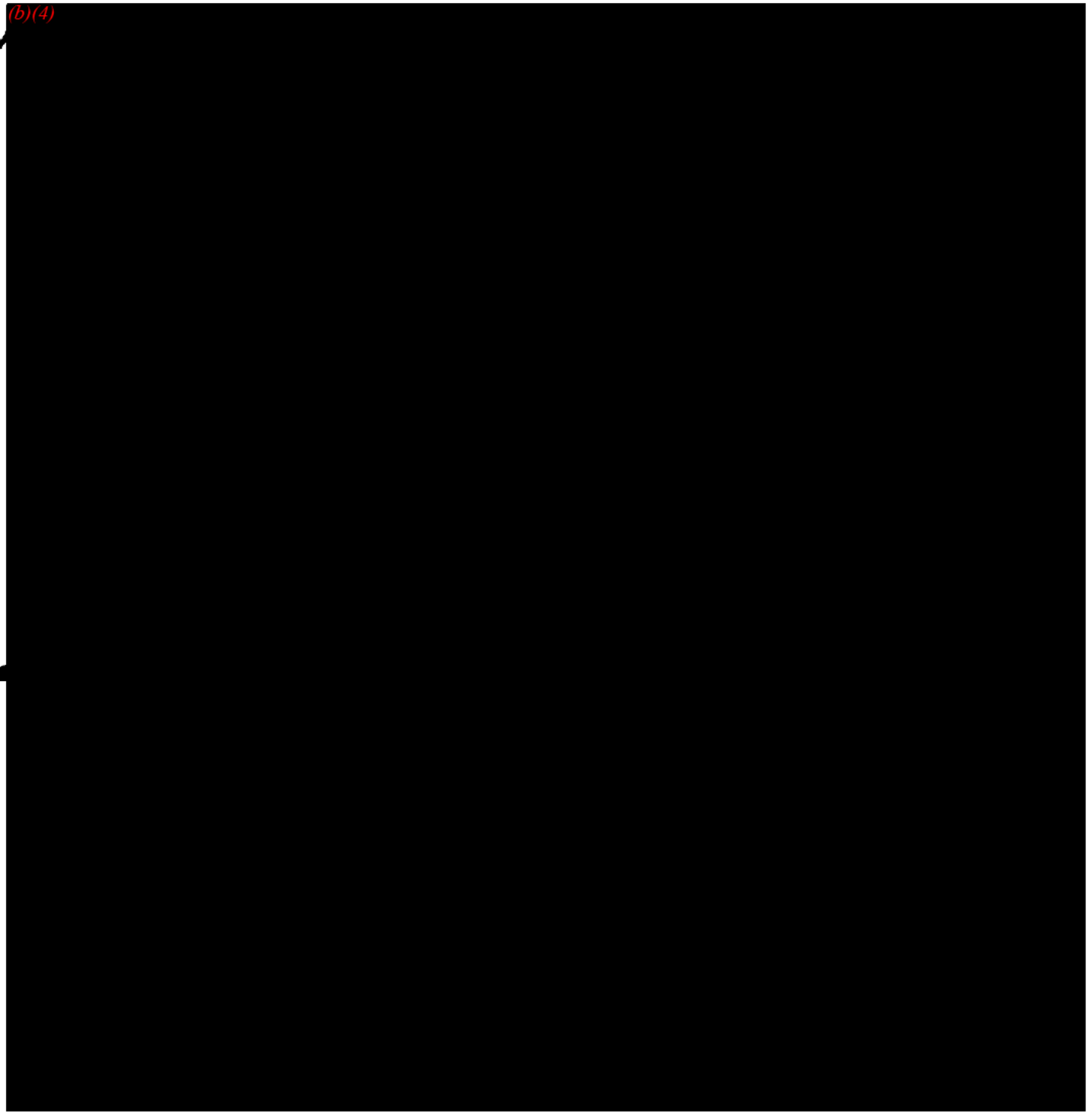

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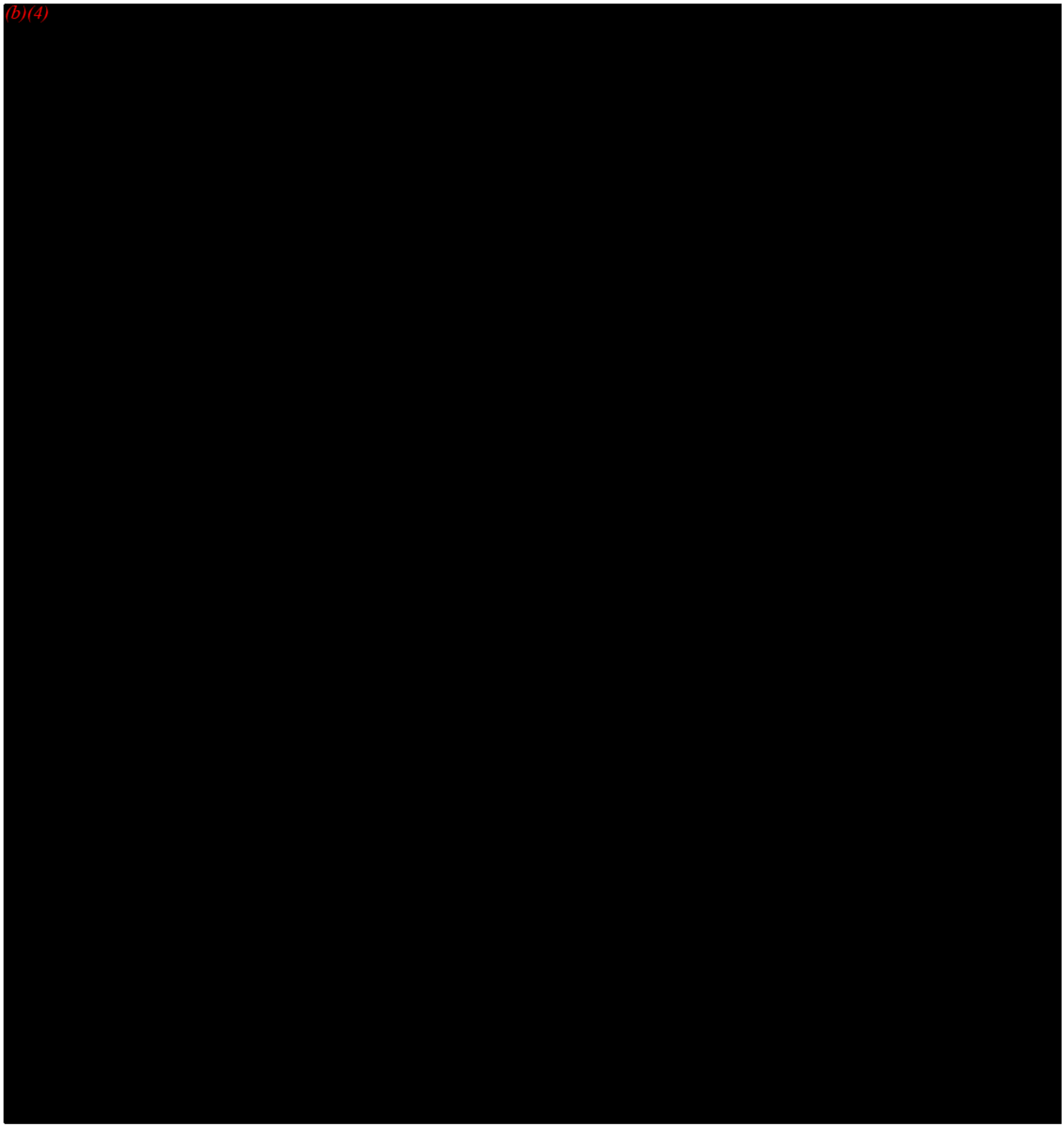

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6.0 Revision Record

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EPD98145
Software Test Plan For NICO - Model 7300

Author: (b) (6) [redacted]

Approvals:

(b) (6) [redacted]

Engineering:

Project Manager — Date 4-Mar-03

Director of Engineering — Date 10-MAR-03

Software Coordinator — Date 6 Mar 2003

Clinical Research Coordinator — Date 10-MAR-03

Quality Engineer — Date 5-Mar-03

Regulatory:

RA/QA — Date 3/11/03

Revision Record

Revision	Date	Prepared By
(b) (6), (b) (4) [redacted]		

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Appendix A – Test Case/Test Type

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Appendix B - Sample Test Case

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Appendix D - Sample Software Validation Summary

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PV 138-9569-07-11p1
Software Validation Summary for NICO Model 7300

(b)(4)

Author (b) (6)

Approvals:

(b) (6)

Engineering:

Project Manager — Date 10 Mar 03

Software Coordinator — Date 10 MAR 2003

Quality Engineering — Date 10-Mar-03

Software Engineering M — Date 10 MAR 2003

Director of Engineering — Date 10-MAR-03

Regulatory:

RA/QA — Date 3/11/03

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1.0 Introduction

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Appendix A - Matrix of Test Cases vs. Release Candidates

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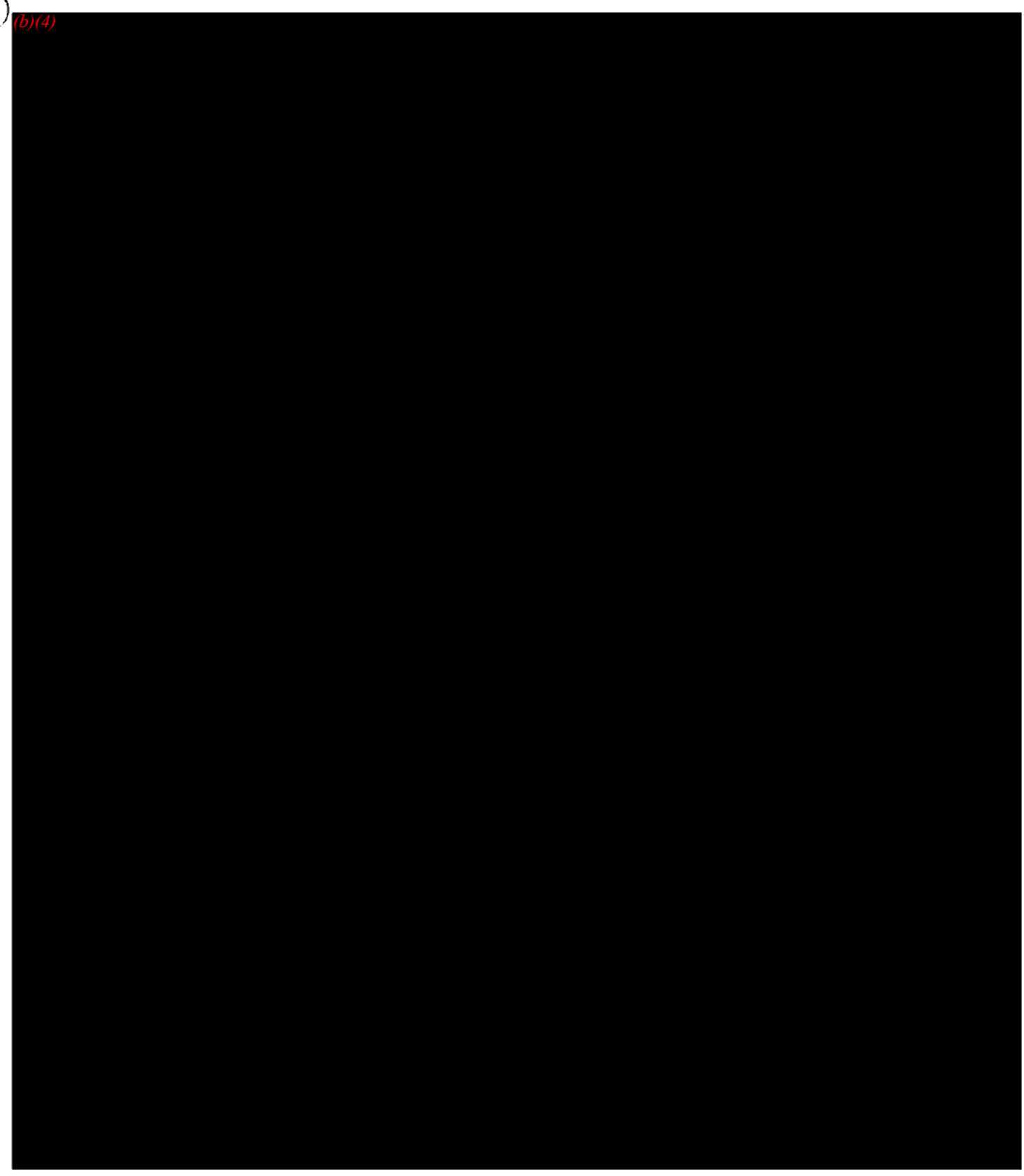

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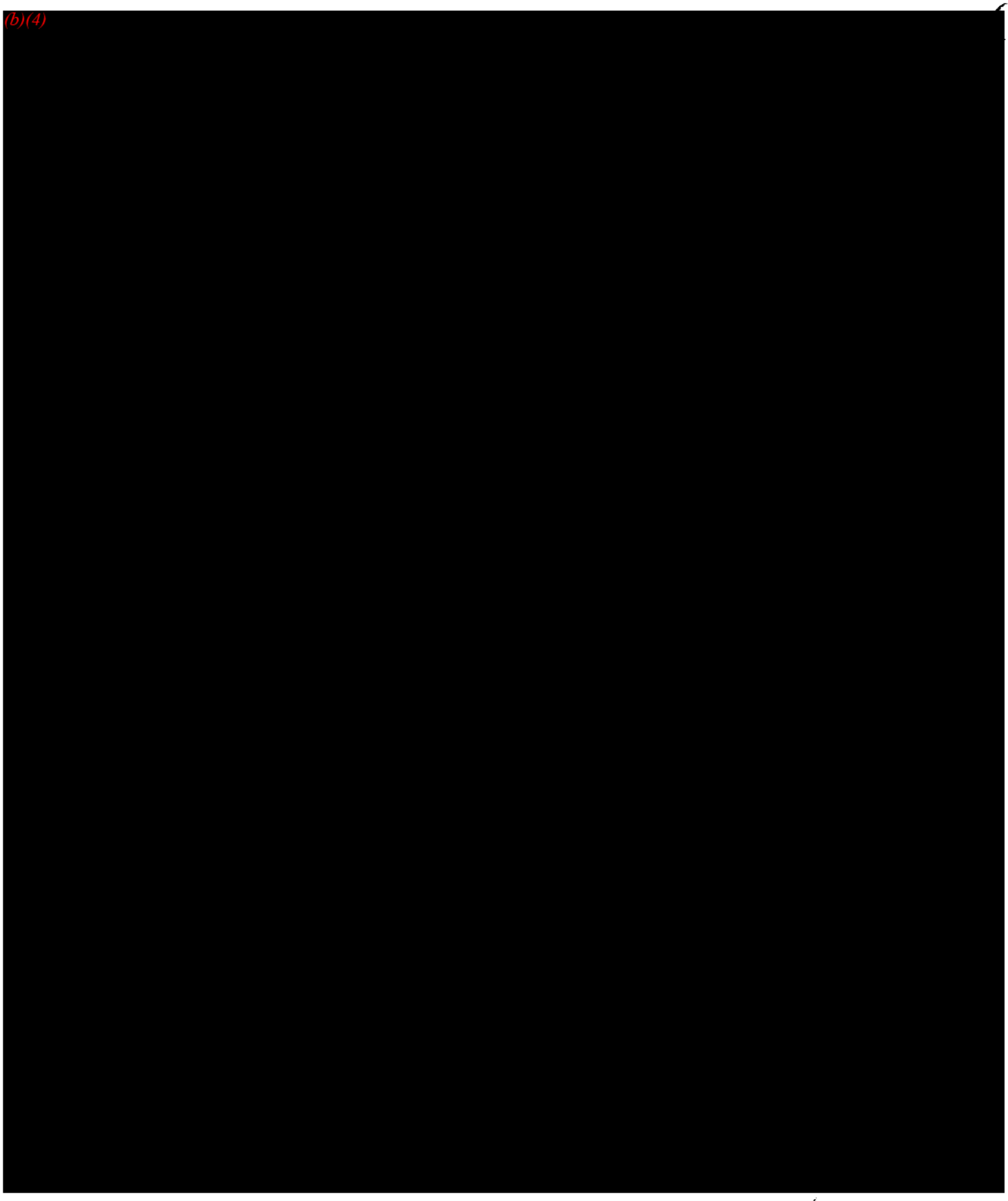

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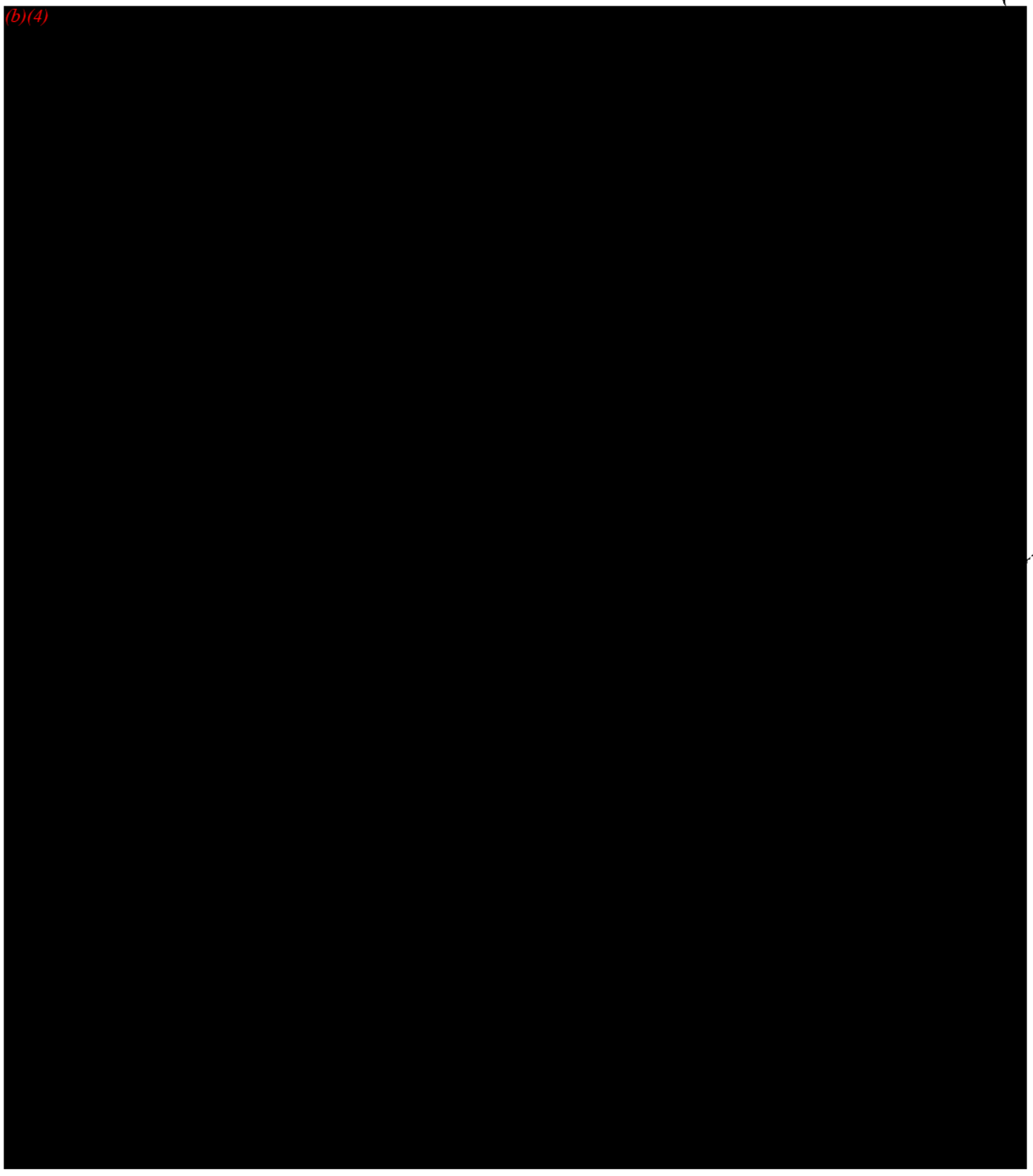

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Appendix C – Test Case vs. Software Revision Summary

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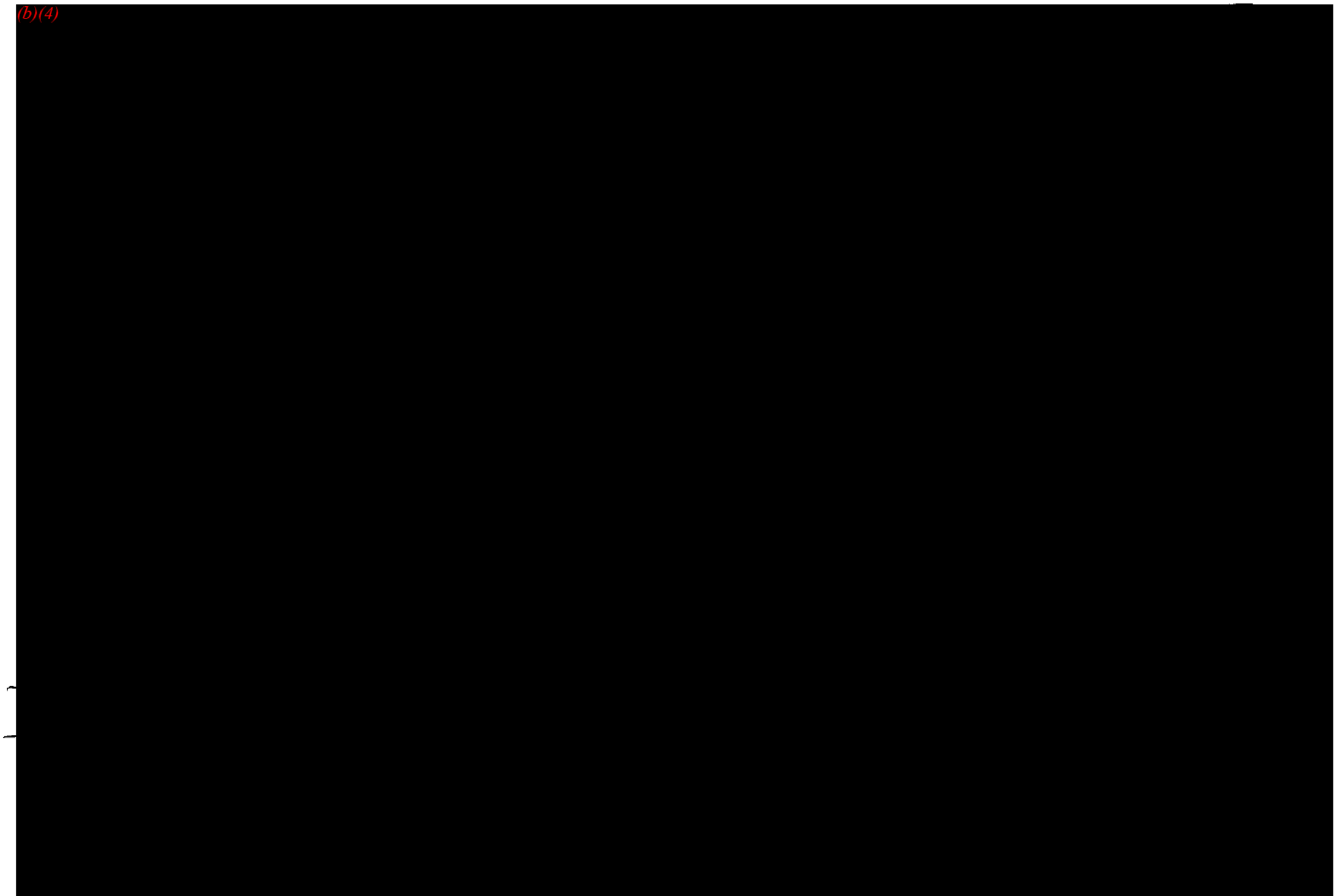

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Appendix D - Software/Product Change Requests

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F. Certification Statement

It is hereby certified that the aforementioned software development procedures were followed; that quality assurance procedures were adhered to; that the testing described demonstrates that the functional requirements were met and that system specifications were fulfilled.

EPW 3-19-03

Eric Wigforss
Project Manager

Supporting Medical Literature

The journal papers provided have evaluated the NICO monitor and found it generally to be clinically acceptable. These papers have been provided for review. Additionally, abstracts that referenced the NICO monitor are provided in a separate section.

NICO References

Journal Papers

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Intensive Care Med (2002) 28:1470–1474
DOI 10.1007/s00134-002-1477-1

ORIGINAL

Evaluation of a noninvasive method for cardiac output measurement in critical care patients

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Abstract *Objective:* Thermodilution (TD) is the gold standard to monitor cardiac output (CO) in critical care. However, there is concern about the safety of right-ventricular catheterization. The CO_2 rebreathing technique allows noninvasive CO determination by means of the indirect Fick principle. Our objectives were: (a) to assess the accuracy of a new system of CO measurement using the CO_2 partial rebreathing method (PRCO); (b) to evaluate whether the PRCO itself may induce changes in CO. *Design and setting:* Prospective study in the intensive care department in a university-affiliated hospital. *Patients:* Twenty-two mechanically ventilated critically ill patients. *Interventions:* CO measured simultaneously by PRCO and TDCO. *Measurements and results:* PRCO and TDCO values were compared by concordance analysis. Stability of cardiac output during PRCO was evaluated by comparing the TDCO measurements before, during, and after the partial rebreathing period using analysis of variance. From a total of 79 valid sets of measurements, bias and precision was calculated at –0.18±1.39 l/min. The concordance analysis of lower and intermediate CO values (<7 l/min) yielded a bias and precision calculation of –0.07±0.91 l/min. No changes in hemodynamics were observed during the partial rebreathing period. *Conclusions:* The noninvasive partial CO_2 rebreathing technique may be an alternative method for CO determination in mechanically ventilated critically ill patients. The rebreathing maneuver alone does not induce changes in CO.

Keywords Cardiac output · Carbon dioxide rebreathing · Thermodilution · Monitoring · Hemodynamics · Critical care

Introduction

Since the introduction of the balloon-directed thermistor-tipped pulmonary artery catheter in critical care medicine in the 1970s [1] thermodilution cardiac output measurements (TDCO) have been available at the bedside. Although some inaccuracies with the method have been reported, it has become the clinical "gold standard." Nevertheless, concern about catheter safety [2, 3] surfaced soon after catheterization of the pulmonary artery was introduced, and several physicians suggested a moratorium in catheter use [4, 5, 6]. However, as recent investigations have highlighted the importance of invasive goal-directed therapy in the earliest stages of severe sepsis and septic shock [7], research and clinical testing of fast, noninvasive methods to monitor hemodynamic status in critically ill patients are necessary.

Various approaches to noninvasive critical care monitoring have been suggested. Analyses of exhaled CO_2 and rebreathing techniques have been tested for CO determination in the critical care setting. Several authors [8, 9, 10, 11] have reported the accuracy of the rebreath-

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ing method for CO measurement in critically ill patients. Unfortunately, however, as this technique is technically difficult and time consuming, its routine use in the critical care arena is limited. To overcome the technical burden of this method the partial rebreathing technique for CO measurement (PRCO) has been commercially developed (NICO, Novametrix) [12]. This is an automated, noninvasive method that uses the indirect Fick principle. The monitor measures end-tidal PCO_2 ($P_{ET}CO_2$) and CO_2 production (VCO_2) in basal conditions during 50 s of partial rebreathing through an added instrumental dead space. By assuming stable hemodynamics, cardiac output is estimated from the changes induced in $P_{ET}CO_2$ and VCO_2.. Nevertheless, during the partial rebreathing period $PaCO_2$ increases in variable amounts (usually 4–5 mmHg) that could alter hemodynamics, mainly CO and systemic vascular resistance. Whether the increase in $PaCO_2$ can modify CO is not known.

We designed this study to answer two questions: first, how accurate are partial rebreathing CO measurements in critical care patients receiving mechanical ventilation, and, second, does the partial rebreathing technique alter cardiac output during the measurement period because of the increase in $PaCO_2$?

Material and methods

We studied 29 critically ill patients recovering from various clinical conditions and receiving mechanical ventilation in volume-controlled mode. The study was performed at the General Intensive Care Department of the Hospital of Sabadell. The protocol was approved by the ethics committee, and informed consent was obtained from the patients' relatives. Inclusion criteria were the need for mechanical ventilation because of acute lung injury, the presence of a thermistor-tipped pulmonary artery catheter (7.5 F catheter, Baxter., Irvine, Calif., USA) for clinical indication, and hemodynamic stability during the procedure. The partial rebreathing device of the monitor (NICO with software version 2.0, Novametrix, Wallingford, Conn., USA) was placed between the Y-piece of the ventilator and the endotracheal tube. After a minimum of 30 min to allow patient stabilization, arterial and mixed venous blood samples were collected to measure shunt fraction, and PRCO was determined with the monitor using the nonaveraged form. We performed TDCO measurements (Hewlett Packard, Palo Alto, Calif., USA) with 10 ml iced DW 5% bolus randomly distributed over the respiratory cycle by using a closed circuit (Co-Set, Baxter). Measurements were performed during the basal period of the NICO monitor (three boluses), during the partial rebreathing period (two boluses), and immediately thereafter (three boluses). With each set of TDCO measurements heart rate, $P_{ET}CO_2$, and mean systemic and pulmonary artery pressures were recorded (Hewlett Packard).

During the partial rebreathing period the increment in dead space increased $P_{ET}CO_2$, while VCO_2 determination showed an artifactual reduction. The monitor measures pulmonary nonshunted capillary blood flow by using a modified indirect Fick equation [12, 13]. By adding shunted blood flow (estimated by Nunn's iso-shunt curves) [14] the equipment calculates CO. Data from NICO were discarded when the monitor was unable to obtain either a stable CO_2 period or PRCO measurements.

We performed a maximum of four sets of measurements in each patient. Between measurements a minimum of 2 h was allowed. A total of 101 pairs of simultaneous measurements were performed. Twenty-two sets of measurements were discarded because the NICO monitor was unable to achieve a stable CO_2 reading. Seven patients were excluded from the study as we were unable to obtain PRCO measurements in these cases. No sets were discarded due to problems with TDCO measurements. We thus analyzed 79 sets of measurements in 22 patients (13 men, 9 women; median age 62 years, range 21–84). The median Acute Physiology and Chronic Health Evaluation II score was 17 (range 9–28).

Correlation between methods was assessed by linear regression analysis. Concordance between methods during the partial rebreathing period was determined by means of bias (mean difference between the two methods) and precision (SD of the mean difference between the two methods) [15]. The relationship between difference and mean CO measurement was assessed by the proportional difference in the CO estimation. Hemodynamic stability during the partial rebreathing period was evaluated by comparing TDCO and hemodynamic data recorded immediately before, during, and immediately after PRCO by using analysis of variance for repeated measurements. Significance was set at $p<0.05$.

Results

Cardiac output ranged from 1.4 to 12.7 l/min when measured with TDCO and from 1.4 to 13.4 l/min when measured with NICO. From a total of 79 sets of measurements we found a significant correlation between NICO and TDCO measurements ($R^2=0.71$, $p<0.001$; Fig. 1). The concordance analysis showed a bias and a precision calculation of –0.18±1.39 l/min and a 95% confidence interval (CI) of +2.59 to –2.95 l/min (Fig. 2A). The proportional difference in CO measurements between the methods was 46% and – 45%. To test the possible impact of a different number of measurements in each patient we repeated the agreement analysis with only the first set of measurements from each patient. We found very similar results, with a bias and precision calculation of 0.16±1.4 l/min and a 95% CI of +2.96 to –2.65 l/min.

Using a clinical decision-making approach, not all CO levels have the same meaning. Accordingly, we decided to analyze lower and intermediate CO, i.e., CO values below 7 l/min, separately. For these sets of measurements concordance analysis showed a bias and precision calculation of –0.07±0.91 l/min and 95% CI of +1.75 to –1.90 l/min (Fig. 2B).

The profile of hemodynamic measurements obtained before, during, and after the partial rebreathing maneuver is shown in Table 1. No changes in TDCO, heart

Table 1 Hemodynamic data during the PRCO measurement period before, during, and after rebreathing (*HR* Heart rate, *MAP* mean systemic arterial pressure, *MPP* mean pulmonary arterial pressure, *TDCO* thermodilution cardiac output)

	Before	During	After	*p*
HR (b/min)	90±18	91±18	91±19	0.993
MAP (mmHg)	81±11	81±12	82±15	0.839
MPP (mmHg)	28±6	29±6	29±6	0.692
TDCO (l/min)	5.9±2.3	6.1±2.4	6.2±2.4	0.740

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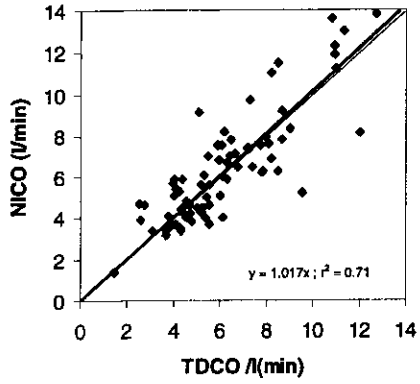

Fig. 1 Correlation plotting cardiac output determined by NICO vs. cardiac output determined by TDCO showing a significant correlation (R^2=0.71, n=79; p<0.001). *Solid line* Regression line; *dotted line* line of identity. *TDCO* Thermodilution cardiac output; *NICO* noninvasive cardiac output

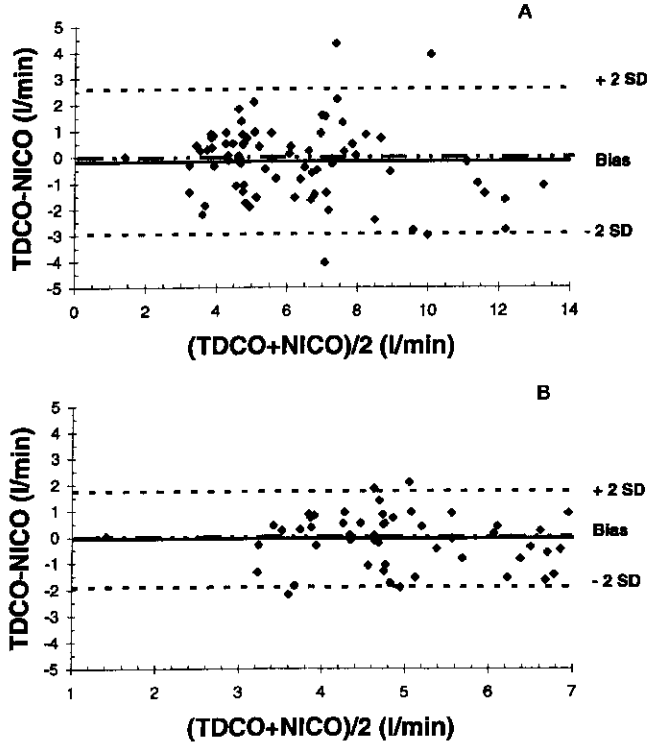

Fig. 2A, B Concordance analysis plots showing bias and agreement between TDCO and NICO. **A** Entire range of measurements. *Solid line* Bias (–0.18 l/min); *dotted lines* 95% confidence limits (±2 SD) for the bias. **B** Lower and intermediate CO values. *Solid line* Bias (–0.07 l/min); *dotted lines* 95% confidence limits (±2 SD) for the bias. *TDCO* Thermodilution cardiac output; *NICO* noninvasive cardiac output

rate, systemic, or pulmonary artery pressures were observed. $P_{ET}CO_2$ increased from 32±4.4 mmHg in the basal period to 38±4.8 mmHg (p<0.01) during the partial rebreathing period.

Discussion

The results of the present study show a good correlation between CO measurements with thermodilution and with the NICO apparatus. Nevertheless, the wide confidence intervals might reduce the possibility of direct substitution of TD for the new partial rebreathing method. An additional issue demonstrated in this study is that the NICO rebreathing maneuver did not induce any detectable changes in cardiac output.

The NICO monitor was first tested in animals [12, 16] and later in patients after cardiac surgery [17, 18]. Results are controversial but encouraging. In the critical care setting there are some limitations to the partial rebreathing technique to measure CO. First, in nonparalyzed patients the increase in instrumental dead space usually induces an increase in patient's respiratory rate to maintain $PaCO_2$, thereby reducing the magnitude of the signal, which limits the monitor's ability to detect changes in $P_{ET}CO_2$ and VCO_2. Second, noise is increased by respiratory pattern irregularities that produce unstable $P_{ET}CO_2$ and VCO_2. This reduction in signal-to-noise ratio could impair monitor accuracy. Third, additional CO not calculated with the Fick equation due to shunt fraction is estimated from pulse oxymetry and inspired oxygen content [12].

A strong limitation of research in this field is the lack of a true gold standard. Clinical use has confirmed TDCO at this site, but limitations of the method are well known [19, 20, 21, 22, 23, 24]. However, as a "clinical gold standard," TDCO offers physicians information for medical decision making. Any alternative method under evaluation must provide information similar to that obtained by means of the gold standard method. When there is a lack of agreement in this scenario, it is not always clear which method is correct and which is not. To minimize the likelihood of TDCO inaccuracies we used 10-ml boluses of iced DW 5% to increase signal magnitude and randomly distributed the bolus injection throughout the respiratory cycle to have a more representative value of the mean cardiac output [20, 25]. We used a closed circuit to minimize problems related to inhomogeneities in injectate temperature [26], and three TDCO boluses in each period were also averaged. A NICO measurement includes a 60-s basal time, a 50-s rebreathing time and a 70-s stabilization time. However, the 50-s rebreathing time was not long enough to perform three TDCO measurements, and consequently only two could be carried out. Therefore TDCO accuracy in this period may be diminished [27]. Moreover, elevation in minute ventilation induced by the increment of instrumental dead space during NICO measurement could have added thermal noise and further impaired TDCO reproducibility [28]. However, the fact that mean and standard deviation did not differ between measurements performed before, during, and after the partial rebreathing period

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markedly reduces the likelihood of substantial TDCO inaccuracies. The results of the present study showed a good correlation between CO measurements with thermodilution and with the NICO apparatus. As with other authors [18], we also found less agreement between NICO and TDCO at higher CO. This could be explained in three different ways. First, at a higher cardiac output, the area under the thermodilution curve is small and signal-to-noise ratio is impaired. This might occur even if measurements are not biased. Second, during PRCO monitoring a short sudden change in instrumental dead space is induced. For a given increase in instrumental dead space (as predicted by the indirect Fick equation), signal magnitude (end-tidal and arterial PCO_2 difference) decreases as CO increases [10], resulting in precision impairment. Third, under conditions of elevated cardiac output the venous-arterial PCO_2 difference narrows, increasing the experimental error of measurement. In fact, at higher CO states both methods could be less accurate and agreement between them would worsen.

Random error tends to cancel out when repeated measurements are performed, thus improving accuracy [29, 30]. However, when a measurement is averaged, the monitor's response time and its ability to detect a sudden change in the monitored variable worsens. A major advantage of continuous or near-continuous monitoring is that it instantly alerts physicians to changes in a patient's state. The sooner a change is detected, the earlier treatment can be modified. Accordingly, we decided to test the device in the nonaveraged mode because, although the accuracy of the method is not enhanced, response time is improved.

In critical care the PRCO technique for CO monitoring has three limitations uncommon in the anesthesia scenario. First, the technique involves a moderate increase in $PaCO_2$ during the rebreathing period that precludes its use in patients with intracranial hypertension. Second, the device requires stable CO_2 elimination for a reliable CO measurement, precluding its use in spontaneously breathing patients in whom tidal volume is variable. Our patients were not paralyzed and were breathing in assisted mandatory ventilation, and therefore minute ventilation could be changed when instrumental dead space increased during the partial rebreathing period. In this situation $P_{ET}CO_2$ becomes unstable and impairs signal-to-noise ratio. In our study 22 of 101 measurements were discarded because the NICO monitor could not obtain a stable CO_2 reading. Nonetheless, none of these patients showed any clinical or hemodynamic signs of intolerance to the rebreathing period. Third, the PRCO method measures only the nonshunted fraction of the cardiac output. Since shunt fraction, hemoglobin content, hemoglobin P50, arterial CO_2 partial pressure, and the difference between arterial and mixed venous O_2 contents might be altered in critically ill patients, miscalculations of estimated shunt fraction by the NICO device could also occur.

A compelling issue in monitoring is the avoidance of any modification in the monitored variable induced by the measuring technique itself. During PRCO measurements, for a given minute ventilation, $PaCO_2$ usually increases up to 6 mmHg while mixed venous PCO_2 basically remains unchanged. Hemodynamic changes related to acute changes in CO_2 levels are well documented [31]. Consequently, to test whether transient increases in $P_{ET}CO_2$ could induce a bias in the measurement we measured TDCO immediately before, during, and immediately after the partial rebreathing period. No changes were found in CO, heart rate, or systemic and pulmonary arterial pressures secondary to the slight and brief increase in $PaCO_2$. To our knowledge, this issue has not been addressed in previous studies.

In conclusion, the NICO monitor provides a near-continuous, automated, and totally noninvasive method for CO measurement in the critical care setting. NICO offers an alternative to invasive CO measurement that could be further improved with new software developments. Nevertheless, the lack of pulmonary vascular pressure determination precludes the replacement of the pulmonary artery catheter in a substantial proportion of critically ill patients.

Acknowledgement The authors thank Novametrix for their technical support.

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„Partielle CO_2-Rückatmungstechnik" versus Thermodilution

Bestimmung des Herzzeitvolumens vor und nach Eingriffen mit extrakorporaler Zirkulation

Zusammenfassung

Fragestellung. Basierend auf der „partiellen CO_2-Rückatmungstechnik" bestimmt der $NICO_2$-Monitor den „pulmonal-kapillären Blutfluss" (Qpc) und das Herzzeitvolumen (Qt). Die Übereinstimmung dieser Technik mit der Thermodilutionsmethode (TD) und die Möglichkeit einer intrapulmonalen Shuntabschätzung (Qs/Qt=1–Qpc/Qt) sollten im Verlauf von herzchirurgischen Eingriffen mit extrakorporaler Zirkulation (EKZ) überprüft werden.
Methodik. Bei 32 Patienten erfolgten vor dem Hautschnitt („prä-EKZ"), 30 min nach Beendigung der EKZ („post-EKZ") und 6–8 h nach Ankunft auf der Intensivstation („post-OP") simultane Messungen von Qt ($NICO_2$-Monitor und TD), Qpc ($NICO_2$-Monitor) sowie des O_2-Shunts (nach der Berggren-Formel). Nach der Formel $Qs/Qt=1-Qpc(NICO_2)/Qt(TD)$ wurde ein intrapulmonaler Shunt berechnet. Die Daten wurden nach den Empfehlungen von Bland u. Altman sowie mit der Regressionsanalyse ausgewertet.
Ergebnisse. „Prä-EKZ" fand sich für Qt eine gute Übereinstimmung zwischen $NICO_2$-Monitor und TD („bias ± precision": −0,13±0,46 l/min; r=0,88±0,47; p<0,001). „Post-EKZ" sowie „post-OP" war das Maß der Übereinstimmung jedoch gering („bias ± precision": 0,97±1,05 l/min bzw. −0,33±0,8 l/min). Zwischen den berechneten Shuntwerten ergab sich zu keinem Zeitpunkt eine signifikante Korrelation.
Schlussfolgerung. Unter „Ruhebedingungen" liefert der $NICO_2$-Monitor zur Herzzeitvolumenbestimmung vergleichbar gute Werte. Nach EKZ ist die Übereinstimmung mit der TD jedoch zu gering. Eine zuverlässige intrapulmonale Shuntbestimmung ist durch das Verfahren nicht möglich.

Schlüsselwörter

Herzzeitvolumen · Thermodilutionsmethode · Partielle CO_2-Rückatmungstechnik · Extrakorporale Zirkulation · Shunt

„Kohlendioxidrückatmungstechniken" zur nichtinvasiven Bestimmung des pulmonalen Blutflusses erleben seit einigen Jahren eine Renaissance. Sie basieren auf dem Fick-Prinzip angewandt auf Kohlendioxid (CO_2). Kohlendioxid hat den Vorteil, dass es im Gegensatz zu Sauerstoff einfacher und mit höherer Genauigkeit in der Ausatemluft gemessen werden kann. Mit dem $NICO_2$-Monitor (Novametrix Medical Systems Inc., Wallingford, USA) steht nun kommerziell ein Gerät zur Verfügung, das über die „partielle CO_2-Rückatmungstechnik" den „pulmonal-kapillären Blutfluss" (Qpc) und daraus das Herzzeitvolumen (Qt) bestimmt.

Die „partielle CO_2-Rückatmungstechnik" wurde erstmals 1980 von Godeon et al. als differenzielle Form der „klassischen CO_2-Rückatmungstechniken" beschrieben [10]. Hierbei kann auf die umständliche Ermittlung des gemischt-venösen CO_2-Partialdrucks ($PvCO_2$) verzichtet werden. Stattdessen werden während einer kurzen Rückatemphase die Veränderungen der CO_2-Abgabe (VCO_2) sowie des endtidalen CO_2-Partialdruckes ($PetCO_2$) gemessen, und hierüber Qpc berechnet. Da alveoläre Einheiten mit sehr kleinem Ventilations-Perfusions-Verhältnis ($0>V/Q<0.1$) oder echtem Shunt ($V/Q=0$) kaum bzw. gar nicht zur Elimination von CO_2 beitragen [8], wird über die „partielle CO_2-Rückatmungstechnik" lediglich derjenige Blutstrom in der Lunge bestimmt, der effektiv am Gasaustausch teilnimmt (Qpc). Die intrapulmonale Shuntfraktion (Qs/Qt) bleibt somit unbekannt. Daher wird zur Bestimmung des Herzzeitvolumens Qs/Qt vom $NICO_2$-Monitor geschätzt und zu Qpc addiert [17].

Zur Zeit liegen noch wenige Studien zum $NICO_2$-Monitor vor. Die Übereinstimmung des durch den $NICO_2$-Monitor ermittelten Qt mit der Thermodilutionsmethode (TD) wurde in einigen Studien als gut [1, 11, 18], in anderen als unzureichend eingestuft [15, 23]. Besonders nach Eingriffen mit extrakorporaler Zirkulation kommt es zu ausgeprä-

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Partial CO_2 rebreathing technique versus thermodilution: measurement of cardiac output before and after operations with extracorporeal circulation

Summary

Background. The $NICO_2$ monitor determines "pulmonary capillary blood flow" (Qpc) and cardiac output (Qt) using the "partial CO_2 rebreathing technique". The agreement between $NICO_2$ and thermodilution (TD) cardiac output was compared before and after cardiac surgery with cardiopulmonary bypass (CBP). In addition, the possibility of calculating the intrapulmonary shunt fraction (Qs/Qt) by combining data from the $NICO_2$ monitor and the TD was investigated.

Methods. In 32 patients measurements were made following induction of anesthesia ("pre-CBP"), 30 min after weaning from CBP ("post-CBP"), and 6–8 h after surgery ("post-OP"). Qt was determined by the $NICO_2$ monitor and TD, Qpc by the $NICO_2$ monitor, and Qs/Qt(O_2) from the standard formula. An intrapulmonary shunt was calculated using Qpc($NICO_2$) and Qt(TD) according to the equation Qs/Qt=1–Qpc/Qt. Bland-Altman and regression analysis techniques were used for statistical evaluation.

Results. "Pre-CBP" there was a good agreement between Qt($NICO_2$) and Qt(TD) with both a bias and precision of -0.13 ± 0.46 l/min and a correlation of $r=0.88\pm0.47$ ($p<0.001$). In contrast, "post-CBP" and "post-OP" there was a lack of agreement for Qt (bias and precision: 0.97 ± 1.05 l/min and -0.33 ± 0.8 l/min, respectively). Regarding the shunt calculations no significant correlations between methods could be found.

Conclusion. Cardiac output measurement by the $NICO_2$ monitor agree well with TD under steady-state conditions but after CBP the agreement was too small. Combining Qpc($NICO_2$) and Qt(TD) does not offer a reliable possibilty for calculating intrapulmonary shunt.

Keywords

Cardiac output · Thermodilution technique · Partial CO_2 rebreathing technique · Shunt · Cardiopulmonary bypass

Originalien

ten und kurzfristigen Veränderungen (Volumenverschiebungen, Schwankungen der Temperatur und Hämoglobinkonzentration etc.), die Einfluss auf die Genauigkeit der „partiellen CO_2-Rückatmungstechnik" haben können. Messungen in den ersten Minuten nach EKZ sind daher problematisch. Eine Verlaufsbeobachtung gibt es bisher nicht. In dieser Studie sollten $NICO_2$-Monitor und TD vor EKZ, 30 min nach EKZ und 6–8 h nach dem Eingriff hinsichtlich Qt verglichen werden. Zudem sollte überprüft werden, ob eine Shuntbestimmung durch Kombination von Qpc ($NICO_2$-Monitor) und Qt (TD) nach der Formel: Qs/Qt=1–Qpc/Qt möglich ist.

Methodik

Nach Zustimmung der Ethikkommission und schriftlicher Einverständniserklärung nahmen 32 Patienten, die sich einem Eingriff mit EKZ unterziehen mussten, an der Untersuchung teil. Patienten mit bekannten Lungenerkrankungen, pulmonalem Hypertonus oder Trikuspidalinsuffizienz waren von der Untersuchung ausgeschlossen. Die intravenöse Narkoseeinleitung erfolgte standardisiert mit Sufentanil (0,2–0,3 $\mu g \times kg^{-1}$ KG), Midazolam (0,05–0,1 $mg \times kg^{-1}$ KG) und Pancuroniumbromid (0,1 $mg \times kg^{-1}$ KG). Die Patienten wurden orotracheal intubiert und volumenkontrolliert beatmet (Servo 900C, Siemens, Erlangen, Deutschland), sodass der $PaCO_2$ im Bereich von 34–44 mmHg lag. Zur Aufrechterhaltung der Narkose wurden in Abständen von je 30 min 25 µg Sufentanil und alle 45 min 5 mg Midazolam verabreicht. Weitere Dosen an Pancuroniumbromid, Sufentanil und Midazolam folgten nach Bedarf. Das invasive hämodynamische Monitoring erfolgte anhand einer Kanüle in der A. radialis zur Blutdruckmessung und über einen Pulmonalarterienkatheter (PA-VIP-Katheter, Edwards Lifescience, Irvine, USA).

Die EKZ wurde in moderater Hypothermie (rektale Temperatur=33°C) mit non-pulsatilem Fluss (2,4 l/min/m^2) und monoartrialer Kanüle durchgeführt; der systemische Blutdruck lag bei 40–80 mmHg. Der Gasaustausch erfolgte über einen Membranoxygenator (Sorin 41, Sorin, Torino, Italia). Das pH-Management folgte der alpha-stat-Methode. Die Herz-Lungen-Maschine (HLM) wurde mit 2000 ml Ringer-Lösung und 250 ml 5%iger Albuminlösung gefüllt. Zur Kardioplegie wurde Bretschneider-Lösung verwendet. Vor dem Entwöhnen von der EKZ wurden die Patienten mit dem integrierten Wärmeaustauscher des Oxygenators und mit einer Wärmematte bis zu einer rektalen Temperatur von 37°C aufgewärmt.

Die Messungen erfolgten bei einer inspiratorischen Sauerstoffkonzentration (FiO_2) von 1,0 an den folgenden Messzeitpunkten:

1) prä-EKZ (nach Narkoseeinleitung, vor dem Hautschnitt),
2) post-EKZ (30 min nach Entwöhnung von der HLM),
3) post-OP (6–8 h nach dem Eingriff auf der Intensivstation).

Vor jeder Messung wurden arterielle und gemischt-venöse Blutproben entnommen. Die arterielle Blutgasanalyse wurde in den Computer des $NICO_2$-Monitor eingegeben und das Rückatemmanöver gestartet. Es wurden 2 Rückatemmanöver (Dauer 6 min) durchgeführt und die Ergebnisse gemittelt. Gleichzeitig wurde das Qt mit der TD bestimmt.

Der $NICO_2$-Monitor ermittelt Qpc nichtinvasiv über die „partielle CO_2-Rückatmungstechnik" (Softwareversion 3.0). Eine Messung dauert 180 s (60 s Nichtrückatemphase (NR), 50 s Rückatemphase (R) und 70 s Stabilisierungsphase ohne Rückatmung). Die Rückatmung wird über die „Zuschaltung" eines seriellen Totraums erreicht. Hierzu dient ein Faltenschlauch (Rückatemschleife), der zwischen 120 und 250 ml vergrößert bzw. verkleinert werden kann, je nach Ausmaß der erforderlichen Rückatmung (Atemzugvolumen adaptiert). Die Umschaltung erfolgt über ein computergesteuertes Ventil. Während der Rückatmung kommt es zum Abfall des VCO_2 und zum Anstieg des $PetCO_2$. Unter der Annahme, dass Blutfluss (Q) und gemischt-venöser CO_2-Gehalt ($CvCO_2$) während der Messphase konstant sind, kann Qpc aus den Veränderungen von VCO_2 und des arteriellen CO_2-Gehalts ($CaCO_2$) berechnet werden (s. Anhang). Zur Bestimmung von Qt erfolgt zusätzlich eine Korrektur für den intrapulmonalen Shunt.

Nach Kalibration bei Raumluft und Null-Fluss wurden das exspiratorische CO_2 über einen Hauptstromkapnometer (Infrarotlicht, Ansprechzeit <60 ms, Ge-

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Tabelle 1
Hämodynamische und respiratorische Parameter sowie Blutgasanalysen

Parameter		„prä-EKZ"	„post-EKZ"	„post-OP"
HF	[/min]	59,9±11,47	89,9±14,96	97,3±14,27
MAP	[mmHg]	76,7±10,41	73,8±8,47	82,3±10,62
MPAP	[mmHg]	18,0±4,76	20,7±4,84	24,2±5,92
ZVD	[mmHg]	7,6±3,27	10±3,17	10,3±3,49
PCWP	[mmHg]	10,5±3,86	13,1±3,95	13,7±3,84
$VCO_{2(NR)}$	[ml/min]	162±31,88	161,3±36,42	220,2±46,62
$PetCO_{2(NR)}$	[mmHg]	35,8±4,32	34,2±3,88	38,5±5,67
AMV	[l/min]	7,7±1,01	8,5±1,00	8,7±1,29
AF	[/min]	12,2±1,19	12,6±1,49	12±1,43
PEEP	[mmHg]	4,7±1,16	6,5±1,31	6,25±1,19
pH		7,40±0,04	7,37±0,04	7,37±0,04
PaO_2	[mmHg]	457±90,83	285,9±106,56	330,6±97,41
$PaCO_2$	[mmHg]	40,8±4,81	40±5,61	41,9±6,03
SaO_2	[%]	99,93±0,07	99,64±0,6	99,96±0,07
PvO_2	[mmHg]	47,1±4,98	41,8±7,33	43,3±5,22
$PvCO_2$	[mmHg]	47,2±4,37	49,4±5,57	47,7±6,33
SvO_2	[%]	80,37±4,86	72,42±7,94	73,86±7,26
Hb	[g/dl]	12,3±1,20	8,4±0,86	10,3±1,21

Dargestellt sind die Mittelwerte (± Standardabweichung) der gemessenen Parameter zu den verschiedenen Messzeitpunkten. Wiedergegeben sind Herzfrequenz (HF), mittlerer arterieller Druck (MAP), mittlerer pulmonalarterieller Druck (MPAP), zentralvenöser Druck (ZVD), pulmonalkapillärer Verschlussdruck (PCWP), CO_2-Abgabe in der Nicht-Rückatemphase ($VCO_{2(NR)}$), endtidaler Kohlendioxidpartialdruck in der Nichtrückatemphase ($PetCO_{2(NR)}$), Atemminutenvolumen (AMV), Atemfrequenz (AF), positiver endexspiratorischer Druck (PEEP), pH-Wert, arterieller und gemischt-venöser Sauerstoff- bzw. Kohlendioxidpartialdruck (PaO_2 und $PaCO_2$ bzw. PvO_2 und $PvCO_2$), arterielle und gemischt-venöse Sättigung (SaO_2 und SvO_2) sowie Hämoglobinkonzentration (Hb).

nauigkeit ±2 mmHg) und der Gasfluss über einen Differenz-Druck-Pneumotachometer (Genauigkeit ±3%) gemessen. Der Hauptstromkapnometer, der Pneumotachometer und die Rückatemschleife wurden zwischen Endotrachealtubus und dem Y-Stück des Beatmungsschlauches angebracht. Die Veränderung der CO_2-Abgabe wird aus dem gemessenen exspiratorischen Atemminutenvolumen und dem CO_2-Gehalt der Ausatemluft berechnet; $CaCO_2$ wird über $PetCO_2$ mittels einer Anpassung an die CO_2-Dissoziationskurve (Standardformel) geschätzt, wobei $PetCO_2$ als nichtinvasive Näherung des $PaCO_2$ dient. Um eine bessere Übereinstimmung von $PetCO_2$ und $PaCO_2$ zu erzielen, werden vom Computer Korrekturen für die Totraumventilation und die pulmonale Perfusionsverteilung vorgenommen. Vor jeder Messung müssen Größe und Gewicht des Patienten, inspiratorische Sauerstoffkonzentration und Gaszusammensetzung (N_2O oder N_2) sowie (wenn möglich) aktueller PaO_2, $PaCO_2$ und Hämoglobinwert (Hb) in den Computer des $NICO_2$-Monitor eingegeben werden. Der intrapulmonale Shunt wird anhand von Iso-Shunt-Kurven (s. Anhang) über die aktuelle periphere Sauerstoffsättigung (SpO_2) und die FiO_2 geschätzt. Durch Eingabe des aktuellen PaO_2 in den Computer erhöht sich die Genauigkeit des geschätzten Shunts. Das integrierte Pulsoxymeter hat eine Genauigkeit von ±3%. Angezeigt wird vom $NICO_2$-Monitor das ermittelte VCO_2 (NR), $PetCO_2$ (NR), Qpc und das berechnete Qt.

Zur Bestimmung des Qt über die TD wurden 10-ml-Boli 4°C-kalter isotoner NaCl-Lösung injiziert. Es erfolgten 3–5 Einzelmessungen über den gesamten Atemzyklus, je 3 Werte wurden gemittelt. Die Berechnung der Temperaturdilutionskurve erfolgte automatisch anhand der modifizierten Steward-Hamilton-Gleichung mit dem integrierten Computer des Siemens-Monitors (Sirecust 1281, Siemens, Erlangen, Deutschland).

Wie beschrieben, schätzt der $NICO_2$-Monitor den intrapulmonalen Shunt anhand von SpO_2, FiO_2 und PaO_2. Da die Pulsoxymetrie während Operationen durch z. B. kalte Extremitäten oder Zentralisation in ihrer Messfähigkeit beeinträchtigt sein kann, sollte überprüft werden, ob durch Kombination von Qpc ($NICO_2$-Monitors) und Qt (Thermodilutionsmethode) eine Shuntbestimmung möglich ist. Dazu wurden Qpc($NICO_2$) und Qt(TD) in die Formel: $Qs/Qt=1 - Qpc/Qt$ eingesetzt und die so ermittelte Shuntfraktion ($Qs/Qt(NICO_2)$) mit der Shuntfraktion für O_2 ($Qs/Qt(O_2)$) verglichen; $Qs/Qt(O_2)$ wurde über eine arterielle und eine gemischtvenöse Blutgasanalyse (Statprofile Nova 9, Nova Biomedical GmbH, Rödermark, Deutschland) nach der Berggren-Formel (s. Anhang) berechnet.

Die Übereinstimmung der Methoden wurde statistisch nach den Empfehlungen von Bland u. Altman geprüft [3]. Angegeben wurden dabei der Mittelwert der Differenzen aus beiden Methoden („bias") sowie die Standardabweichung der Differenzen („precision"). Zuvor wurden die Ergebnisse der Methoden nach Bland u. Altman auf Wiederholbarkeit geprüft [3]. Das Maß der Korrelation zwischen den Methoden wurde mit der Regressionsanalyse berechnet. Die Mittelwerte von $Qt(NICO_2)$ und Qt(TD) wurden mit einem ungepaarten Student-*t*-Test verglichen. Ein $p<0,05$ wurde als signifikant angenommen.

Nach Critchley u. Critchley wurden die Grenzen der Genauigkeit (maximaler tolerabler prozentualer Fehler bzw. „percentage error") des Methodenvergleichs geschätzt [6]. Der maximal tolerable prozentuale Fehler berechnet sich aus der Summe der Varianzen der einzelnen Methoden. Ein Fehler von <20% gilt in der Praxis als zulässige Messungenauigkeit. Bei einem Vergleich zweier Methoden mit einem Fehler von je ±20% ergibt sich daher ein maximal tolerabler prozentualer Fehler von ±28,28% $((0,2^2+0,2^2)^{1/2})$. Er wird auf den Mittelwert des Methodenvergleichs bezogen. Sind die Grenzen der Übereinstimmung (2-mal die Standardabweichung der Differenzen) geringer als die Grenzen der Genauigkeit (±28,28% vom jeweiligen Mittelwert eines Methodenvergleichs), so sind die Methoden durch einander ersetzbar (d. h. vergleichbar gut bzw. vergleichbar schlecht).

Ergebnisse

Insgesamt wurden bei 32 Patienten (8 Frauen und 24 Männer) 96 Messpaare

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Tabelle 2
Herzzeitvolumina (Qt), „pulmonal kapillärer Blutfluss" (Qpc) und Shuntfraktionen (Qs/Qt)

Parameter	Qt(TD) [l/min]	Qt($NICO_2$) [l/min]	Qpc($NICO_2$) [l/min]	Qs/Qt(O_2) [%]	Qs/Qt($NICO_2$) [%]
„prä-EKZ"	3,8±0,88	3,9±0,97	3,4±0,76	16,7±5,0	7,0±11,55
„post-EKZ"	5,1±1,03	4,1±0,99*	3,7±0,83	25,4±6,32	26,9±16,02
„post-OP"	5,5±1,19	5,9±1,42	5,5±1,24	20,5±5,24	3,2±16,53

*Dargestellt sind die Mittelwerte (± Standardabweichung) der gemessenen Parameter zu den verschiedenen Messzeitpunkten. Gegenübergestellt sind die Herzzeitvolumina gemessen durch die Thermodilutionsmethode (Qt(TD)) und den $NICO_2$-Monitor (Qt($NICO_2$)). Signifikant unterschiedliche Ergebnisse ($p < 0,05$) sind durch einen * gekennzeichnet. Der mit dem $NICO_2$-Monitor bestimmte „pulmonal kapillären Blutfluss" Qpc($NICO_2$) ist wiedergegeben. Die durch Kombination von Qt(TD) und Qpc($NICO_2$) berechnete Shuntfraktion (Qs/Qt($NICO_2$)) ist der Shuntfraktion nach der Berggren-Formel Qs/Qt(O_2) gegenübergestellt.*

für Qt(TD) und Qt($NICO_2$) untersucht. Alle Patienten mussten sich einer koronaren Bypassoperation mit EKZ unterziehen. Das Alter der Patienten lag zwischen 46 und 86 Jahren (Median 74 Jahre), das Gewicht zwischen 55–116 kg (Median 80,5 kg) und die Größe zwischen 154–191 cm (Median 172,5 cm). Bei keinem der Patienten war nach EKZ eine Kreislaufunterstützung mit Katecholaminen oder mit der intraortalen Ballonpumpe (IABP) nötig. Der Verlauf der hämodynamischen und respiratorischen Parameter sowie von pH- und Hämoglobinwert sind in Tabelle 1 wiedergegeben. Die rektale Temperatur lag z. Z. der Messung: „prä-EKZ" bei 36,4±0,9°C, „post-EKZ" bei 37,1±0,7°C und „post-OP" bei 36,2±1,1°C. Die Dauer der EKZ lag zwischen 41 und 112 min (Median: 84 min).

Herzzeitvolumina vor extrakorporaler Zirkulation („prä-EKZ")

Mittelwerte (± Standardabweichung) sind in Tabelle 2 wiedergeben; sie waren nicht signifikant unterschiedlich. Die Wiederholbarkeit der TD lag bei −0,06±0,18 l/min (Koeffizient der Wiederholbarkeit: 0,36 l/min) und für den $NICO_2$-Monitor bei −0,04±0,28 l/min (Koeffizient der Wiederholbarkeit: 0,56 l/min).

In der Bland-Altman-Darstellung (Abb. 1a) ergab sich ein „bias" von −0,13 l/min, mit einer „precision" von ±0,46 l/min. Die Grenzen der Übereinstimmung lagen bei ±0,92 l/min (von −1,05–0,79 l/min). Der maximal tolerable prozentuale Fehler wurde mit ±1,08 l/min (±28.28% von 3,85 l/min) angenommen. Da die Grenzen der Übereinstimmung geringer waren als die Grenzen der Genauigkeit, waren die Methoden als vergleichbar einzuschätzen.

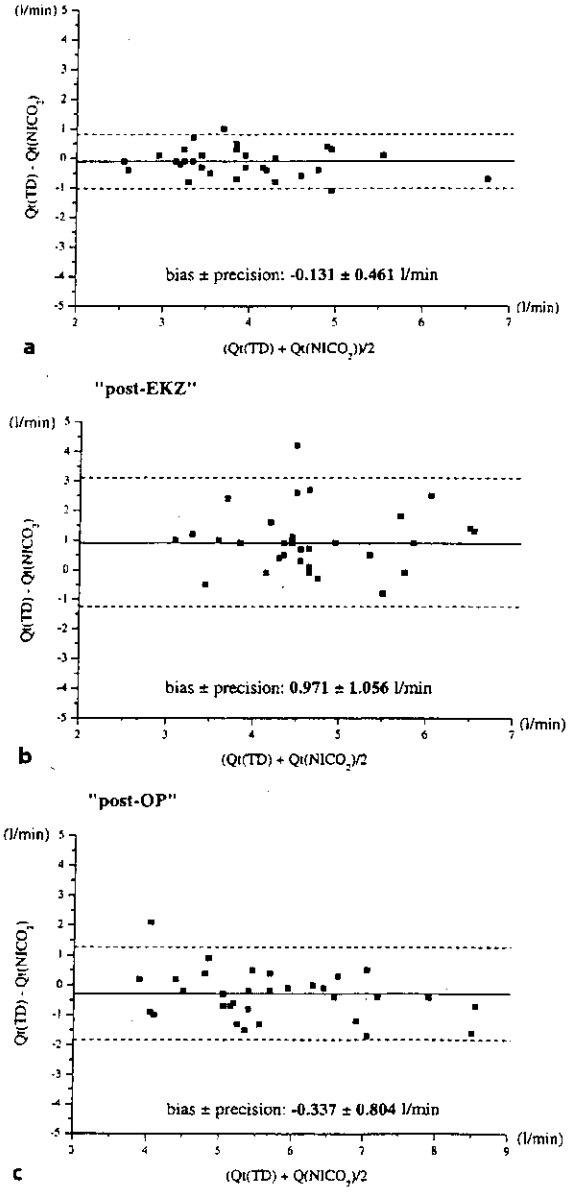

Abb. 1a–c ▶ Bland-Altman-Darstellung der Herzzeitvolumina zu den 3 Messzeitpunkten, bestimmt mit dem $NICO_2$-Monitor (Qt($NICO_2$)) und der Thermodilutionsmethode (Qt(TD)). Aufgetragen sind die Mittelwerte der Wertepaare (Qt(TD) + Qt($NICO_2$)/2) gegen die Differenzen der Wertepaare (Qt(TD)–Qt($NICO_2$)). Die durchgezogene Linie markiert den Mittelwert der Differenzen, die gestrichelten Linien die 95%-Konfidenzintervalle der Differenzen (2-mal die Standardabweichung der Differenzen). Angegeben sind „bias" und „precision" in l/min. a prä-EKZ; b post-EKZ; c post-OP

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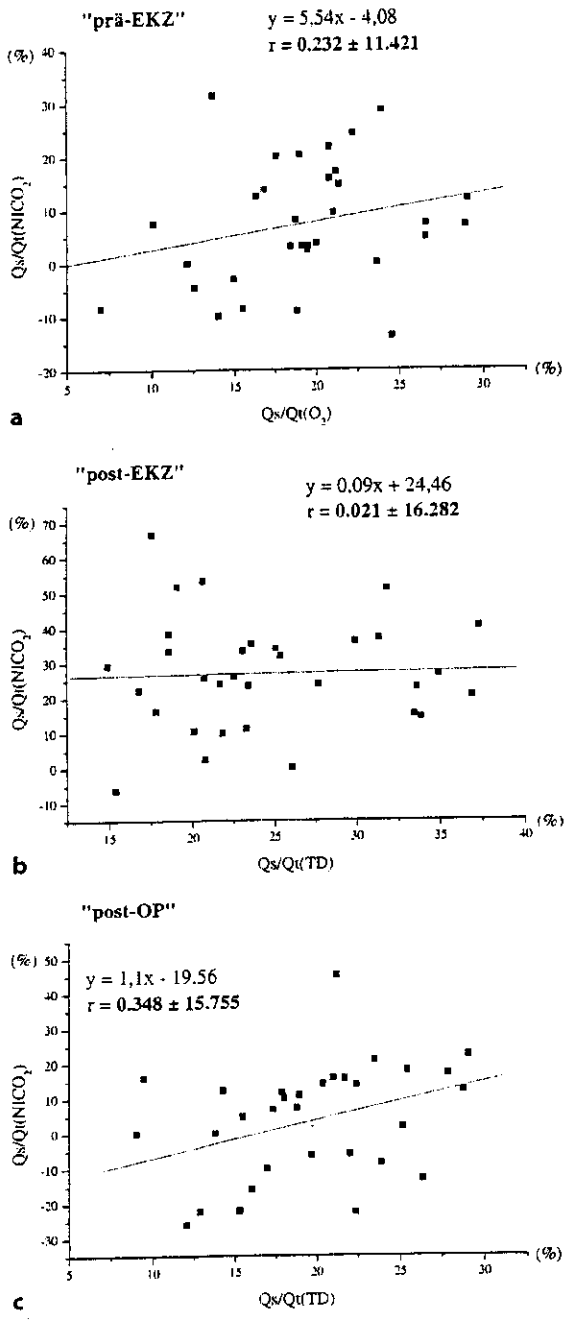

Abb. 2a–c ◀ Darstellung der Regressionsanalyse der Shuntfraktionen zu den verschiedenen Messzeitpunkten. Die Shuntfraktion, berechnet nach der Berggren-Formel ($Qs/Qt(O_2)$), ist gegen die Shuntfraktion, berechnet durch Kombination von $Qpc(NICO_2)$ und Qt(TD) ($Qs/Qt(NICO_2)$), aufgetragen. Angegeben ist der Korrelationskoeffizient *(r)* und die Steigung der Regressionsgeraden *(y)*. a prä-EKZ; b post-EKZ; c post-OP

Auch zeigte sich in der Regressionsanalyse zwischen Qt(TD) und $Qt(NICO_2)$ eine gute Korrelation der Daten (r=0,88 ±0,46; p<0,001).

Herzzeitvolumina 30 Minuten nach extrakorporaler Zirkulation („post-EKZ")

Mittelwerte (± Standardabweichung) sind in Tabelle 2 wiedergegeben. Es fand sich ein signifikanter Unterschied zwischen Qt(TD) und $Qt(NICO_2)$ (p<0,05).

Die Wiederholbarkeit der TD lag bei −0,03±0,22 l/min (Koeffizient der Wiederholbarkeit: 0,44 l/min) und für den $NICO_2$-Monitor bei 0,003±0,41 l/min (Koeffizient der Wiederholbarkeit: 0,82 l/min).

In der Bland-Altman-Darstellung (Abb. 1b) ergab sich ein „bias" von 0,97 l/min, mit einer „precision" von ±1,05 l/min. Die Grenzen der Übereinstimmung lagen bei ±2,1 l/min (von −1,14–3,08 l/min). Der maximal tolerabler prozentualer Fehler wurde mit ±1,31 l/min (±28,28% von 4,66 l/min) angenommen. Da die Grenzen der Übereinstimmung größer waren als die Grenzen der Genauigkeit, sind die verglichenen Methoden nicht durch einander ersetzbar.

In der Regressionsanalyse zwischen Qt(TD) und $Qt(NICO_2)$ ergab sich für Qt ein r=0,46±0,89 mit einem Signifikanzniveau von p<0,01.

Herzzeitvolumina 6–8 Stunden nach dem Eingriff („post-OP")

Mittelwerte (± Standardabweichung) sind in Tabelle 2 wiedergegeben. Die Werte waren nicht signifikant unterschiedlich.

Die Wiederholbarkeit der TD lag bei −0,02±0,22 l/min (Koeffizient der Wiederholbarkeit: 0,44 l/min) und für den $NICO_2$-Monitor bei 0,04±0,33 l/min (Koeffizient der Wiederholbarkeit: 0,66 l/min).

In der Bland-Altman-Darstellung (Abb. 1c) ergab sich ein „bias" von −0,33 l/min, mit einer „precision" von ±0,8 l/min. Die Grenzen der Übereinstimmung lagen bei ±1,6 l/min (von −1,93–1,27 l/min). Mit einem maximal tolerablen prozentualen Fehler von ±1,62 l/min (±28,28% von 5,74 l/min) ist hier wieder eine bessere Übereinstimmung der Methoden festzustellen.

In der Regressionsanalyse zwischen Qt(TD) und $Qt(NICO_2)$ ergab sich für Qt ein r=0,82±0,81 mit einem Signifikanzniveau von p<0,001.

Shuntfraktionen

Mittelwerte (± Standardabweichung) sind in Tabelle 2 wiedergegeben. In der Regressionsanalyse (Abb. 2a–c) zwischen O_2-Shunt ($Qs/Qt(O_2)$ und „$NICO_2$-Shunt" ($Qs/Qt(NICO_2)$) ergab sich zu keinem Zeitpunkt eine signifikante Korrelation zwischen den Werten.

Diskussion

Eine physiologische Größe kann durch die jeweils angewandte Methode meist nur mit einer gewissen Ungenauigkeit bestimmt werden. Der „wahre" Wert bleibt unbekannt. Durch die von Bland u.

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Altman vorgeschlagene Darstellung lassen sich neue Methoden mit etablierten Techniken hinsichtlich ihrer Übereinstimmung vergleichen. Liegt ein hohes Maß an Übereinstimmung vor, sind die gemessenen Werte der Methoden gleich gut (bzw. gleich schlecht). Die Ergebnisse der Methoden müssen jedoch reproduzierbar sein, da bei fehlender Reproduzierbarkeit einer oder beider Methoden eine geringe Übereinstimmung resultiert [3]. In der klinischen Praxis gilt die Thermodilutionsmethode (TD) als „Goldstandard" der Herzzeitvolumenbestimmung und ist in zahlreichen Studien validiert worden. Die Messungenauigkeit der TD wird mit 4–10% angegeben, wenn jeweils 3 aufeinanderfolgende Einzelmessungen vorgenommen werden [27]. Mit dem $NICO_2$-Monitor steht nun ein, im Gegensatz zur TD, non-invasives Herzzeitvolumen-Monitoring zur Verfügung.

Tsujimoto et al. fanden beim Vergleich Qt(TD) versus Qt($NICO_2$) ein gutes Ergebnis („bias" und „precision" −0,21±0,715 l/min) während der Narkose [29]. Auch in der vorliegenden Studie war unter Ruhebedingungen („prä-EKZ") eine gute Übereinstimmung zwischen $NICO_2$-Monitor und TD hinsichtlich der Bestimmung von Qt festzustellen (Abb. 1a). Verglichen mit der TD scheint der $NICO_2$-Monitor Qt leicht zu überschätzen.

Im Gegensatz dazu zeigte sich 30 min nach EKZ eine beträchtliche Diskrepanz zwischen den Ergebnissen beider Methoden (Abb. 1b). Eine geringere Messgenauigkeit durch die TD wäre hier zu diskutieren. In den ersten 30 min nach hypothermer EKZ (Kerntemperatur 28°C) sind Fehler bis zu 50% bei der Bestimmung von Qt durch die TD beschrieben worden [2, 4, 19]. Ursache sind v. a. Schwankungen der Temperatur im Blutstrom (relevant >0,05°C) [19]. In dieser Untersuchung wurden die Messungen 30 min nach EKZ durchgeführt. Ein durch Temperaturschwankungen hervorgerufener Messfehler bei der Bestimmung von Qt(TD) kann zwar nicht völlig ausgeschlossen werden, ist aber aufgrund der hohen Reproduzierbarkeit von Qt(TD) unwahrscheinlich. Dagegen scheint die „partielle CO_2-Rückatmungstechnik" Qt auch 30 min nach EKZ weniger genau bestimmen zu können. Als mögliche Ursachen müssen die der Methodik zugrunde liegenden Annahmen (s. Anhang) betrachtet werden.

1. Annahme. *Der Blutfluss (Q) ist während Nichtrückatemphase (NR) und Rückatemphase (R) konstant.*

Diese Bedingung kann unter Ruhebedingungen als erfüllt gelten. Nach EKZ dagegen sind auch kurzfristige Schwankungen des pulmonalen Blutflusses (instabiles Qt, Volumenverschiebungen, pulmonale Veränderungen) häufig [20, 22]. Steigt z. B. der Blutfluss während der Rückatemphase an, verringert sich die arteriovenöse CO_2-Differenz. Für die Berechnung von Qpc nach der differenziellen Fick-Gleichung bedeutet dies, dass sich die Differenz von $CaCO_2$(R) und $CaCO_2$(NR) vergrößert. Dadurch wird Qpc falsch-niedrig bestimmt.

2. Annahme. *Der $PvCO_2$ (bzw. $CvCO_2$) bleibt während der Rückatemphase konstant.*

Der $PvCO_2$ entspricht dem Mittel der venösen CO_2-Partialdrücke aus den verschieden Geweben. Je nach Metabolismus und Durchblutung tragen sie unterschiedlich zu $PvCO_2$ bei. Sind CO_2-Abgabe und CO_2-Produktion ideal aufeinander abgestimmt, bleibt $PvCO_2$ konstant. Unter Ruhebedingungen steigt der $PvCO_2$ nur sehr langsam infolge einer Hypoventilation (z. B. Rückatemphase) an, abhängig von der CO_2-Produktion und dem Verteilungsvolumen für CO_2 [21]. Während einer kurzen Rückatemphase ist der Anstieg zu vernachlässigen. Nach EKZ ist aber eine Konstanz des $PvCO_2$ wahrscheinlich nicht gegeben. Trotz reduziertem Metabolismus können Gewebe, die während der EKZ inadäquat durchblutet werden, CO_2 akkumulieren. Auch scheint der CO_2-Transport im Blut während der EKZ eingeschränkt zu sein [5]. Nach EKZ kommt es in der Regel zu ausgeprägten Umverteilungsphänomenen des Blutflusses [16, 20, 22]. Das CO_2 wird je nach Durchblutung „ausgewaschen", sodass unabhängig von der Atemphase der $PvCO_2$ variabel sein könnte [30]. Einen Anstieg des $PvCO_2$ während der Rückatemphase konnten Nilsson et al. auch Stunden nach herzchirurgischen Eingriffen dokumentieren [23].

3. Annahme. *Die Änderung des $PetCO_2$ ($\Delta PetCO_2$) entspricht der Änderung des $PaCO_2$ ($\Delta PaCO_2$).*

Normalerweise sind $PetCO_2$ und $PaCO_2$ eng miteinander korreliert. Die arterioendtidale CO_2-Differenz hängt von der Ventilations-Perfusions-Verteilung (V/Q) in der Lunge ab. Sie nimmt mit größerem alveolärem Totraum zu [24]. Der $NICO_2$-Monitor versucht daher, über Totraumberechnungen eine bessere Anpassung des $PetCO_2$ an den alveolären und damit arteriellen CO_2-Partialdruck zu erzielen [14]. Nach EKZ kann es aber durch kurzfristige Schwankungen des Lungenblutflusses sowie pulmonale Veränderungen zum Anstieg bzw. Abfall von Totraumventilation und intrapulmonalem Shunt kommen [9, 12]. Dadurch können Fehler bei der Schätzung von $\Delta PaCO_2$ resultieren. Dies ist um so mehr von Bedeutung, da während der Rückatemphase $\Delta PetCO_2$ mit durchschnittlich 4 mmHg relativ klein ist. Ein Unterschied zwischen $\Delta PaCO_2$ und $\Delta PetCO_2$ von nur 1 mmHg würde somit in einem Fehler von 25% bei der Berechnung von Qpc (bzw. Qt) resultieren.

4. Annahme: $\Delta PetCO_2 \times S = \Delta CaCO_2$.

Die Schätzung des CO_2-Gehalts im Blut über das $PetCO_2$ erfolgt durch den Computer anhand der Steigung der CO_2-Dissoziationskurve (S) über eine Standardformel [17]. Hierbei spielt der Hämoglobinwert eine wesentliche Rolle. Nach EKZ kann es aber aufgrund von Volumenverschiebungen, Bluttransfusionen, Blutungen etc. zu Schwankungen der Hämoglobinkonzentration kommen. Unterscheiden sich aktueller und eingegebener Hb-Wert um 3 g/dl, resultiert ein Fehler von ungefähr 10% für den berechneten Blutfluss.

Viele dieser Veränderungen scheinen auch im weiteren Verlauf für Stunden zu bestehen. In einer Studie an herzchirurgischen Patienten auf der Intensivstation fanden Nilsson et al. zwar eine hohe Wiederholbarkeit für das Qt($NICO_2$) (Koeffizient der Wiederholbarkeit =0,6 l/min) und nahezu gleiche Mittelwerte im Vergleich zum TD (4,4 l/min vs. 4,6 l/min), in der Bland-Altman-Analyse ergab sich aber nur eine geringe Übereinstimmung der beiden Methoden mit einer „precision" von ±1,8 l/min [23]. Van Heerden et al. fanden in einer ähnlichen Studie bei herzchirurgischen Intensivpatienten lediglich eine geringe Korrelation zwischen der TD und dem $NICO_2$-Monitor (r=0,691). Das Qt gemessen mit der TD war signifikant höher als die $NICO_2$-Werte (p=0,0003) und in der Bland-Alt-

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man-Analyse ergab sich besonders für hohe Qt eine geringe Übereinstimmung [15]. Auch bei Tachibana et al. war 1–3 h nach Herzoperationen lediglich eine Übereinstimmung von 0,28±1,03 l/min (r=0,63) festzustellen, wenn mit hohem Atemzugvolumen (12 ml/kg) beatmet wurde [28]. Beatmungsmodus, positiver endexspiratorischer Beatmungsdruck (PEEP) sowie hoher FiO_2 hatten keinen Einfluss auf die Messung. Bei kleinem Atemzugvolumen (6 ml/kg) war die Übereinstimmung sogar geringer. In einer weiteren Untersuchung an herzchirurgischen Patienten 5 und 18 h nach Operation fanden Osterlund et al. eine Korrelation zwischen TD und der „partiellen CO_2-Rückatemtechnik" von r=0,8 und in der Bland-Altman-Analyse eine gute Übereinstimmung („bias" und „precision": −0,14±0,77 l/min) [25]. Die Reproduzierbarkeit der Ergebnisse war auch hier hoch. In der vorliegenden Untersuchung ergab sich eine gerade eben akzeptable Übereinstimmung zwischen TD und $NICO_2$-Monitor 6–8 h nach EKZ (Abb. 1c). Tendenziell scheint es bei zunehmender postoperativer Stabilisierung der Patienten wieder zu einer besseren Übereinstimmung der Methoden zu kommen.

Crichley u. Crichley empfahlen in einer Metaanalyse von Herzzeitvolumenmessungen, dass die Grenzen der Übereinstimmung (2-mal die Standardabweichung der Differenzen) kleiner sein sollten als die Grenzen der Ungenauigkeit (geometrisches Mittel der Fehler aus jeder Methode) [6]. Wir gingen davon aus, dass jede der verglichenen Methoden einen klinisch tolerablen Fehler von maximal ±20% haben darf und damit eine Grenze der Ungenauigkeit von ±28%. Legt man diese Kriterien zugrunde, war nur für die Messungen vor EKZ von einer sicher annehmbaren Übereinstimmung auszugehen. Nach EKZ hingegen war das Maß der Übereinstimmung geringer, als es der maximal tolerable Fehler erlaubt. Insofern kann lediglich unter Ruhebedingungen die TD durch den $NICO_2$-Monitor ersetzt werden, dies limitiert den Einsatz während und nach herzchirurgischen Eingriffen mit EKZ.

Zwischen $Qs/Qt(NICO_2)$ und $Qs/Qt(O_2)$ konnten wir keine signifikante Korrelation feststellen (Abb. 2a–c). Problematisch hierbei ist v. a. die Bestimmung von $Qs/Qt(NICO_2)$, da sich durch Kombination von $Qpc(NICO_2)$ und Qt(TD) die Fehler der 2 Methoden addieren (besonders nach EKZ). Dies macht das Ergebnis unvorhersehbar. Eine Betrachtung der Standardabweichungen von $Qs/Qt(NICO_2)$ verdeutlicht dies (Tabelle 2).

Auffällig war aber, dass die über die Berggren-Formel bestimmten Shuntfraktionen relativ groß waren (z. B. 16% „prä-EKZ"). Hierbei könnte der vielfach diskutierte Effekt einer Shuntzunahme aufgrund von hohen FiO_2 eine Rolle gespielt haben [7]. Dies ließ sich in der Untersuchung durch einen Vergleich mit $Qs/Qt(NICO_2)$ nicht klären. Nilsson et al. verglichen $Qs/Qt(O_2)$ und den vom $NICO_2$-Monitor geschätzten Shuntanteil (Differenz zwischen $Qt(NICO_2)$ und $Qpc(NICO_2)$). Auch hier ergab sich keine gute Übereinstimmung („bias" und „precision": 0,08±10,75%) [23]. Für die Berechnung von $Qt(NICO_2)$ scheint sich aber eine ungenaue Schätzung des Shunts durch den $NICO_2$-Monitor nur geringfügig auszuwirken. Ein Fehler in der Schätzung des Shunts von 25% resultiert nach Haryadi et al. lediglich in einem Fehler von 5% bei der Bestimmung von $Qt(NICO_2)$ [13].

Würden die hier angewandten Methoden Qpc und Qt mit absoluter Genauigkeit messen, könnte der Shunt anhand von CO_2 bestimmt werden. Ein Unterschied zwischen $Qs/Qt(O_2)$ und $Qs/Qt(NICO_2)$ wäre selbst dann zu erwarten (bei allerdings guter Korrelation). Dies liegt daran, dass $Qs/Qt(NICO_2)$ ausschließlich dem intrapulmonalen Shunt (echter Shunt + „venöse Beimischung"), $Qs/Qt(O_2)$ dagegen dem transpulmonalen (intrapulmonaler Shunt + „venöse Beimischung" von bronchialen und thebesischen Venen) entspricht. Ein weiterer Grund liegt in den unterschiedlichen Bindungs- bzw. Dissoziationskurven von O_2 und CO_2 in Blut. Je unlöslicher ein Gas, desto besser wird es selbst durch Alveolen mit kleinem V/Q eliminiert [8]. Da CO_2 eine, verglichen mit O_2, höhere effektive Löslichkeit besitzt (6,0 für CO_2 gegenüber 0,6 für O_2), ist die CO_2-Abgabe in Alveolen mit kleinem V/Q verhältnismäßig stärker beeinträchtigt als die O_2-Aufnahme [31]. Dadurch wird der Anteil der „venösen Beimischung", die dem echten Shunt durch die Messmethoden hinzugeschlagen wird, für CO_2 größer sein als für O_2.

Einschränkungen dieser Studie sind, dass die diskutierten Fehlerquellen des $NICO_2$-Monitors nach EKZ (potentieller $PvCO_2$-Anstieg während der Rückatemphase, instabiler Blutfluss während der Messphase, Differenz zwischen $\Delta PetCO_2$ und $\Delta PaCO_2$ etc.) durch die Untersuchung nicht belegt werden können. Dies muss in kontrollierten Studien erfolgen. So lag z. B. der von Nilsson et al. beobachtete Anstieg des $PvCO_2$ während der Rückatmung bei ca. 0,61 mmHg [23]. Ein Wert, der innerhalb der Messungenauigkeit vieler Blutgasanalysegeräte liegen dürfte. Dennoch schließen wir uns der Meinung dieser Autoren an, dass die z. Z. bestehenden Algorithmen des $NICO_2$-Monitors optimiert werden müssen, um bessere Ergebnisse nach EKZ zu erzielen.

Fazit für die Praxis

Zusammenfassend lässt sich feststellen, dass der $NICO_2$-Monitor unter Ruhebedingungen verglichen mit der TD ähnlich gute Ergebnisse für Qt liefert. Nach EKZ ist aber die Herzzeitvolumenbestimmung durch den $NICO_2$-Monitor weniger zuverlässig. Dieser Zustand kann in der postoperativen Phase für mehrere Stunden anhalten. Eine verlässliche Bestimmung der Shuntfraktion ist durch die vorgestellte Methode nicht möglich.

Anhang

1. Berechnung des Blutflusses (Q) nach dem Fick-Prinzip angewandt auf CO_2:

$$Qpc = VCO_2/CvCO_2 - CaCO_2,$$

für Q konstant (Q Nichtrückatemphase (NR)=Q Rückatemphase (R)), gilt:

$$VCO_2(NR)/CvCO_2(NR) - CaCO_2(NR) = Qpc = VCO_2(R)/CvCO_2(R) - CaCO_2(R),$$

für $CvCO_2$ konstant ($CvCO_2(NR)$= $CvCO_2(R)$), gilt:

$$Qpc = VCO_2(NR) - VCO_2(R)/CaCO_2(R) - CaCO_2(NR), \text{ bzw.}$$

$$Qpc = \Delta VCO_2/\Delta CaCO_2;$$

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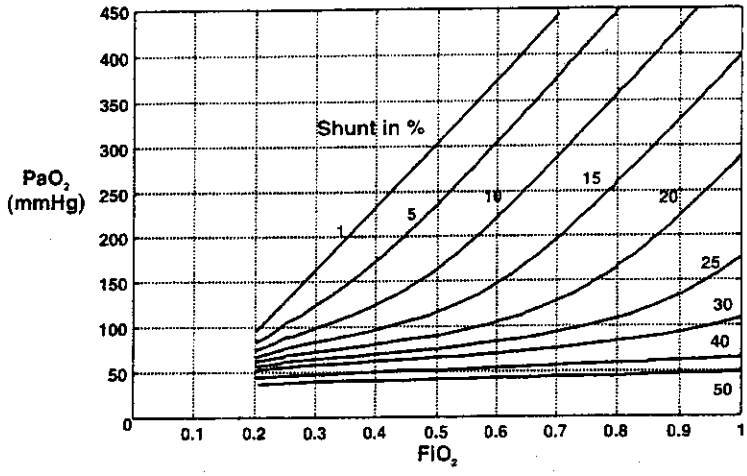

Abb. 3 ▲ **Auswirkung eines intrapulmonalen Shunt's auf den PaO_2 bei unterschiedlicher FiO_2**

Qpc steht für den „pulmonal-kapillären Blutfluss" (l/min), VCO_2 für die CO_2-Abgabe (ml/min), $CvCO_2$ und $CaCO_2$ für den gemischt-venösen bzw. arteriellen CO_2-Gehalt in Blut (ml/dl).

$$\Delta CaCO_2 = \Delta PaCO_2 * S,$$

für die „partielle CO_2-Rückatmungstechnik": $\Delta PetCO_2 \approx \Delta P_ACO_2 \approx \Delta PaCO_2$;

$PetCO_2$, P_ACO_2 und $PaCO_2$ stehen für den endtidalen, alveolären bzw. arteriellen Kohlendioxidpartialdruck (mmHg), S für die Steigung der CO_2-Dissoziationskurve (durch den Computer des $NICO_2$-Monitors anhand einer Standardformel berechnet).

Daher gilt vereinfacht:

$$Qpc = \Delta VCO_2 / \Delta PetCO_2 * K * S,$$

K ist ein Korrekturfaktor für den alveolaren Totraum.

$$Qt(NICO_2) = Qpc/(1 - Qs/Qt)$$

Qs/Qt wird durch den $NICO_2$-Monitor geschätzt (s. unter 3.).

2. Berechnung des O_2-Shunt's nach der Berggren-Formel:

$$Qs/Qt(O_2) = CcO_2 - CaO_2/CcO_2 - CvO_2,$$

$CcO_2 = (Hb * 1{,}39) + (P_AO_2 * 0{,}0031)$;
$CaO_2 = (Hb * 1{,}38 * SaO_2) + (PaO_2 * 0{,}0031)$;
$CvO_2 = (Hb * 1{,}38 * SvO_2) + (PvO_2 * 0{,}0031)$;
$P_AO_2 = (P_{ATM} - P_{H_2O}) * FiO_2 - PaCO_2/RQ$;

$Qs/Qt(O_2)$ steht für den transpulmonalen Shunt (%), CcO_2, CaO_2 u. CvO_2 für den kapillären, arteriellen und gemischt-venösen Sauerstoffgehalt in Blut (ml/dl), P_AO_2 für den alveolären Sauerstoffpartialdruck (mmHg), P_{ATM} für den aktuellen Luftdruck (mmHg), P_{H_2O} für den Wasserdampfdruck (47 mmHg) und RQ für den respiratorischen Quotienten (dieser wurde mit 1 angenommen).

3. Schätzung des intrapulmonalen Shunt's durch den $NICO_2$-Monitor: Die Schätzung des intrapulmonalen Shunt's durch den $NICO_2$-Monitor orientiert sich an den Nunn-Iso-Shunt-Kurven (Abb. 3). Der $NICO_2$-Monitor verwendet dazu die aktuelle SpO_2 sowie die angegebene FiO_2 [26]. Die Schätzung wird genauer, wenn dem Computer ein aktueller PaO_2 mitgeteilt wird [17].

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Clinical evaluation of a partial CO_2 rebreathing technique for cardiac output monitoring in critically ill patients

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Background: Monitoring central hemodynamics is essential in critically ill patients and less invasive techniques are needed. In this study, the clinical and technical performance of a new non-invasive cardiac output monitor (NICO) based on partial CO_2 rebreathing technique and a modified Fick equation were evaluated. The various sources of possible errors in measurement of cardiac output (CO), carbon dioxide production ($\dot{V}CO_2$) and pulmonary shunt were also assessed.
Methods: Simultaneous measurements of CO with partial CO_2 rebreathing technique (CO_{NICO}) and thermodilution (CO_{TD}) were performed in 15 patients during major surgery or in the ICU. Pulmonary shunt was estimated from this device and compared to values obtained by standard shunt formula. The accuracy of $\dot{V}CO_2$ measurements was assessed in a mechanical lung model.
Results: A good correlation was found between CO_{NICO} and CO_{TD} ($r = 0.96$, within-subject correlation $r = 0.88$) with a small underestimation of cardiac output by the NICO of 0.04 L/min, limits of agreement (±2SD) being −1.68 and 1.76 L/min. In hemodynamic unstable patients the method closely tracked changes in CO. Pulmonary shunt was underestimated by approximately 11%-units compared to standard shunt calculations using arterial and mixed venous blood gases. We also observed an underestimation in $\dot{V}CO_2$ measurements.
Conclusion: Clinical evaluation shows that partial CO_2 rebreathing technique provides a useful and accurate non-invasive estimate of cardiac output. Although this technique cannot fully replace the pulmonary artery catheter, it may be used to monitor central hemodynamics in a large number of critically ill patients.

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Key words: cardiac output; monitoring; non-invasive; partial CO_2 rebreathing.

THE HEMODYNAMIC management of critically ill patients in the operating room (OR) and in the ICU is markedly facilitated if key parameters such as cardiac output can be continuously monitored. Since the use of pulmonary artery catheters has been questioned (1, 2) there is a need for alternative methods. Several less invasive techniques for cardiac output measurements have been developed and tested. There are different Doppler-based techniques, among them the transesophageal echo-Doppler technique. With a Doppler probe placed in the esophagus, the descending aortic blood flow is monitored (3, 4). It provides almost continuous information but has the disadvantage that it is still somewhat invasive and sensitive to movements of the probe or the patient. This method has its definite place in studying rapid hemodynamic changes and trends in the OR and in well-sedated patients in the ICU. The transthoracic electrical bioimpedance method is a completely non-invasive technique but suffers from several clinically significant errors (5). The pulse contour cardiac output technique can be performed using an indwelling pressure-transduced radial or femoral catheter. However, this method can not be used for quantification of cardiac output unless a calibration, for instance by thermodilution, is performed at intervals (6). Different CO_2 rebreathing techniques using the Fick principle to calculate cardiac output have also been suggested, but most of these techniques depend on total CO_2 rebreathing for estimation of mixed venous CO_2 content. However, total rebreathing is difficult to perform in critically ill patients (7). In 1980, Gedeon and coworkers described a new non-invasive method for calculating cardiac output which is based on a partial CO_2 rebreathing technique and uses a differential Fick equation (8). This method has been further developed and computerized in the NICO system (Novametrix Medical Systems Inc., Connecticut, USA) (9).

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The goal of the present study was to assess the validity of this partial CO_2 rebreathing technique for cardiac output measurement compared to thermodilution technique in mechanically ventilated patients in the OR and in the ICU. To challenge the method, the patient group studied included hemodynamically unstable patients as well as patients with large intrapulmonary shunt and alveolar dead space. The performance of this device in measuring carbon dioxide elimination and estimating pulmonary shunt (venous admixture) was assessed. Changes in arterial and mixed venous CO_2 tension due to rebreathing were also studied.

Patients, material and methods

With approval of the Human Ethics Committee of the University of Göteborg and after informed consent from the patient or a relative, 15 patients (12 patients undergoing major surgery and three patients in the ICU) were included in the study (Table 1). The patients studied were those already monitored with a pulmonary artery catheter or those in whom additional monitoring was indicated apart from the study. The mean (range) age of the patients, three female and 12 male, was 62 years (34–84 years). The main diagnosis of the three patients in the ICU was sepsis. Seven patients scheduled for liver transplantation, four patients for vascular surgery due to aortic aneurysm and one patient for surgery due to adrenal carcinoma were studied in the OR.

Patients undergoing surgery were studied during general anesthesia with pentothal, fentanyl, an inhalation agent and intermittently administered muscle relaxant. In the ICU, the patients were sedated using continuous infusions of propofol or midazolam in combination with fentanyl. All patients were endotracheally intubated and mechanically ventilated in volume-controlled mode with a Servo 300 ventilator (Siemens-Elema, Solna, Sweden) in the ICU or a Siemens UV 705 ventilator with a circle system including a CO_2 absorber in the OR. Fraction of inspiratory oxygen (FiO_2) varied between 0.27 and 0.72 and positive end expiratory pressure between 4 and 17 cm H_2O.

Respiratory measurements

Side stream spirometry (Datex-Ohmeda, Helsinki, Finland) was used for respiratory monitoring of expiratory volumes. Inspiratory and expiratory oxygen and carbon dioxide concentrations (FiO_2, $FETO_2$, $FiCO_2$, and $FETCO_2$) were measured continuously with infrared and paramagnetic technology, respectively, using the AS/3 multimode monitoring system (Datex-Ohmeda).

Hemodynamic measurements

All patients were monitored using a radial artery and central venous catheter. In 11 patients measurements of bolus thermodilution cardiac output ($CO_{TD}b$) were performed using a 7.5 F flow-directed thermodilution fiberoptic pulmonary artery catheter (Oximetrix® SvO_2 Systems, Opticath, Abbott Laboratories, North Chicago, IL, USA) connected to a monitor. In four pa-

Table 1

Patient *characteristics.*

Patient No.	Sex, M/F	Age, years	BSA, m^2	Diagnosis	CO_{TD} technique	CO_{TD} range, L/min	PEEP cmH_2O	FiO_2	Maximal pulmonary shunt refraction
1	M	56	1.70	Liver cirrhosis	bolus	4.3–13.0	3–4	0.31–0.38	0.25
2	M	49	1.78	Sepsis	continuous	5.7–7.5	10–13	0.40	0.19
3	M	74	2.20	Aortic aneurysm	bolus	2.3–10.1	4	0.41–0.51	0.21
4	M	84	1.86	Sepsis	continuous	5.0–7.4	14–15	0.57–0.72	0.38
5	M	34	1.86	Liver cirrhosis	bolus	6.6–12.7	3	0.27–0.36	*
6	M	84	1.79	Aortic aneurysm	bolus	3.6–4.7	4	0.27–0.39	0.21
7	M	77	1.85	Aortic aneurysm	continuous	3.5–6.1	4	0.35	*
8	M	52	1.74	Liver cirrhosis	bolus	6.8–15.7	3	0.34–0.40	0.42
9	F	42	2.17	Liver cirrhosis	continuous	6.6–8.4	16–17	0.27–0.71	0.53
10	M	44	2.42	Liver cirrhosis	bolus	7.4–14.4	10	0.30–0.46	0.29
11	M	65	1.95	Sepsis	bolus	4.9–5.8	13	0.65	*
12	F	58	1.82	Liver cirrhosis	bolus	5.6–8.6	4	0.37–0.43	0.30
13	M	78	1.91	Aortic aneurysm	bolus	2.7–4.6	14–15	0.37–0.43	0.31
14	M	59	1.98	Familiar amyloid neuropathy	bolus	3.9–6.4	4	0.46–0.50	0.15
15	F	67	1.68	Adrenal carcinoma	bolus	3.6–5.9	4	0.35–0.37	0.22

BSA, body surface area. M/F, male/female. CO_{TD},thermodilution cardiac output. *Missing value.

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tients 'continuous' cardiac output (CO_{TDC}) was obtained using a 7.5 F pulmonary artery catheter (Swan-Ganz CCOmbo, Baxter Healthcare Corporation, Irvine, CA, USA) connected to a Vigilance monitor.

Partial CO_2 rebreathing technique

The NICO monitor measures carbon dioxide, volume and flow. It consists of a disposable device that is connected to the breathing circuit between the endotracheal tube and the Y-piece, distal to the humidifier. It contains a pneumatically controlled valve that can automatically direct flow through an extra and adjustable dead space to achieve a partial rebreathing state (50–90% of tidal volume). For analysis of CO_2 and ventilatory flow/volumes, a mainstream infrared analyzer and a flow/volume sensor based on the Pitot technique is used. The monitor is equipped with a separate pulse oximeter. Carbon dioxide elimination ($\dot{V}CO_2$) is calculated as the sum of the product of carbon dioxide concentration and flow during each breathing cycle. Arterial CO_2 content is estimated from end-tidal CO_2 and the CO_2 dissociation curve.

Every 3 min an extra dead space is added for 50 s to achieve partial CO_2 rebreathing. This causes $FETCO_2$ to rise and $\dot{V}CO_2$ to decrease. Differences in CO_2 elimination and end-tidal CO_2 between the normal and the rebreathing state are used to calculate cardiac output using the Fick principle and a differential Fick equation. This is possible under the assumption that pulmonary capillary blood flow (PCBF) is constant during the measurement cycle and that the rebreathing period is short enough not to change mixed venous CO_2. Two different equations for cardiac output, during normal condition and during the rebreathing period, can be expressed:

$$Q = \frac{\dot{V}CO_2 \text{ nonrebreathing}}{C\bar{v}CO_2 - CaCO_2 \text{ nonrebreathing}} \quad \text{eqn. 1}$$

$$Q = \frac{\dot{V}CO_2 \text{ rebreathing}}{C\bar{v}CO_2 - CaCO_2 \text{ rebreathing}} \quad \text{eqn. 2}$$

where Q is blood flow and $C\bar{v}CO_2$ and $CaCO_2$ represent mixed venous and arterial carbon dioxide content, respectively. By combining eqns 1 and 2 into one differential Fick equation the term for mixed venous CO_2 content will be eliminated.

$$Q = \frac{\dot{V}CO_2 \text{nonrebreathing} - \dot{V}CO_2 \text{ rebreathing}}{CaCO_2 \text{rebreathing} - CaCO_2 \text{ nonrebreathing}} \quad \text{eqn. 3}$$

$$Q = \frac{\Delta\dot{V}CO_2}{\Delta CaCO_2} \quad \text{eqn. 4}$$

The equation is then reduced to compare changes in carbon dioxide elimination and changes in arterial CO_2 content, reflected by the change in end-tidal CO_2 as a result of a change in ventilation, assuming that the arterial–alveolar CO_2 difference is the same during non-rebreathing and rebreathing periods.

$$Q = \frac{\Delta\dot{V}CO_2}{\Delta FET CO_2 \times CO_2 - \text{dissociationcurve}} \quad \text{eqn. 5}$$

By measuring cardiac output indirectly via CO_2 in exhaled gas, calculated blood flow will only represent that part of the cardiac output that has passed through ventilated parts of the lungs; pulmonary capillary blood flow. Accordingly, the part of cardiac output that does not take part in gas exchange; the shunt fraction, has to be added to obtain the total cardiac output. It is estimated from the FiO_2 and SpO_2 and iso-shunt diagrams assuming an arterial–mixed venous oxygen content (a–$\bar{v}$ O_2) difference of 50 mL/L (9) with enhanced accuracy if values for PaO_2 are added.

The NICO displays the cardiac output measurements after every completed cycle and the PCBF as aan average over time as well as values for $FETCO_2$, $\dot{V}CO_2$ and spirometry data.

Experimental procedure

The NICO measures cardiac output (CO_{NICO}) over a 3-min period. Simultaneous measurements of cardiac output were performed in triplicate by bolus thermodilution (CO_{TDb}) with 10 ml iced saline randomly throughout the breathing cycle (accepting ≤10% spread of the values). When continuous thermodilution cardiac output technique (CO_{TDC}) was used, the Vigilance monitor was set on stat mode and a mean value obtained during the 3-min NICO cycle was calculated. Respiratory measurements and arterial and mixed venous blood gas samples were obtained just before a rebreathing cycle to avoid influences of the extra dead space.

Technical evaluation

Pulmonary shunt calculations were made according to the standard shunt formula (10) and compared to the estimated shunt from the NICO using displayed values for PCBF and CO.

In four patients, paired blood gas samples from arterial and mixed venous blood were collected before and at the end of a rebreathing period during several rebreathing cycles to evaluate changes in CO_2 tension during rebreathing.

The accuracy of the $\dot{V}CO_2$ measurement by the NICO was studied in a mechanical lung model connected to a Servo 900 C ventilator (Siemens-Elema)

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where CO_2 could be added in defined amounts (11). The respiratory frequency, minute ventilation, dead space, PEEP and inspiratory/expiratory time were varied at two levels of CO_2 in the system.

Statistical analysis

Values are presented as mean ± SD or SEM as indicated. Correlation between techniques was determined using linear regression analysis and Bland & Altman presentation (12). Within-subject correlation was assessed by using multiple regression as described by Bland & Altman (13).

Results

A total of 125 paired measurements of cardiac output were obtained, 4–24 in each patient, over a period of 1.5–8 h: 74 measurements by bolus thermodilution ($CO_{TD}b$) and 51 by continuous thermodilution ($CO_{TD}c$). Cardiac output ranged from 2.3 to 18.1 L/min using the partial CO_2 rebreathing (CO_{NICO}) technique and from 2.3 to 15.7 L/min using thermodilution techniques (CO_{TD}) (Table 1). Figure 1A demonstrates the close correlation ($r = 0.96$), between cardiac output measured with the partial CO_2 rebreathing technique and with the thermodilution method. The within-subject correlation between NICO and thermodilution was also excellent ($r = 0.88$). The mean difference between paired values ($CO_{TD} - CO_{NICO}$) was 0.04 L/min, while the limits of agreement (bias ± 2 SD) were −1.68 and 1.76 L/min (Fig. 1B). Bias and limits of agreement were similar when comparing the two thermodilution techniques, bolus and continuous, with NICO (−0.05 ± 1.92 and 0.18 ± 1.38 L/min, respectively), the within-subject correlation being r = 0.90 and r = 0.73, respectively. Figure 2 shows hemodynamic measurements during an operation for an aortic aneurysm. The partial CO_2 rebreathing technique for the measurement of cardiac output closely followed changes in cardiac output by the bolus thermodilution method.

Alveolar dead space from 48 measurements in nine patients ranged from 7% to 40%. In 12 of the patients, 56 pairwise measurements of pulmonary shunt fraction were obtained using the standard shunt formula compared to the displayed values for pulmonary capillary blood flow and cardiac output from the NICO monitor. ((CO_{NICO} − PCBF)/CO_{NICO}). The range of the shunt according to the shunt formula was 10–53% (mean 22%). The corresponding NICO estimation of shunt was markedly lower, 1–34% (mean 11%). As shown in Fig. 3A and B, pulmonary shunt fraction was markedly underestimated by the NICO technique as compared to calculation using the standard shunt formula. Arterial–mixed venous oxygen content difference (a–$\bar{v}$ O_2) was also determined ($n = 61$). Average values in these patients ranged between 10 and 64 mL/min (mean 29 mL/min).

In four patients, 11 paired gas analyses of arterial and mixed venous blood were obtained before and at the end of a rebreathing period (Fig. 4A and B). The increase in mixed venous CO_2 concentration following the rebreathing period was 2.5 ± 0.3% (SEM) from the initial value while arterial CO_2 tension increased by 9.8 ± 0.8% (SEM).

The NICO underestimated $\dot{V}CO_2$ as measured in a mechanical lung model. This underestimation was

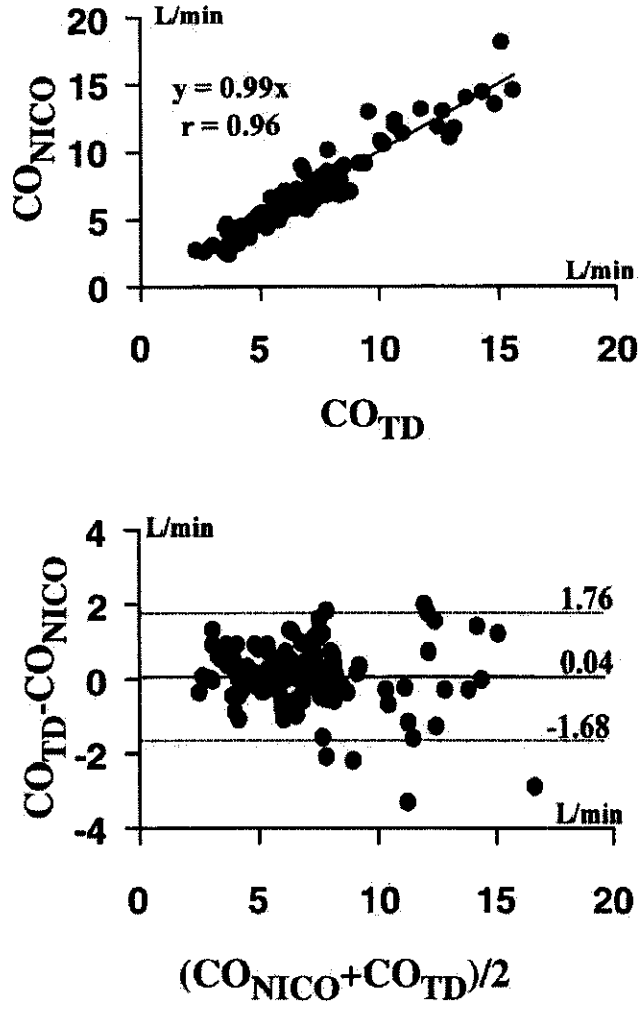

Fig. 1. A. Scatterplot of paired cardiac output measurements obtained by thermodilution (CO_{TD}) and partial CO_2 rebreathing technique (CO_{NICO}) with the solid line representing linear regression. B. Bland-Altman analysis showing the agreement between the two techniques. The solid line represents the mean difference between CO_{TD} and CO_{NICO} (systematic bias) and the dotted lines define the limits of agreement (± 2 SD).

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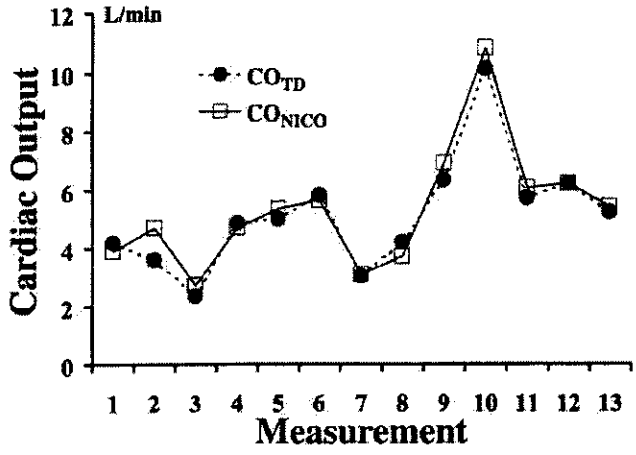

Fig. 2. Values from pairwise measurements of cardiac output using bolus thermodilution and the non-invasive partial CO_2 rebreathing technique (NICO) in a patient undergoing operation for an aortic aneurysm.

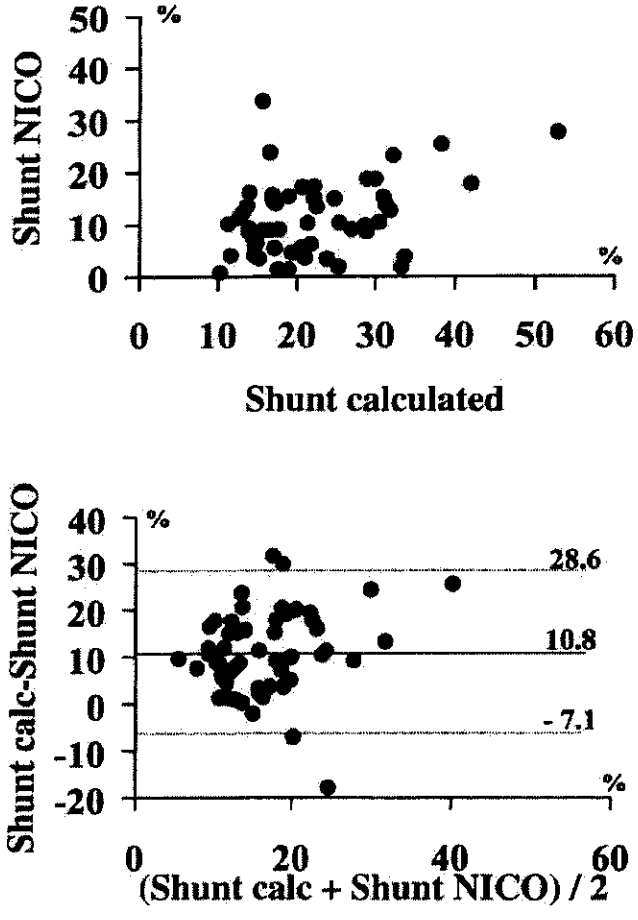

Fig. 3. (A) Scatterplot of correlation between pulmonary shunt calculated from the standard shunt formula and pulmonary shunt estimated by the NICO. (B) Bland-Altman analysis showing bias and limits of agreement (±2 SD) for the pulmonary shunt calculated from arterial and mixed venous blood samples and pulmonary shunt estimated by the NICO.

greater with increased respiratory frequency, being 2–9% (range) at a respiratory frequency of 10 compared to 5–13% and 10–19% at frequencies of 15 and 20, respectively. Changes in I:E ratio or PEEP at a fixed respiratory rate did not affect the $\dot{V}CO_2$ measurement.

Discussion

The partial CO_2 rebreathing method for cardiac output estimation has been implemented with newly developed equipment and assessed in critically ill patients during major surgery in the intensive care unit. In this study, cardiac output values measured with this technique correlated well with cardiac output obtained from thermodilution techniques. There was a minimal average (0.04 L/min) underestimation of CO_{NICO} as compared to cardiac output determined with thermodilution techniques, with limits of agreement being −1.68 and 1.76 L/min, respectively. Two methods of thermodilution were used in the present study – bolus and 'continuous'. A similar good agreement was obtained between CO_{NICO} and both methods.

The problem when comparing alternative methods for cardiac output measurement is that the usual reference method, thermodilution, is not a true 'gold standard' and has a substantial variability of its own (14). Consequently, an important part of the observed difference between the two techniques (Fig. 1B) is due to variability in the thermodilution technique itself. The high within-subject correlation ($r = 0.88$) demonstrated that changes in cardiac output observed with the thermodilution technique were reliably detected with the partial CO_2 rebreathing technique even when used in patients with large pulmonary shunt or alveolar dead space. Still, studies assessing the thermodilution technique indicate that a substantial change in cardiac output of 15–20% has to occur before a sig-

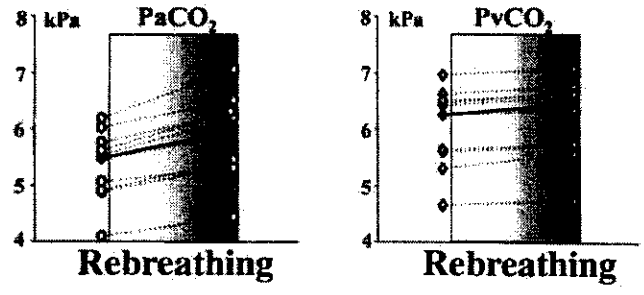

Fig. 4. A and B. Eleven paired blood gas analyses of arterial and mixed venous blood obtained before and at the end of a rebreathing period. The bold lines represents median values.

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nificant change in cardiac output can be concluded (14).

Methodological considerations

The Fick method is considered to be the gold standard for cardiac output measurement. It is based on the principle of conservation of mass. It states that the amount of oxygen extracted from the respired gases equals the amount added to the blood, which passes through the lungs (15). This can be expressed as

$$Q = \dot{V}O_2/(CaO_2 - C\bar{v}O_2)$$

where Q is the blood flow, $\dot{V}O_2$ the oxygen consumption and CaO_2 and $C\bar{v}O_2$ the arterial and the mixed venous oxygen content, respectively. If Fick's equation on CO_2, which is preferable to measure and less sensitive to high FiO_2, is used instead, the equation analogously becomes

$$Q = \dot{V}CO_2/(C\bar{v}CO_2 - CaCO_2) \ .$$

Partial rebreathing in the present study is achieved by addition of an expandable dead space (16). The technique combines measurements obtained during a non-rebreathing period with the ones obtained during a subsequent rebreathing period. The changes in $FET-CO_2$ and in $\dot{V}CO_2$ in response to a change in ventilation are used to calculate PCBF and an estimated pulmonary shunt fraction is added to achieve the total cardiac output. Cardiac output, as well as the carbon dioxide production, is assumed to be stable and the ventilation kept constant during the 3-min measurement cycle. The most important factors for the accuracy of the technique are that:

1 both the changes in $\dot{V}CO_2$ elimination and the changes in end-tidal CO_2 are measured correctly;
2 mixed venous CO_2 content remains relatively constant during the rebreathing period, explained partly by the large CO_2 body stores;
3 pulmonary shunting can be correctly estimated by pulse oximetry, FiO_2 and iso-shunt calculations.

In this study these issues have been addressed.

(1) The accuracy of the $\dot{V}CO_2$ measurements by the NICO was assessed in a mechanical lung model. It was observed that increased respiratory frequency led to a substantial underestimation of $\dot{V}CO_2$, while changes in PEEP and I:E ratio had little impact on measurements. The underestimation caused by frequencies over 15 may introduce a systematic underestimation of cardiac output, unless it is accompanied by a corresponding underestimation of end-tidal CO_2. Although we have found a significant and variable underestimation of $\dot{V}CO_2$ in terms of the absolute values, this has clearly not introduced substantial bias in the cardiac output measurements (Fig. 1B). This may be due to the measurement of $\dot{V}CO_2$ and end-tidal CO_2 with the same gas monitor, minimizing the effect of the CO_2 measurement error. It indicates further that the underestimation is due to an error in the CO_2 measurement and not in the volume measurement of the equipment. Any over/underestimation in the concentration measurement will according to eqn. 4 (see Methods) not affect the bias or accuracy of the cardiac output data. A bias in the gas volume measurement will immediately show up in the cardiac output determination.

(2) Blood gases taken before and at the end of rebreathing cycles showed an expected increase in arterial CO_2 tension during rebreathing by $9.8 \pm 0.8\%$. This change is utilized in the calculation of cardiac output (see above). The basic assumption for the partial CO_2 rebreathing technique postulates that $P\bar{v}CO_2$ should remain constant during the rebreathing manoeuvre (8). We observed a moderate ($2.5 \pm 0.3\%$), but significant increase, in $P\bar{v}CO_2$ during rebreathing. It is possible that this change in mixed venous CO_2 contributes to the increase in arterial CO_2 and thus results in a possible underestimation of pulmonary capillary blood flow and finally of cardiac output.

(3) The cardiac output measurements in this study were very close to those obtained with the thermodilution technique. However, the displayed cardiac output using the partial CO_2 rebreathing technique consists of two parts: measured pulmonary capillary blood flow and estimated pulmonary shunt. The shunt estimation systematically showed too low values, on average 11%-units below true pulmonary shunt based on arterial and mixed venous blood gases. This underestimation should have resulted in 11% too low cardiac output value of the partial rebreathing device, but it did not. The explanation may be sought in the fact that pulmonary capillary blood flow calculated by the partial rebreathing technique is basically made up of the sum of all the partial blood flows passing through the various parts of the lung, where the contribution of each part depends on the actual ventilation/perfusion ratio ($\dot{V}/\dot{Q}$) applicable locally to that part. The contribution of any lung area where the $\dot{V}/\dot{Q}$ is much less than 1 will be less weighted in this sum of flows than contributions coming from areas where ventilation/perfusion ratios are equal to or larger than 1. However, our patients had quite a large part of the lung with $\dot{V}/\dot{Q}$ of ~0.5, i.e. with a normal alveolar ventilation but with twice as high circulation (17). The partial CO_2 rebreathing device may therefore indicate a somewhat higher pul-

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monary blood flow for our patients than would have been the case had our patients (with the same total pulmonary capillary blood flow) been characterized by ventilation/perfusion distribution based on the $\dot{V}/\dot{Q}=1$ (16). In patients with such a 'normal' ventilation/perfusion distribution, it is possible to make the most truthful comparison with thermodilution measurements of cardiac output. The addition of the true shunted flow (where $\dot{V}/\dot{Q}=0$) to the pulmonary capillary blood flow makes comparison with thermodilution cardiac output entirely feasible even for the less than ideal cases. However, the difference in the two concepts of cardiac output measurements must not be overlooked. The partial rebreathing technique of determining cardiac output focuses on the effective part of the cardiac output, meaning that only that portion of the blood flow that is actively involved in the gas exchange is taken fully into account.

The calculated shunt in the partial CO_2 rebreathing device is probably underestimated because the chosen default value for the arterial-mixed venous oxygen content difference is set at 50 mL/L, whereas the true a–$\bar{v}$ O_2 difference directly measured in 12 patients was markedly lower. Using this value instead of the default value, the estimated shunt would have been much closer to the true calculated shunt. To avoid an incorrect shunt calculation we suggest that the a–$\bar{v}$ O_2 difference should be calculated based on the carbon dioxide output measurement, the cardiac output calculation and a default value for the respiratory quotient of 0.85 using the following formula:

$$a-\bar{v}\ O_2 \text{ difference (mL/L)} = \dot{V}CO_2/(0.85 \times CO_{NICO})$$

If this a–$\bar{v}$ O_2 difference markedly differs from the used default value of 50 mL/min, a correcting of the shunt calculation should be performed. If this technique for correction of estimated shunt were applied in the present study, the estimated shunt would be higher and closer to the calculated shunt using arterial and mixed venous blood gases.

It is difficult to assess the effect of these different errors on the final cardiac output value of the studied device. The net effect seems very small, as the bias between the partial CO_2 rebreathing technique and thermodilution is as low as 40 mL/min. It can not be ruled out that these over- and underestimations are balancing each other by coincidence. Further evaluation of the influence of these factors may, however, lead to an increase in precision and stability of measurements.

Clinical applications

In the present study, the clinical application of the partial rebreathing technique was also assessed. It was observed that it is simple to initiate measurements and that the technique is easy to use without any previous experience. It is important that the patient is adequately sedated or anesthetized, tolerates controlled mechanical ventilation and that spontaneous breathing efforts are avoided. This restriction may be solved by new software for the device, which allows cardiac output measurements during more spontaneous modes of breathing. One of the major advantages is that the method is non-invasive and harmless to the patient. It affects the patient only by intermittently adding an extra dead space, which causes a transient rise in arterial CO_2 tension of about 10% of the initial value. This is negligible and rarely a problem, except possibly in patients with severe respiratory failure and hypercapnia or in patients with critically elevated intracranial pressure. It is also important that CO_2 body stores are stable during the measurements (9). This may probably explain variable results on cardiac output measurements with this technique obtained in cardiac surgery patients studied after their return from the OR (18). It is also unclear whether the technique is possible to use during laparoscopy and CO_2 insufflation.

In the present study it was observed that the absolute deviation between the two techniques (partial CO_2 rebreathing and thermodilution) was somewhat higher at higher cardiac output levels (Fig. 2). From a clinical point of view, however, it is crucial that the method is more accurate at low/normal cardiac output than at supra-normal levels (> 10 L/min).

This technique competes favorably with other non-invasive cardiac output techniques available. The transesophageal echo-Doppler technique with a similar correlation and precision as the NICO compared to thermodilution technique (3) has the disadvantage that frequent repositioning of the esophageal probe by a trained investigator may be needed (3), which makes it unsuitable for long-term clinical monitoring. The pulse contour method appears to be less precise than the partial CO_2 rebreathing technique, with wider limits of agreement (2SD = 2.5 L/min) at least in postsurgical cardiac patients (6). The disadvantage with this method is also the necessity for calibration using another method of cardiac output determination and the possible changes in calibration factors with changes in vascular tone (6).

In conclusion, this clinical evaluation shows that partial CO_2 rebreathing technique provides a useful non-invasive estimate of cardiac output in critically ill patients. It closely tracks changes in cardiac output in hemodynamically unstable patients. Further development of the underlying methodology such as shunt

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calculation appears to be possible. Improvement of the software for use in spontaneously breathing patients would also widen the use of the technique. Still, even if the technique can not fully replace the pulmonary artery catheter, it can be of great value in the monitoring of a large number of critically ill patients both in the OR and in the ICU.

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NONINVASIVE CARDIAC OUTPUT ASSESSMENT DURING HEART SURGERY

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Ceriana P, Maurelli M, Braschi A, Baiardi P, De Amici D. Noninvasive cardiac output assessment during heart surgery.
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ABSTRACT. Objective. To evaluate the reliability of a new noninvasive method for the assessment of cardiac output with the partial carbon dioxide rebreathing technique. **Methods.** This technique was applied to patients undergoing heart surgery. Values of cardiac index obtained with this equipment were compared with the artero-venous CO_2 gradient, a reliable index of cardiovascular status. Positive and negative predictive values of the test were assessed. **Results.** A total of 21 simultaneous measurement of the cardiac index and of the artero-venous CO_2 gradient were obtained. The positive predictive value of the test was 67% while the negative predictive value was 100%, indicating that a normal value of cardiac index recorded with the rebreathing technique predicts with a good reliability a normal cardiovascular state. **Conclusions.** Working through a series of mathematical algorithms, accuracy in the computation of cardiac output can be decreased with this equipment; however, this limitation seems to be outweighed by the simplicity and noninvasive nature of the methods.

KEY WORDS. Carbon dioxide, rebreathing, cardiac output, noninvasive.

INTRODUCTION

The continuous search for new monitoring tools capable of acquiring signals of vital functions in a noninvasive way has stimulated the biomedical research to release innovative equipments; at present three systems can measure cardiac output in a non-invasive way: a) the bio-impedance, b) the ultrasound method (echo scan + doppler effect), c) the partial CO_2 rebreathing technique.

This last method is based on the fact that pulmonary blood flow is proportional to the ratio between CO_2 production and arterial-mixed venous CO_2 content difference and employs a modified form of the Fick equation for CO_2 [1] that estimates total non-shunted pulmonary capillary blood flow as the ratio between changes of CO_2 elimination rate and end-tidal CO_2 in response to a short period of rebreathing. The most innovative aspect is the assumption that during this period of rebreathing venous CO_2 content does not change and thus can be omitted.

A recently introduced instrument (NICO, Novametrix Medical System, Wallingford, CT) performs a continuous noninvasive determination of cardiac output by means of the abovementioned technique; it has already been used in the clinical setting and compared with the standard method of thermodilution with rather conflicting results [2, 3]: in fact some authors

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found a fair correlation between the two methods, while other authors did not.

Purpose of the present study is to assess the reliability of this instrument for the evaluation of cardiac index in patients undergoing open-heart procedures.

METHODS

a) The equipment

The NICO instrument controls a valve that allows partial rebreathing of expired gas; a combination flow and CO_2 sensor is positioned between the tracheal tube and the Y-piece of the respiratory circuit. The sensor and valve assembly automatically introduces a certain amount of series deadspace for 50 seconds every 3 minutes.

Furthermore, this equipment gives an estimate of alveolar dead space from the alveolar-arterial CO_2 difference, provided that the operator introduces the arterial CO_2 value with an arterial blood sample. An estimate of shunt fraction is given by the instrument according to the Nunn's nomogram [4], by computing oxygen saturation with pulse oxymetry and inspired oxygen fraction (inserted by the operator). Finally, the haemoglobin blood level must be inserted too, since the machine employs the CO_2 dissociation curve for the computation of pulmonary capillary blood flow.

b) Study design

The first step was the choice of a reference technique with which to compare the data obtained with the CO_2 rebreathing technique. As we mentioned in the introduction section, thermodilution was excluded having already been tested by other authors with conflicting results, furthermore, we considered it more appropriate, even from a conceptual point of view, to compare with another non invasive technique.

Therefore, our choice was the artero-venous CO_2 (ΔAV) gradient, obtained by subtracting the arterial CO_2 value from the central venous value provided that the two samples of blood are simultaneously drawn: this parameter has a close "physiological" affinity with the methodology of CO_2 rebreathing, is non invasive (since venous CO_2 does not need to be sampled from the pulmonary artery) and has been validated [5] as a reliable indicator of the cardiovascular status. In practice, when the patient has a $\Delta AV \leq 6$ mmHg he has a satisfactory cardiovascular status and when the value is > 6 mmHg its cardiovascular function is poor.

c) Patients

Our group consisted of 10 patients who gave their consent to the study: 9 males and 1 female with a mean age of 63.9 years. The planned surgical procedure was coronary artery bypass graft (3 cases), aortic valve replacement (5 cases) or these two associated procedures (2 cases). Anaesthesia was induced and maintained with a triple regimen including propofol-sufentanyl-cisatracurium in continuous infusion through a central venous catheter, while monitoring included electrocardiogram (two leads), pulseoximetry, invasive arterial blood pressure, capnography and body temperature. Upon the institution of mechanical ventilation (Servo 900 C, Siemens) in pressure-controlled mode, in order to achieve an expired tidal volume of 10 ml/kg, non-invasive cardiac output monitoring with NICO was started.

Our protocol included the recording of cardiac output (indexed to body surface area) and ΔAV twice for every patient during the course of the operation: the first time before cardiopulmonary bypass (CPB) and the second time after CPB, during phases of cardiovascular stability, without any surgical manipulation that could alter myocardial performance. Both measurements were taken during the interval between two rebreathing cycles. ΔAV was assessed with two simultaneous samples from the radial artery and the central venous catheter. The samples were promptly analyzed with a blood gas analyzer (ABL 4, Radiometer, Copenhagen); the value of end-tidal CO_2 was recorded while the arterial blood was drawn in order to validate a simultaneous alveolar-arterial gradient. The cardiovascular status was considered satisfactory when the patient had a cardiac index 2.2 l/min/m^2 or an artero-venous CO_2 gradient ≤ 6 mmHg.

d) Data analysis

In order to verify how reliably this new equipment could assess cardiac output, the recorded values, cardiac index and ΔAV, were plotted on a two-axis graph, and two perpendicular lines were drawn at the threshold of normality for each parameter, in order to obtain four frames. Then the positive predictive value and the negative predictive value of the test, together with their 95% confidence intervals were calculated.

RESULTS

A total of twenty-one simultaneous measurements of the

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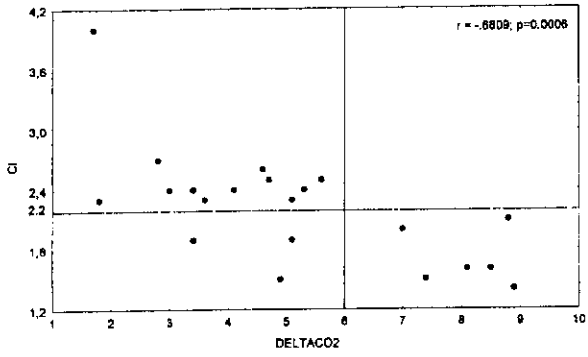

Fig. 1. Simultaneous measurements of cardiac index and artero-venous CO_2 gradient are divided in four frames by two perpendicular lines drawn at the threshold of normality for each parameter. The majority of these points are in the two frames where the two parameters measure in the same direction: upper left frame = normal cardiac output; lower right frame = low cardiac output.
Legend: A–V CO_2 gradient = artero-venous CO_2 gradient expressed in mmHg. CI = cardiac index expressed in l/min/m^2.

cardiac index and of the artero-venous CO_2 gradient were obtained and were plotted in Figure 1. The positive predictive value of the test was 67% (confidence interval 95% = 47–87%) while the negative predictive value was 100%; the test turned out to have an accuracy of 86% (confidence interval 95% = 71–100%). With respect to the alveolar-arterial CO_2 gradient, a mean value of 2.7 ± 0.8 mmHg has been recorded.

COMMENT

As reported in Figure 1, we can see that the great majority of the points (18/21, 86%) measure in the same directions, i.e. they are in the two frames of low or fair cardiac output, respectively, while only three points fall in a frame where the two parameters measure in opposite directions. In essence, given the assumption that the ΔAV is a reliable indicator of the cardiovascular status, although not in a quantitative manner, we can see that in the majority of cases the value of cardiac index recorded with the rebreathing method is in accordance with it and gives the physician a valuable piece of information regarding the patient's cardiovascular function.

It is noteworthy the negative predictive value of 100%: so a normal value of cardiac index recorded with the rebreathing technique predicts with a high degree of reliability a good cardiovascular state; on the other hand, when the instrument releases a low value, a further verification is needed.

In summary, this equipment calculates cardiac output noninvasively through a series of mathematical algorithms, and it is likely that a certain amount of accuracy can be lost. This limitation is in our opinion outweighed by the simple, non-invasive nature of the method.

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Effect of Ventilatory Settings on Accuracy of Cardiac Output Measurement Using Partial CO_2 Rebreathing

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Background: **Recently, a new device has been developed to measure cardiac output noninvasively using partial carbon dioxide (CO_2) rebreathing. Because this technique uses CO_2 rebreathing, the authors suspected that ventilatory settings, such as tidal volume and ventilatory mode, would affect its accuracy: they conducted this study to investigate which parameters affect the accuracy of the measurement.**

Methods: **The authors enrolled 25 pharmacologically paralyzed adult post–cardiac surgery patients. They applied six ventilatory settings in random order: (1) volume-controlled ventilation with inspired tidal volume (V_T) of 12 ml/kg; (2) volume-controlled ventilation with V_T of 6 ml/kg; (3) pressure-controlled ventilation with V_T of 12 ml/kg; (4) pressure-controlled ventilation with V_T of 6 ml/kg; (5) inspired oxygen fraction of 1.0; and (6) high positive end-expiratory pressure. Then, they changed the maximum or minimum length of rebreathing loop with V_T set at 12 ml/kg. After establishing steady-state conditions (15 min), they measured cardiac output using CO_2 rebreathing and thermodilution *via* a pulmonary artery catheter. Finally, they repeated the measurements during pressure support ventilation, when the patients had restored spontaneous breathing. The correlation between two methods was evaluated with linear regression and Bland-Altman analysis.**

Results: **When V_T was set at 12 ml/kg, cardiac output with the CO_2 rebreathing technique correlated moderately with that measured by thermodilution ($y = 1.02x$, $R = 0.63$; bias, 0.28 l/min; limits of agreement, −1.78 to +2.34 l/min), regardless of ventilatory mode, oxygen concentration, or positive end-expiratory pressure. However, at a lower V_T of 6 ml/kg, the CO_2 rebreathing technique underestimated cardiac output compared with thermodilution ($y = 0.70x$; $R = 0.70$; bias, −1.66 l/min; limits of agreement, −3.90 to +0.58 l/min). When the loop was fully retracted, the CO_2 rebreathing technique overestimated cardiac output.**

Conclusions: **Although cardiac output was underreported at small V_T values, cardiac output measured by the CO_2 rebreathing technique correlates fairly with that measured by the thermodilution method.**

ALTHOUGH there is controversy over the cost benefit of pulmonary artery catheterization,[1,2] cardiac output (CO) is commonly monitored when treating critically ill patients. Recently, a new device, the $NICO_2$ system (Novametrix Medical Systems Inc., Wallingford, CT), has been developed to measure CO noninvasively using partial carbon dioxide (CO_2) rebreathing.[3,4] This device uses periodic partial CO_2 rebreathing to create a CO_2 disturbance, which is then used in a differential Fick CO_2 equation to calculate CO.[3]

There have been few studies to investigate how well the results obtained by CO_2 rebreathing correlate with those obtained by the conventional thermodilution technique.[5–7] Furthermore, it remains to be clarified which ventilatory or hemodynamic parameters affect the measured values when the CO_2 rebreathing technique is used. Because noninvasive CO measurement depends on CO_2 rebreathing and assumes constant dead space and mixed venous CO_2 content through the CO_2 rebreathing procedure,[3,4] we suspected that change in ventilatory settings might affect accuracy of the CO measurement. Consequently, we performed a prospective comparative study to evaluate the effects of tidal volume (V_T), ventilatory mode, inspired oxygen fraction (F_{IO_2}), and positive end-expiratory pressure (PEEP) on the accuracy of the measurement. The $NICO_2$ system uses a rebreathing loop in which volume is adjustable according to tidal volume. We suspected that a too-short loop may affect the accuracy due to poor signal-to-noise ratio. Therefore, we investigated, as a factor of the machine itself, the effect of adjusting the length of the rebreathing loop.

Subjects and Methods

The study was approved by the institutional ethics committee of the National Cardiovascular Center (Osaka, Japan), and written informed consent was obtained from each patient.

Patients

Twenty-five adult patients aged 48–78 yr (median, 61 yr) who had undergone cardiac surgery (table 1) were enrolled in this study. Enrollment criteria were (1) insertion of a Swan-Ganz catheter; (2) stable hemodynamics in the intensive care unit; and (3) no leakage around the endotracheal tube. We excluded candidates who (1) had central nervous system disorders; (2) might be adversely affected by induced hypercapnia (risk of severe pulmonary hypertension or increased intracranial pressure); or (3) demonstrated severe tricuspid regurgitation on intraoperative examination of transesophageal echocardiography, which interferes with the accuracy of thermodilution CO measurement. Arterial blood pressure, heart rate, pulmonary artery pressure, central venous pressure, and pulse oximeter signal (PM-1000; Nellcor Inc., Hayward, CA) were continuously monitored in all pa-

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Table 1. Patient Profile

No. of patients	25
M/F	19/6
Age (yr)	61 ± 9
Height (cm)	163 ± 7
Body Weight (kg)	63 ± 11
Background diseases	
Coronary artery disease	11
Acquired valve disease	8
Thoracic aortic aneurysm or dissection	4
Miscellaneous	2

tients. After waiting 1–3 h for hemodynamics to stabilize after surgery, we started the measurements.

Measurements

We measured CO using two methods. Values for CO derived from a thermodilution technique (CO_{TD}) were obtained using a Swan-Ganz catheter (7.5 French; Abbott Laboratories, North Chicago, IL). Injection of 10 ml cold saline (0°C) was performed in triplicate, and the values were averaged. Because the CO measurement varies depending on when in the respiratory cycle the measurement is initiated,[8] we standardized the timing of bolus injection after the first half of the expiratory phase. We confirmed the injection timing by watching the waveform of airway pressure *versus* time on the graphic monitor of a ventilator (Bird Corp., Palm Springs, CA). Noninvasive measurement of CO (CO_{NI}) was performed with a $NICO_2$ system (software version 3.1, fast mode). This procedure has been presented in detail elsewhere.[3,4] Briefly, on a breath-by-breath basis, CO_2 production ($\dot{V}co_2$) is calculated from the flow and CO_2 concentration at the airway opening. Then, to establish the relation between $\dot{V}co_2$ and CO, the Fick principle is applied as follows:

$$\dot{V}co_2 = CO \times (C\bar{v}co_2 - Caco_2), \quad (1)$$

where $C\bar{v}co_2$ and $Caco_2$ represent the CO_2 content in mixed venous and arterial blood, respectively. In the $NICO_2$ system, CO_2 rebreathing is performed for 50 s every 3 min using a disposable sensor (Novametrix Medical Systems). A brief period of CO_2 rebreathing caused a change in $Paco_2$ and a change in $\dot{V}co_2$ but little or no change in $C\bar{v}co_2$ in anesthetized dogs,[3] probably because the quantity of CO_2 stores in the body is large, and new equilibrium levels are attained after 20–30 min.[9] Assuming that CO and $C\bar{v}co_2$ remain constant during the CO_2 rebreathing procedure, the following equation can be substituted for the previous one:

$$\Delta\dot{V}co_2 = CO \times (-\Delta Caco_2), \quad (2)$$

where $\Delta\dot{V}co_2$ is the change in $\dot{V}co_2$ between normal breathing and CO_2 rebreathing, and $\Delta Caco_2$ is the change in arterial CO_2 content. Assuming here that dead space fraction (V_D/V_T) remains constant during the CO_2 rebreathing and that $\Delta Caco_2$ is proportional to changes in arterial carbon dioxide pressure ($Paco_2$) and end-tidal CO_2 pressure ($PETco_2$), the following equation can be plotted:

$$CO = \Delta\dot{V}co_2/S \times \Delta PETco_2, \quad (3)$$

where $\Delta PETco_2$ is the change in $PETco_2$ between normal breathing and CO_2 rebreathing, and S is the slope of the CO_2 dissociation curve from hemoglobin. The constant S can be expressed as a function of hemoglobin concentration and $Paco_2$ as follows[3]:

$$S = (1.34 \times [Hb] + 18.34)/(1 + 0.193 \times Paco_2)$$

$$[ml\ CO_2 \cdot l^{-1}\ blood \cdot mmHg^{-1}], \quad (4)$$

where [Hb] is hemoglobin concentration.

Before the start of the study protocol, the $NICO_2$ system was calibrated for zero CO_2 by opening the system to the atmosphere, according to the manufacturer's instructions. We entered the results of arterial oxygen pressure (Pao_2), $Paco_2$, Fio_2 (0.4–0.7), and hemoglobin concentrations (7.9–11.9 g/dl) into the machine when each patient was under the baseline ventilation. Inclusion of these parameters is used to calculate shunt fraction (Pao_2 and Fio_2), alveolar dead space ($Paco_2$), and the slope of the CO_2 dissociation curve (hemoglobin).[3,4]

Study Protocol

We used Bird 8400*STi* ventilators (Bird Corp.). At the time of admission to the intensive care unit, initial ventilatory settings were as follows: synchronized intermittent mandatory ventilation mode; volume-controlled ventilation (VCV); inspired V_T of 10 ml/kg; decelerating flow pattern; respiratory rate of 10–12 breaths/min; and inspiratory time of 1.0 s. The Fio_2 was adjusted by attending physicians to maintain a Pao_2 greater than 100 mmHg. Baseline PEEP was set at 4 cm H_2O in 23 patients; because of hypoxemia, the remaining 2 patients needed PEEP of 6 and 8 cm H_2O, respectively. With the patients maintained in the supine position, sedated with continuous intravenous injection of propofol (2–3 mg · kg^{-1} · h^{-1}), and paralyzed with bolus administration of vecuronium bromide (4–8 mg), we started the measurement protocol.

In random order, we applied six ventilatory settings to all of the 25 patients, and then we applied three additional settings in a fixed order (table 2). To test the effects of ventilatory mode and V_T, we chose VCV with inspired V_T of 12 or 6 ml/kg and pressure-controlled ventilation (PCV) with the same V_T settings. The Fio_2 and respiratory rate were fixed identical to baseline. The PEEP was also fixed identical to the baseline measurement (4 cm H_2O in 23 patients, 6 cm H_2O in 1, and 8 cm H_2O in 1). The inspiratory time was set to 1.0 s for both VCV and PCV. The level of pressure control was adjusted

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Table 2. Ventilatory Settings

Ventilatory mode	VCV	VCV	PCV	PCV	VCV	VCV	VCV	VCV	PSV
Inspired tidal volume (ml/kg)	12	6	12	6	12	12	12	12	8.8
F_{IO_2}	0.5	0.5	0.5	0.5	1.0	0.5	0.5	0.5	0.5
PEEP*	4	4	4	4	4	15	4	4	4
Rebreathing loop	†	†	†	†	†	†	Long (400 ml)	Short (150 ml)	†
No. of patients	25	25	25	25	25	25	17	17	23

Median values are presented for fraction of inspired oxygen (F_{IO_2}) and positive end-expiratory pressure (PEEP).

VCV = volume-controlled ventilation; PCV = pressure-controlled ventilation; PSV = pressure-support ventilation.

* In two patients, PEEP of 6 and 8 cm H_2O was used because of hypoxemia. † The rebreathing loop was sized according to the manufacturer's instructions recommended for set tidal volume of 12 ml/kg.

to obtain the same V_T during VCV. The rebreathing loop was sized according to the manufacturer's instructions recommended for a set V_T of 12 ml/kg. To examine the effects of F_{IO_2}, we increased the F_{IO_2} to 1.0 with VCV and 12 ml/kg V_T. To examine the effects of high PEEP, we increased PEEP to 12–15 cm H_2O with VCV and 12 ml/kg V_T, depending on the patient's hemodynamic stability. The order of these six conditions was randomized. Then, to examine the effects of varying the length of the rebreathing loop, in 17 patients, measurements were performed with the loop maximally expanded (400 ml) or fully retracted (150 ml) while VCV and 12 ml/kg V_T were used. After the measurements were completed, vecuronium infusion was stopped. When the patient recovered stable spontaneous breathing, we switched the ventilatory mode to continuous positive airway pressure of 4 cm H_2O plus pressure-support ventilation (PSV) of 10 cm H_2O.

After establishing steady-state conditions (approximately 15 min) at each setting, we measured both CO_{NI} and CO_{TD}. We limited ourselves perform only nine measurements (one measurement for each ventilatory setting) per patient. Arterial blood samples were analyzed with a calibrated blood gas analyzer (ABL 505; Radiometer, Copenhagen, Denmark). Hemodynamic data were also recorded. V_D/V_T and venous admixture fraction

Table 3. Respiratory and Hemodynamic Parameters at Each Ventilatory Setting

Ventilatory Setting	VCV Large V_T	VCV Small V_T	PCV Large V_T	PCV Small V_T	VCV F_{IO_2} 1.0	VCV High PEEP	VCV Long Loop	VCV Short Loop	PSV
V_T (ml/kg)	13.0 ± 0.6	6.9 ± 0.9*	13.2 ± 0.8	6.9 ± 0.9*	12.9 ± 0.7	13.2 ± 0.7	13.1 ± 0.8	13.1 ± 0.8	8.8 ± 2.6†
$\dot{V}_E$ (l · min^{-1} · kg^{-1})	0.13 ± 0.01	0.07 ± 0.02*	0.13 ± 0.01	0.07 ± 0.02*	0.13 ± 0.01	0.13 ± 0.01	0.13 ± 0.01	0.13 ± 0.01	0.14 ± 0.04
PIP (cm H_2O)	27.5 ± 5.8	17.0 ± 3.5	27.0 ± 6.4	16.4 ± 3.9	27.2 ± 5.8	36.6 ± 7.1	26.9 ± 7.1	26.9 ± 7.0	15.2 ± 2.7
PEEP (cm H_2O)	4.2 ± 0.9	4.2 ± 0.9	4.2 ± 0.9	4.2 ± 0.9	4.2 ± 0.9	14.0 ± 1.7	4.4 ± 1.1	4.4 ± 1.1	4.1 ± 0.4
pH	7.45 ± 0.04	7.32 ± 0.04*	7.44 ± 0.05	7.31 ± 0.03*	7.42 ± 0.04	7.44 ± 0.05	7.42 ± 0.05	7.45 ± 0.04	7.39 ± 0.05
$Paco_2$ (mmHg)	37.7 ± 5.4	55.2 ± 6.8*	39.2 ± 6.4	56.1 ± 6.4*	40.4 ± 6.4	38.8 ± 7.5	40.5 ± 7.8	36.6 ± 7.1	43.6 ± 5.9
P/F	292 ± 87	239 ± 69	299 ± 88	238 ± 58	376 ± 87‡	357 ± 113‡	324 ± 95	330 ± 94	275 ± 87
Lactate (mM)	2.0 ± 1.2	1.9 ± 1.2	2.1 ± 1.2	1.9 ± 1.1	1.9 ± 1.1	2.0 ± 1.0	2.0 ± 0.9	2.1 ± 1.0	2.1 ± 1.2
CO_{TD} (l/min)	5.24 ± 1.45	5.69 ± 1.58	5.23 ± 1.56	5.87 ± 1.79	5.10 ± 1.50	4.46 ± 1.45	5.34 ± 1.67	5.19 ± 1.33	5.43 ± 1.40
CO_{NI} (l/min)	5.41 ± 1.36	4.02 ± 1.00§	5.60 ± 1.40	4.23 ± 1.36‖	5.30 ± 1.45	4.82 ± 1.24	5.81 ± 1.58	6.49 ± 1.58	5.95 ± 1.38
$\dot{V}co_2$ (ml · min^{-1} · kg^{-1})	3.0 ± 0.3	2.0 ± 0.4*	3.1 ± 0.5	2.2 ± 0.5*	3.1 ± 0.4	3.0 ± 0.4	3.2 ± 0.5	3.0 ± 0.5	3.2 ± 0.9
$PETco_2$ (mmHg)	34.5 ± 3.8	49.9 ± 6.8*	35.4 ± 4.9	50.4 ± 6.1*	35.7 ± 4.7	34.7 ± 4.9	36.7 ± 5.3	34.6 ± 4.8	42.4 ± 7.4#
V_D/V_T	0.43 ± 0.09	0.50 ± 0.10**	0.43 ± 0.10	0.45 ± 0.13	0.45 ± 0.09	0.43 ± 0.09	0.43 ± 0.11	0.41 ± 0.12	0.53 ± 0.17
$\dot{Q}_S/\dot{Q}_T$	0.05 ± 0.03	0.10 ± 0.07	0.06 ± 0.04	0.10 ± 0.04	0.03 ± 0.03	0.04 ± 0.03	0.05 ± 0.04	0.06 ± 0.03	0.07 ± 0.05
HR (beats/min)	92 ± 7	95 ± 9	93 ± 8	95 ± 9	94 ± 8	92 ± 9	92 ± 9	91 ± 8	94 ± 8
BP (mmHg)	79 ± 9	77 ± 10	77 ± 10	77 ± 12	79 ± 11	74 ± 11	76 ± 8	77 ± 9	79 ± 11
PA (mmHg)	19.3 ± 5.6	25.3 ± 7.8	18.6 ± 5.5	24.6 ± 5.8	19.0 ± 6.1	21.3 ± 5.5	20.2 ± 6.6	19.6 ± 6.0	20.1 ± 5.7
CVP (mmHg)	7.9 ± 2.5	9.6 ± 3.5	7.5 ± 2.7	9.4 ± 3.3	7.6 ± 2.6	10.4 ± 2.4††	7.6 ± 2.9	7.7 ± 2.3	8.6 ± 3.0
PCWP (mmHg)	9.8 ± 2.2	11.5 ± 3.9	9.6 ± 2.5	11.8 ± 2.8	10.1 ± 2.5	11.8 ± 2.1	10.2 ± 2.8	10.0 ± 2.5	10.4 ± 3.8
PVR (dyn · s · cm^{-5})	158 ± 89	212 ± 120	153 ± 100	194 ± 111	149 ± 93	185 ± 105	167 ± 108	161 ± 102	157 ± 84
SVR (dyn · s · cm^{-5})	1,162 ± 372	997 ± 243	1,145 ± 379	974 ± 216	1,191 ± 315	1,237 ± 405	1,106 ± 335	1,126 ± 302	1,101 ± 320
$S\bar{v}o_2$ (%)	72 ± 7	73 ± 7	73 ± 7	73 ± 7	79 ± 6‡‡	70 ± 8	73 ± 7	72 ± 6	72 ± 7

* $P < 0.05$ *versus* volume-controlled ventilation (VCV)–large tidal volume (V_T), pressure-controlled ventilation (PCV)–large V_T, fraction of inspired oxygen (F_{IO_2}) 1.0, high positive end-expiratory pressure (PEEP), long loop, short loop, and pressure-support ventilation (PSV). † $P < 0.05$ *versus* other ventilatory settings. ‡ $P < 0.05$ *versus* VCV–small V_T, PCV–small V_T, and PSV. § $P < 0.05$ *versus* VCV–large V_T, PCV–large V_T, F_{IO_2} 1.0, long loop, short loop, and PSV. ‖ $P < 0.05$ *versus* PCV–large V_T, long loop, short loop, and PSV. # $P < 0.05$ *versus* VCV–large V_T, VCV–small V_T, PCV–large V_T, PCV–small V_T, F_{IO_2} 1.0, high PEEP, and short loop. ** $P < 0.05$ *versus* VCV–large V_T and short loop. †† $P < 0.05$ *versus* PCV–large V_T and F_{IO_2} 1.0. ‡‡ $P < 0.05$ *versus* VCV–large V_T, PCV–large V_T, high PEEP, and PSV.

$\dot{V}_E$ = minute ventilation; PIP = peak inspiratory pressure; $Paco_2$ = arterial carbon dioxide tension; P/F = ratio of arterial oxygen tension to F_{IO_2}; CO_{TD} = cardiac output with thermodilution; CO_{NI} = cardiac output with carbon dioxide rebreathing; $\dot{V}co_2$ = carbon dioxide production; $PETco_2$ = end-tidal carbon dioxide pressure; V_D/V_T = dead-space fraction; $\dot{Q}_S/\dot{Q}_T$ = venous admixture fraction; HR = heart rate; BP = mean artery pressure; PA = mean pulmonary artery pressure; CVP = central venous pressure; PCWP = pulmonary capillary wedge pressure; PVR = pulmonary vascular resistance; SVR = systemic vascular resistance; $S\bar{v}o_2$ = mixed venous oxygen saturation.

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Table 4. Results of Bland-Altman Analysis and Regression Analysis

Ventilatory Setting	VCV Large V_T	VCV Small V_T	PCV Large V_T	PCV Small V_T	VCV F_{IO_2} 1.0	VCV High PEEP	VCV Long Loop	VCV Short Loop	PSV
Bias (l/min)	0.18	−1.67	0.37	−1.64	0.19	0.37	0.48	1.30	0.52
Precision (l/min)	1.04	1.06	1.17	1.19	1.12	0.81	1.27	1.15	1.02
Limits of agreement (l/min)	−1.90 to +2.26	−3.79 to +0.45	−1.97 to +2.71	−4.02 to +0.74	−2.05 to +2.43	−1.25 to +1.99	−2.06 to +3.02	−1.00 to +3.60	−1.52 to +2.56
Slope of linear regression	1.01	0.69	1.04	0.71	1.01	1.05	1.05	1.23	1.07
Correlation coefficient (R)	0.63	0.66	0.50	0.72	0.62	0.72	0.54	0.61	0.63

VCV = volume-controlled ventilation; PCV = pressure-controlled ventilation; PSV = pressure-support ventilation; V_T = tidal volume; F_{IO_2} = fraction of inspired oxygen; PEEP = positive end-expiratory pressure.

($\dot{Q}_S/\dot{Q}_T$) were calculated using the following equations[10,11]:

$$V_D/V_T = 1 - (0.863 \cdot \dot{V}co_2)/(\dot{V}_E \cdot Paco_2) \quad (5)$$

and

$$\dot{Q}_S/\dot{Q}_T = (Cc'o_2 - Cao_2)/(Cc'o_2 - C\bar{v}o_2), \quad (6)$$

where $\dot{V}_E$ is minute ventilation, $Cc'o_2$ is oxygen content at the pulmonary capillary, Cao_2 is arterial oxygen content, and $C\bar{v}o_2$ is mixed venous blood oxygen content. Assuming that pulmonary capillary blood is fully saturated with oxygen and that oxygen content is roughly proportional to oxygen saturation, the second equation can be revised as follows:

$$\dot{Q}_S/\dot{Q}_T = (1 - Sao_2)/(1 - S\bar{v}o_2), \quad (7)$$

where Sao_2 and $S\bar{v}o_2$ are oxygen saturation at the artery and mixed venous blood, respectively.

Statistical Analysis

Data are presented as mean ± SD. Using analysis of variance with repeated measures, mean values were compared across different settings. When significance was observed, the mean values were tested by multiple comparison with the Bonferroni correction. We evaluated the correlation between CO_{NI} and CO_{TD} with linear regression and Bland-Altman analysis.[12,13] To investigate which parameters contributed to the discrepancy between CO_{NI} and CO_{TD}, we also performed linear multiple regression analysis among F_{IO_2}, V_T, V_E, PEEP, peak inspiratory pressure, pH, Pao_2, $Paco_2$, $PETco_2$, $\dot{V}co_2$, and $S\bar{v}o_2$. Statistical significance was set at $P < 0.05$.

Results

Blood gas and hemodynamic results are summarized in table 3. Minute ventilation was stable at all 12-ml/kg V_T settings. Regardless of ventilatory mode, the 6-ml/kg V_T settings resulted in higher $Paco_2$, higher $PETco_2$, and less $\dot{V}co_2$, compared with the 12-ml/kg V_T settings. During PSV, V_T values (8.8 ± 2.6 ml/kg) decreased to between those for 12- and 6-ml/kg V_T settings, whereas minute ventilation was similar to that at the 12-ml/kg V_T settings. CO_{TD} values were similar at each 12-ml/kg V_T setting, although CO_{TD} values at the 6-ml/kg V_T settings were slightly larger in comparison. At high PEEP, CO_{TD} values were lower.

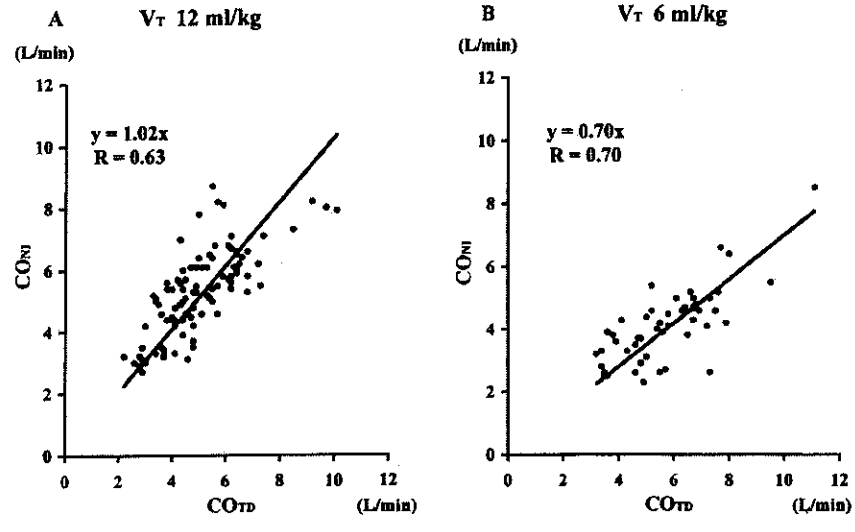

Fig. 1. Agreement between cardiac output measurements obtained by carbon dioxide rebreathing (CO_{NI}) and those obtained by thermodilution technique (CO_{TD}). (*A*) Large tidal volumes (V_T, 12 ml/kg) during both volume-controlled ventilation and pressure-controlled ventilation. (*B*) Same modes, but with small tidal volumes (6 ml/kg). Equations and result curves for linear regression analysis are also shown.

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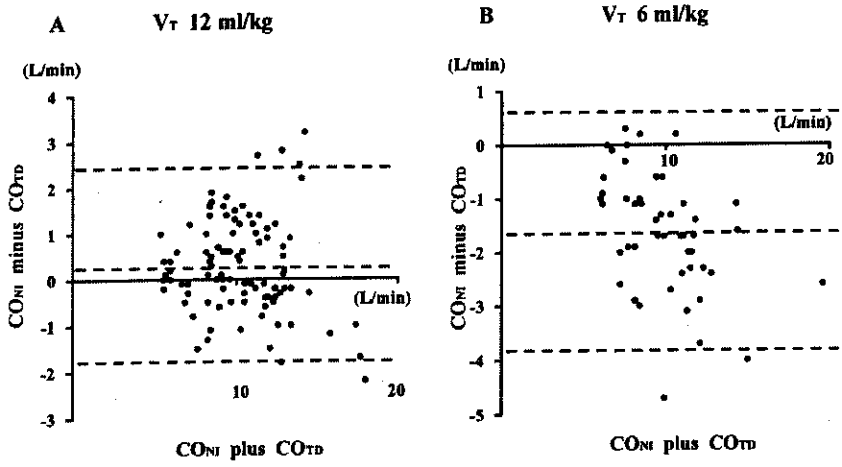

Fig. 2. Bias analysis between cardiac output measurements obtained by carbon dioxide rebreathing (CO_{NI}) and one those obtained by thermodilution technique (CO_{TD}). (*A*) Large tidal volumes (V_T; 12 ml/kg) during both volume-controlled ventilation and pressure-controlled ventilation. (*B*) Same modes, but with small tidal volumes (6 ml/kg). Dotted lines show bias and limits of agreement between the two methods.

Levels of pressure control were 24 ± 7 (16–36) cm H_2O with inspired V_T of 12 ml/kg and 13 ± 4 (8–22) cm H_2O with V_T of 6 ml/kg. As a result, there was no difference in peak inspiratory pressure for VCV and PCV at either V_T setting (table 3).

Results of Bland-Altman analysis and linear regression analysis are shown in table 4 for each ventilatory setting. When V_T values were the same, Bland-Altman analysis characteristics between CO_{TD} and CO_{NI} were almost identical (bias and precision: 12-ml/kg V_T VCV, 0.18 and 1.04; 12-ml/kg V_T PCV, 0.37 and 1.17; 6-ml/kg V_T VCV, −1.67 and 1.06; and 6-ml/kg V_T PCV, −1.64 and 1.19, table 4). Consequently, for the same V_T values, CO data during both VCV and PCV were analyzed together.

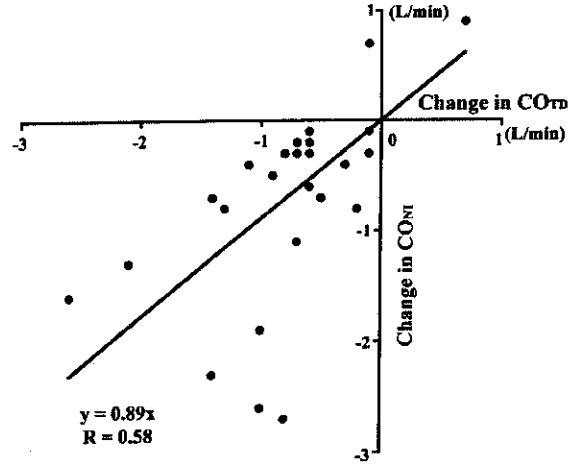

Fig. 3. Relation between changes in cardiac output measurements obtained by thermodilution technique and those obtained by carbon dioxide rebreathing when positive end-expiratory pressure was increased. Ventilatory settings are volume-controlled and 12 ml/kg tidal volume. When positive end-expiratory pressure was increased from 4.2 to 14.0 cm H_2O in average, cardiac output measurements obtained both by thermodilution technique and by carbon dioxide rebreathing decreased in almost all patients. Each point corresponds to a different patient. Note that both values moved in identical directions in all patients but one. Equations and result curves for linear regression analysis are also shown.

When V_T was 12 ml/kg, a fair correlation was observed between CO_{NI} and CO_{TD} (fig. 1). The slope of linear regression was 1.02 (R = 0.63, fig. 1), and bias was small (0.28 l/min, fig. 2), although limits of agreement were wide (−1.78 to +2.34 l/min, fig. 2). This is the case with ventilatory setting of high F_{IO_2} or high PEEP (table 4). By contrast, when V_T was small (6 ml/kg), the CO_{NI} underestimated the CO_{TD} with a slope of 0.70 (fig. 1), a bias of −1.66 l/min, and limits of agreement of −3.9 to +0.58 l/min (fig. 2). During PSV, the correlation between CO_{NI} and CO_{TD} was also close to identical (slope = 1.07, R = 0.63, bias = 0.52 l/min, table 4). With the loop maximally expanded, the CO_{NI} correlated moderately with CO_{TD} (slope = 1.05, bias = 0.48, table 4); however, with the loop fully retracted, CO_{NI} overestimated CO_{TD} (slope = 1.23, bias = 1.30, table 4). Linear multiple regression analysis revealed that the setting most affecting the discrepancy between CO_{NI} and CO_{TD} was minute ventilation (R = 0.616).

Figure 3 shows a relation between changes in CO_{TD} and those in CO_{NI} when PEEP was increased during VCV and 12-ml/kg V_T. When average PEEP was increased from 4.2 to 14.0 cm H_2O, both CO_{TD} and CO_{NI} decreased. Both values moved in identical directions in all patients but one. The value of CVP increased from 7.9 ± 2.5 to 10.4 ± 2.4 mmHg at higher PEEP, and pulmonary capillary wedge pressure also increased from 9.8 ± 2.2 to 11.8 ± 2.1 mmHg (table 3).

Discussion

The main findings of this study are as follows. (1) During mechanical ventilation with large constant V_T or during PSV, CO measurements obtained by CO_2 rebreathing technique correlate with those obtained by thermodilution method. (2) When minute ventilation is large, the accuracy of the CO_2 rebreathing technique is not affected by a selection of VCV, PCV, spontaneous breathing (PSV), PEEP, or F_{IO_2}. (3) When V_T and minute ventilation are reduced, the CO_2 rebreathing technique

underreports CO. (4) CO measurements are accurate when the rebreathing loop is maximally expanded but is overestimated when the loop is fully retracted.

Clinical Implications

Using partial CO_2 rebreathing, CO can be measured noninvasively.[3,4] However, there have been few clinical reports, on the accuracy of this technique.[5-7] We need to confirm that it provides effective monitoring for critically ill patients and discover parameters that might affect accuracy. Our results suggest that at a large V_T setting and with constant minute ventilation, CO measurements obtained from this technology correlate fairly with those from the thermodilution method. When inspired V_T is set at 12 ml/kg and respiratory rate is set at 10-12 breaths/min, which results in an actual minute ventilation of 0.13-0.14 $l \cdot min^{-1} \cdot kg^{-1}$, the linear regression slopes for CO_{NI} and CO_{TD} were almost identical (1.01:1.05). Bias analysis also indicated small bias and moderate precision (fig. 2), while accuracy was consistent regardless of ventilatory mode (VCV or PCV), PEEP, or F_{IO_2}. Correlation of results from CO_{NI} and CO_{TD} was also satisfactory during PSV (table 4). These observations suggest that this CO_2 rebreathing technique is reliable both with large constant V_T and during PSV. In addition, because the maximally expanded loop did not affect accuracy (table 4), rather than it being necessary to strictly adjust the loops, there may be some leeway in adjusting them for the maximal expected V_T. In contrast, when the rebreathing loop was set too short for a given V_T, CO_{NI} measurements had greater values than those obtained by CO_{TD} (table 4). This may be due to the small changes in $PETco_2$ that occur with the shortest loop during CO_2 rebreathing, when a slight amount of noise would likely generate large errors.

To our surprise, when V_T was small (6 ml/kg), CO_{NI} measurements showed consistently lower values than those produced by CO_{TD}, resulting in a linear regression slope of 0.70 and a negative value of bias (figs. 1 and 2). Low V_T (6 ml/kg) is currently recommended for ventilator management in acute respiratory failure,[14] so attention needs to be drawn to the lack of reliable measurement using CO_{NI} at the low V_T setting. Reasons for these discrepant results have not been clarified, but there are several possible explanations.

First, after we adjusted the length of rebreathing loops for high V_T, when V_T was decreased, results may have been affected because the loop had become relatively too long. However, we found that the maximally expanded loop did not make CO_{NI} measurements less accurate (table 4). This finding suggests that the combination of long loop and small V_T are unlikely to impair the accuracy of CO_{NI}.

Second, at small V_T settings, $PETco_2$ increased to almost 60 mmHg in several patients. The software (version 3.1) that we used suspends rebreathing when the baseline $PETco_2$ is greater than 65 mmHg or $PETco_2$ is greater than 80 mmHg during CO_2 rebreathing. It could be that the linearity between $Caco_2$ and $PETco_2$ is less accurate when $PETco_2$ is extremely high.

Finally, the assumed constancy of mixed venous CO_2 content may be false for some time after V_T and minute ventilation are changed. The measured values of $\dot{V}co_2$ were smaller at low V_T than at high V_T (table 3). Although we waited for 15 min, this may not have been enough time for CO_2 stores to reach a steady state, which is 100 times larger than oxygen stores.[9] In addition, the time course of the increase in $Paco_2$ after abrupt decrease of ventilation is much slower than the rate of decrease after abrupt increase of ventilation.[9] These facts suggest that CO_2 stores and mixed venous CO_2 content may continue to change even after $Paco_2$ and $PETco_2$ seem to have reached plateau values. If this is the case, the accuracy of the CO_2 rebreathing technique may be compromised when there are abrupt changes in minute ventilation and $\dot{V}co_2$. Further study is needed to find out exactly what happens after these sudden changes and whether these mechanisms affect the accuracy of the CO_2 rebreathing technique.

Limitations

The current study has several limitations. First, the patients in our study were sedated and paralyzed initially, resulting in constant V_T and stable $\dot{V}co_2$. Even during PSV, they breathed quietly with small variation in V_T. Therefore, our results may not be directly extrapolated to populations of patients whose V_T and $\dot{V}co_2$ are changing.[6] Secondly, our patients had relatively normal lung mechanics (respiratory system compliance, 45.4 ± 12.8 ml/cm H_2O; resistance, 11.2 ± 4.1 cm $H_2O \cdot s \cdot l^{-1}$), and their hemodynamics had been stabilized at time of entry into the study. In more seriously compromised patients, the accuracy may be quite different. To corroborate the relevance of our findings for acutely ill and ventilator-dependent patients, it is prudent to perform further studies. Third, we did not examine how the ventilatory pattern alterations affect the assumptions underlying the fundamental equation of the $NICO_2$ technique: *e.g.*, constant V_D/V_T, constant CO, and constant mixed venous CO_2 content during the CO_2 rebreathing procedure. Finally, it remains to be clarified whether the impaired accuracy of CO_{NI} with small V_T results from small V_T itself or from reduced minute ventilation. During PSV, when V_T was smaller (8.8 ± 2.6 ml/kg) but minute ventilation was similar to that at the high V_T settings, CO_{NI} and CO_{TD} values correlated fairly ($y = 1.07x$); we speculate that if normocapnia is sustained by adjusting the respiratory rate, the accuracy of the CO_{NI} technique can be maintained at small V_T.

In conclusion, noninvasive measurement of CO using CO_2 rebreathing is reliable with a bias of less than 0.5 l/min and a precision of 1 l/min when the tidal

volume is large and constant, regardless of ventilatory modes. However, at small tidal volume, the rebreathing system underreports CO, compared with the conventional thermodilution technique.

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EMERGING TECHNOLOGY

David Reich, MD
Section Editor

Advances in Noninvasive Cardiac Output Monitoring: An Update

Monica Botero, MD, and Emilio B Lobato, MD

It is a source of regret that the measurement of flow is so much more difficult than the measurement of pressure. This has led to an undue interest in the blood pressure manometer. Most organs, however, require flow rather than pressure.

Jarisch, 1928[1]

Routine monitoring of circulatory function during the perioperative period has generally consisted of heart rate, blood pressure, and electrocardiography. Clinical signs, such as urine output, jugular venous distention, skin turgor, and skin perfusion have been used to estimate cardiac function. These signs may be unreliable, particularly in critically ill patients.[2-4]

Although Harvey discovered the circulation of the blood more than 300 years ago, routine measurements of cardiac output (CO) have been available to clinicians only since 1970.[5] Since its introduction in 1970, pulmonary artery catheterization has been considered the gold standard for the measurement of CO in humans. Although its risk-to-benefit ratio has not been determined, this procedure has become one of the most common procedures performed in critically ill patients around the world.[6-8] During anesthesia, CO determination is traditionally reserved for patients with severe circulatory instability or patients undergoing major surgery because the standard technique for CO measurement requires right heart catheterization with its attendant costs and risks.[6]

Ideally, the technology that provides CO estimation should be noninvasive, accurate, reliable, and continuous. At present, no single monitoring method meets all of these criteria.[3] New methods of noninvasive CO monitoring have become available for use in the operating room. In addition to being able to use them at the bedside, a major advantage of many noninvasive techniques is that they avoid the risks of morbidity as well as discomfort associated with more invasive techniques.

Because many of these techniques have developed so quickly, anesthesiologists may be unfamiliar with all their clinical applications. Even more challenging may be to decide if the new method can replace the old gold standard based on clinical evidence and the appropriate statistical analysis. Previous studies comparing CO measurement techniques suffered from deficiencies in design or suboptimal statistical methodology,[9] leading to the erroneous belief that these techniques are interchangeable when significant differences exist. The purpose of this review is twofold: (1) to outline the utility and limitations of new methods of noninvasive CO monitoring (without the use of an intravascular catheter) currently available to anesthesiologists and (2) to assist practitioners to more critically review new reports on these techniques.

MAGNITUDE OF THE PROBLEM

At present, cardiovascular disease remains the most widespread major medical problem in patients in the United States, and it is predicted that its incidence will increase 25% to 35% during the next 30 years in the population >65 years old. Overall, this is also the group with the highest incidence for undergoing surgical procedures.[10]

There are 25 million noncardiac operations performed annually in the United States[11]; of these, 3 million are performed on patients at risk for coronary artery disease.[11,12] More than 1 million pulmonary artery catheters are sold in the United States each year, and the annual costs associated with their use are >$2 billion. Since Dexter et al[13] performed the first pulmonary artery catheterization in 1945, the field of hemodynamic monitoring has significantly evolved. Pulmonary artery catheterization was initially used in cardiac catheterization laboratories to diagnose a wide variety of congenital heart lesions by measuring pressures and oxygen content in the right heart chambers. It was not until 1970, however, when Swan et al[14] reported that pulmonary artery catheterization could be performed at the bedside by use of a specially designed balloon-tipped catheter, that this technique became commercially available and began to be used in a variety of clinical settings.[15,16] Clinicians began to use the hemodynamic data derived from pulmonary artery catheterization to select, modify, and monitor medical treatment, particularly in patients with acute myocardial infarction. The benefits seemed obvious, and it was assumed that the therapeutic decisions made using the hemodynamic data derived from pulmonary artery catheterization improved patient outcomes.[15] To date, however, there is no evidence that patient outcomes are improved by the use of pulmonary artery catheterization. Randomized clinical trials have never been performed to evaluate the benefits and safety of this procedure.

BIAS, PRECISION, AND LIMITS OF AGREEMENT: THE BLAND-ALTMAN METHOD

For clinicians, it is sometimes difficult to assess the adequacy of a new technique because some familiarity with statistical

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analysis is required. To assess the value of new technologies, standardization of reporting results is necessary. Mantha et al[17] studied statistical reports of comparison studies in which interchangeability of a new measurement technique with an established method was the primary goal and found several inadequacies. Until recently, new techniques were compared using correlation and regression analysis. This type of analysis has deficiencies, however, as highlighted by Bland and Altman in 1986.[9,18] Bland and Altman[18] recommended a simple descriptive analysis to compare simultaneous measurements of the same physiologic variable, such as CO. Computing the differences between all paired measurements provides the simplest measure of disagreement between 2 measurements: bias. Bias is the mean of the differences between the 2 observations. Bias measures the systematic tendency of one technique to read consistently higher or lower than the other. The SD of all the individual bias measurements can be calculated: precision and 95% confidence limits ($u \pm 2$ SD), which are referred to as *limits of agreement*.[9,19] Precision is a measure of the reproducibility of the measurements. Systematic errors between 2 measurement techniques as a function of the range of the physiologic parameter being measured can occur (ie, a new technique that tends to underestimate at low values and overestimate at high values of CO). Plotting the difference between the 2 methods versus their mean usually discloses this error (Fig 1).[16,19,20]

Bias and precision statistics have replaced correlation and regression as the accepted statistical technique of comparing 2 techniques measuring the same physiologic variable, such as CO.[9,18] In addition, when reporting the results of comparison studies, Critchley and Critchley[9] recommended quoting the mean CO (u), the bias, the limits of agreement (u ± 2 SD), and the percentage error (± 2 SD/u), unless the mean CO for the study approximates 5.0 L/min. The acceptance of a new method should be judged against the ± 10% to 20% accuracy of the current reference method (eg, thermodilution). Consequently, Critchley and Critchley[9] recommended that limits of agreement between the new and the reference technique of ± 30% be accepted.

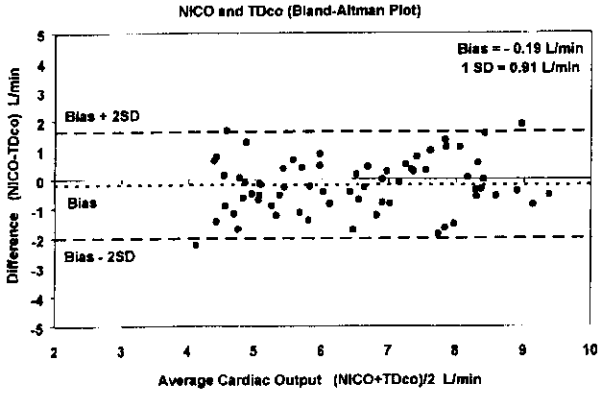


Fig 1. Bland-Altman plot of cardiac output measurements from bolus thermodilution and partial carbon dioxide rebreathing techniques after coronary artery bypass graft surgery in the intensive care unit.[50] It provides mean bias (−0.19 L/min) and lower and upper limits of agreement (−0.19 ± 1.82), within which 95% of bias measurements should lie. Abbreviations: TDco, bolus thermodilution; NICO, partial carbon dioxide rebreathing technique.

NONINVASIVE TECHNIQUES FOR CARDIAC OUTPUT MEASUREMENT

There are 3 current techniques that can determine CO noninvasively: (1) Doppler ultrasound, (2) partial carbon dioxide (CO_2) rebreathing, and (3) thoracic bioimpedance.

Doppler Measurement of Cardiac Output

Consisting of high-frequency sound waves, ultrasound easily penetrates skin and other body tissues. As it encounters tissues of different acoustic density, a fraction of an emitted ultrasound signal is reflected.[21] When an ultrasound beam is directed to a moving target (eg, column of flowing blood), the reflected sound wave changes its frequency, a phenomenon known as *Doppler shift*. The magnitude of this Doppler shift is directly proportional to the velocity of blood flow. This is expressed mathematically by the following equation:

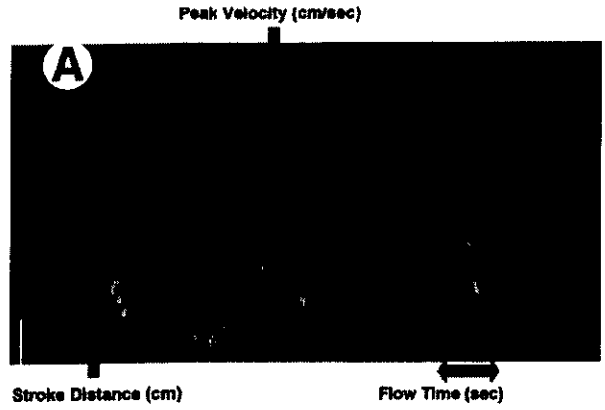
$$Fd = 2fo/C \; V \cos\theta$$

Where *Fd* represents the change in frequency or Doppler shift, *fo* is the transmitted frequency, and *V* is the velocity of the moving blood. *C* is the velocity of ultrasound in blood and remains constant. The angle θ is the angle between the direction of the moving blood and the transmitted ultrasound beam.[22]

Stroke volume can be calculated by multiplying the average blood velocity during a systolic cycle by the ejection time (stroke distance) and by the cross-sectional area through which blood flows (Fig 2A).[4,23] Doppler signals can be obtained with an ultrasound probe placed externally at the suprasternal notch and directed at the ascending aorta, at the tip of an endotracheal tube, or at the tip of an esophageal probe (esophageal Doppler monitor [EDM]) and directed at the descending thoracic aorta (Fig 2B). With transesophageal echocardiography (TEE), CO can be derived by measurement of flow through a cardiac valve (most commonly, mitral or aortic), left ventricular outflow tract, or main pulmonary artery.

To measure ascending aortic blood flow with surface ultrasound, the suprasternal transducer is positioned to receive an audible signal from the aortic root that indicates the peak velocity of flow. The ultrasound beam needs to be transmitted parallel to the direction of blood flow through the aortic valve. Generally, angles ϕ of $>20°$ yield clinically unacceptable underestimation measurements of velocity and consequently of CO. The velocity is entered into the formula together with the cross-sectional area of the aorta. This area has been determined in many instances by two-dimensional or M-mode echocardiography but most commonly is derived from a nomogram stored in the computer based on age, sex, height, and weight.[22] Variations in the cross-sectional area of the aorta from 5% to 17% between systole and diastole are known to introduce error in this calculation, however. In addition, although nomograms may correlate well in large population studies, they may be invalid for an individual patient.[21]

Esophageal Doppler monitoring has many advantages over the transcutaneous approach. The close proximity of the de-



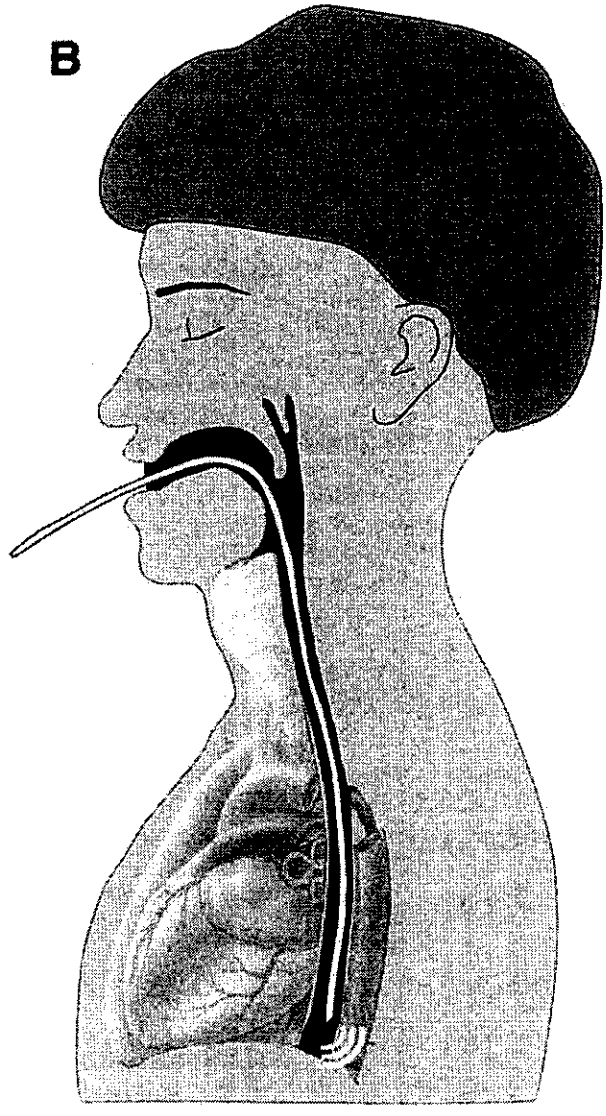


Fig 2. (A) Esophageal Doppler flow-velocity waveform. (B) Doppler measurement of cardiac output. The transducer is located at the tip of an esophageal probe and directed at the descending thoracic aorta.

scending aorta to the esophagus provides an excellent window for obtaining Doppler signals, allows continuous monitoring, and provides stability for the transducer. To measure descending aortic flow, the esophageal probe is positioned to maximize descending aortic flow signals. A correction factor (K-factor) is necessary to account for blood flow distributed to the head and upper extremities. When calibrated, the esophageal Doppler signals continuously monitor CO based on descending aortic flow. Several studies have suggested that the K-factor may introduce a source of error in the measurement of CO because it can fluctuate during surgery as a response to changes in sympathetic tone, arterial blood pressure, and alterations in anesthetic depth.[21,24,25]

In clinical trials, esophageal Doppler measurements have given inconsistent results. Initial studies reported significant variability between Doppler and thermodilution measurements unacceptable for clinical CO monitoring. The authors of these trials concluded that Doppler techniques were operator dependent[26-28] and that frequent manipulation of the probe was necessary to obtain accurate data. An esophageal probe that allows the near-simultaneous measurement of the velocity of the descending aortic flow and the descending aortic diameter has been described.[29] The aortic cross-sectional diameter as measured with this device has been reported to closely correlate with that determined by TEE, and the descending aortic blood flow showed good agreement with the CO as measured by thermodilution.[4,29] To date, a small amount of literature has detailed the clinical use and accuracy of the EDM.[30-32] In cardiac surgery, the EDM has been shown to assist in optimizing gut perfusion in conjunction with a gastric tonometer and to decrease perioperative complications.[33] Sinclair et al[34] successfully used the EDM in patients undergoing proximal femoral fracture repair in a high-risk population. In this prospective, randomized, and blinded study, intraoperative intravascular volume loading to optimal stroke volume guided by the use of the EDM resulted in a more rapid postoperative recovery and a significantly reduced hospital stay.[34] A relevant finding from these studies was the greater sensitivity of stroke volume over CO, as compensatory tachycardia tended to maintain CO in the face of mild-to-moderate hypovolemia. Overall, the control groups showed no change in output but had significant falls in stroke volume.[35] Outcome was improved by acting on the information provided to achieve the set goal of optimal filling. Whether this noninvasive technique can be considered equivalent or superior to invasive monitoring techniques requires further investigation, but encouragement can be drawn from these initial investigations. The EDM may develop into a widely used tool as a perioperative and critical care monitoring device.

Transesophageal Echocardiography

Two-dimensional echocardiography is an essential tool for preoperative and postoperative diagnosis, and TEE has become a widely used intraoperative monitor to assess cardiac anatomy, left ventricular function, preload, myocardial ischemia, and myocardial infarction. Two-dimensional TEE can detect small quantities of intravascular air and can reliably diagnose atrial septal defects.

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To date, clinical trials support TEE as a reliable alternative for intraoperative CO measurement and for its ability to track serial changes throughout the surgical procedure.[36-38] Initial studies used pulmonary artery blood flow to measure CO and reported strong agreement with thermodilution.[37] This technique requires substantial probe manipulation, however, and poor image quality is frequently obtained because of interference from air in the left mainstem bronchus. Savino et al[37] reported adequate imaging in 25 of 33 patients (76%). Another alternative approach to Doppler CO measurements uses the transgastric, apical view to assess aortic blood flow (Fig 3). A limitation of this approach is that obtaining this view is technically more difficult and may not be achieved in 12% of patients.[39]

Perrino et al[38] used an alternative approach to Doppler CO measurement and reported excellent agreement with thermodi-

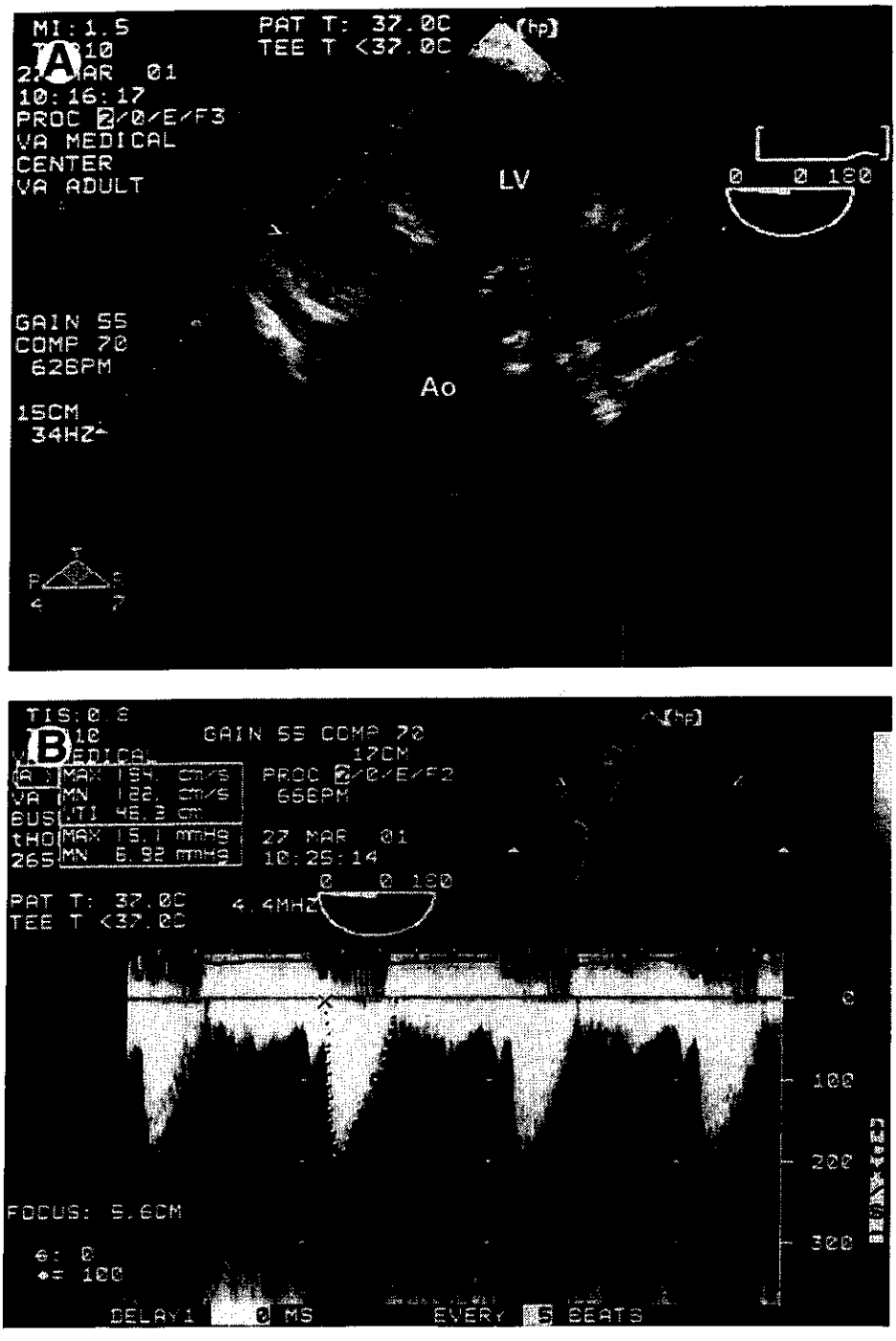

Fig 3. (A) Two-dimensional multiplane esophageal echocardiographic image of the apical transgastric left ventricular outflow tract view. This position provides an ultrasound beam oriented near parallel to blood flow within the aortic valve. (B) Continuous-wave Doppler signal of aortic blood flow velocities. Abbreviations: Ao, aorta; LV, left ventricle.

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lution and adequate imaging easily obtained in 32 of 33 patients. Perrino et al[38] positioned the transesophageal ultrasound probe to obtain a transverse plane, transgastric short-axis view of the left ventricle at the midpapillary level. By rotating the imaging array to approximately 120°, the left ventricular outflow tract and ascending aorta were imaged lying parallel to the ultrasound beam, and aortic blood flow velocities were measured by a continuous-wave Doppler beam focused at the level of the aortic valve (Fig 4). The aortic valve area was measured by planimetry using the triangular model proposed by Darmon et al[36] (Fig 5). A major advantage of Perrino's approach lies in the minimal probe positioning adjustment needed. Consequently, from a single probe location, the anesthesiologist can monitor left ventricular regional and global wall motion using the short-axis view and measure CO rotating the imaging plane to measure aortic flow velocities, expanding the intraoperative usefulness of TEE.

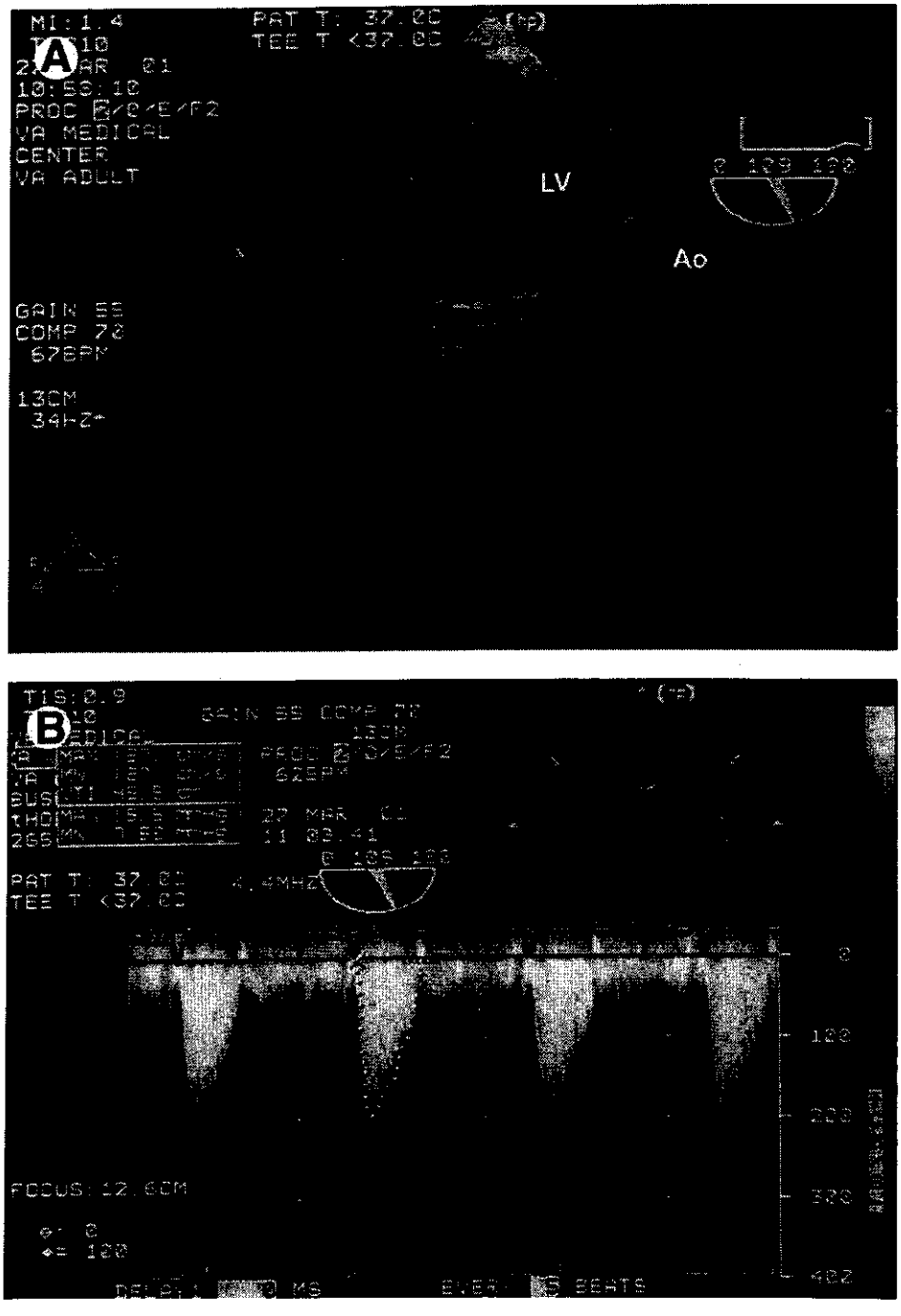

Fig 4. (A) Two-dimensional multiplane esophageal echocardiographic image of the 120° transgastric left ventricular outflow tract view. (B) Continuous-wave Doppler signal of aortic blood flow velocities. Abbreviations: Ao, aorta; LV, left ventricle.

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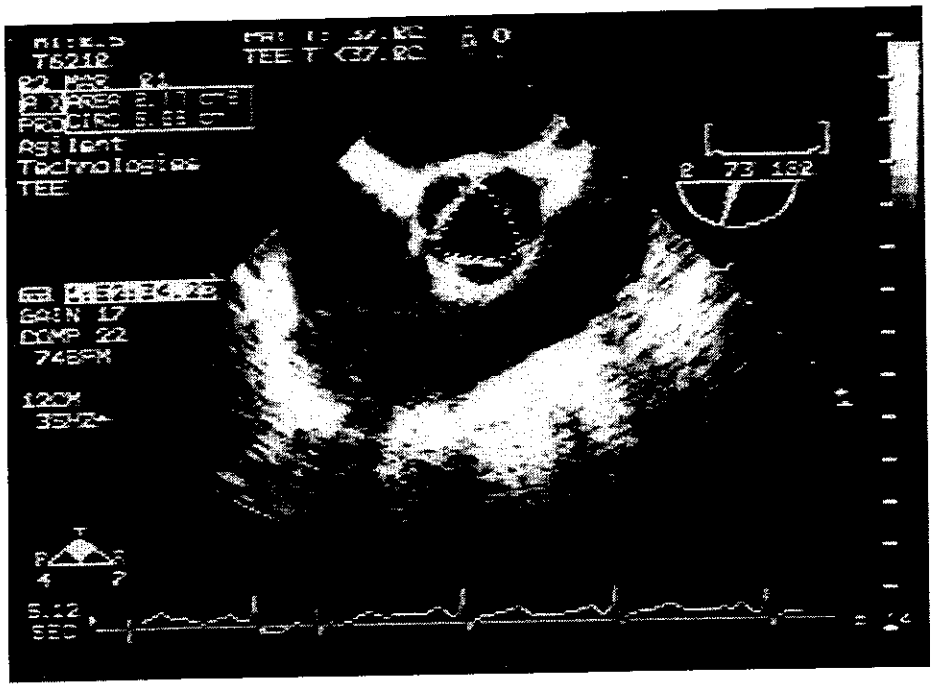

Fig 5. Two-dimensional multiplane esophageal echocardiographic image of the basal short-axis view of the aortic valve. Valve orifice planimetered using the triangular model.

DIFFERENTIAL CARBON DIOXIDE FICK PARTIAL REBREATHING TECHNIQUE

The Fick principle is based on the conservation of mass. This principle postulates that blood flow through the alveoli is equal to the ratio of the uptake or elimination of a gas and the difference in concentration of that gas in the blood flowing into and out of the lungs. Although used primarily in cardiac catheterization laboratories and traditionally considered the gold standard to measure CO, this technique is invasive, and methodologic error is common. The major limitations of the direct Fick technique are related to errors in sampling and analysis, difficulty in obtaining oxygen uptake continuously in the operating room, the presence of bulky equipment surrounding the endotracheal tube, and the inability to maintain steady-state hemodynamic and respiratory conditions. More recent technology relies on the elimination of CO_2, and it is totally noninvasive. The Fick equation using CO_2 can be formulated as:

$$Q = \dot{V}CO_2/C\bar{V}CO_2 - CaCO_2 \quad (1)$$

In which Q is the cardiac output, $\dot{V}CO_2$ is the CO_2 elimination, and $C\bar{V}CO_2$ and $CaCO_2$ are the mixed venous and arterial CO_2 blood contents. Using the CO_2 version of the Fick equation has the advantages that CO_2 elimination is easier to accurately measure than oxygen uptake, and that estimates of arterial CO_2 concentration may be made from the gas exhaled by the lungs. The CO_2 concentration in the alveolar end-capillary blood can be noninvasively estimated by monitoring the CO_2 partial pressure in the expired gas and relating it to the blood concentration with the help of the CO_2 dissociation curve.[40]

A similar form of the Fick equation, the differential CO_2 Fick partial rebreathing method, uses the ratio of the change in CO_2 elimination and in end-tidal CO_2 in response to a brief period of partial rebreathing. The partial rebreathing method combines measurements obtained during a nonrebreathing period with measurements obtained during a subsequent rebreathing period. This form of the Fick equation can be derived by combining the CO_2 Fick equations during baseline (nonrebreathing [nonrebr]) and rebreathing (rebr) periods. These equations can be formulated as follows:

$$Q_{PCBF} = \dot{V}CO_{2\ nonrebr}/C\bar{V}CO_{2\ nonrebr} - CaCO_{2\ nonrebr} \quad (2)$$

$$Q_{PCBF} = \dot{V}CO_{2\ rebr}/C\bar{V}CO_{2\ rebr} - CaCO_{2\ rebr} \quad (3)$$

In which Q_{PCBF} is the pulmonary capillary blood flow; $\dot{V}CO_{2\ nonrebr}$ and $\dot{V}CO_{2\ rebr}$ are the CO_2 eliminations in mL/min during nonrebreathing and rebreathing; and $C\bar{V}CO_{2\ nonrebr}$, $C\bar{V}CO_{2\ rebr}$, $CaCO_{2nonrebr}$, and $CaCO_{2\ rebr}$ are the mixed venous and arterial CO_2 blood contents in mL/mL of blood during nonrebreathing and rebreathing.[40] Assuming no significant change of pulmonary capillary blood flow during the measurement period, equations [2] and [3] can be combined to yield:

$$Q_{PCBF} = \dot{V}CO_{2\ nonrebr} - \dot{V}CO_{2\ rebr}/(C\bar{V}CO_{2\ nonrebr} - CaCO_{2\ nonrebr}) - (C\bar{V}CO_{2\ rebr} - CaCO_{2\ rebr}) \quad (4)$$

Based on the large size of the CO_2 body stores and slow time constant of the CO_2 stores relative to the time of rebreathing, the assumption is made that the mixed venous CO_2 concentration remains relatively constant throughout the rebreathing and nonrebreathing periods. As a result, the terms associated with mixed venous CO_2 concentration during baseline and rebreathing cancel, and the equation can be formulated as follows:

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$$Q_{PCBF} = \dot{V}CO_{2\ nonrebr} - \dot{V}CO_{2\ rebr}/CaCO_{2\ rebr} - CaCO_{2\ nonrebr} \quad (5)$$

Therefore:

$$Q_{PCBF} \Delta \dot{V}CO_2/\Delta CaCO_2 \quad (6)$$

Where $\Delta \dot{V}CO_2$ is the change in CO_2 elimination in mL/min, and $\Delta CaCO_2$ is the change in alveolar blood CO_2 content in mL/mL blood between the baseline and rebreathing periods.[40]

The $NICO_2$ system (Novametrix Medical Systems, Inc, Wallingford, CT) continuously measures airway flow, pressure, and CO_2 concentration (Fig 6). The $NICO_2$ system controls and monitors the performance of a pneumatically controlled valve assembly, which consists of a rebreathing valve with large-bore tubing and a combination CO_2/flow sensor. This assembly is inserted in the ventilator circuit between the patient and the Y piece of the breathing circuit. The flow through the valve during the normal (baseline) mode is straight through the valve. The flow through the valve during rebreathing is diverted through the expandable rebreathing loop (Fig 7). The sequence of rebreathing and stabilization is shown in Fig 8. During the baseline period, which lasts 60 seconds, the valve is in the nonrebreathing mode. During the rebreathing period, the valve is activated by the application of positive pressure. A quantity of end-exhaled gas, equal to the volume of the expandable loop and the valve, is accumulated for inhalation (rebreathing) with the next breath. This inhaled CO_2 increases the alveolar CO_2 concentration, reduces the net flux of CO_2 diffusing into the alveoli from the blood, reduces the CO_2 eliminated from the lung, and increases the arterial CO_2 content. During the restabilization period, which lasts 70 seconds, the valve is switched so that the control line pressure falls to ambient pressure level, and the mechanism returns the valve to normal mode. This period allows the patient's CO_2 stores to recover.[40]

To calculate alveolar content of CO_2, the $NICO_2$ uses the following equation:[40]

$$CaCO_2 = (6.957[Hb] + 94.864) * \log (1.0 + 0.1933PaCO_2)$$

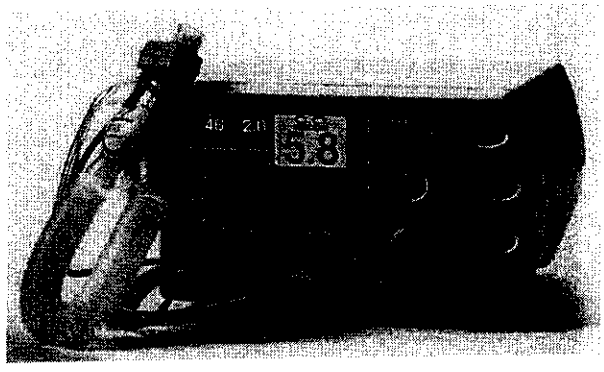

Fig 6. The $NICO_2$ system (Novametrix Medical Systems, Inc, Wallingford, CT) measures cardiac output based on changes in end-tidal carbon dioxide after a brief period of rebreathing.

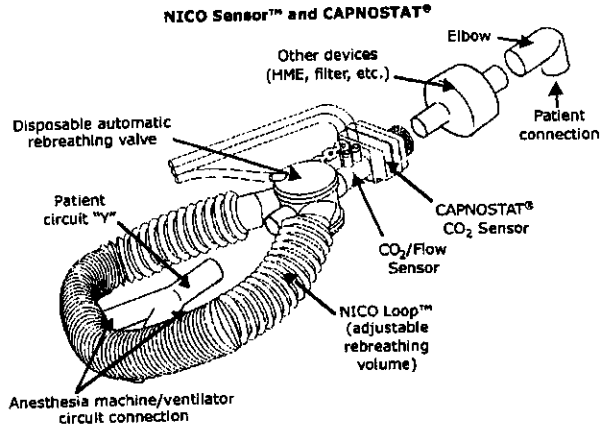

Fig 7. The $NICO_2$ sensor, a combination of an on-airway flow sensor, on-airway/mainstream carbon dioxide (CO_2) sensor, an adjustable deadspace tubing, and a pneumatic valve, is connected in between the endotracheal tube of the patient and the Y-piece of the breathing circuit. Abbreviation: HME, heat and moisture exchanger.

Where *Hb* is hemoglobin in g/dL, $PaCO_2$ is the alveolar CO_2 partial pressure in mmHg, and $CaCO_2$ is the alveolar CO_2 content in mL CO_2/mL blood. Using $PaCO_2$ and the CO_2 dissociation curve, the arterial CO_2 content is estimated.[40]

Because the partial rebreathing method measures only the nonshunted portion of the CO, the $NICO_2$ uses arterial blood oxygen saturation (SaO_2) measured by pulse oximetry (SpO_2), and the inspired oxygen concentration (F_IO_2) to estimate the shunt[40] based on the following equation:

$$Q_S/Q_T = CcO_2 - CaO_2/CcO_2 - C\bar{V}O_2 \quad (7)$$

Where CcO_2, CaO_2, and $C\bar{V}O_2$ are the end-capillary, arterial, and mixed venous oxygen contents; Q_S is the shunt flow; and Q_T is the CO. This noninvasive method of shunt estimation is an adaptation of Nunn's isoshunt plots[42] that describe the relationship between arterial oxygen tension (PaO_2) and F_IO_2 for different levels of intrapulmonary shunt.

Although rebreathing methods have been criticized in the past,[43] technologic improvements and subsequent experience with their use suggest that they may be useful additions to the perioperative and critical care of patients. Initial laboratory trials reported good agreement and precision between the CO_2-rebreathing and Fick methods,[44] with larger variability in others.[45,46] To date, a few clinical studies have detailed the accuracy of the $NICO_2$ compared with invasive techniques of CO measurement.[47-52] The authors' group compared 191 paired measurements of CO using the $NICO_2$, a pulmonary artery catheter, and an ultrasonic flow probe in 34 consenting adults undergoing coronary artery bypass graft surgery.[48] A transit-time ultrasonic flow probe that was placed directly on the ascending aorta by the surgical team was chosen as the reference CO because thermodilution has proved to be less than an optimal reference method in comparison studies.[44,46,47] A comparable accuracy was found between CO values obtained with the $NICO_2$, thermodilution, and directly measured aortic blood flow. These data suggest that this noninvasive technique offers a good alternative to invasive CO measurement during coro-

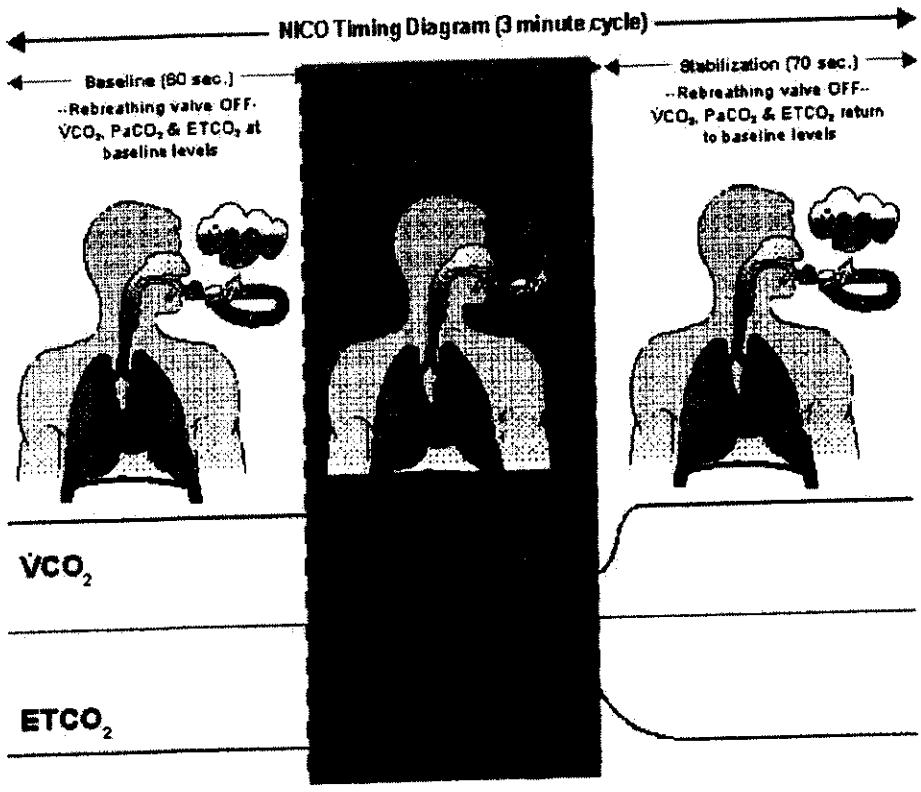

Fig 8. $NICO_2$ timing diagram (3-minute cycle). $NICO_2$ cycles automatically among baseline, rebreathing, and stabilization periods. During partial rebreathing, a transient increase in carbon dioxide and a decrease in carbon dioxide elimination provide the data required for the differential Fick cardiac output calculation.

nary artery bypass graft surgery. Gray and Perrino[51] compared 31 matched sets of CO measurements from the $NICO_2$ and TEE in 8 patients undergoing noncardiac surgery. These authors concluded that the $NICO_2$ produces little systematic error in CO determinations.[51] Van Heerden et al[52] compared 42 paired CO measurements from the $NICO_2$ and the standard thermodilution technique in 12 patients who had recently undergone cardiac surgery. Comparison of the 2 techniques using the Bland-Altman method showed good correlation; however, this decreased at higher levels of CO. Despite the potential advantages of continuous partial CO_2 rebreathing CO monitoring, the clinical experience with this technique is still limited. Additional data from ongoing investigations are necessary to clarify the clinical use of this promising application of the Fick technique.[48-52]

Thoracic Bioimpedance

The assessment of stroke volume relies on the measurement of changes in transthoracic electrical resistivity. These changes are due to the ejection of blood into the ascending aorta with each cardiac cycle and are phasic in nature.[53] In 1966, Kubicek[54] described the thorax as a cylinder evenly perfused with blood of specific resistivity. Later, Sramek[55] showed that the thorax behaves electrically more like a truncated cone. To measure thoracic electrical impedance, an alternating current of low amplitude and high frequency is introduced and simultaneously sensed by 2 sets of electrodes placed around the neck and xiphoid process (Fig 9).

In clinical trials, bioimpedance CO measurements have shown inconsistent results. The technique appears to be reliable in healthy volunteers but performs unpredictably in critically ill patients, in high-risk surgical patients, and in the operating room.[56-58] Critchley et al[59] found a major bias between the 2 methods during abdominal surgery. Perrino et al[56] reported clinically significant disagreement between thermodilution and bioimpedance in 50 patients undergoing noncardiac surgery. The intraoperative environment with electrocautery, mechanical ventilation, and surgical manipulations may have caused

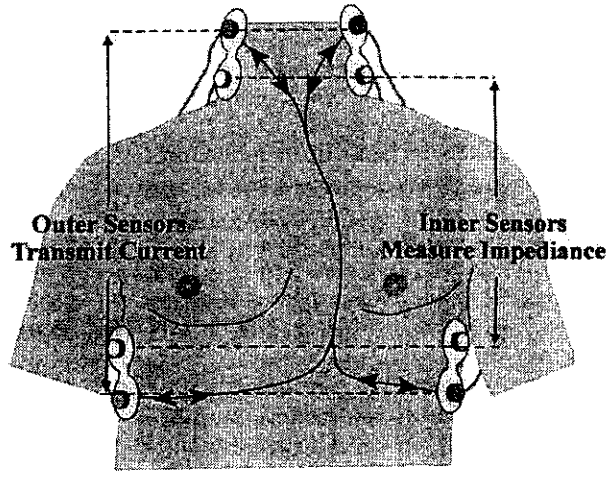

Fig 9. Placement of sets of electrodes around the neck and xiphoid process that measure thoracic electrical impedance.

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distortion of the impedance signal leading to inaccurate readings. Alterations in cardiac performance resulting from anesthetics, myocardial ischemia, and alterations in loading conditions may have caused errors in bioimpedance measurements,[56] limiting its usefulness in patients with coronary artery disease and impaired ventricular function. In addition, minor changes in lead placement or changes in tissue water content that frequently occur with perioperative fluid shifts and pulmonary edema may interfere with the signal. To date, further investigation of signal processing techniques to improve performance in the intraoperative setting is necessary if bioimpedance is to develop as a reliable clinical tool.

CONCLUSION

Noninvasive measurement of CO, although initially confined to the experimental laboratory, is now available in the clinical arena as a result of refinements in technology. Current evidence suggests that in selected populations these techniques represent a reasonable alternative to more invasive methods without the associated morbidity.

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Noninvasive Cardiac Output by Partial CO_2 Rebreathing after Severe Chest Trauma

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Background: **In multiple trauma patients, early continuous cardiac output (CCO) monitoring is frequently desired but is difficult to routinely employ in most emergency departments because it requires invasive procedures. Recently, a noninvasive cardiac output (NICO) technique based on the Fick principle and partial CO_2 rebreathing has shown promise under a variety of conditions. Since this method has not been tested after lung damage, we evaluated its utility in a clinically relevant model.**

Methods: **Anesthetized, ventilated swine (n = 11, 35–45 kg) received a unilateral blunt trauma via a captive bolt gun followed by a 25% hemorrhage. After 60 min of shock, crystalloid resuscitation was given as needed to maintain heart rate < 100 beats/min and mean arterial pressure > 70 mm Hg. Standard CCO by thermodilution (Baxter Vigilance, Irvine, CA) was compared with NICO (Novametrix Medical Systems Inc., Wallingford, CT) for 8 hr.**

Results: **The severity of the injury is reflected by seven deaths (average survival time = 4.25 hr). Trauma increased dead space ventilation (19%), airway resistance (30%), and lactate (3.2 mmol/L), and decreased dynamic compliance (48%) and Pao_2/Fio_2 (54%). In these extreme conditions, the time course and magnitude of change of CCO and NICO were superimposed. Bland-Altman analysis reveal a bias and precision of 0.01 ± 0.69 liters/min. The linear relationship between individual CCO and NICO values was significant ($p < 0.0001$) and was described by the equation NICO = (0.74 ± 0.1)CCO + (0.65 ± 0.16 liters/min) but the correlation coefficient ($r^2 = 0.541$) was relatively low. The cause for the low correlation could not be attributed to increased pulmonary shunt, venous desaturation, anemia, hypercapnia, increased dead space ventilation, or hyperlactacidemia.**

Conclusion: **NICO correlated with thermodilution CCO, but underestimated this standard by 26% in extreme laboratory conditions of trauma-induced cardiopulmonary dysfunction; 95% of the NICO values fall within 1.38 liters/min of CCO; and with further improvements, NICO may be useful in multiple trauma patients requiring emergency intubation during initial assessment and workup.**

Key Words: **Noninvasive cardiac output monitoring, Fick principle, Pulmonary contusion, Swine.**

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Trauma patients often spend extended periods of time in the emergency department during the admission process acquiring radiologic evaluations, receiving fracture reduction, and awaiting bed assignment. Sedatives are frequently administered. The early resuscitation and stabilization of these patients can be challenging, especially in the elderly, because it is mostly based on simple physiologic parameters such as heart rate and blood pressure. On the other hand, routine invasive hemodynamic monitoring with pulmonary artery catheters or other devices is impractical due to time constraints and technical limitations.

A new technique of noninvasive cardiac output (NICO) monitoring using the Fick principle and partial CO_2 rebreathing may have a role in the early hemodynamic monitoring of critically ill trauma patients following endotracheal intubation.[1–3] By intermittently altering the dead space within the ventilator circuit via a rebreathing valve, changes in CO_2 production (Vco_2) and end-tidal CO_2 ($ETco_2$) are measured and applied to a differential form of the Fick equation ($\Delta Vco_2/\Delta ETco_2$). Additional CO not calculated with the Fick equation due to shunt fraction is estimated from continuous on-line pulse oximetry and inspired oxygen content (Fio_2). Thus, the NICO technique is potentially useful even with trauma-induced pulmonary dysfunction, but it has never been tested in these conditions. To fill this gap, we compared standard thermodilution CO with the NICO method in an experimental model of severe chest trauma with respiratory failure.

MATERIALS AND METHODS

All protocols were performed in strict accordance to the guidelines for the care and use of experimental animals as outlined by the NIH. All animals were housed in a facility approved by the American Association for the Accreditation of Laboratory Animal Care and were monitored by staff veterinarians for any signs of unnecessary pain or distress.

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Except for 12 hr before surgery when there was access to water only, food and water were provided ad lib.

General Instrumentation

After an overnight fast, farm-raised, crossbred pigs of either sex (35.1 ± 0.9 kg, n = 11) were induced with ketamine i.m. (25 mg/kg) + xylazine i.m. (2.5 mg/kg), anesthetized with continuous i.v. infusions of fentanyl (40 μg/kg/hr) and ketamine (12.5 mg/kg/hr), and mechanically ventilated in the supine position via cricothyroidotomy (8–10 mL/kg tidal volume, 40% F_{IO_2} with respiratory rate adjusted to keep initial P_{aCO_2} 40–50 mm Hg). Large-bore catheters were placed in the carotid artery and internal jugular vein via cervical cutdown for measurement of mean arterial blood pressure (MAP) and for fluid administration. Multilumen, flow-directed fiberoptic pulmonary artery catheters (Swan-Ganz Combo Thermodilution Catheter, Baxter Labs, Irvine, CA) were placed into the external jugular vein via an introducer sheath (Arrow International, Inc., Reading, PA) and advanced into the pulmonary artery for continuous measurement of filling pressure, mixed-venous oxygen saturation (S_{VO_2}), and continuous cardiac output (CCO, Vigilance Computer, Baxter Labs) by thermodilution. Flow-through pressure transducers were used on appropriate catheter ports to eliminate the use of heparin. Body temperature was maintained at 36–38°C with a heating blanket. EKG was continuously monitored.

The NICO monitor (Novametrix Medical Systems Inc., Wallingford, CT) was connected between the ventilator circuit and tracheostomy tube. The system cycled every 3 min with 50-sec rebreathing periods thereby updating CO approximately every 4 min. The pulse oximeter used in shunt fraction calculations was placed on the ear.

Trauma/Resuscitation Protocol

A captive bolt gun (Model ME, Karl Schermer & Co., Germany) delivered a blunt injury to the right hemithorax by a previously described technique.[4,5] Tube thoracostomy immediately followed to prevent tension pneumothorax. At 5 min after injury, 25% of the estimated blood volume was withdrawn through the carotid artery catheter in three increments (15%, 5%, 5%) over 30 min. After an additional 60 min of shock, resuscitation was initiated by replacing 3× the shed blood volume with 0.9% NaCl over 30 min. For the remaining 6-hr observation period, supplemental 0.9% NaCl was administered as needed for hypotension (mean arterial pressure < 70 mm Hg) or tachycardia (heart rate > 100 beats/min).

Data Collection

The following were monitored continuously on-line: NICO, CCO, core temperature, heart rate, mean arterial pressure, pulmonary capillary wedge pressure, S_{VO_2}, end tidal CO_2, peak inspiratory pressure, mean inspiratory pressure, and pulse oximetry. Additional pulmonary function data were monitored continuously with an inline computer (Bicore CP-100, Allied Health Care Products, Riverside, CA) connected to an esophageal balloon catheter (SmartCath, Allied Health Care) and flow transducer (VarFlex, Allied Health Care). With serial sampling, arterial blood gases (P_{O_2}, P_{CO_2}, pH, base excess, and arterial O_2 saturation) and lactate were measured on a Nova Stat Profile Ultra (Waltham, MA) and complete blood counts were measured on an Abbott CellDyn 1600 (Abbott Park, IL).

Statistical Analysis

The time-related changes in CCO and NICO are expressed as means ± SE. Correlation between the two methods was determined by linear regression. A Bland-Altman analysis[6] was used to compare the bias and precision of the two methods. Significance was assessed at the 95% confidence interval.

RESULTS

The combined injury and hemorrhage protocol produced seven deaths (mortality = 64%), two during resuscitation and five thereafter (average survival time was 4.25 hr). Injury and hemorrhage produced profound derangements in hemodynamics and pulmonary function: mean arterial pressure (62%), S_{VO_2} (49%), dynamic compliance (27%), and P_{O_2}/F_{IO_2} (P/F) (56%) were all decreased from preinjury baseline values. Increases in heart rate (224%), dead space ventilation (20%), airway resistance (309%), and lactate (3.15 mmol/liter) were also observed. These data are comparable to those in our previous studies[4,5] so additional figures are not shown. In these conditions, there were 129 paired data points for comparison between the NICO and CCO methods.

Figure 1 shows that the phase and magnitude of the NICO and CCO values were comparable over the entire observation period. After baseline NICO and CCO average values (3.5 ± 0.2 and 3.4 ± 0.3 liters/min), there was a decrease of more than 50% to hemorrhage values (1.6 ± 0.2 vs. 1.6 ± 0.1 liters/min). Thereafter, there was a rapid recovery following resuscitation (2.3 ± 0.4 vs. 2.7 ± 0.3 liters/min).

Figure 2 shows a plot of the difference in the two methods versus the average of the two methods (Bland-Altman analysis). Basically, these data show that at low CO, the two methods most closely agree, but at higher average CO, the difference between the two methods tends to increase. These data showed a bias and precision of 0.01 ± 0.69 liters/min.

Figure 3 shows a linear regression analysis for individual NICO and CCO values (n = 129). The correlation was significantly linear ($r^2 = 0.541$; $p < 0.0001$), which means that 54% of a NICO increase was directly correlated with a CCO increase. The regression was described by the linear equation: $Y = (0.739 \pm 0.060)X + 0.648 \pm 0.162$, in which there was a tendency for NICO to underestimate CCO by 27%.

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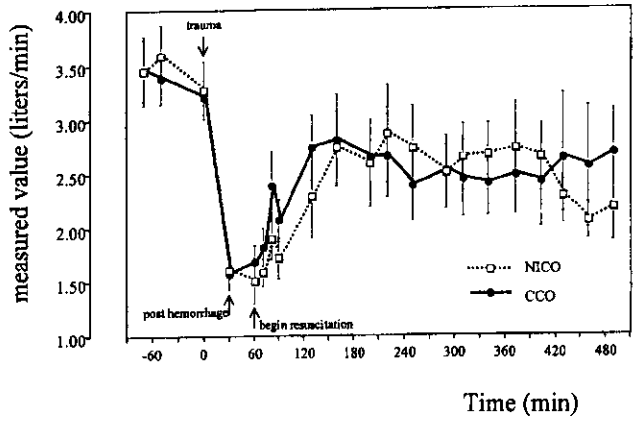

Fig. 1. *Time course of average NICO and CCO values over the duration of the experiment (n = 11 animals).*

Figure 4 shows how the agreement between the two methods was influenced by six common pathophysiologic conditions likely encountered in severely injured patients. These data show that no more than 5% of the total number of paired CCO and NICO measurements deviated by more than 1.4 liters/min as a function of increased pulmonary shunt, venous desaturation, anemia, hypercapnia, increased dead space ventilation, or hyperlactacidemia.

DISCUSSION

NICO monitoring is safe, simple, and apparently accurate in the laboratory after shock, pulmonary edema, and inotrope administration.[7–9] In addition, NICO has been tested in intensive care patients with respiratory failure, and during heart surgery and liver transplantation.[3,10–12] The general experience with the device has been favorable, with an overall correlation coefficient > 0.70 and bias and precision of 0.12 ± 0.78 liters/min.

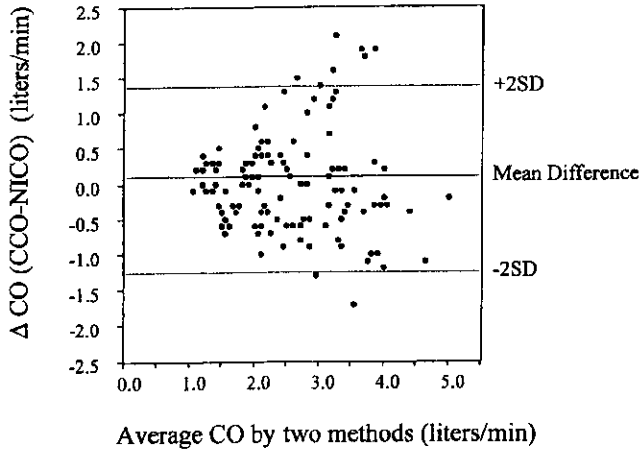

Fig. 2. *Bland-Altman analysis showing difference between CCO and NICO plotted against the average of the two techniques (n = 120 measurements).* Solid line, *Mean difference between the two techniques (0.01 liters/min);* dashed lines, *95% confidence limits (± 2 SD) for the mean difference.*

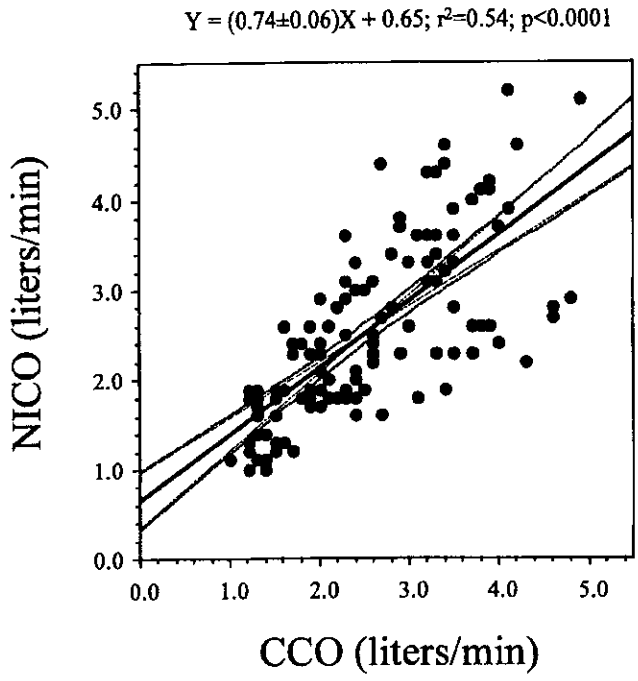

Fig. 3. *Scatter plot of individual CCO and NICO values. Linear regression shows that NICO has a tendency to underestimate CCO (slope = 0.73). Correlation is significant (r^2 = 0.54; n = 129; p < 0.0001).*

The present study evaluated the 8-hr interval after a severe chest injury. This extreme state of cardiopulmonary dysfunction was associated with 64% mortality and tests the limits of reliability of the NICO device in the early postinjury phase when invasive cardiopulmonary monitoring is frequently desired but difficult to employ.

Figure 1 demonstrates that the phase and magnitude of the average NICO values almost exactly tracked average CCO. The bias and precision shown in Figure 2 (0.01 ± 0.69 liters/min) demonstrates that NICO compares reasonably well with CCO over a range of 0–6 liters/min. However, Figure 3 shows that individual NICO values tend to underestimate individual CCO by 27%. The observed correlation coefficient (r^2) of 0.54, is generally lower than others have reported.[3,7–12] The explanation for this discrepancy is unclear.

We cannot rule out CCO inaccuracies even though this technique favorably compares with the manual thermodilution technique.[13] Potential pitfalls of CCO monitoring, relative to bolus thermodilution CO, include thermal noise caused by incomplete mixing of cold peripheral blood with warmer central blood and variabilities of heart rate over the time course of a CCO reading. To directly address the accuracy issue, both the CCO and NICO methods should be compared with an independent method for measuring CO, such as an aortic flow probe.

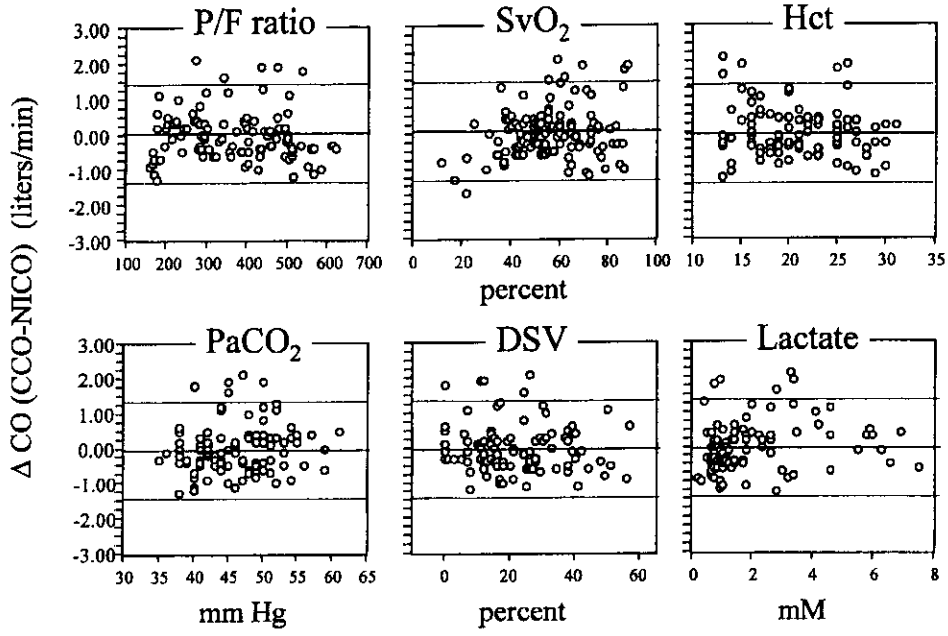

Fig. 4. *These scatter plots show that no more than 5% of the total number of paired CCO and NICO measurements deviated by more than 1.4 liters/min as a function of increased pulmonary shunt, venous desaturation, anemia, hypercapnia, increased dead space ventilation, or hyperlactacidemia.*

We suspect, but have no direct proof, that the severity of lung injury in this model may have overcome the NICO's ability to correct for shunt fraction and that this may have contributed to observed decreases in r^2. For example, according to our data, and if it can be assumed that CCO is 100% accurate, then it is theoretically possible that a real increase from 2 liters/min to 4 liters/min in CO after severe chest trauma could be masked or misinterpreted by a 50–75% variability in the NICO value.

The current NICO allows for real-time determination of shunt fraction using pulse oximetry and F_{IO_2}. The classic Fick technique can underestimate true CO when there is underlying pulmonary dysfunction because of blood flow lost to shunt fraction, which has been a criticism of previous NICO prototypes. However, the data in Figure 4 show no correlation between the decrease in P/F ratio and the difference between the two methods, which suggests that shunt fraction per se did not alter NICO any more than it altered CCO. Similarly, increased dead space ventilation, hypercapnia, and hyperlactacidemia did not correlate with the difference between the two methods. The NICO-CCO variability may have trended slightly higher at lower hematocrits and higher mixed venous oxygen saturations, which, in theory, could reflect displacement of CO_2 from hemoglobin by the Bohr effect. Nevertheless, the results in Figure 4 suggest that several common conditions in severely injured trauma victims were not likely to interfere with the reliability of the NICO technique any more than they would interfere with the reliability of the CCO technique.

In conclusion, NICO tracked reasonably well with thermodilution CCO in extreme conditions of trauma-induced cardiopulmonary dysfunction, especially at the low range of CO. This suggests that NICO monitoring might have a potential role in field situations or in the emergency department before invasive techniques can be implemented. However, it must be emphasized that large errors persisted despite the general congruence between the NICO and CCO values, so without further refinements, NICO will probably continue to have a limited role in the emergency department. The overall agreement between NICO and CCO monitoring was lower after chest trauma than that generally reported in other intensive care patients with respiratory failure, during heart surgery, and during liver transplantation. The explanation is unclear. Extreme caution should be exercised in patients with head injury because the rebreathing cycle can cause transient increases in P_{aCO_2} of 2–5 mm Hg.[13] Further evaluations of NICO in clinically relevant models and in patients are necessary to confirm these predictions.

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□紹　介□

CO_2 再呼吸法による新しい非侵襲的心拍出量モニター（NICO™）

辻本三郎* 有村佳修* 黒田信人*
呉原英和* 太城力良*

要　旨

Fickの原理を応用し，二酸化炭素（CO_2）を一部再呼吸させてCO_2の呼出量の変化より心拍出量（CO）を算出する非侵襲的心拍出量モニターNovametrix社のNICO™を紹介する。NICO™によるCO_2再呼吸式CO測定法の測定精度を，Bland-Altmanらの方法によりスワン・ガンツカテーテルを利用した持続的熱希釈法およびパルス式色素希釈法と比較・検討した。前者間のbias（n＝46）は$-0.21\,l\cdot m^{-1}$，precisionは-1.65から$1.22\,l\cdot m^{-1}$で，後者間のbias（n＝53）は$-0.1\,l\cdot m^{-1}$，precisionは-2.14から$1.94\,l\cdot m^{-1}$であった。NICO™による心拍出量は，熱希釈法による場合に比べて$0.21\,l\cdot min^{-1}$，またパルス式色素希釈法による場合に比べると$0.1\,l\cdot min^{-1}$とともに低く測定されたが，臨床的に有意なバイアスはないと考えられた。スワン・ガンツカテーテル挿入が禁忌の患者や挿入困難な患者，またはそれ以外の比較的循環動態の安定した患者の麻酔管理にはNICO™は有用なモニターと思われた。

心拍出量とは，1分間に左心室から大動脈に送り出される血液量（あるいは右心室より肺動脈へ送り出される血液量）と定義される。心拍出量測定は，麻酔管理や集中治療を行ううえで重要な循環系のモニターである。心拍出量の測定には，従来より，直接Fick法，色素希釈法，熱希釈法で行われてきた。このうち，直接Fick法による心拍出量測定は正確でゴールドスタンダードな方法であるが，臨床的にはスワン・ガンツカテーテルを挿入して測定する熱希釈法がもっとも広く行われている。また，最近ではより侵襲の少ないパルス式色素希釈法による心拍出量測定も開発され，熱希釈法による心拍出量測定との精度比較がなされている[1]。

新しく開発されたNovametrix社のNICO™は，Fickの原理を応用し，二酸化炭素（CO_2）を一部再呼吸させたときのCO_2産生量の変化と終末呼気CO_2分圧の変化より心拍出量（CO）を測定する非侵襲的心拍出量モニターである[2)3)]。今回，NICO™によるCO_2再呼吸式CO測定法の測定精度を，スワン・ガンツカテーテルを利用した持続的熱希釈法およびインドシアニングリーンを用いたパルス式色素希釈法と比較・検討した。

1. 機器の概要と測定原理

1）概　要

NICO™は，NICOモニター（モデル7300），ディスポーザブルのNICOセンサー™，カプノスタットCO_2センサーおよびオキシメトリセンサーより構成されている。

(a) NICOモニター（モデル7300，図1）

前面パネルは，表示スクリーン，センサーコネクター，コントロールノブ，操作用プッシュボタンなどよりなり，心拍出量，心係数，一回心拍出量，CO_2放出量（VCO_2），肺胞換気量を含む種々の呼吸モニタリングパラメータが表示できる。背面パネルには，AC電源入力モジュール，3つのRS 232シリアル通信ポート，アナログ入出力ポートなどが配備されている。

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(b) NICOセンサー™（図2）

NICOセンサー™は，再呼吸弁，NICO LoopおよびCO_2・流量センサーより構成されている。NICO Loopを呼気量の設定と一致するように伸展させ，再呼吸弁が開くとLoop内の再呼吸量が回路内に追加されて，このときのCO_2流量をCO_2・流量センサーで測定する。本製品はディスポーザブルである。

(c) カプノスタットCO_2センサー，およびオキシメトリセンサー

カプノスタットCO_2センサーはメインストリーム方式で，NICOセンサー™の遠位側（患者側）に装着する。専用のオキシメトリセンサーにより，シャント補正と脈拍数により一回心拍出量が計算できる。

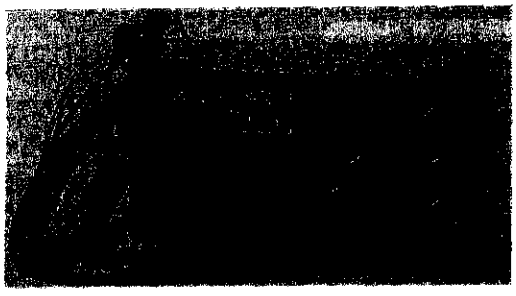

図1　NICO™モニター7300

2）測定原理

NICO™による心拍出量の測定は，直接Fickの原理を応用したものである[2)3)]。Fickの原理では，1分間に肺から摂取される酸素量を動静脈酸素含量の較差で割った値として心拍出量が求められる（図3）。混合静脈血の採取のためには，肺動脈カテーテルの挿入が必要である。

これに対して，NICO™では，呼出されるCO_2量をCO_2動静脈含量較差で割ることで心拍出量を計算するCO_2に対するFickの式を用いている。再呼吸の時間を50秒とすることで，混合静脈血CO_2含量の測定が不要となり，非観血的に心拍出量が求められる（式）。すなわち，呼出ガスの一部を再呼吸させて呼出されるCO_2の変化量（ΔVco_2）を終末呼気CO_2分圧の変化量（$\Delta ETco_2$）で割った値として心拍出量を算出する。NICOセンサー™を患者の呼吸回路に装着し，CO_2・流量センサーによりΔVco_2が測定される。一方，$\Delta ETco_2$はメインストリーム方式のカプノスタットCO_2センサーで測定される。測定は60秒間および70秒間のsteady stateを挟んでNICOセンサー™の再呼吸弁の開放によりCO_2の再呼吸を50秒間行う合計3分間のサイクルでなされる。

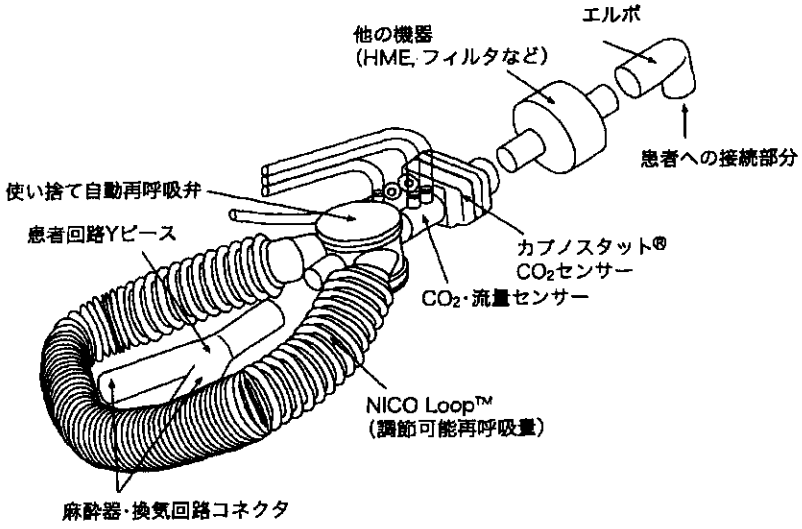

図2　NICOループ™

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$$CO_2\ \text{Fick equation}: C.O.=\frac{\dot{V}CO_2}{C\bar{v}CO_2-CaCO_2}$$

Applied with & without rebrathing

$$C.O.=\frac{\dot{V}CO_{2N}}{C\bar{v}CO_{2N}-CaCO_{2N}}=\frac{\dot{V}CO_{2R}}{C\bar{v}CO_{2R}-CaCO_{2R}}$$

Using the law of ratios to form the differential Fick equation :

$$C.O.=\frac{\dot{V}CO_{2N}-\dot{V}CO_{2R}}{(C\bar{v}CO_{2N}-CaCO_{2N})-(C\bar{v}CO_{2R}-CaCO_{2R})}=\frac{\Delta\dot{V}CO_2}{\Delta CaCO_2}=\frac{\Delta\dot{V}CO_2}{S\Delta PetCO_2}$$

式　CO_2 に対する modified Fick 式

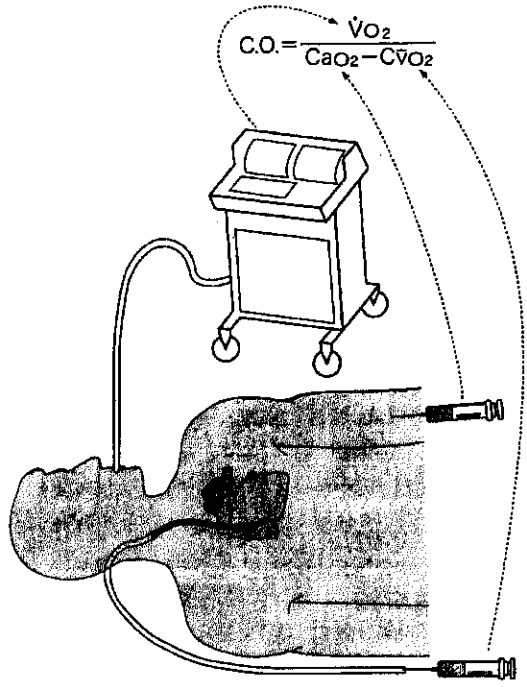

図 3　Fick の原理に基づく心拍出量測定

2. 臨床研究

NICO™ による CO_2 再呼吸式 CO 測定法（RBCO）の測定精度を，肺動脈カテーテルを利用した持続的熱希釈法（TDCCO）およびインドシアニングリーンを用いたパルス式色素希釈法（PDD）とで比較・検討した。

1）対象と方法

(a) 研究 1：CO_2 再呼吸式測定法（RBCO）と持続的熱希釈法（TDCCO）との比較

スワン・ガンツカテーテルを挿入されて手術が行われた 4 症例（心臓弁置換術 2 症例，CABG 1 症例，肝切除術 1 症例）の成人患者を対象とした。測定は麻酔導入後に行い，心臓手術症例では人工心肺開始前までの任意の時点で行った。NICO™ による CO 測定は流量/CO_2 センサーと再呼吸バルブ回路を気管チューブと Y アダプタとの間に連結し，3 分間のサイクルで 50 秒間，約 150-200 cc の呼気ガスを再呼吸させて測定した。TDCCO による CO 測定は，Baxter 社の Vigilance Monitor™ で行った。なお，NICO™ の安全性は保証されているので，患者の承諾は得なかった。

(b) 研究 2：CO_2 再呼吸式測定法（RBCO）とパルス式色素希釈法（PDD）との比較

あらかじめ本研究の趣旨を患者に説明し，口頭で協力の了承を得てから研究を行った。開腹手術症例 14 症例（男 6 症例，女 8 症例）の成人患者を対象とした。測定は麻酔導入後から手術終了時までの任意の時点で行った。PDD による CO 測定は，一定量のインドシアニングリーンを静脈路より急速注入し，鼻に装着したパルスオキシメトリ用プローブで ICG 吸光の変化を測定し，ICG 希釈曲線が描出できることより求められる。今回の研究では，日本光電社の DDG アナライザー™（DDG 1101）を使用し，生理食塩液 1 ml で溶解したインドシアニングリーン（5 mg）を右内頸静脈もしくは末梢静脈路より急速投与して CO を測定した。各時点で 2-3 回測定して，その平均値を CO 値とした。

(c) 統計検定：Bland-Altman らの一致性の分析（analysis of agreement）により，同一のパラメータ（この場合は CO 値）を測定した 2 種類の測定方法の精度（precision）を検討した[4]。す

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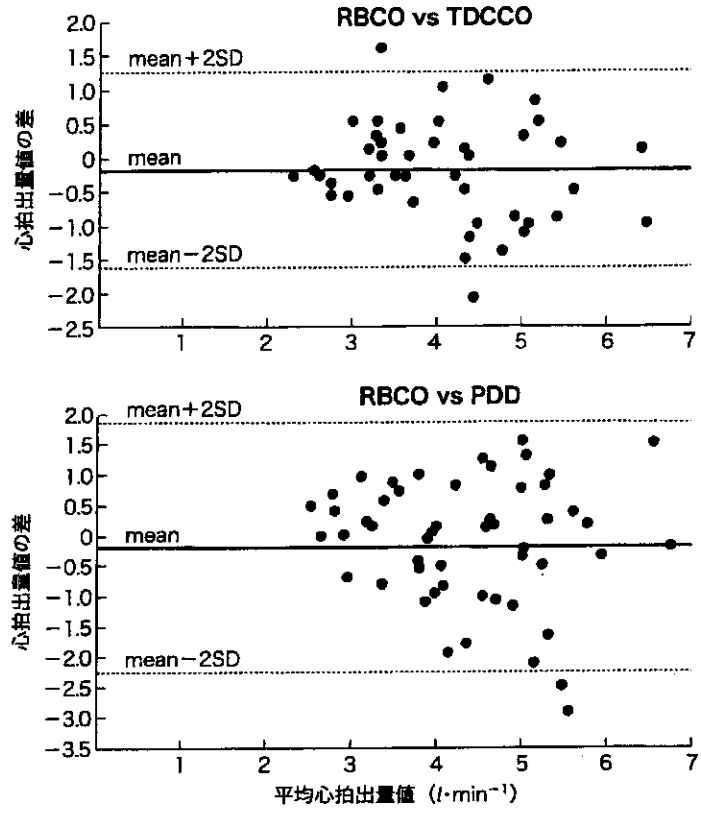

図 4　結果のグラフ
上段は CO_2 再呼吸式測定法（RBCO）と持続的熱希釈法（TDCCO）との bias と precision を，下段は CO_2 再呼吸式測定（RBCO）とパルス式色素希釈法（PDD）との bias と precision を示す。

なわち，2種類の方法で得られたCO値の平均値に対してCO値の較差をプロットし，biasとprecisionを2種類の方法で得られた値の較差の平均値と標準偏差を用いて求めた。biasは較差の平均値で2種類の方法間のシステムエラーを表わし，precisionはばらつきを表わし，±2 SD，95%信頼区間で定義した。また，最小2乗法により直線回帰式を求めた。

2）結果（図4）

(a) 研究1

測定データは46時点で得られた。RBCOとTDCCOによるCO測定法のbiasは$-0.21\,l\cdot m^{-1}$であり，precisionは-1.65から$1.22\,l\cdot m^{-1}$であった。直線回帰式は，$y=0.69x+1.0$（$r=0.78$）であった。

(b) 研究2

測定データは53時点で得られた。RBCOとPDDによるCO測定法のbiasは$-0.1\,l\cdot m^{-1}$であり，precisionは-2.14から$1.94\,l\cdot m^{-1}$であった。直線回帰式は，$y=0.57+1.8$（$r=0.62$）であった。

3. 考　察

今回の研究では，NICO™による心拍出量は熱希釈法による場合に比べて$0.21\,l\cdot min^{-1}$，またパルス式色素希釈法による場合に比べると$0.1\,l\cdot min^{-1}$とともに低く測定されたが，臨床的に有意なバイアスはないと考えられた。測定のばらつき（precision）は，熱希釈法との比較では$1.43\,l\cdot min^{-1}$とほぼ良好な結果であった。この

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結果は他の報告と一致しており[5)~8)]，臨床的にNICO™による心拍出量測定は有用であると思われる。一方，熱希釈法との比較では，測定のばらつきは2.04 $l \cdot min^{-1}$ とやや大きかった。これには抽出サンプル数が少なかったことや，パルス式色素希釈法による測定には一回一回の測定値にばらつきがあり測定者の測定技術の問題などが関与したのかもしれない。

心拍出量の測定方法としては，直接Fick法，色素希釈法および熱希釈法が代表的な方法として挙げられる。これらはすべて侵襲的な方法で，直接Fick法と色素希釈法は測定が煩雑で，かつ繰り返しの測定が困難であり，臨床的には有用でない。スワン・ガンツカテーテルを用いた熱希釈法も侵襲的な方法ではあるが，右心系および左心系の圧測定ができ，また各種の薬物の投与ルートとしても利用できる。このためスワン・ガンツカテーテルは重症患者の麻酔管理や集中治療に必須のモニターとして，現時点ではもっとも広く利用されている。

一方，最近，パルス式色素希釈法や食道超音波ドップラー法，あるいはCO_2再呼吸式法などの非侵襲的な心拍出量モニターが開発されてきた。パルス式色素希釈法は，色素を静脈内に注入したり，動脈血のヘモグロビン濃度の測定が必要であるため，やや侵襲的な方法といえる。欠点として，注入した色素の再循環のために繰り返しの測定に限度があること，測定に時間がかかること，ある程度の測定技術が必要なことなどが考えられる。食道超音波ドップラー法は，血流速度と下行大動脈径の測定より心拍出量を測定するために，より正確な値が得られること，心拍ごとの血行動態がリアルタイムでモニターできる点で優れている。しかし，食道内への超音波プローブの挿入はやや侵襲的であること，超音波プローブを適正な位置に挿入するのにやや技術を要すること，プローブの位置がずれるなどが欠点として考えられる。これらに比べて，CO_2再呼吸式法によるNICO™は気管挿管下で人工呼吸されている成人患者であれば，気管チューブの先端に装着するだけで容易に心拍出量の測定ができ，簡便でもっとも非侵襲的なモニターであろう。測定に3分とやや時間がかかること，この測定期間中，心拍出量の変化はないと仮定している点が欠点として挙げられる。また，CO_2の再呼吸時に終末呼気CO_2濃度および動脈血CO_2分圧の5 mmHg前後程度の上昇が認められるが，その場合のCO_2の再呼吸による生体への影響がどうなのか，CO_2の再呼吸時に肺塞栓が発生した場合の発見が遅れる可能性があるかなどの問題点が挙げられるが，今後の検討すべき課題であろう。将来的には，より短時間で測定が可能になるように改良されることを期待したい。

以上，現時点においては，呼吸・循環系に問題のある患者の麻酔管理や集中治療には，スワン・ガンツカテーテルを用いたモニターが侵襲的方法ではあるが，もっとも有用であろう。しかし，スワン・ガンツカテーテル挿入が禁忌の患者や挿入困難な患者，またはそれ以外の比較的循環動態の安定した患者の麻酔管理にはNICO™は有用なモニターとなると思われる。

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ABSTRACT

Introduction and Clinical Evaluation of a New Non-invasive Cardiac Output Monitor (NICO™) Based on Fick Partial CO_2 Rebreathing Method

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A newly developed non-invasive monitor, NICO™ (Novametrix Medical Systems Inc.), measures cardiac output based on changes in respiratory CO_2 concentration caused by a brief period of rebreathing. By applying modified form of the CO_2 Fick principle, cardiac output is caluculated. We determined the accuracy and precision of this technique (RBCO) by comparing it with continuous thermodilution technique (TDCCO) and pulse dye densitometry thechnique (PDD). The overall difference between RBCO and TDCCO(n=46) was -0.21 ± 1.43 (bias$\pm$2 SD) $l \cdot min^{-1}$. On the other hand, the overall difference between RBCO and PDD (n=53) was -0.1 ± 2.04 (bias$\pm$2 SD) $l \cdot min^{-1}$. The degree of accuracy of RBCO was thought to be the same as those of TDCCO and PDD. We expect that NICO™ will be a usuful cardiac output monitor in any method of general anesthesia in which PA catheterization is difficult or not indicated.

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PARTIAL CO_2 REBREATHING INDIRECT FICK TECHNIQUE FOR NON-INVASIVE MEASUREMENT OF CARDIAC OUTPUT

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Haryadi DG, Orr JA, Kuck K, McJames S, Westenskow DR. Partial CO_2 rebreathing indirect Fick technique for non-invasive measurement of cardiac output.

J Clin Monit 2000; 16: 361–374

ABSTRACT. Objective. Evaluation in animals of a non-invasive and continuous cardiac output monitoring system based on partial carbon-dioxide (CO_2) rebreathing indirect Fick technique. **Methods.** We have developed a non-invasive cardiac output (NICO) monitoring system, based on the partial rebreathing method. The partial rebreathing technique employs a differential form of the Fick equation for calculating cardiac output ($\dot{Q}_T$) using non-invasive measurements. Changes in CO_2 elimination ($\Delta\dot{V}CO_2$) and partial pressure of end-tidal CO_2 ($\Delta P_{ET}CO_2$) in response to a brief period of partial rebreathing are used to measure pulmonary capillary blood flow ($\dot{Q}_{PCBF}$). A non-invasive estimate of anatomic and intrapulmonary shunt fraction ($\dot{Q}_S/\dot{Q}_T$), based on oxygen saturation from pulse oximetry (SpO_2) and inspired oxygen concentration (FiO_2), is added to compute total cardiac output [$\dot{Q}_T = \dot{Q}_{PCBF}/(1 - \dot{Q}_S/\dot{Q}_T)$]. The performance of the NICO was compared with iced 5% dextrose bolus thermodilution cardiac output (TDco) measurements in 6 dogs. Cardiac output was varied using dobutamine, and halothane, and by clamping of the inferior vena cava. Two hundred and forty-six ($n = 246$) paired measurements of TDco and NICO over a range of cardiac outputs (TDco range = 0.60–8.87 l/min) were compared using Bland-Altman analysis and weighted correlation coefficient. **Results.** The Bland–Altman technique yielded a NICO precision of ±0.70 l/min (13.8%) with a mean bias of −0.07 l/min (−1.4%) compared to TDco. The weighted correlation coefficient between TDco and NICO values was: $r = 0.93$ ($n = 246$). **Conclusion.** The partial CO_2 rebreathing technique for measurement of cardiac output is non-invasive, automated, and based on the well accepted Fick principle. The limits of agreement between NICO and TDco is within the recommended value for NICO to be a clinically acceptable method for cardiac output measurement. The results of this canine study show that NICO performed as well, and in some cases better, than other currently available non-invasive cardiac output techniques over a wide range of cardiac outputs.

KEY WORDS. Cardiac output, partial rebreathing, NICO, carbon dioxide, non-invasive monitoring, thermodilution cardiac output.

INTRODUCTION

Cardiac output, the volume of blood pumped by the heart per unit time, is an important, essential, and a comprehensive measure of a patient's cardiovascular status. It has proven value in hemodynamic assessment for both surgical and critical care intervention. The introduction of the balloon-tipped, flow directed Swan–Ganz pulmonary artery (PA) catheter in the early 1970s enabled bedside thermodilution cardiac output (TDco)

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measurement [1]. Despite concerns regarding it's precision and accuracy TDco is currently the most widely used and clinically accepted standard [2, 3]. Even though the additional filling pressure information obtained from the PA catheter is useful, the monitoring costs associated with it's use are substantial while its associated morbidity and mortality is hardly insignificant [4]. With increasing evidence on the risk of infections and other serious complications associated with the use of PA catheters, a controversy exists over its risk/benefit ratio [5, 6]. Non-invasive measurement of cardiac output would therefore be desirable in patients whose cardiac performance is in question while the risk and costs associated with a PA catheter are unwarranted. Presently, non-invasive methods for estimating cardiac output, including transthoracic bioimpedance, esophageal Doppler and trans-esophageal echocardiography are undergoing refinement. However, none have achieved widespread clinical use.

Fick method for measurement of cardiac output

The Fick method for measurement of cardiac output is based on the theoretical principle enunciated by Adolf Fick in 1870 [7, 8]. The principle states that over a given time period, the quantity of a gas such as O_2 or CO_2 entering or leaving the lungs is equal to the quantity of the gas taken up or expelled by the blood flowing in the pulmonary capillaries. The Fick technique for cardiac output measurement has long been a standard by which other methods of determining cardiac output have been compared. The Fick equation expressed with CO_2 as the indicator gas is:

$$\dot{Q}_T = \frac{\dot{V}CO_2}{(CvCO_2 - CaCO_2)} . \quad (1)$$

Where $\dot{Q}_T$ is the cardiac output $\dot{V}CO_2$, is CO_2 excreted by the lungs, and $CaCO_2$ and $CvCO_2$ are the arterial and mixed venous CO_2 contents, respectively. The direct Fick method is considered the "gold standard" for measurement of cardiac output; however its practical application in a clinical setting is limited due to technical issues involved in accurate metabolic gas measurements and the need for invasive arterial and mixed venous O_2 or CO_2 content measurements.

Rebreathing indirect Fick method

To eliminate the need for invasive blood gas samples, indirect Fick methods known as rebreathing techniques have been developed [9–11]. Rebreathing techniques use estimates of arterial and mixed venous CO_2 contents obtained from measurements of end-tidal CO_2 partial pressure ($PETCO_2$) made at the mouth during normal breathing and rebreathing maneuvers. $\dot{V}CO_2$ can be measured to an acceptable level of accuracy using commercially available metabolic gas monitors [12]. The arterial CO_2 content ($CaCO_2$) is estimated from the measurement of $PETCO_2$ during normal periods of ventilation. During rebreathing the lungs are used as an aero-tonometer to measure mixed venous CO_2 partial pressure ($PvCO_2$) from which CO_2 content ($CvCO_2$) is calculated. The partial pressure of CO_2 in the mixed venous blood ($PvCO_2$) is obtained when the patient breathes into a bag attached to the mouth. As the patient rebreathes, the level of $PETCO_2$ rises asymptotically to a plateau level corresponding to the partial pressure of CO_2 in the blood entering the lungs (or mixed venous blood). At equilibrium, the partial pressure of CO_2 in the end pulmonary capillary blood can be assumed equal to the partial pressure of CO_2 in the alveoli, and the CO_2 elimination from the lungs approaches zero ($\dot{V}CO_2 \sim 0$). This is commonly known as the "total-rebreathing" technique [13]. Even though the total CO_2 rebreathing technique allows non-invasive cardiac output estimation based on routinely obtained respiratory gas measurements, the compliant rebreathing bag and the need for patient cooperation makes it impractical for use in mechanically ventilated patients.

Partial rebreathing indirect Fick method

A variation of the rebreathing technique has been adapted for use with ventilated patients whose cooperation cannot be assured [14–17]. The partial rebreathing technique uses a differential form of the Fick equation to calculate cardiac output. The technique uses the ratio of the change in the numerator and denominator of the Fick equation to measure cardiac output. Changes in CO_2 elimination ($\Delta\dot{V}CO_2$) and partial pressure of end-tidal CO_2 ($\Delta PETCO_2$) in response to a brief change in effective ventilation are used to measure cardiac output. The Fick Equation (Equation (1)) for two separate levels of ventilation at time 1 and time 2, can be written as:

$$\dot{Q}_T = \frac{\dot{V}CO_{2,1}}{Cv_1CO_2 - Ca_1CO_2} = \frac{\dot{V}CO_{2,2}}{Cv_2CO_2 - Ca_2CO_2} . \quad (2)$$

Where subscripts 1 and 2 indicate values at time 1 and 2 respectively. Equation (2) assumes that the cardiac output remains constant from time 1 to time 2. From basic

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algebra (X = A/B = C/D = (A−C)/(B−D)] Equation (2) can be rearranged to obtain:

$$\dot{Q}_T = \frac{\dot{V}CO_{2,1} - \dot{V}CO_{2,2}}{(Cv_1CO_2 - Ca_1CO_2) - (Cv_2CO_2 - Ca_2CO_2)} . \quad (3)$$

Rearranging terms in the denominator of Equation (3):

$$\dot{Q}_T = \frac{\dot{V}CO_{2,1} - \dot{V}CO_{2,2}}{(Cv_1CO_2 - Cv_2CO_2) - (Ca_1CO_2 - Ca_2CO_2)} . \quad (4)$$

Assuming that the mixed venous CO_2 content does not change during a brief change in effective ventilation ($Cv_1CO_2 = Cv_2CO_2$), Equation (4) reduces to:

$$\dot{Q}_T = \frac{\Delta\dot{V}CO_2}{\Delta CaCO_2} , \quad (5)$$

where $\Delta\dot{V}CO_2 = \dot{V}CO_{2,1} - \dot{V}CO_{2,2}$ and $\Delta CaCO_2 = Ca_2CO_2 - Ca_1CO_2$.

The change in effective ventilation necessary for implementation of the partial rebreathing Fick technique can be achieved in many ways. Gedeon et al. in 1980 first described a method where effective ventilation was altered by a bidirectional change in ventilation (hyperfollowed by hypoventilation by changing respiratory rate) [14]. Subsequently, Gedeon, Roy and Capek, described a method wherein a serial dead space added in the breathing circuit was used to alter effective ventilation [15–17]. We have developed a partial rebreathing non-invasive cardiac output (NICO) system that uses a pneumatically driven valve to temporarily add an adjustable serial dead space to the breathing circuit. This added dead space permits a subject to rebreathe only a part of his exhaled gases.

When alveolar or end-capillary CO_2 content ($CcCO_2$) is used in the Fick equation in place of arterial CO_2 content ($CaCO_2$) then pulmonary capillary blood flow ($\dot{Q}_{PCBF}$) is measured rather than cardiac output ($\dot{Q}_T$). The cardiac output ($\dot{Q}_T$) is the sum of the blood flowing through the lungs ($\dot{Q}_{PCBF}$) that participates in alveolar gas exchange and blood that bypasses the lungs without exposure to gas exchanging alveoli, namely intrapulmonary shunt blood flow ($\dot{Q}_S$), in addition to anatomic shunt. Expressed in equation form:

$$\dot{Q}_{PCBF} = \frac{\Delta\dot{V}CO_2}{\Delta CcCO_2} \quad (6)$$

$$\dot{Q}_T = \dot{Q}_{PCBF} + \dot{Q}_S . \quad (7)$$

The NICO system uses a non-invasive estimate of intrapulmonary and anatomic shunt fraction ($\dot{Q}_S/\dot{Q}_T$) based on oxygen saturation from pulse oximetry (SpO_2) and inspired oxygen concentration (FiO_2) to compute cardiac output.

$$\dot{Q}_T = \frac{\dot{Q}_{PCBF}}{(1 - \dot{Q}_S/\dot{Q}_T)} . \quad (8)$$

The non-invasive method for estimating shunt fraction in the NICO system is adapted from Nunn's iso-shunt plots, which are a series of continuous curves that indicate the relationship between partial pressure of oxygen in the arterial blood (PaO_2) and fraction of inspired oxygen concentration (FiO_2) for different levels of shunt (%) [18]. The partial pressure of oxygen (PaO_2) is a function of the saturation of oxygen in the arterial blood (SaO_2) and their inter-relationship can be defined using an invertible version of the blood oxygen tension-saturation curve [19–20]. The arterial blood oxygen saturation (SaO_2) may be non-invasively determined using a pulse oximeter. The NICO system makes use of oxygen saturation from pulse oximetry (SpO_2) and the fractional concentration of inspired oxygen (FiO_2) as entered by the user, in conjunction with Nunn's iso-shunt plots to obtain a non-invasive estimate of shunt fraction ($\dot{Q}_S/\dot{Q}_T$) [21].

The CO_2 dissociation curve defines the relationship between CO_2 content and partial pressure of CO_2. At equilibrium the partial pressure of CO_2 in the end pulmonary capillary blood can be assumed equal to the partial pressure of CO_2 in the alveoli, and the CO_2 dissociation relationship can be expressed as [17]:

$$CcCo_2 = (6.957[Hb] + 94.864) * \ln(1.0 + 0.1933 \cdot PACO_2) , \quad (9)$$

where $PACO_2$ = partial pressure of CO_2 in the alveoli; $CcCO_2$ = content of CO_2 in the end pulmonary capillary blood; Hb = hemoglobin concentration.

Previous investigators have assumed that the gradient between the partial pressure of end-tidal CO_2 ($PETCO_2$) and alveolar CO_2 ($PACO_2$) does not change during rebreathing [14–17]. This assumption is unacceptable when $\Delta PETCO_2$ is small because the partial pressure of CO_2 in alveolar deadspace changes in proportion to inspired CO_2 during rebreathing. Because $PETCO_2$ is a weighted sum of the partial pressure of CO_2 from perfused ($PACO_2$) and un-perfused alveoli ($PUCO_2$), large changes in $PUCO_2$ in the alveolar dead space (unperfused alveoli) as a result of rebreathing cause a small change in $PETCO_2$ that is not related to cardiac output. We have therefore made use of a two compartment

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mathematical model of the lung to account for the observed differences between $P_{ET}CO_2$ and P_ACO_2 (model described in the Appendix).

If $P_{ET}CO_2$ measured at the mouth is corrected for alveolar dead space then it can be assumed to equal partial pressure of CO_2 in the end capillary blood (which is assumed to be in equilibrium with partial pressure of CO_2 in the alveoli (P_ACO_2)) [22, 23]. Combining Equations (6) and (9)

$$\dot{Q}_{PCBF} = \frac{\Delta \dot{V}CO_2}{Cc\left(P'_{ET}CO_2(t_2)\right) - Cc\left(P'_{ET}CO_2(t_1)\right)}, \quad (10)$$

where $Cc(P'_{ET}CO_2(t))$ is the CO_2 content in the capillary blood calculated from $P'_{ET}CO_2$ at time t, after taking into consideration the dilution of $P_{ET}CO_2$ due to the alveolar dead space. Therefore the Fick cardiac output equation becomes simply the ratio of change in CO_2 elimination ($\Delta \dot{V}CO_2$) to a corresponding change in CO_2 content (ΔCCO_2) as calculated from corresponding changes in partial pressures of CO_2 measured at the mouth ($\Delta P_{ET}CO_2$).

The goal of the present study was to assess the performance of the NICO when compared with bolus thermodilution cardiac output measurements in animals over a wide range of cardiac outputs.

METHODS

System description

The NICO monitor consists of a microprocessor based data acquisition system that measures on-airway flow, pressure and mainstream partial pressure of CO_2 ($NICO_2$®, Novametrix Medical Systems Inc., Wallingford, CT). It also has an integrated pulse oximeter to measure oxygen saturation (SpO_2). The partial pressure of CO_2 is measured by a mainstream infrared absorption technique with a solid state sensor. CO_2 elimination ($\dot{V}CO_2$) is calculated breath-by-breath by integrating the product of the CO_2 concentration over the entire respiratory cycle (inspiratory and expiratory) of each breath [24].

The disposable NICO sensor shown in Figure 1 is a combination of an on-airway flow sensor, on-airway CO_2 sensor, adjustable dead space tubing, and a pneumatic valve. In use, the NICO sensor is connected between the breathing circuit (at the Y-piece) and the endotracheal tube of the patient. The NICO monitor controls the operation of the pneumatic valve by application of positive pressure (~140 mmHg). In its default position, the pneumatic valve causes gas from the breathing circuit to bypass the adjustable deadspace. When actuated, the pneumatic valve places the adjustable deadspace (150–450 ml) serially in the breathing circuit between the Y piece of the breathing circuit and the endotracheal tube connected to the patient. This causes the patient to rebreathe a portion of his/her exhaled CO_2 remaining in the deadspace during the subsequent respiratory cycles. The increase in inhaled CO_2 due to rebreathing results in an increase in the partial pressure of alveolar CO_2 (P_ACO_2) and therefore a reduction in the net flux of CO_2 diffusion from the pulmonary capillary blood into the alveoli. This causes a reduction in the CO_2 eliminated from the lung (fall in $\dot{V}CO_2$) and a corresponding increase in alveolar and arterial CO_2 tension (increase in P_ACO_2 and $P_{ET}CO_2$).

The percentage rebreathing is approximately equal to the fraction of the total volume of the added deadspace (range 150 ml to 450 ml) and anatomical deadspace over the tidal volume. Expansion or retraction of the adjustable NICO loop is used to achieve 40–80% rebreathing in order to obtain a significant change in and $P_{ET}CO_2$ signals.

Signal processing

The rebreathing valve is activated for 50 seconds once every three minutes. The resulting changes in and $P_{ET}CO_2$ are shown in Figure 2. Sixty seconds of baseline measurements of and $P_{ET}CO_2$ are recorded before the rebreathing period. A recovery period of 70 seconds allows for CO_2 stores to recover after which another cycle is begun. The flow and CO_2 signals are sampled at 100 Hz with a resolution of 0.1 l/min for flow and 0.1 mm Hg for $P_{ET}CO_2$. The NICO monitor computes and displays and $P_{ET}CO_2$ data on a breath-to-breath basis. Baseline values for and $P_{ET}CO_2$ were calculated as the average of a group of samples between 27 and 0 seconds before the start of a known rebreathing process. During rebreathing, values for and $P_{ET}CO_2$ were calculated as the average of a group of samples during the interval of 25 to 50 seconds into the rebreathing period. The two compartment mathematical model of the lung described in the appendix was used to account for the expected differences between $P_{ET}CO_2$ and P_ACO_2. The changes in P_ACO_2 and are then used along with Equations (6) and (8) to calculate $\dot{Q}_{PCBF}$. The intrapulmonary shunt fraction ($\dot{Q}_S/\dot{Q}_T$) was calculated based on Nunn's iso-shunt plots from user entered F_IO_2 values and the average of the last one minute of SpO_2 values. The cardiac output values for the NICO were then calculated from Equation (10).

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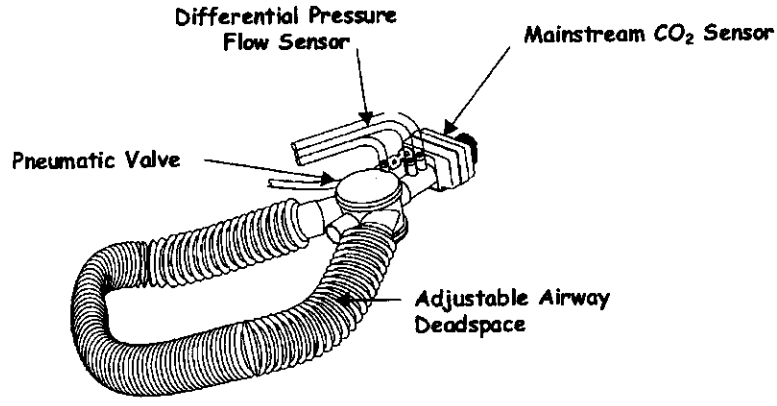

Fig. 1. The disposable NICO sensor for single patient use is a combination of an on-airway flow sensor, on-airway/mainstream CO_2 sensor, an adjustable deadspace tubing, and a pneumatic valve. It is connected in between the endotracheal tube of the patient and the Y-piece of the breathing circuit.

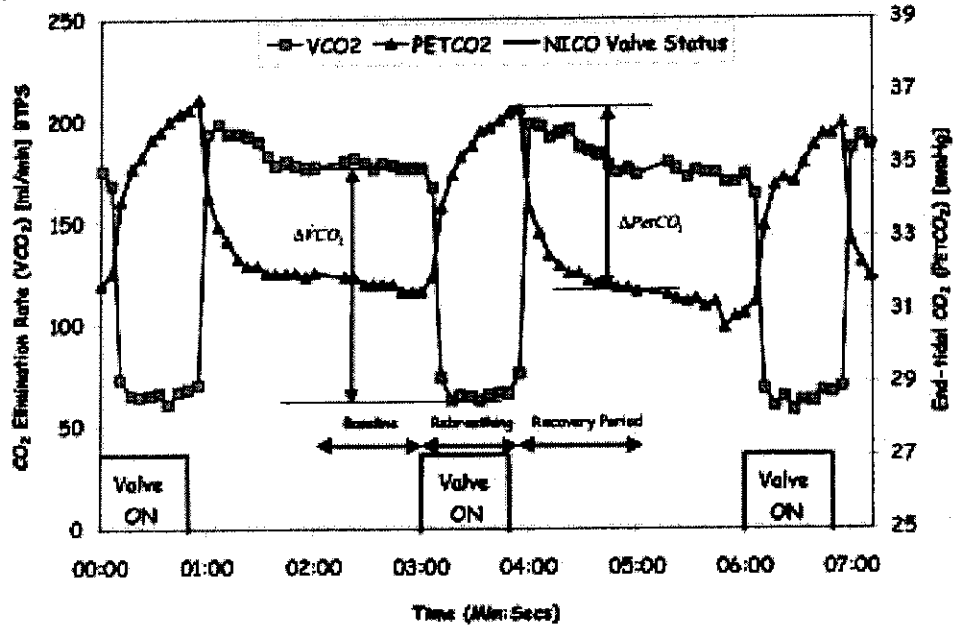

Fig. 2. Typical waveforms: Figure showing breath-to-breath measurements of $\dot{V}CO_2$ and $P_{ET}CO_2$ during periods of baseline or normal ventilation (60 seconds), rebreathing (50 seconds) and recovery periods (70 seconds).

Animal study protocol

After approval from the University of Utah Institutional Animal Care and Usage Committee, we studied six dogs weighing 18.2–39.5 kg (average weight = 26.05 kg). The dogs were studied in the supine position. Endotracheal intubation was performed with a cuffed tube taking care to avoid air leaks. The dogs were mechanically ventilated and anesthesia maintained with halothane. Muscle paralysis was achieved using periodic bolus injections of pancuronium bromide.

Thermodilution CO (TDco) was measured using a DualTherm cardiac output computer (DualTherm®, B. Braun Medical Inc., Bethlehem, PA). The Dualtherm system makes use of PA catheters equipped with a second thermistor located at the right atrial injectate

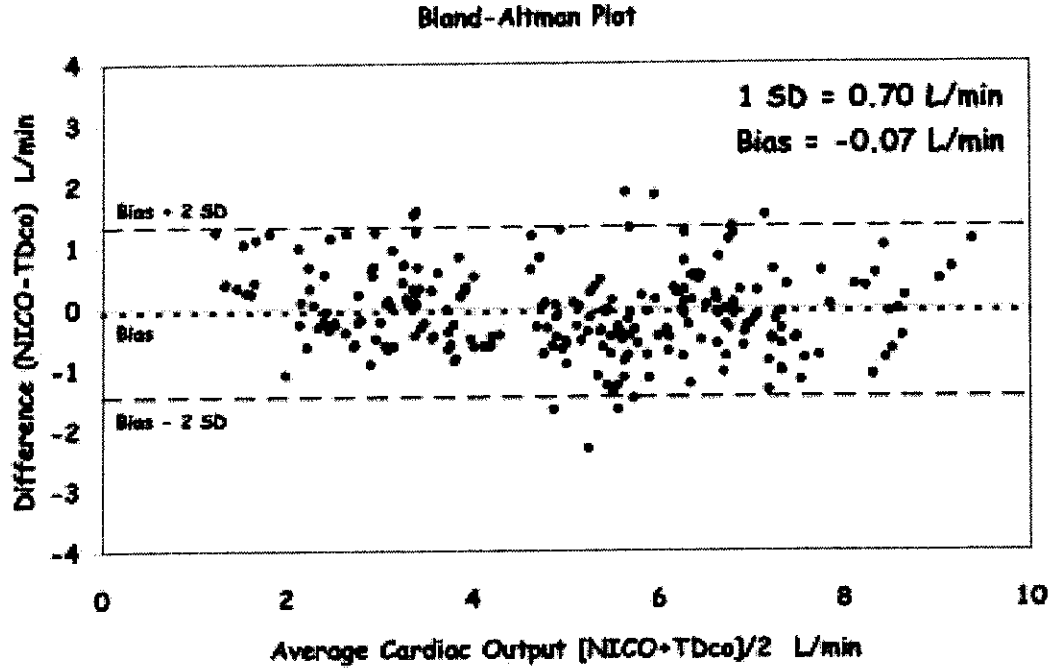

Fig. 3. Bland–Altman plot: differences between NICO and TDco plotted against the average of the two. Bias = average (NICO − TDco) is shown by the dotted line. The dashed lines indicate ± 2 standard deviation from the bias.

port on the catheter [25, 26]. The measurement of the injectate temperature eliminates the need for a correction factor to estimate heat gain of the injectate as it passes through the lumen of the catheter. Thermodilution measurements were made at approximately 10–15 minute intervals using the average of three sequential measurements with 10 ml iced 5% dextrose injections, phased randomly with respect to respiration. Correct positioning of the catheter was ensured using the PA pressure waveforms and the injectate temperature waveforms as reference.

A continuous intravenous infusion of Dobutamine (2.5 to 15 μg/kg/min) was administered to increase cardiac output to two to three times its initial resting state. With dobutamine the percentage increase in stroke volume was typically 2–3 times the percentage increase in heart rate. Increased levels of halothane (0.5 to 4%) and/or clamping of the inferior vena cava was used to reduce cardiac output. Controlled clamping of the inferior vena cava caused a reduction in venous return, resulting in a decrease in cardiac output.

Arterial blood gas and hematocrit measurements were obtained once every two hours (STAT Profile, NOVA Biomedical, Waltham, MA, USA) and used to enhance the accuracy of NICO measurements.

Statistical analysis

TDco values immediately preceding the cyclic NICO were defined as matched cardiac output measurements and used for analysis. Bland–Altman statistics were used to compare the degree of agreement and to determine if a significant difference existed between the two methods of cardiac output measurement [27]. The number of data points collected in each dog differed (average = 41, range = 17–62), therefore, a weighted correlation coefficient was used to take into account the repeated observations from several subjects [28, 29]. Bias was defined as the mean value of the differences between NICO and TDco. Precision was defined as the standard deviation of the differences. Limits of agreement were defined by the bias ± two standard deviations. Percentage limits of agreement were calculated as the ratio of two times the standard deviation to mean cardiac output [30]. Results are presented for each animal and as pooled data.

RESULTS

The pooled data from six dogs consisted of 246 paired measurements of cardiac output obtained over the range

Table 1. Bland–Altman results from individual dogs

Dog	*n*	Bias (l/min)	SD (l/min)	TDco range (l/min)	Mean CO (l/min)	Percentage limits of agreement[a]	Correlation coeff (*r*)
1	17	0.02	0.58	1.13–6.27	4.03	± 28.8%	0.96
2	16	0.21	0.53	2.03–6.47	4.28	± 24.8%	0.95
3	55	−0.17	0.56	2.27–7.73	4.81	± 23.3%	0.94
4	57	−0.38	0.46	1.29–8.00	4.85	± 19.0%	0.98
5	62	0.26	0.91	0.60–8.83	5.86	± 31.1%	0.91
6	39	−0.12	0.64	2.60–8.87	5.40	± 23.7%	0.94
All dogs	246	−0.07	0.70	0.60–8.87	5.09	± 27.5%	0.93

Mean CO is the average of the individual [TDco+NICO]/2 values.
[a] Limits of agreement = 2 SD/mean CO.

from 0.60 to 8.87 l/min (TDco range). The weighted correlation coefficient between TDco and NICO was $r = 0.93$. The regression equation was NICO = 0.89 TDco + 0.52. The standard deviation of the difference between NICO and TDco was 0.70 l/min (precision) with a mean difference of −0.07 l/min (bias) (Figure 3). Expressed as a percentage of the mean cardiac output (average of matched NICO and TDco pairs = 5.09 l/min) the bias was −1.4% and the precision was 13.8%. The Bland–Altman plot shows that the error is not a function of cardiac output, since the scatter in the data is similar at low and high cardiac outputs (Figure 3). Of the differences, 95.9% were within the limits of agreement (+1.33 to −1.47 l/min) which represents ± 2 SD from the bias. The overall limits of agreement between the two methods for the pooled data in the study was 27.4% (= 2 · SD/average CO). The results from Bland–Altman analysis for individual dogs are presented in Table 1. The precision for individual dogs varied from 0.46 to 0.91 l/min and the % limits of agreement from 19.0% to 31.1% (mean = 25.1%).

DISCUSSION

The results from this animal study show good agreement between TDco and NICO measurements. The systematic bias between NICO and TDco was small (−1.4%). NICO measurements closely followed changes in TDco measurements as seen in Figure 4. The standard deviation of the differences in the two techniques (± 0.70 l/min, 13.8%) is comparable and in some cases better than that reported for other non-invasive cardiac output technologies such as thoracic bioimpedance and Doppler [30]. Critchley and Critchely, from a meta-analysis, have reported the overall limits of agreement in studies evaluating Bioimpedance to be ± 37% and in those evaluating Doppler ultrasound to be ± 65% [30]. The limits of agreement between NICO and TDco (27.4%) is within the recommended value (of up to ± 30%) for NICO to be a clinically acceptable method for cardiac output measurement.

The measurement of cardiac output using total rebreathing techniques is based on the Fick principle. Cardiac output is the ratio between CO_2 elimination rate ($\dot{V}CO_2$) and mixed venous–arterial CO_2 content difference ($CvCO_2$–$CaCo_2$). While $CaCO_2$ can be estimated from $P_{ET}CO_2$ with correction for physiological dead space, the estimation of $CvCO_2$ requires complex rebreathing maneuvers or analysis of single breath CO_2 curves [31]. Systematic errors, which tend to accumulate, are introduced when calculating the mixed venous-arterial CO_2 content difference since the mixed venous and arterial contents are established by separate procedures. The partial CO_2 rebreathing technique obviates the need for estimating $CvCO_2$ by using a differential form of the Fick Equation [13–17]. Changes in CO_2 elimination ($\Delta\dot{V}CO_2$) and partial pressure of end-tidal CO_2 ($\Delta P_{ET}CO_2$) in response to a brief change in effective ventilation are used to measure pulmonary capillary blood flow ($\dot{Q}_{PCBF}$).

During the partial rebreathing procedure, CO_2 concentrations in the arterial blood are raised to a lesser degree (2–6 mmHg) than during complete rebreathing (> 5–10 mmHg). Using the same assumptions as for total rebreathing (no change $\dot{Q}_{PCBF}$ in and mixed venous CO_2 content), this method allows estimation of with a lesser impact on ventilation than total rebreathing. The assumption that venous CO_2 content does not change from the nonrebreathing to the rebreathing period has been previously validated [17]. Venous CO_2 content does not change because it corresponds to total CO_2 stores in the body. CO_2 stores are large relative to both metabolic CO_2 production in the tissue and the

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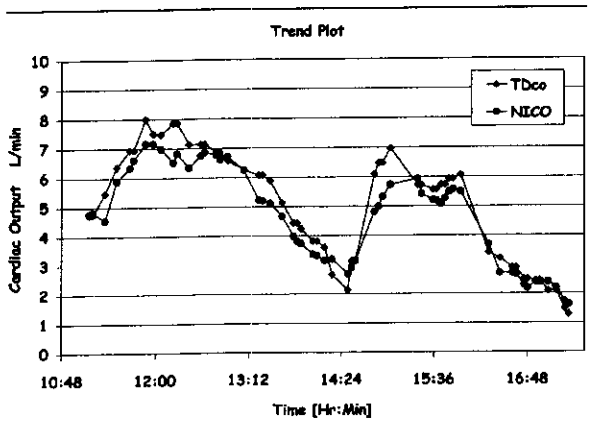

Fig. 4. Typical trend plot showing NICO measurements closely following changes in cardiac output measured using the bolus thermodilution technique. Cardiac output was varied using Dobutamine and increased levels of halothane.

CO_2 eliminated from the lungs. These CO_2 stores in the body act as a low pass filter and change very slightly over short periods of time [18, 22].

A number of investigators have validated the partial CO_2 rebreathing technique for measurement of cardiac output since it was first described by Gedeon in 1980 [14]. Table 2 provides a summary of these studies and the results obtained. This technique is now more viable for practical implementation than it has been in the past due to the availability of accurate and reliable disposable pneumotachographs and fast response on-airway CO_2 sensors.

We used a two-compartment mathematical lung model to account for the observed differences between partial pressure of end-tidal CO_2 ($PETCO_2$) and the partial pressure of CO_2 in the end-capillary blood (assumed equal to partial pressure of CO_2 in the perfused alveoli = $PACO_2$). During rebreathing, partial pressure of CO_2 in the un-perfused alveoli ($PUCO_2$) changes drastically and partial pressure of CO_2 in perfused alveoli ($PACO_2$) changes less. Because of the large change in $PUCO_2$, the change in $PETCO_2$ caused by re-breathing does not reflect $\Delta PACO_2$ in cases when the difference is small or when there is a large un-perfused volume. The model also helped explain the slow change in $PETCO_2$ and the observed overshoot in signals following re-breathing.

The FRC gas stored in the un-perfused alveoli act as a low-pass filter that limits the rate of change in CO_2 concentration in the un-perfused volume. During re-breathing, the partial pressure of CO_2 in the un-perfused alveoli ($PUCO_2$) increases more slowly than $PACO_2$. In published rebreathing studies, the late occurring increase in $PETCO_2$ was attributed to re-circulation [35]. Our models indicate that the late change in $PETCO_2$ is due to the contribution of the slowly changing concentration in the un-perfused alveoli.

The most important reason for using $PACO_2$ in the denominator of the partial Fick equation as opposed to $PETCO_2$, is that the gradient between $PETCO_2$ and perfused alveolar CO_2 changes during rebreathing. If this gradient is not accounted for, measurements can be in error, especially at high cardiac outputs when observed $\Delta PETCO_2$ is small. Rebreathing causes large changes in the inspired CO_2 concentration and therefore large changes in the CO_2 concentration in the un-perfused space. Our model accounts for these changes and therefore improves the estimation of cardiac output using the partial rebreathing method.

The more accurate estimates of $PACO_2$ provided by the model are used in the NICO algorithms. In the numerator of the differential Fick equation, the change in CO_2 excretion measured at the mouth is replaced by the estimate of CO_2 flow out of the blood as provided by the model. In the denominator of the partial Fick equation, the change in end tidal CO_2 partial pressure is replaced by the change in alveolar partial pressure as calculated by the model. These modifications to the published equations make the system more robust especially at the extremes of high and low cardiac output. We realize that in reality, the actual lungs are made up of many alveoli that lie on a continuum ranging from complete perfusion to no perfusion. However, for our purposes, the two-compartment model was adequate.

The present study was done in dogs under controlled mechanical ventilation. Occasional small spontaneous breaths did not affect the NICO measurements. In order to use this technique in non-intubated patients, several modifications are necessary including use of an air-tight face mask, algorithms to include compensation for irregular tidal volume and increased signal to noise levels [36].

The partial CO_2 rebreathing technique has worked reasonably well in patients with pulmonary disease [39] and in dogs with oleic acid lung injury [17, 43]. The additional NICO sensor deadspace (~32 ml) and resistance (4 cmH_2O at 40 LPM flow) introduced in the breathing circuit during normal ventilation is negligible when compared to anatomical and apparatus deadspace. The use of the NICO may impose a slight increase in the partial pressure of CO_2 in the arterial blood of approximately 2–6 mmHg for a very short duration. This change is well tolerated in most patients. If necessary, the minute ventilation provided to the patient can be increased slightly to maintain desired baseline CO_2 levels.

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Table 2. Studies reviewing performance of partial CO_2 rebreathing indirect Fick technique for non-invasive measurement of cardiac output

Lead author, year	Ref.	Method description	Study population	No. of data points (N)	TDco range (l/m)	Regression equation Y = m X + c	Correlation coeff (r)	Bias (l/m)	Precision (l/m)
Gedeon, 1980	[14]	Hyper-Hypoventilation	5 dogs 6 pts	35 6	0.5–6.5 2.5–5.0	Y = 0.97x + 0.00	NR	NR	(20%) (8%)
Roy, 1985	[16]	Switched serial DS	25 dogs	322	1.5–7.0	Y = 0.94x + 0.24	0.91	NR	NR
Blomqvist, 1986	[32]	Inserted DS for 8 breaths Oleic acid lavage	14 dogs 12 dogs	NR	Mean 2.14	NR	0.94 0.91	0.17	(CV = 12%)
Capek, 1988	[33]	Switched serial deadspace	29 pts	329	NR	Y = 0.76x + 1.39	0.70	NR	NR
Capek, 1988	[17]	Switched serial DS Lavage w/oleic acid	16 dogs	458	1.5–7.5	Y = 0.92x + 0.30	0.91	0.01	0.51
Bosman, 1990	[34]	Hyper-hypoventilation Switched serial DS	44 postoperative CABG pts	40 41	3.2–9.6	Y = 0.27x + 1.86 Y = 0.88x + 0.75	0.40 0.93	–0.12 0.18	0.57 0.57
Gedeon, 1992	[35]	Rebreathing apparatus	6 pigs	64	1.5–11.5	Y = 0.95x + 0.38	0.92	–0.13	0.78
Osterlund, 1995	[36]	Rebreathing apparatus	40 postoperative cardiac pts	80	1.8–8.9	Y = 0.76x + 1.2	0.81	–0.14	0.77
Gamma de Abreu, 1995	[37]	Switched serial DS	15 sheep 8 ARDS pts	23	2.7–10.9	NR	0.54	–1.69	1.90
Orr, 1996	[38]	Switched serial DS	5 dogs	272	1.8–13.5	NR	0.92	NR	(SEE = 0.96 l/m)
Gamma de Abreu, 1997	[39]	Switched serial DS	15 sheep	15	2.9–10.7	Y = 0.60x + 1.53	0.73	NR	NR
Orr, 1998	[40]	Switched serial DS	5 dogs	176	1.0–8.0	Y = 1.04x – 0.78	0.94	–1.1	0.62
Bailey, 1998	[41]	Switched serial DS	7 CABG pts	44	2.5–9.4	Y = 0.71x + 1.5	0.90	0.07	0.85
Haryadi, 1998	[42]	Switched serial DS	4 dogs	115	1.9–12.2	Y = 0.99x + 0.25	0.91	0.21	0.76
Johnson, 1998	[43]	Switched serial DS Oleic acid lavage	4 dogs	41	1.8–6.5	Y = 0.91x + 0.41	0.83	0.02	0.65
Watt, 1998	[44]	Switched serial DS	5 CABG pts	NR	NR	NR	NR	0.20	0.79
Kuck, 1998	[45]	Switched serial DS	10 CABG pts	36	2.61–8.1	NR	0.92	0.02	0.70
Guzzi, 1998	[46]	Switched serial DS	27 CABG pts	69	NR	NR	0.85	–0.01	0.62
Jopling, 1998	[47]	Switched serial DS	NR	48	NR	NR	NR	0.26	NR
Orr, 1999	[48]	Switched serial DS (Breath-to-breath CO)	42 CABG pts	117	2.6–8.2	NR	NR	0.07	0.81
Haryadi, 1999	[49]	Switched serial DS	10 CABG pts	48	1.9–7.8	NR	NR	0.46	0.85
Loeb, 1999	[50]	Switched serial DS	21 CABG pts	NR	3.00–10.00	NR	NR	0.11	0.95
Present study		Switched serial DS	6 dogs	246	0.60–8.87	Y = 0.89x + 0.52	0.93	–0.07	0.70

Pts – patients; NR – not reported; TDco – thermodilution cardiac output; CABG – coronary artery bypass grafting procedure; DS – dead space; CV – coefficient of variation; SEE – standard error of the estimate.

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A limitation of all rebreathing cardiac output methods is that they only measure that portion of cardiac output that participates in gas exchange in the lung. Intrapulmonary and anatomic shunt fraction ($\dot{Q}_S/\dot{Q}_T$) measured using invasive and non-invasive techniques have been used to compute total cardiac output [35, 36]. The NICO system estimates shunt fraction ($\dot{Q}_S/\dot{Q}_T$) based on oxygen saturation from pulse oximetry (SpO_2) and fractional concentration of inspired oxygen (FiO_2) [21]. The limited accuracy of pulse oximetry measurements of SpO_2 (1–2%) and the steepness of the oxygen tension-saturation curve (especially for $SpO_2 > 95\%$) may lead to inaccuracies in the non-invasive estimates of shunt fraction. Therefore, when arterial blood gas measurements are available, the NICO computes a correction summand based on the difference between the current SpO_2 and the SaO_2 derived from the invasive blood gas measurement. The correction summand is then applied to subsequent pulse oximetry measurements to modify these pulse oximetry measurements and more accurately determine the partial pressure of oxygen in the patient's arterial blood. The SaO_2 or PaO_2 value is then employed in the shunt equations to facilitate an accurate, non-invasive determination of the patient's intrapulmonary shunt. We have previously shown that these non-invasive estimates of intrapulmonary shunt compare well with invasive estimates of shunt [51]. In most cases the shunt fraction is small and therefore even a large error in the estimate of shunt fraction leads to a small error in cardiac output. An accuracy of $\pm 20\%$ in the estimation of shunt fraction is sufficient to ensure that the error in the estimation of cardiac output is less than $\pm 5\%$, even under conditions of 25% shunt [52].

Errors introduced in the NICO measurements from any inaccuracy in the estimation of intrapulmonary shunt are within the range of the confidence interval of the standard it is usually compared to (bolus thermodilution). We expect that patients in whom a significant shunt flow is suspected or when using elevated levels of FiO_2, arterial blood gas data will be available. Entry of arterial blood gas improves NICO measurements, however to a relatively small degree [53]. NICO may be completely noninvasive and still deliver clinically useful cardiac output measurements. In the present study the average value for the non-invasively estimated intrapulmonary shunt was 10.4% (range = 3.6 to 29.1%, 1 SD = 6.8%).

TDco is at present the most commonly used clinical standard for the measurement of cardiac output. The accuracy of bolus TDco measurements may be poor if strict guidelines in its practice are not adhered to [2, 3]. The limited reproducibility of thermodilution cardiac output measurements hampers evaluation of new cardiac output techniques [54]. When compared to cardiac output measurements using a transit time ultrasonic flow probe we have observed at times TDco overestimated cardiac output by 50% for CO > 6 l/min [55]. In this study, we used iced 5% dextrose and a catheter equipped with an additional thermistor located close to the proximal injectate port. The use of the additional thermistor to measure the injectate temperature as it enters the blood stream avoids the use of correction factors or computation constants and therefore enhances accuracy of cardiac output determination [25, 26].

At lower cardiac outputs it has been shown that a 500% change in alveolar deadspace causes only a 11% change in cardiac output measured using partial rebreathing Fick technique [17]. When large alveolar deadspace changes are suspected the accuracy of the NICO measurements can be enhanced by entry of arterial blood gas values.

Large changes in hemoglobin concentration can have a small effect on NICO measurements. The CO_2 dissociation curve, in which hemoglobin is a factor, is used to convert the partial pressure of CO_2 (PCO_2) into CO_2 content (CCO_2). The NICO system assumes normal hemoglobin of 14 gm/dl unless overridden by a manually entered value. A 30% change in hemoglobin, which roughly corresponds to loss of 3-4 units of blood, will cause an error in Q_{PCBF} of 15%. The error in the calculation of cardiac output from changes in the pH and temperature and its resulting effects in the CO_2 dissociation curve are small [17].

The NICO system provides updates in cardiac output once every 3 minutes. The response time for a step change in cardiac output could be 1–2 cycles and depends on the quality of the signals monitored. Other continuous cardiac output monitoring devices based on a heated catheter that are currently available in the market take an average of 9 minutes to respond to a change in cardiac output [56].

CONCLUSION

NICO is a non-invasive, easy to use, and automated method that can provide semi-continuous cardiac output measurements in mechanically ventilated subjects. It is based on the partial CO_2 rebreathing technique, wherein changes in CO_2 elimination ($\Delta\dot{V}CO_2$) and partial pressure of end-tidal CO_2 ($\Delta PETCO_2$) in response to a brief change in effective ventilation are used to measure cardiac output. The technique is based on the Fick principle against which all other cardiac output techniques have been evaluated. NICO allows measurement of cardiac output from routinely monitored clinical

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signals. The results from the canine study show that NICO performed well over a wide range of cardiac outputs. The limits of agreement between NICO and TDco (27.4%) is within the recommended value (of up to ±30%) for NICO to be a clinically acceptable method for cardiac output measurement.

APPENDIX

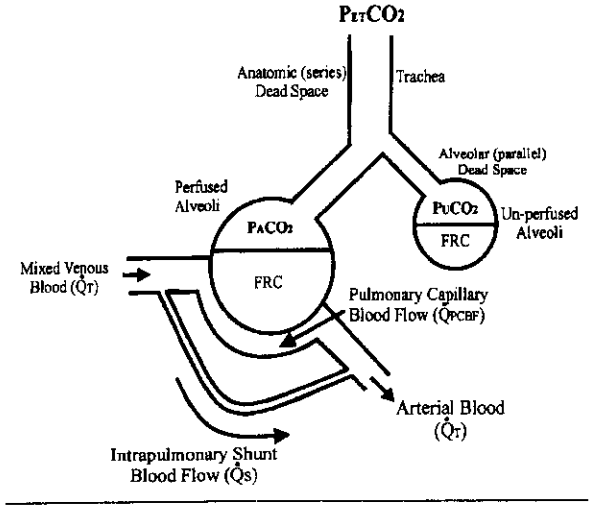
CO_2 gas exchange model

A two-compartment mathematical lung model as described below was used to account for the observed differences between partial pressure of end-tidal CO_2 ($P_{ET}CO_2$) and the partial pressure of CO_2 in the end-capillary blood (assumed equal to partial pressure of CO_2 in the perfused alveoli = P_ACO_2).

In this model the lung is comprised of two large alveoli, one of which is completely perfused and another which is completely un-perfused [57–58]. The $P_{ET}CO_2$ measured at the mouth is the weighted sum of the partial pressure of CO_2 in the perfused (P_ACO_2) and the un-perfused alveoli (P_UCO_2).

$$P_{ET}CO_2 = rP_ACO_2 + (1 - r)P_UCO_2\,, \tag{A.1}$$

where, r is the perfusion ratio, which indicates the fraction of the total alveoli that are perfused. To measure pulmonary capillary blood flow ($\dot{Q}_{PCBF}$), we need to analyze the change in the partial pressure of CO_2 in the perfused alveoli (P_ACO_2) rather than change in the $P_{ET}CO_2$. We therefore need to calculate P_ACO_2 from Equation (a).



$$P_ACO_2 = \frac{[P_{ET}CO_2 - (1 - r)P_UCO_2]}{r}\,. \tag{A.2}$$

Since CO_2 does not enter the un-perfused alveoli from the pulmonary capillary blood flow ($\dot{Q}_{PCBF}$), it therefore must enter only from the airway, i.e., it is inhaled. Rebreathing causes a step increase in the concentration of the inhaled CO_2. The rate at which P_UCO_2 changes is a function of the respiratory rate and the ratio of the tidal volume to functional residual capacity (FRC). The CO_2 concentration in the un-perfused alveoli is modeled as:

$$P_UCO_2[n] = P_UCO_2[n-1]\frac{V_{FRC}}{(V_t + V_{FRC})} + P_ICO_2\frac{V_t}{(V_t + V_{FRC})}\,, \tag{A.3}$$

where

$$P_ICO_2 = \frac{(V_ICO_2 + V_{DS} \cdot P_{ET}CO_2[n-1])}{V_t}\,. \tag{A.4}$$

$P_UCO_2[n-1]$ = partial pressure of CO_2 in the un-perfused alveoli at the end of the previous breath; V_{FRC} = volume in the functional residual capacity; V_t = tidal volume; P_ICO_2 = partial pressure of CO_2 in the inspired gas as it enters the alveoli; V_ICO_2 = volume of inspired CO_2; V_{DS} = series (anatomic) dead space volume.

The volume in the functional residual capacity is a function of body weight and is estimated by the dead space volume measured using Fowlers method [59]. The FRC gas stored in the un-perfused alveoli acts as a low-pass filter that limits the rate of change in CO_2 concentration in the un-perfused volume. During rebreathing, P_UCO_2 increases more slowly than P_ACO_2. The FRC volume is a function of the anatomic (or series) dead space volume (V_{DS}) and is also proportional to patient size.

$$V_{FRC} = kV_{DS}\,, \tag{A.5}$$

where k is a constant which can either be assumed to be of a particular value or experimentally determined. V_{DS} is measured directly from the single breath CO_2 curve and is known to be an indicator of patient size.

The two-compartment model also accounts for the rapid change in $\dot{V}CO_2$ at the start and end of rebreathing. As rebreathing begins, the concentration of CO_2 in the alveoli increases, decreasing the partial pressure gradient between alveoli and blood, thereby decreasing CO_2 elimination ($\dot{V}CO_2$). Careful observation of the $\dot{V}CO_2$ signal shows that the $\dot{V}CO_2$ measured at the mouth decreases rapidly and reaches a minimum during the first or second breath of rebreathing even though the

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partial pressure gradient in the alveoli continues to decrease in later breaths. This observation is accounted for by flow of CO_2 into the FRC. As $PaCO_2$ increases, a fraction of the CO_2 coming from the blood remains in the FRC and is therefore not eliminated through the mouth. The amount of CO_2 flowing in and out of the FRC gas is proportional to the change in gas concentration. The corrected $\dot{V}CO_2$ (amount of the actual CO_2 moving from blood to alveolar space) is calculated by:

$$\dot{V}CO_2 = \dot{V}mCO_2 + (V_{FRC} + V_t)\Delta feCO_2\,, \qquad (A.6)$$

where $\dot{V}mCO_2$ = CO_2 elimination measured at the mouth; V_{FRC} = FRC volume; V_t = tidal volume; $\Delta feCO_2$ = concentration of end-tidal CO_2.

These model parameters are updated following every breath. The corrected $PaCO_2$ and values are used to calculate cardiac output. The default perfusion ratio was assumed to equal to 0.94 when no blood gas data was available. When blood gas data was available the perfusion ratio was adjusted based on the difference between $PetCO_2$ and $PaCO_2$ measured directly.

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GLOSSARY

TDco	Bolus thermodilution cardiac output (l/min)
NICO	non-invasive cardiac output
$\dot{Q}_T$	Cardiac output (l/min) obtained using NICO
$\dot{Q}_{PCBF}$	Pulmonary capillary blood flow (l/min)
$\dot{Q}_S$	Intrapulmonary shunt blood flow (l/min)
$\dot{Q}_S/\dot{Q}_T$	Intrapulmonary shunt fraction (%)
$CaCO_2$	arterial blood CO_2 content (ml of CO_2/100 ml of blood)
$CvCO_2$	mixed venous blood CO_2 content (ml of CO_2/100 ml of blood)
$CcCO_2$	end capillary blood CO_2 content (ml of CO_2/100 ml of blood)
$PetCO_2$	partial pressure of end-tidal CO_2 (mmHg)
$PaCO_2$	partial pressure of CO_2 in the end-capillary blood (assumed equal to partial pressure of CO_2 in the alveoli) (mmHg)
$PuCO_2$	partial pressure of CO_2 in the un-perfused alveoli (mmHg)
$\dot{V}CO_2$	CO_2 elimination rate (ml/min, ATPS)
Hb	hemoglobin concentration (dl/l)

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PARTIAL CO_2 REBREATHING CARDIAC OUTPUT – OPERATING PRINCIPLES OF THE NICO™ SYSTEM

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Jaffe MB. Partial CO_2 rebreathing cardiac output – operating principles of the NICO™ system.
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ABSTRACT. The partial rebreathing method of cardiac output estimation is reviewed with a particular focus on its application for continuous monitoring, rebreathing and implementations and from both a historical and technical perspective. The assumptions of the method are discussed as well as the various implementations. The NICO monitor and rebreathing valve are described from a functional view. The clinical data including (a) comparisons between bolus thermodilution and continuous thermodilution in patients in the OR setting, (b) comparisons to continuous thermodilution with both the Baxter and Abbott continuous cardiac output devices and (c) comparison between different means of shunt correction are presented. Compared to conventional cardiac output methods, the partial CO_2 rebreathing technique is non-invasive, can easily be automated and can provide real-time and continuous cardiac output monitoring. Taking advantage of modern sophisticated sensor and signal processing technology and integrating multiple monitored physiological variables the NICO monitor is the first commercially available cardiac output system making use of the partial rebreathing of CO_2.

KEY WORDS. Cardiac output, pulmonary capillary blood flow, Fick equation, partial rebreathing, carbon dioxide elimination, non-invasive.

INTRODUCTION

Adolph Fick described the first method of cardiac output estimation in 1870 [1]. This method remains the original reference standard by which all other means of determining cardiac output are evaluated. Cardiac output monitoring with a pulmonary artery (PA) catheter using the bolus thermodilution method became the de facto "gold" standard shortly after its introduction in the 1970's. Continued questions about the PA catheter's effect on morbidity and mortality [2] have led to an increased interest in other methods, particularly non-invasive methods for cardiac output monitoring. In particular, non-invasive CO_2 Fick methods are seeing resurgence in research and clinical interest. This paper describes Novametrix's implementation of a non-invasive CO_2 method known as the partial rebreathing method of cardiac output estimation.

During the last twenty years, technological changes such as improvements in pulse and venous oximetry have prompted several investigators to explore the possibility of using the oxygen Fick method for cardiac output monitoring. However, a number of problems with the O_2 Fick equation still limit its clinical application in the ICU. Using the CO_2 version of the Fick equation has the advantages that CO_2 elimination

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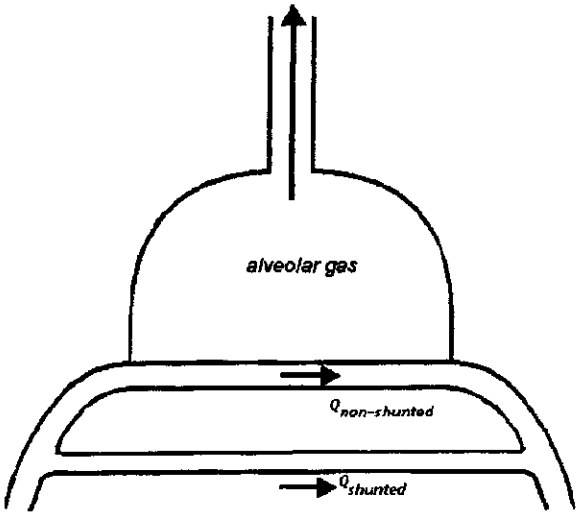

Fig. 1. Ideal lung model showing shunted ($Q_{shunted}$) and non-shunted ($Q_{non-shunted}$) blood flow. Alveolar deadspace is not shown in this model.

(VCO_2) is easier to accurately measure than oxygen uptake and that estimates of arterial CO_2 concentration may be made from the gas exhaled by the lungs. Furthermore, the CO_2 concentration in the alveolar end-capillary blood can be estimated non-invasively by monitoring the CO_2 partial pressure in the expired gas and relating it to the blood concentration with the help of the CO_2 dissociation curve.

The Fick principle is based on the conservation of mass (Figure 1). It postulates that blood flow through the alveoli is equal to the uptake or elimination of a gas divided by the difference in concentrations of that gas in the blood flowing into and out of the lungs. The Fick equation using carbon dioxide is:

$$Q = \frac{\dot{V}CO_2}{CvCO_2 - CaCO_2} \quad (1)$$

where, VCO_2 is the carbon dioxide elimination of CO_2 in ml/min, Q is the cardiac output in ml/min, and $CaCO_2$ and $CvCO_2$ are the arterial and venous carbon dioxide blood contents in ml/ml of blood, respectively.

The CO_2 concentrations may be estimated from exhaled gas. This modification considers only that part of the cardiac output that participates in gas exchange, i.e., the non-shunted blood flow or the pulmonary capillary blood flow (PCBF). By estimating the amount of blood flow bypassing the lung (shunt flow) and adding it to the PCBF, cardiac output may be determined. The shunt flow can be estimated using, for example, data from a pulse oximeter combined with the inspired oxygen gas fraction (FtO_2) or with blood gas measurements and the well-known shunt fraction equation (Qs/Qt).

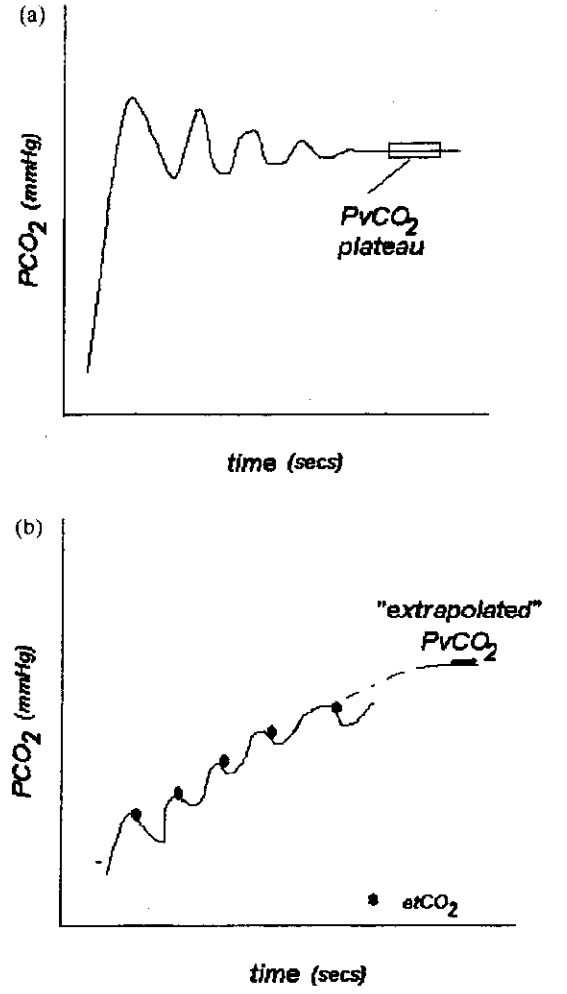

Fig. 2. Complete rebreathing methods – (a) plateau (Collier) and (b) exponential (Defares) methods.

The cardiac output or the pulmonary capillary blood flow (PCBF) in many rebreathing methods is calculated by estimating both arterial and venous concentrations of CO_2 from measurements made at the mouth. These noninvasive methods, which employ complete CO_2 rebreathing, have evolved from the desire for a "simpler" noninvasive Fick method and are based on various schemes indirectly to measure mixed venous partial pressure of carbon dioxide ($PvCO_2$). The two principal CO_2 complete rebreathing approaches, the Defares and Collier CO_2 rebreathing techniques (Figure 2), require

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that the subject rebreathes from a bag with CO_2 accumulating until the mixed venous partial pressure can be estimated or extrapolated. With the Collier method, the subject rebreathes from a bag in which the concentration of CO_2 is significantly higher than the mixed venous CO_2 concentration. The subject rebreathes until the CO_2 waveform "dampens" out and a plateau is reached for a few seconds. The Defares method uses a lower concentration of CO_2 and performs an extrapolation of the end tidal values of CO_2. Breathholding methods with various inhaled concentrations of CO_2 take advantage of the observation that during a breathhold, the alveolar PCO_2 either rises or falls exponentially and asymptotically approaches $PvCO_2$. However, complete rebreathing methods such as these require the patient's cooperation, provide intermittent measurements and are unsuitable as monitoring modalities. The different complete rebreathing methods, including methods that employ breathholding, rebreathing, and single- or multi-breath approaches with physiologic gases (O_2, CO_2) and inert, soluble gases, are reviewed by Sackner (1987) [3].

DIFFERENTIAL FICK PARTIAL REBREATHING METHOD

The differential CO_2 Fick partial rebreathing technique, which is a variation on the traditional rebreathing methods, was first described with an end-expiratory hold [4] and later with the addition of deadspace [5, 6]. The partial rebreathing method combines measurements obtained during a non-rebreathing period with the ones obtained during a subsequent rebreathing period. With partial rebreathing, as opposed to total or complete rebreathing, an amount less than the total CO_2 volume from the previous expired tidal volume is rebreathed during the rebreathing period. Cardiac output is then computed with an alternate form of the Fick equation that has been termed the differential Fick partial rebreathing method. It uses the change in carbon dioxide elimination (VCO_2) and the change in end-tidal CO_2 in response to a change in ventilation to calculate a cardiac output value. This form of the Fick equation can be simply derived by combining the CO_2 Fick equations from the baseline (nonrebr) and rebreathing (rebr) periods. The CO_2 Fick equation for each period are:

$$\dot{Q}_{PCBF} = \frac{\dot{V}CO_{2_{nonrebr}}}{CvCO_{2_{nonrebr}} - CaCO_{2_{nonrebr}}} \tag{2}$$

$$\dot{Q}_{PCBF} = \frac{\dot{V}CO_{2_{rebr}}}{CvCO_{2_{rebr}} - CaCO_{2_{rebr}}} \tag{3}$$

where, PCBF is the pulmonary capillary blood flow in ml/min, $VCO_{2_{nonrebr}}$ and $VCO_{2_{rebr}}$ are the carbon dioxide eliminations of CO_2 in ml/min during non-rebreathing and rebreathing, respectively. Similarly, the non-rebreathing and rebreathing $CaCO_2$ and $CvCO_2$ are the alveolar and mixed venous carbon dioxide blood contents in ml/ml of blood, respectively.

Assuming no significant change of pulmonary capillary blood flow during the measurement period, Equations (2) and (3) can be combined to yield:

$$\dot{Q}_{PCBF} = \frac{\dot{V}CO_{2_{nonrebr}} - \dot{V}CO_{2_{rebr}}}{(CvCO_{2_{nonrebr}} - CaCO_{2_{nonrebr}}) - (CvCO_{2_{rebr}} - CaCO_{2_{rebr}})} \tag{4}$$

Conventional partial CO_2 rebreathing (as does total) assumes that the venous CO_2 concentration remains relatively constant throughout the rebreathing and the non-rebreathing periods. That assumption is based on the relatively large size of the CO_2 body stores and slow time constant of the CO_2 stores relative to the time of rebreathing. Thus, the terms associated with venous CO_2 concentration during baseline and rebreathing cancel:

$$\dot{Q}_{PCBF} = \frac{\dot{V}CO_{2_{nonrebr}} - \dot{V}CO_{2_{rebr}}}{CaCO_{2_{rebr}} - CaCo_{2_{nonrebr}}} \tag{5}$$

This can be rewritten as:

$$\dot{Q}_{PCBF} = -\frac{\Delta\dot{V}CO_2}{\Delta CaCO_2} \tag{6}$$

where $\Delta\dot{V}CO_2$ and ΔCaO_2 are the change in carbon dioxide elimination in ml/min and change in alveolar blood content in ml/ml blood between the baseline and rebreathing periods, respectively.

The NICO system has expanded upon equation (6) and used expressions for calculating alveolar content of carbon dioxide.

$$CaCO_2 = (6.957[Hb] + 94.864) * \log(1.0 + 0.1933\,PaCO_2) \tag{7}$$

where Hb is hemoglobin in g/dl, $PaCO_2$ is the alveolar CO_2 partial pressure in mm Hg and $CaCO_2$ is the alveolar CO_2 content in ml CO_2/ml blood.

Using the alveolar partial pressure of CO_2 ($PaCO_2$) and the CO_2 dissociation curve, the arterial CO_2 content may be estimated. Furthermore, some investigators [7, 8] have equated end-tidal CO_2 to arterial CO_2 and have used a simple equation, which is a function of hemoglobin and alveolar CO_2, for the slope of the CO_2

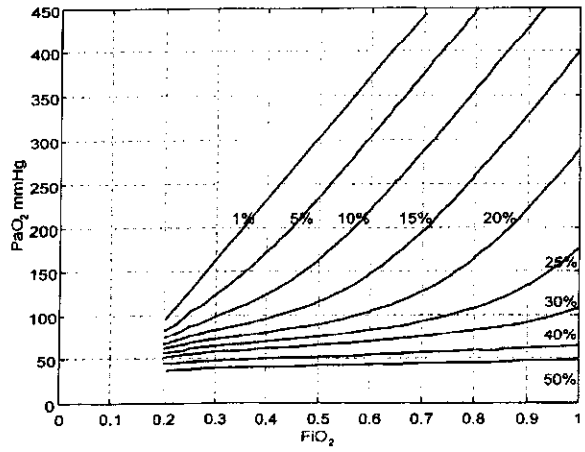

Fig. 3. Iso-shunt plots (adapted from [12]). Shunt fraction percentages are shown on each isocline.

dissociation curve. The alveolar CO_2 partial pressure is estimated using the end-tidal CO_2 concentration and a mathematical model of the lung that includes an alveolar deadspace.

SHUNT CORRECTION

The partial rebreathing method by itself measures the non-shunted portion of the cardiac output. The shunt may be a physical shunt or due to alveolar ventilation/pulmonary perfusion mismatching (V/Q). Pulmonary shunting has been defined as "the passage of blood through the lungs without taking part in gas exchange" [9]. The most common means of compensating for the shunted blood flow (Qs) is to employ venous and arterial blood gases if they are available. The well-known shunt equation (Equation (8)) can be used to convert the PCBF value to a value that better reflects cardiac output by dividing the PCBF value by $1 - Qs/Qt$.

$$Qs/Qt = \frac{CcO_2 - CaO_2}{CcO_2 - C\bar{v}O_2} \quad (8)$$

where, CcO_2, CaO_2 and CvO_2 are the end-capillary, arterial and mixed venous oxygen contents, respectively and where Qs is the shunt flow and Qt is the cardiac output.

Oxygen content of blood consists of the bound and dissolved portions and is written as:

$$CxO_2 = Hb \times SxO_2 \times 1.38 - PxO_2 \times 0.0031 \quad (9)$$

where, Hb is the hemoglobin in, SxO_2 is the saturation of x in percent, PxO_2 is the partial pressure of x in mmHg, and x is arterial, venous or end-capillary.

Other methods including those used in the NICO system (patent pending) for estimating a shunt employ SpO_2 and FiO_2 [10, 11]. The noninvasive method of shunt estimation is an adaptation of Nunn's iso-shunt plots [12]. These plots (Figure 3) are a series of continuous curves that describe the relationship between arterial pO_2 and inspired oxygen concentration (FiO_2) for different levels of intrapulmonary shunt (%). Arterial blood oxygen saturation (SaO_2) is determined non-invasively with pulse oximetry (SpO_2). The SaO_2 or PaO_2 value is estimated and then employed in the shunt equations to make a non-invasive estimation of the patient's intrapulmonary shunt.

IMPLEMENTATIONS

Various implementations of partial rebreathing have been tested in either research or commercial configurations (e.g., Novametrix NICO). These methods differ in aspects such as measurement, signal processing and breathing circuit/valve configuration.

Measurement

Breath-to-breath flow and CO_2 can be measured by a mainstream breath-to-breath method (Novametrix NICO); a mainstream CO_2 and a downstream flow sensor [4, 15]; or, by a mainstream flow sensor and sidestream gas sampling [7].

Signal processing

The signal processing consists of the calculation of the $ETCO_2$ and VCO_2 from the raw signals, the filtering of the breath-to-breath values of $ETCO_2$, VCO_2 and other parameters, and filtering of the cardiac output (Figure 4). $PETCO_2$ is calculated as the CO_2 partial pressure in mm Hg at the end of expiration. This may be a single point or an average of several data points. One has to be careful when and how this value is determined (filtering etc.) so that a more robust $PETCO_2$ is used. For example with NICO, this value is not directly used in the denominator (as in Equation (6)) or used to calculate CO_2 content but instead is corrected by the estimated functional residual capacity (FRC) and alveolar deadspace so that alveolar PCO_2 may be calculated and used to estimate CO_2 content. The VCO_2 is

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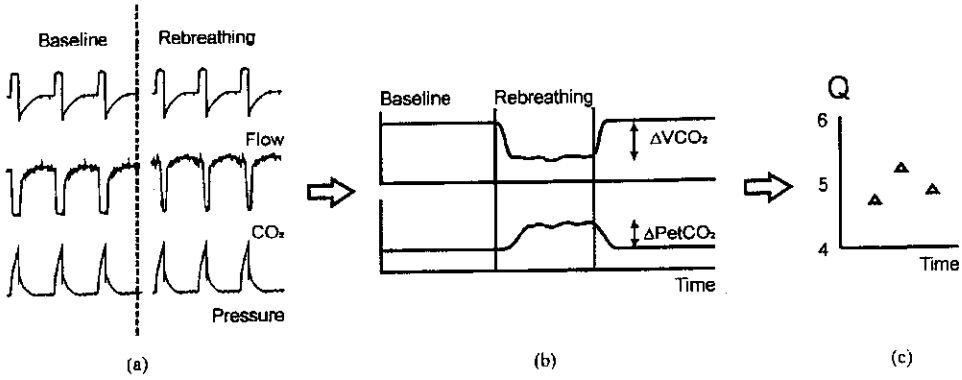

Fig. 4. Schematic representation of partial rebreathing (a) flow, pressure and CO_2 waveforms (baseline and rebreathing shown), (b) breath to breath estimates of carbon dioxide elimination and endtidal CO_2, and (c) cardiac output estimates.

computed as the sum of the product of flow and airway CO_2 fraction data samples over each breath cycle. It may be corrected for changes in the functional residual capacity (FRC). For both the baseline and rebreathing period a representative value must be determined for VCO_2 and $PETCO_2$ (Figure 5). While representative baseline values are relatively simple to determine, the rebreathing values are not. The VCO_2 changes from baseline to the rebreathing level within 2–3 breaths while $PETCO_2$ changes tend to be a little slower. To determine values during rebreathing in particular, simple time or breath-based averaging, curve fitting, or more sophisticated signal processing methods as used by Novametrix have been applied. The variables used for estimating cardiac output are evaluated with respect to their noise levels. Based on this evaluation the algorithm determines the confidence in the cardiac output estimation, which is displayed on a five segment bar graph (CObar™) on the monitor screen. Successive cardiac output estimations are filtered with an adaptive and weighted moving average filter. Filter coefficients are determined based on the input variables' signal qualities. The maximal average group delay of the filtered cardiac output is less than ten minutes.

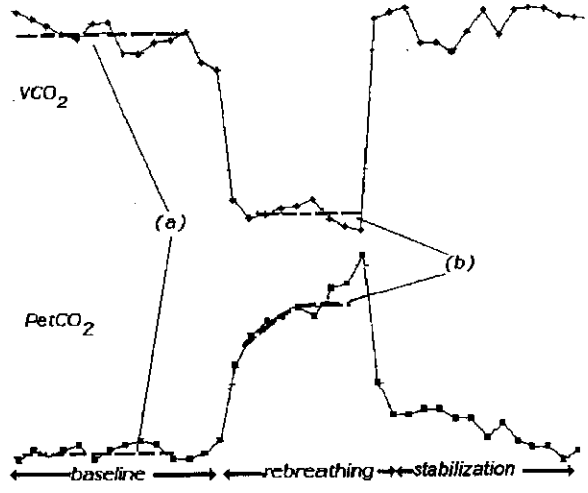

Fig. 5. VCO_2 and $ETCO_2$ changes during baseline, rebreathing and stabilization. (a) Representative baseline values determined as average, (b) representative rebreathing values determined as average for VCO_2 and curvefit/extrapolation for $PETCO_2$.

Breathing circuit/valve

Gedeon (1985) [5] introduced a deadspace using a cross-bar approach which tied the inspiratory and expiratory limbs of the breathing circuit together via an "externally controlled" valve. The valve, when activated, increases deadspace by the volume of the inspiratory and expiratory limbs and "cross-bar." This method requires either modifications of the ventilator circuit or custom ventilator circuits and is not adaptable for spontaneous breathing. An approach that is more conducive to use on almost any ventilator circuit is one in which the measurement sensors and rebreathing valve are inserted between the elbow and "Y" adding minimal additional deadspace. Capek (1988) [7] first placed a flow sensor (and later a mainstream CO_2 sensor) with the rebreathing valve and fixed deadspace between the subject and the "Y" of the ventilator circuit. The Novametrix NICO monitor improves upon earlier research rebreathing systems with an adjustable deadspace breath-

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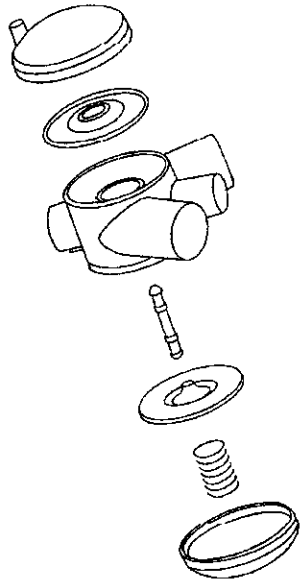

Fig. 6. Exploded view of partial rebreathing valve (patents pending).

ing loop (patent pending). It also employs an inexpensive, single patient use pneumatically controlled valve assembly that is easily inserted in the ventilator circuit between the patient and "Y". This valve assembly is a variation on the commonly used exhalation valve using a dual diaphragm design with a spring return (Figure 6). It has been tested on the bench [16] and found to provide a low deadspace of 32 ml (including sensor) in normal (non-rebreathing) operation, to add a small pressure drop of <2 cm H_2O/l/sec at 60 LPM and to be reliable at pressures as high as 110 cm H_2O.

NICO MONITOR

The NICO monitor (Figure 7), introduced in early 1999, is the first monitor to implement the partial rebreathing method in a commercial device. The monitor is a Motorola 68332 microprocessor based data acquisition system consisting of differential, absolute and gage pressure transducers, CO_2 measurement and control circuitry, pulse oximetry measurement and control circuitry, valving, purge and valve actuation pumps, inter-connecting tubing and a high speed serial interface. The monitor's firmware resides in a Flash RAM. The system uses SRAM for data storage and an EEPROM to store system parameters. The operations performed by the system include data acquisition, zeroing, purging, heater control, parameter calculation, waveform display and corrections to the flow signal for gas composition, airway pressure, and barometric pressure. The firmware is organized around a multitasking operating system that divides the functions of the system into independent entities, or tasks, that run on a time-scheduled basis. In addition, interrupts, running at a rate of 100 Hz, are used to gather data and provide serial communications.

Functional tasks

a) Flow signal data acquisition

Because of the need for a high resolution system with a fixed orifice sensor, a high resolution (20 bit) and high frequency analog to digital conversion circuit is used to obtain the needed high dynamic range for flows (1–180) l/min passing through the fixed orifice sensor.

b) CO_2 signal data acquistion

When the source pulses, it generates infrared energy over a broad band of wavelengths. Two detectors of this energy are placed on the opposite side of the CAPNOSTAT. One detector is shielded by a filter, which only passes the wavelengths in the CO_2 absorption spectra. This channel, the data channel, is proportional to intensity of the energy modulated by the concentration of CO_2. The second detector has a filter, which passes IR energy not in the CO_2 spectra. This channel, the reference channel, is related to the intensity of the energy of the source. Therefore, any change to the intensity of the overall band is measured by the reference channel. The actual measurement of concentration is performed by the data channel. The greater the concentration of CO_2 the more IR energy is absorbed; therefore, less energy hits the detector and a lower intensity is read. The signals from the data and reference channels are filtered, baseline corrected and amplified prior to sampling at 100 Hz by 12-bit analog to digital converters.

c) SpO_2 signal data acquistion

After filtering, the red and IR signals are sampled by a 20 bit A/D converter. Baseline removal, artifact detection and the measurements are performed by the software based algorithms.

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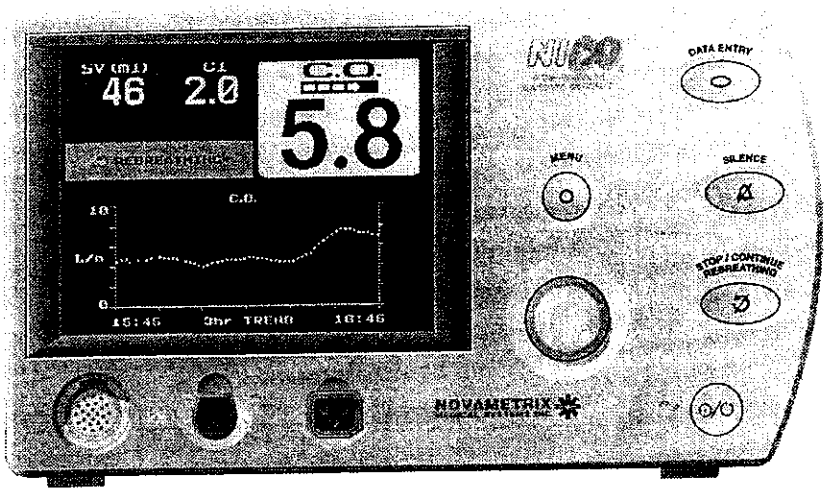

Fig. 7. Non-invasive cardiac output monitor.

d) Parameter calculation

The software processes the acquired waveforms and calculates on a breath-by-breath basis or at a predetermined or user configurable averaging interval. These include simple flow based parameters such as frequency, and expired volume, CO_2 based parameters such as $ETCO_2$, oxygen saturation based parameters such as SpO_2 and pulse rate and more complicated parameters such as carbon dioxide production, airway deadspace and cardiac output.

e) Zeroing-pressure sensors

Because of baseline changes and limited analog to digital conversion resolution, linearization of the differential pressure signal from a fixed orifice device is not possible without additional signal conditioning. The monitor periodically actuates valves that open the absolute pressure transducer to the atmosphere and connect the ports across the differential pressure transducer. This latter step simulates a zero-flow signal which in turn is subtracted from the differential pressure transducer output to compensate for baseline changes.

f) Zeroing – CO_2

The CO_2 zero values are different for each type of adapter (neonatal and adult reusable and single patient use and sampling adapter). The user zeros the CAPNOSTAT CO_2 sensor to the type of sensor being used and does not have to re-zero until the type of adapter is changed or the monitor requests a re-zero.

g) Partial rebreathing valve control

The partial rebreathing valve is pneumatically controlled using solenoid valves and a pump for actuation. The safety of the valve as used for rebreathing has been enhanced by monitoring of the control line pressure and other parameters such as inspired CO_2 volume. Also, a spring restores the valve to the normal (non-rebreathing) mode of operation in the event of a leak, tube disconnect or system failure such as loss of power. The valve control pneumatics are designed in such a way that a disconnect or pump or valve failure would cause the valve to be restored to the non-rebreathing mode rather than the rebreathing mode of operation.

h) Heater control

To maintain a constant temperature within the CAPNOSTAT, a software based Proportional-Integral-Derivative (PID) control loop is used. Both hardware and software monitor the temperature of the heaters, providing redundant safety measures. Each can independently turn off the power to the heaters if the upper temperature limit is exceeded. The controlling pulses generated by the software are AC coupled through the hardware to prevent the heater power from being

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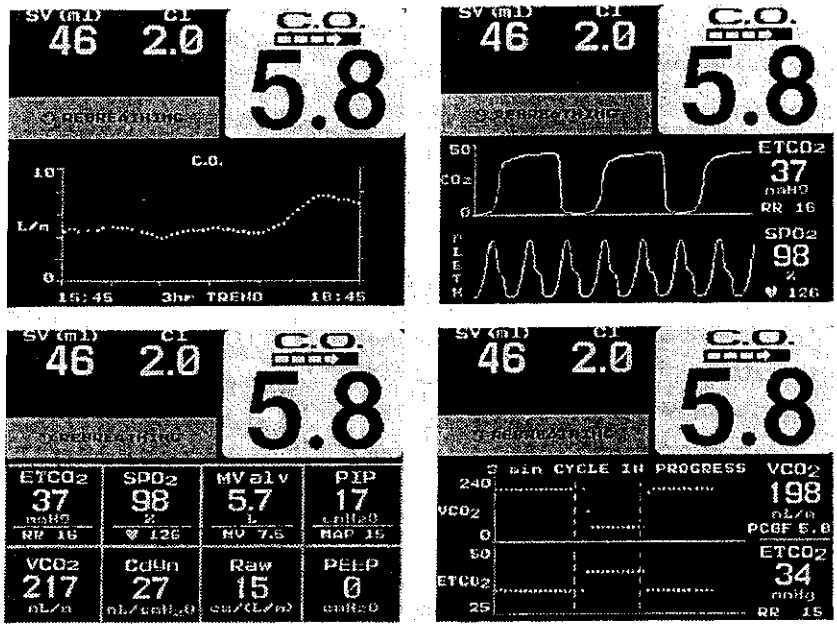

Fig. 8. Representative screens from NICO – (a) cardiac output trend screen, (b) waveform screen, (c) numerical screen and (d) rebreathing cycle screen (with demo data).

latched on. Additionally, a solid-state electronic thermostat in the CAPNOSTAT will disable power to the heater if a hard limit is exceeded.

i) Gas compensation

The effects of various gas compositions found in critical care and in anesthesia have an effect on most flowmeter systems. The monitor allows the user to select between different default gas concentrations so that appropriate compensations can be made.

j) User interface

The user communicates with the software using several push button switches and a navigation knob on the front panel on the monitor. The user can switch between waveforms, cardiac output or rebreathing cycle trends, or numeric data screens (Figure 8). Additionally, the display presents the cardiac output in a large visible format with a confidence bar consisting of 5 segments. The "signal quality" which determines the number of segments displayed is related to measurements such as the stability of the CO_2 stores.

(k) System outputs

The monitor can communicate with external devices via bi-directional serial communications.

OPERATION OF THE VALVE

As shown in the exploded view (Figure 6), the rebreathing valve consists of a body, 2 domes which enclose 2 diagraphms that are interconnected with a rod, and a spring to return the valve to normal mode. Additionally tubing for control and expandable, corrugated tubing to adjust the deadspace is attached to the valve assembly. The NICO sensor assembly, consisting of a rebreathing valve with large bore tubing and a combination CO_2/flow sensor, is connected to the NICO monitor which controls and monitors the performance of the valve (Figure 9). The valve is placed into rebreathing mode using active pneumatic controls and returned to normal mode via the recoil of a spring. The pneumatic control of the monitor contains a pump and solenoids. A watchdog circuit and software task is included to prevent improper "on" operation of the control pump. The flow through the valve during normal mode (Figure 10a) is straight through the valve. The

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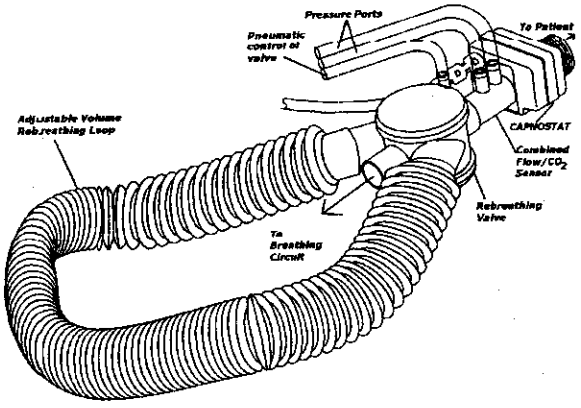

Fig. 9. Novametrix rebreathing configuration (patents pending). CO_2/flow sensor with valve and rebreathing loop shown. Rebreathing loop can be retracted and expanded between 120 and 250 ml to optimize the level of rebreathing.

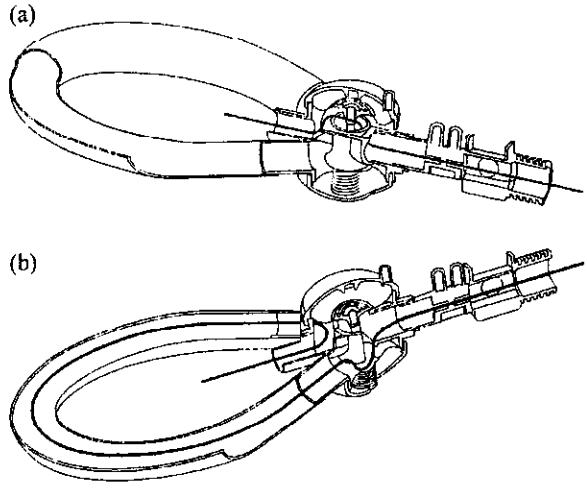

Fig. 10. Normal (a) and rebreathing (b) modes of NICO valve and sensor. Thick lines show path of flow through the device for each mode. (Image created by John Sandor.)

flow through the valve during rebreathing is diverted through the expandable rebreathing loop (Figure 10b).

The rebreathing valve allows the addition and removal of the rebreathed volume. If that volume is not removed after an appropriate time the patients breathes an increased volume of inspired CO_2 resulting in decreased ventilation and a higher level of arterial CO_2. This increase is typically a few mm Hg and is only of clinical concern in a small percentage of patients. However, to address this concern the safety of the valve as used for rebreathing has been enhanced by:

- maintaining known pressures in the control line, monitoring of the control line pressure, adjusting and warning the user as needed;
- monitoring of other parameters such as inspired volume of CO_2, and SpO_2 and warning as needed;
- placing a spring to restore the valve to the normal (non-rebreathing) mode of operation in the event of a leak, control line tube disconnect or system failure such as loss of power operating the valve with control pneumatics such that a disconnect or pump or valve failure would cause the valve to enhance the restoration to the normal mode rather than the rebreathing mode of operation.

The control line pressure transducer is used to monitor the pressure in the tubing connecting the monitor to this valve. Positive pressure applied to the rebreathing valve places it in the rebreathing state. Venting the rebreathing valve to atmosphere places the valve in the non-rebreathing state. A pressure sensor is used to monitor the pressure being applied to the rebreathing valve. By monitoring this pressure, the system can determine if the rebreathing valve is working correctly, and pressure adjustments can be made to assure the correct pressure is applied to the valve.

REBREATHING SPECIFICS

During rebreathing a portion of the CO_2 expired during the previous breath (determined by the volume of the loop and valve) is inhaled in the early portion of inspiration. The inhaled CO_2 increases the alveolar CO_2 concentration, reduces the net flux of CO_2 diffusing into the alveoli from the blood, reduces the CO_2 eliminated from the lung, and increases the arterial CO_2 content. During exhalation, the expired volume is redirected through the rebreathing loop by the valve. The later portions of the breath (equal to approximately the volume of the loop and valve) are "stored" for inhalation of the next breath. This rebreathing continues for approximately one minute. The sequence of rebreathing and stabilization is shown in Figure 11. Baseline measurements precede the period of rebreathing. During the baseline period, which lasts 60 seconds, the valve is in the non-rebreathing mode. During the rebreathing period, which last 50 seconds, the valve is actuated by the application of positive pressure and the patient rebreathes some of his own exhaled CO_2. During the stabilization period, which lasts 70 seconds, the valve is switched so that the control line pressure falls to ambi-

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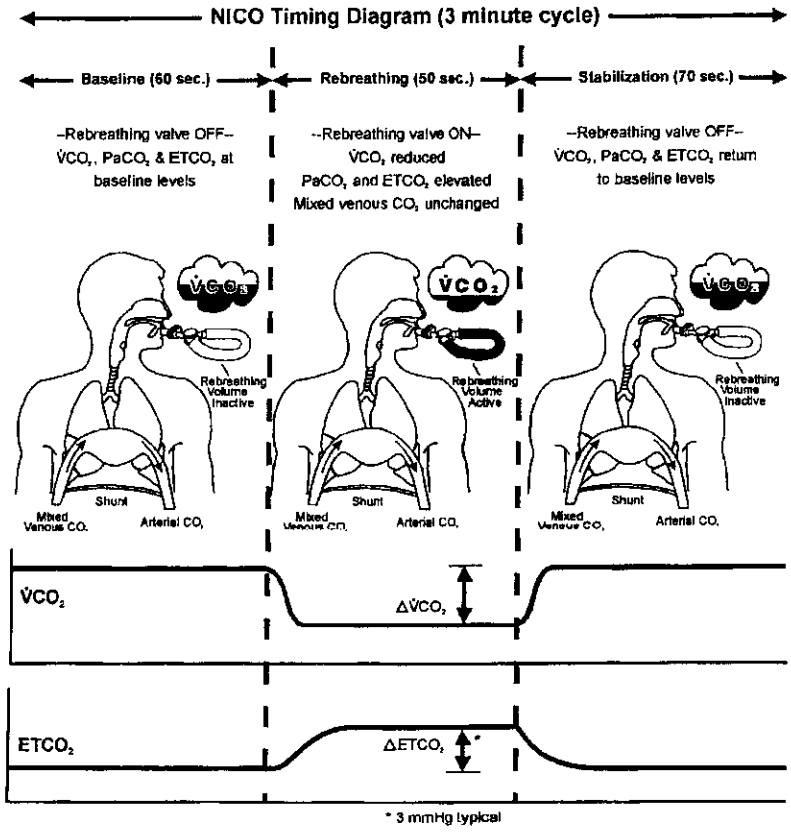

Fig. 11. NICO rebreathing cycle.

ent pressure level and the spring returns the valve to normal mode. The stabilization period also allows the patient's CO_2 stores to recover.

RESULTS OF STUDIES TO DATE

The results of the animal and patient studies of partial rebreathing methods conducted to date are summarized in Table 2. Most of these studies compare bolus thermodilution to the partial rebreathing method. However, the comparison of cardiac output data between different measurement methodologies such as partial rebreathing and thermodilution requires consideration of a number of issues [17].

Bolus thermodilution, the current clinical standard, is repeated at predetermined intervals or as deemed needed by the clinician to assess a change in the patient's status. Two or more boluses of saline are often injected over a minute or more time interval. The repeatability of these boluses determines the degree of confidence in the average. Often the data show an increasing spread with higher cardiac outputs. The clinical variability between boluses may be large [18].

Particularly in a hemodynamically unstable situation it is important to compare thermodilution series with other methods that reflect the same time interval. In addition, spontaneous breaths, manipulation of the lungs, and changes in ventilation may temporarily preclude the use of the partial rebreathing measurement.

Prior work

In a 1980 paper [4], Gedeon highlighted the problems with the CO_2 Fick methods, particularly issues with related to patient cooperation and the estimation of arterial and mixed venous CO_2 content by the different approaches. Systematic errors are additive and with small arteriovenous differences a small error in either

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Table 1. Summary of selected investigators' deadspace implementations

Investigator [reference]	Rebreathed volume	Cycle time/ rebreathing time	Averaging baseline/ rebreathing[a]	Sample rate (/sec)	Sensors	Corrections/notes
Capek [7]	170 ml	3.5 min/30 sec	15 breaths/all breaths but first	40	Siemens 930 both with/without mainstream flow sensor	Vd_{alv}/VT constant during measurements
Gama de Abreu [8, 15]	200 ml	3 min/35 sec	60 sec/last 15 sec	60	Siemens 930 with mainstream flow sensor	Reports only PCBF
Novametrix NICO	Variable	3 min/50 sec	30 sec/15–35 sec	100	Mainstream CO_2 and flow	VCO_2 for FRC $P_{ET}CO_2$ for perfusion ratio[b]

Abbreviations: PCBF – pulmonary capillary blood flow; FRC – functional residual capacity.
[a] Averaging time in breaths or seconds for baseline and rebreathing periods.
[b] Perfusion ratio corrects for parallel deadspace effect.

Table 2. Selected partial rebreathing cardiac output studies using bolus thermodilution as the reference method [39]

Author, date [reference]	Method	Study population	Number of data points	CO range (l/m)	r	Bias (l/min)	Precision (l/min)
Gedeon A, 1980 [4]	Hyper-hypoventilation	5 dogs 6 patients	35 6	0.5–6.5 2.5–5.0	NR	NR	(20%) (8%)
Roy RJ, 1985 [6]	Switched serial DS	25 dogs	322	1.5–7.0	0.91	NR	NR
Blomqvist H, 1986 [25]	DS for 8 breaths. Oleic acid lavage	14 dogs 12 dogs	NR	Mean 2.14	0.94 0.91	0.17	(CV = 12%)
Capek JM, 1988 [20]	Switched serial deadspace	29 patients	329	NR	0.70	NR	NR
Capek JM, 1988 [7]	Switched serial DS Lavage w/oleic acid	16 dogs	458	1.5–7.5	0.91	0.01	0.51
Bosman RJ, 1990 [26]	Hyper-hypoventilation Switched DS	44 postoperative CABG patients	40 41	3.2–9.6	0.40 0.93	–0.12 0.18	0.57 0.57
Gedeon A, 1992 [19]	Rebreathing apparatus	6 pigs	64	1.5–11.5	0.92	–0.13	0.78
Osterlund B, 1995 [27]	Rebreathing apparatus	40 postoperative cardiac patients	80	1.8–8.9	0.81	–0.14	0.77
Gama de Abreu, 1995 [8]	Switched DS	15 sheep 8 ARDS patients	23	2.7–10.9	0.54	–1.69	1.90

Abbreviations: NR – not reported; TDco – thermodilution cardiac output; CABG – coronary artery bypass grafting procedure; DS – dead space; CV – coefficient of variation; r – correlation coefficient.

measurement can result in a rather large error in estimating the cardiac output. Gedeon was the first to describe a method that relies upon a change in arterial CO_2 content while at the same time maintaining a constant venous CO_2 content. This required that these measurements be performed in a time short enough such that recirculation was not a factor. To accomplish this he adjusted the ventilator's end-inspiratory pause and minute ventilation to provide a baseline period followed by periods of slight hyper- and hypo-ventilation.

In later papers, Gedeon suggested adding deadspace to achieve a similar effect [5] and additional measure-

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Table 3. Selected NICO studies [39]

Author, date [reference]	Study population	Number of data points	CO range (l/m)	r	Bias (l/min)	Precision (l/min)
Orr JA, 1996 [28]	5 dogs	272	1.8–13.5	0.92	NR	(SEE = 0.9)
Orr JA, 1998 [29]	5 dogs	176	1.0–8.0	0.94	–1.1	0.62
Bailey PL, 1998 [30]	7 CABG patients	44	2.5–9.4	0.90	0.07	0.85
Haryadi DG, 1998 [31]	4 dogs	115	1.9–12.2	0.91	0.21	0.76
Johnson KB, 1998 [32]	4 dogs Oleic acid lavage	41	1.8–6.5	0.83	0.02	0.65
Watt RC, 1998 [33]	5 CABG patients	NR	NR	NR	0.20	0.79
Kück K, 1998 [34]	10 CABG patients	36	2.63–8.1	0.92	0.02	0.70
Guzzi L, 1998 [24]	27 CABG patients	69	NR	0.85	–0.01	0.62
Jopling MW, 1998 [35]	NR	48	NR	NR	0.26	NR
Orr JA, 1999 [36]	42 CABG patients	117	2.6–8.2	NR	0.07	0.81
Haryadi DG, 1999 [37]	10 CABG patients	48	1.85–7.78	NR	0.46	0.85
Loeb RG, 1999 [38]	21 CABG patients	NR	3–10	NR	0.11	0.95

Abbreviations: NR – not reported; TDco = thermodilution cardiac output; CABG – coronary artery bypass grafting procedure; DS – dead space; SEE – standard error of the estimat; r – correlation coefficient.

ments such as oxygen consumption to better correct for shunt [19]. For his doctoral dissertation [20] at Rensselaer Polytechnic Institute, Troy, NY, John Capek further expanded upon the early work of Gedeon by (a) adding a fixed deadspace, (b) performing more frequent (once per $3\frac{1}{2}$ minute) rebreathing intervals, (c) correcting for alveolar deadspace assuming a constant Vd_{alv}/VT during the rebreathing, and (d) including hemoglobin as a factor in the slope of the CO_2 dissociation curve. Besides monitoring of cardiac output, PCBF and other parameters, Gama de Abreu (1997) [22] and Gedeon (1985) [5] reported the use of PCBF for optimizing the level of PEEP.

NICO

The Novametrix NICO system and its prototypes have been tested in a number of animal and clinical studies.

Animal studies

The animal experiments allowed the methodology to be studied over a wide range of cardiac output, rapidly changing cardiac output, and wide range and rapidly changing shunt conditions. The animal studies included comparisons to ultrasonic flow probes placed around the pulmonary artery and to bolus thermodilution with traditional and DualTherm (B. Braun) technologies.

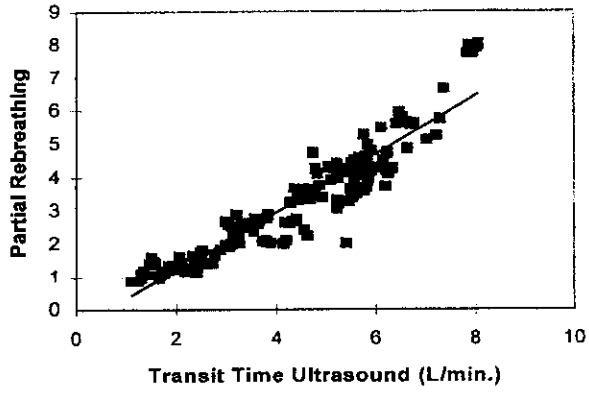

Fig. 12. Scatterplot of partial rebreathing vs. ultrasonics flow probe (r = 0.94 −1.1 ± 0.62 l/min, n = 176) [23] (unpublished plot) (used with permission from J. A. Orr).

In an ultrasonic flow probe comparison study [23] 6 dogs with a flow probe around their pulmonary artery had their cardiac output raised using a continuous infusion of epinephrine and dobutamine and lowered using increased inhaled concentration of halothane (Figure 12). The data indicated that the system compared well to this reference device. Comparison studies

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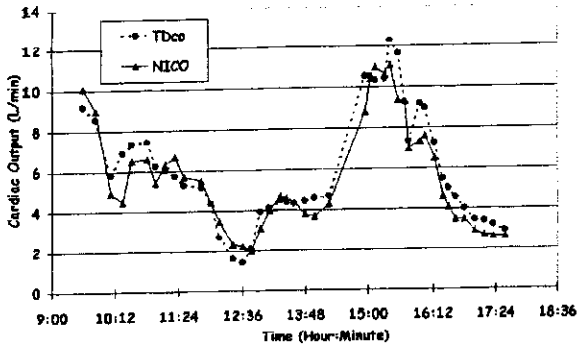

Fig. 13. Time plot of partial rebreathing (NICO) vs. dual therm bolus thermodilution (TDco) for a 9 hr animal study in which cardiac output was raised and lowered over a 1.5–12,3 l/min range (n = 43, r = 0.96 bias ± precision of −0.39 ± 0.83 LPM) (unpublished plot).

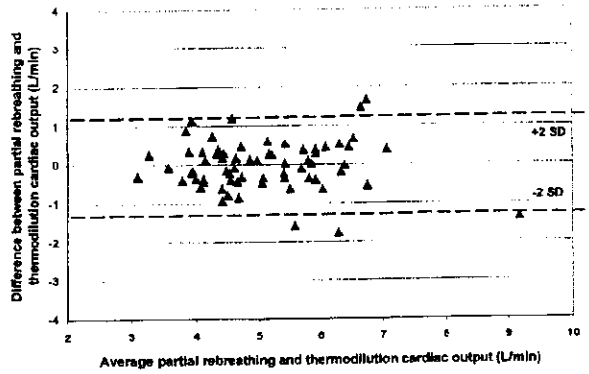

Fig. 14. Bland–Altman plot from CABG patietns [adapted from 24]. Overall bias and precision is − 0.01 ± 0.62 LPM and r = 0.85.

in animals to bolus thermodilution with traditional and DualTherm technologies have showed excellent bias, precision and tracking (Figure 13).

Clinical studies

A number of the clinical studies were presented at recent scientific meetings. The clinical abstracts presented included (a) comparisons between bolus thermodilution and continuous thermodilution in patients in the OR setting, (b) comparisons to continuous thermodilution with both the Baxter and Abbott devices and (c) comparison between different means of shunt correction. Figure 14 presents the data from a study of patients undergoing cardiopulmonary bypass procedures [24]. The other clinical studies showed results consistent with the data from this study. The NICO system uses a switched serial deadspace approach whereas some of the earlier NICO abstracts used a cross-bar approach for the addition of deadspace. Clinical studies were performed to evaluate the shunt correction algorithm employed in the NICO system [10]. The Novametrix shunt correction algorithm, which uses SpO_2 and FiO_2, was compared with measured and assumed blood gas values in 42 patients (30–85 years) in the OR and post-operatively in the ICU. The PCBF was separately adjusted using the measured and assumed blood gas values. The results were compared against thermodilution cardiac output. The data indicates that using the blood gases in the NICO shunt correction algorithm only improves overall performance to a relatively small degree over the noninvasive method ($r = 0.82$ vs. $r = 0.78$ and bias ± precision of 0.34 ± 0.88 vs. 0.69 ± 6.94 LPM) [10].

LIMITATIONS

The partial rebreathing method assumes that the following parameters do not significantly change during the baseline and rebreathing periods of each measurement cycle. It will be shown that each is a reasonable assumption.

Cardiac output remains constant

This is a fundamental assumption of the Fick method [13] and all methods that do not make beat-to-beat estimates including thermodilution. Any change in the cardiac output during the measurement periods should result in an error not to exceed the amount of the change.

Partial pressure of mixed venous CO_2($PvCO_2$) remains relatively constant

The $PvCO_2$ reflects the level of the CO_2 stores. Due to the buffering and large size of these stores a significant change in ventilation is required before a change in the venous CO_2 partial pressure is measured. Changes in ventilation such as hyper- or hypo-ventilation, changes in metabolism, or a sudden release of metabolites can alter the mixed venous CO_2 partial pressure. As long as these changes have a time constant on the order of the 2–3 minutes, the method as implemented in the NICO system can compensate for these changes.

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Intrapulmonary shunt constant and can be estimated non-invasively

The method measures pulmonary capillary blood flow, the non-shunted portion of the cardiac output. To calculate total cardiac output, the shunted portion of cardiac output must be included. The measurement of intrapulmonary shunt (Qs/Qt) requires the calculation of arterial and mixed venous oxygen contents. When mixed venous blood samples are not available, various oxygen tension-based indices are often used to estimate Qs/Qt. Additionally, noninvasive methods of estimating Qs/Qt based upon SpO_2 and FiO_2 measurements have been used. A recent study [14] examined the reliability of invasive *versus* noninvasive indices of Qs/Qt and found that the noninvasive estimates compare well with the invasive estimate of shunt (i.e. all r except one between 0.83–0.93). If the shunt changes during the measurement period, the error in cardiac output due to this effect will be no more than the change in the shunt. Errors in the shunt estimate will similarly affect the cardiac output. Thus, a large shunt estimation error has only a small effect on cardiac output. For example, if the true shunt was 10% but the estimated shunt has a 20% error (i.e., the shunt may be 12% or 8%) then this translates only to a 2% error in cardiac output.

Hemoglobin

The equations for the CO_2 dissociation curve used by most investigators include hemoglobin. The hemoglobin can be measured or assumed. If it is assumed to be 11 and there is an error of 3 g/dl (i.e., actual hemoglobin is 8), an error of approximately 10% is introduced in the estimate of cardiac output.

In addition to these assumptions, the method at present is only being applied to mechanically ventilated patients. Currently research is underway to expand the scope of the method to include spontaneously breathing subjects. Also, use of the system is contraindicated in patients that cannot tolerate a change of up to several torr in the arterial CO_2 partial pressure.

CONCLUSIONS

Compared to conventional cardiac output methods, the partial CO_2 rebreathing technique is non-invasive, can easily be automated and can provide real-time and continuous cardiac output monitoring. Taking advantage of modern sophisticated sensor and signal processing technology and integrating multiple monitored physiological variables the NICO monitor is the first commercially available implementation of partial CO_2 rebreathing.

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Anesthesiology 2002; 96:A-493
October 15, 2002, 2:00:00 PM - 4:00:00 PM, Orange County Convention Center, Room F

Is the Patient's Temperature the Cause of the Underestimation of Cardiac Output Using the NICO System Compared with the Swan Ganz Catheter?

Gildas Gueret, M.D.; Benoit Rossignol, M.D.; Jean Paul Wargnier, M.D.; Andre Miossec, M.D.; Charles C. Arvieux, M.D., Ph.D.
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Introduction: Cardiac output may be measured from expired CO_2 using the NICO device (Non Invasive Cardiac Output NICO®; Novametrix). Such a measurement is based on the Fick principle with CO_2 as the marker assayed by VCO_2 and $ETCO_2$[1] .A variation exist between cardiac output determined by Swan Ganz catheter (CCO®- Continuous Cardiac Output, Baxter) and the NICO. We wondered if the variation of body temperature during anaesthetic recovery may explain such a discrepancy. We tried to answer such a question by comparing the variation of cardiac output between the two techniques when the body temperature of the patients changed during and after the surgery.

Method: After informed consent had been obtained, 25 patients operated on for CABG (off pump technique) or major aortic surgery were studied. Only patients whose haemodynamic status required an invasive assessment of the cardiac function were included. Anaesthesia was induced and maintained with propofol and remifentanil using TCI protocol and curarized with cisatracurium. The main goal was stable anaesthesia without haemodynamic depression.

Results: 3646 points of comparison were obtained. An under estimation of the CO by the NICO was consistently observed (-0.05 litre min^{-1}; CI 95% = -2.43; +2.23 litre min^{-1}). This difference was not affected by the variation of the body temperature as shown on the diagram by the relative variations between the two techniques which remain parallel to the axis of the temperature between 33.5 and 40.5°C.

Discussion: Variations of the temperature of the patients did not affect the measurement of the cardiac output by the NICO device and cannot be a factor to explain why the NICO underestimates CO by comparison with the Swan Ganz catheter.

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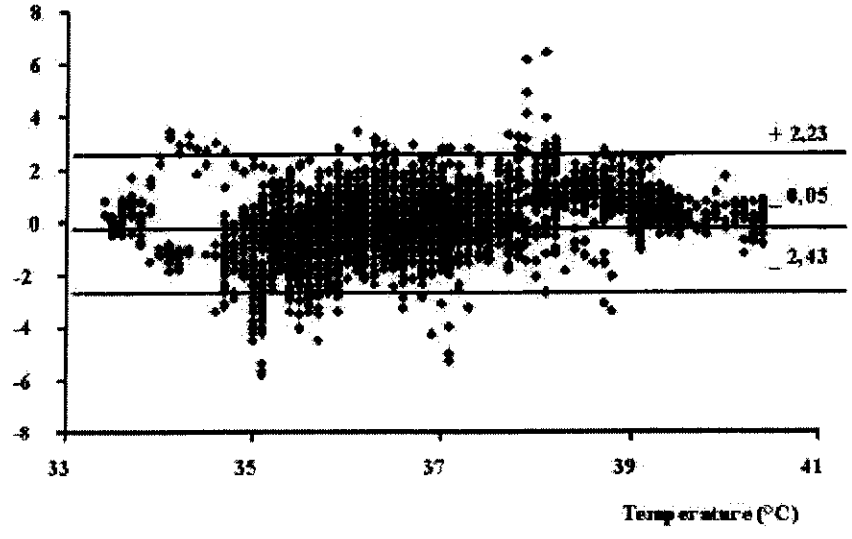

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Anesthesiology 2002; 96:A492
October 15, 2002, 2:00:00 PM - 4:00:00 PM, Orange County Convention Center, Room F

A Comparison of Flow Guided Versus Conventional Volume Replacement in Major Elective Surgery

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The study was performed to examine the hypothesis that intraoperative resuscitation would be better guided by continuous measurements of cardiac output than the conventional measurements of blood pressure and heart rate. Twenty four patients scheduled for either nephrectomy or radical cystectomy were consecutively enrolled into the study. Exclusion criteria were current history of angina or congestive heart failure, significant chronic lung disease, morbid obesity and the need for more extensive surgery. All patients had a radial arterial line and thoracic epidural catheter placed preinducion, and received a standardized anesthetic consisting of a sufentanil infusion supplemented by inhalational agent and neuromuscular relaxation. A continuous epidural infusion of bupivacaine (0.125%) and hydromorphone (6μg/cc) was given for postoperative analgesia. In the intervention group, the NICO noninvasive cardiac output monitor (Novametrix,CT) was used to guide intraoperative resuscitation. The goal was to maintain the cardiac index above 3 L.min-1.m-2 throughout the case with either volume replacement, or a dobutamine infusion if volume alone failed to achieve this goal. In the control group, blood pressure, heart rate and, where possible, urine output were used to guide resuscitative efforts. In both groups, the hemoglobin was maintained between 9 to 11 g/dl with packed red cell transfusions. Measured outcomes included speed of recovery of gastrointestinal function, as measured by the postoperative time required before the patient could tolerate a soft diet, and the time to hospital discharge. Between group statistical comparisons were performed using the unpaired Students t-Test.

The NICO monitor performed reliably in all cases and no patient was excluded because of failure of the device to provide consistent recordings. There was no difference in mean age between the NICO (65 yrs) and the control (57 yrs) groups. Overall, the difference in the times to diet toleration (84 vs 113 hrs) and hospital discharge (5.1 vs 6.6 days) in the NICO (n=12) vs control (n=12) group were not significantly different. However examining the radical cystectomy patients separately (n=12) showed that both the time to diet toleration (123 vs 176 hours) and hospital discharge (6.8 vs 9.3 days) were significantly different ($p< 0.05$) in the NICO vs control group. In contrast, in the nephrectomy patients (n=12) there was no difference in either time to diet toleration (46 vs 50 hrs) or hospital discharge (3.5 vs 3.8 days) in the NICO vs control group. The mean duration of surgery was 9.0 hrs for a radical cystectomy vs 4.4 hrs for a nephrectomy ($p <0.01$), and the mean difference in intraoperative volume replacement was 15 vs 7.3 litres ($p<0.01$).

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Anesthesiology 2002; 96:A489
October 15, 2002, 2:00:00 PM - 4:00:00 PM, Orange County Convention Center, Room F

Noninvasive Cardiac Output Measurements: Comparison of Partial CO_2 Rebreathing Technique and Pulse Dye Densitometry Technique

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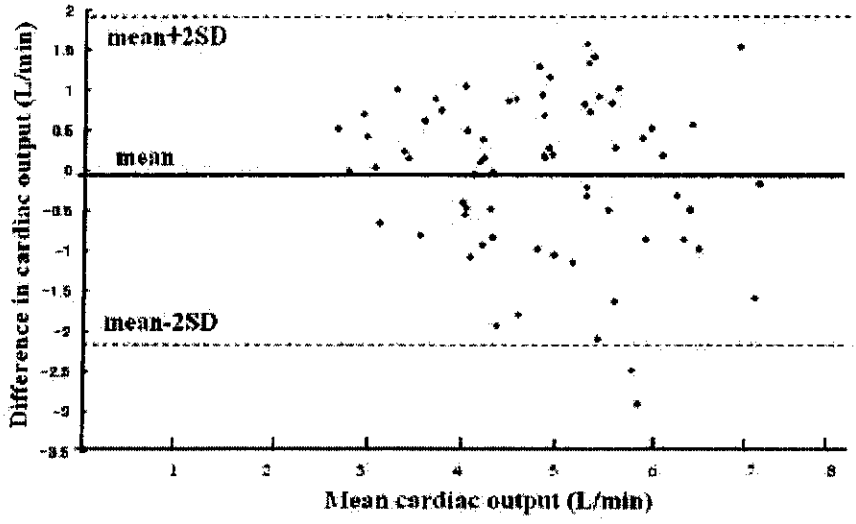
Introduction: Thermodilution method using PA catheter still remains a clinical standard for measuring cardiac output (CO), but several less invasive methods such as transesophageal doppler echocardiography, pulse dye densitometry using indocyanine green (ICG) (PDD; DDG1101: Nihon-Koden, Tokyo, Japan), and CO_2 rebreathing method (NICO, Novametrix Medical Systems Inc., USA) have been developed recently. Pulse dye densitometry technique has been developed in Japan to measure CO by analyzing the pulsatile change in ICG concentration in the peripheral arterial blood without direct blood sampling. CO by PDD is calculated from dye dilution curve of ICG at the nasal wing by an optical sensor and the agreement of CO determinations by PPD comparing it with thermodilution method has been assessed. Because there has been previously no report that has compared CO_2 rebreathing method with PDD method, we studied to assess the agreement of CO determinations by NICO to those obtained by PDD.

Method: Adult patients undergoing elective laparotomy were selected for inclusion in this study. CO was measured at any time during operation. As it took 3 minutes to measure CO by NICO and about 2 minutes by PDD, we obtained each point data during 6 minutes (2 NICO cycles). Injections of 2.5 mg of ICG from right internal jugural vein were repeated two to three times and the average value as set to CO. The agreement between the different methods was compared by Bland-Altman analysis.

Results: 70 data points from 19 patients were examined. NICO has a bias and precision (2SD) of -0.04 ± 1.96 L/min when compared to PPD as shown in Bland-Altman plot (below).



Discussion: Results show both monitoring systems may be clinically acceptable devices for noninvasive measurement of CO. From the point of view of the ease of use, minimal set up time, and cost effectiveness, NICO may be a most useful alternative as noninvasive CO monitoring at present.
References: (1) Anesthesiology 87:816, 1997, (2) Anesthesiology 92:A323, 2000, (3) Masui 50:799, 2001.

1004

Anesthesiology 2002; 96:A486
October 15, 2002, 2:00:00 PM - 4:00:00 PM, Orange County Convention Center, Room F

Flow Versus Pressure-Based Variables for Monitoring Fluid Administration

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Introduction: Accurate assessment of circulating volume is important during the intraoperative period. Both central venous pressure (CVP) and pulmonary artery occlusion pressure (PAOP) are routinely used as indicators of both circulating blood volume and cardiac preload. However, there are many intrinsic and extrinsic factors which may cause CVP and PAOP to be inaccurate measures of preload. With the advent of less invasive hemodynamic monitors, cardiac output (CO) has been increasingly used as an indicator of blood flow. Non-Invasive cardiac Output (NICO) (Novametrix Medical Systems, Wallingford, CT) device uses the principle of CO_2 dilution via a rebreathing circuit. NICO derived CO has been shown to correlate well with that obtained from PA catheter. We hypothesize that CO is a more reliable measure of preload compared with CVP and PAOP.

Methods: With IRB approval and patient signed informed consent, 30 ASA I-III adult patients undergoing cystectomy or cystoprostatectomy received a standardized anesthetic incorporating a balanced inhalational technique. Depth of anesthesia was maintained at a constant level as judged by standard clinical criteria. In addition to the standard monitoring, an arterial and a Continuous Cardiac Output (CCO) PA catheter (Baxter Healthcare Corporation, Irvine, CA) were placed following induction of anesthesia. Intraoperative fluid management were guided by a fluid challenge algorithm triggered by a change from baseline of BP <20% or Systolic BP < 85 mmHg, HR>20% or >110/min, or urine output <0.5 mL/kg/h. A colloid (Hextend) bolus of 250 mL was administered under pressure delivered within 2 min. Hemodynamic variables (CVP, PAOP, NICO-CO, PA-CCO) were measured at baseline (immediately before colloid bolus), 5 and 15 min after each fluid bolus. NICO CO determination was performed with the NICO 'FAST' mode which avoids algorithm averaging of COs from sequential rebreathing cycles. A response was defined as a change at each of the two time points from baseline of > "0" while no response was defined as a change of > "0". Descriptive statistics and chi-square test were performed as appropriate. A p value <0.05 was considered significant.

Results: The average age was 65±7 with a duration of surgery of 473±183 min (mean±sd). Data were collected for 102 fluid boluses with an average of 3 boluses for each patient. The results are presented in Table 1. NICO and PA derived CO are associated with more frequent positive responses following a colloid fluid bolus compared with CVP or PAOP.

Conclusions: Flow based variable, e.g. cardiac output, may be a more sensitive indicator of intraoperative colloid bolus administration compared with pressure based variables. The use of NICO may be a viable alternative to PA derived cardiac output.

Table 1. Percentage of patients with a response (change of >0) at 5 and 15 minutes from baseline.

	CVP (mmHg)	PAOP (mmHg)	PA-CCO (L/min)	NICO-CO (L/min)	P value
% of patients with response between 5 min and baseline	50	62	73	71	0.001
% of patients with response between 15 min and baseline	46	59	65	66	0.01

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Anesthesiology 2002; 96:A480
October 15, 2002, 2:00:00 PM - 4:00:00 PM, Orange County Convention Center, Room F

Evaluation of the Cardiac Output Measured with the NICO Device, the Swan Ganz Catheter and the SVO_2 in Cardiovascular Patients

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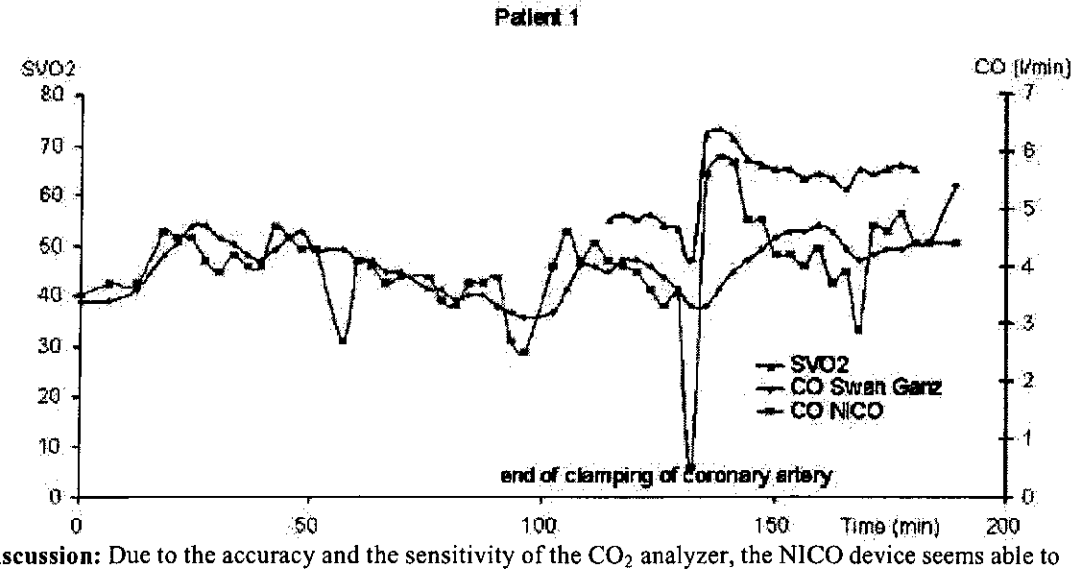
Anesthesiology, CHRU, Brest, France, Metropolitan.

Introduction: Evaluation of the cardiac output may be done using the expired CO_2 with the NICO device (Non Invasive Cardiac Output NICO®, Novametrix). Such a measurement is based on the Fick's principle with the CO_2 as the marker assayed by the VCO_2 and $ETCO_2$[1]. Actually, the technique includes the measurement of the pulmonary capillary output and adds an estimation of the pulmonary shunt. In order to test the accuracy of the measure, we evaluated at the same time the cardiac output both with the NICO device and with the Swan Ganz catheter (CCO®: continuous cardiac output with SVO_2 Baxter), and the SVO_2 in major cardiovascular surgery.

Methods: After the informed consent has been obtained, 25 patients operated on CABG (off pump technique) or major aortic surgery have been studied. Only the patients whom haemodynamic status required an invasive assessment of the cardiac function were tested. Induction and maintenance of anesthesia were done with propofol and remifentanil using TCI protocol and curarized with cisatracurium. The main goal was a stable anesthesia without haemodynamic depression.

Results: The NICO device has detected positive (patient 2 at the incision time) and negative (patient 1: unclamping the coronary artery, patient 2: heart luxation and beginning of the CBP)(figure 1 and 2) variations in cardiac output per operatively. With the later, negative variations of cardiac output were only detected with the SVO_2.
Figure 1 and 2: evolution of the SVO2 and the cardiac output measured with both methods.



Discussion: Due to the accuracy and the sensitivity of the CO_2 analyzer, the NICO device seems able to detect positive or negative variations of the cardiac output than the CCO Swan Ganz catheter was not able to detect in cardiovascular surgery patients. The SVO_2 device may detect only a decrease in oxygen delivery. Thus, the NICO device seems sensitive enough to detect sharp variations in cardiac output that the CCO Swan Ganz catheter could not detect with the advantage of a truly non invasive device.

1. Crit Care Med 1997; 25: 675-83.

1066

Anesthesiology 2002; 96:A479
October 15, 2002, 2:00:00 PM - 4:00:00 PM, Orange County Convention Center, Room F

Comparison of the Cardiac Output Measured with the NICO Device or the Swan Ganz Catheter in Major Cardiovascular Surgery

Gildas Gueret, M.D.; Benoit Rossignol, M.D.; Jean Paul Wargnier, M.D.; Daniel Deredec, M.D.; Charles C. Arvieux, M.D., Ph.D.
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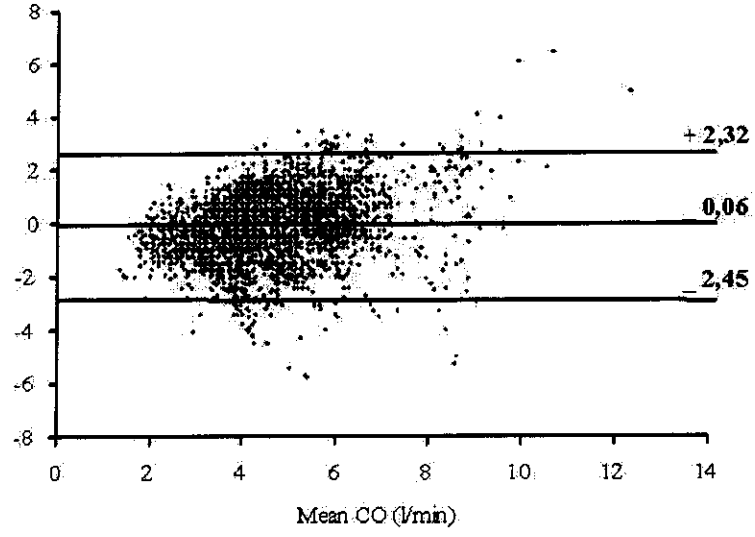
Introduction: Evaluation of the cardiac output may be done using the expired CO_2 with the NICO device (Non Invasive Cardiac Output NICO® Novametrix). Such a measurement is based on the Fick's principle with the CO_2 as the marker assayed by the VCO_2 and $ETCO_2$[1]. Actually, the technique includes the measurement of the pulmonary capillary output and adds an estimation of the pulmonary shunt. In order to test the accuracy of the measure we evaluated at the same time the cardiac output both with the NICO device and with the Swan Ganz catheter (CCO®: continuous cardiac output with SVO_2 Baxter) in major cardiovascular surgery.

Methods: After the informed consent has been obtained, 25 patients operated on CABG (off pump technique) or major aortic surgery have been studied. Only the patients whom haemodynamic status required an invasive assessment of the cardiac function were tested. Induction and maintenance of anaesthesia were done with propofol and remifentanil using TCI protocol and curarized using cisatracurium. The main goal was a stable anaesthesia without haemodynamic depression. Data were compared with student t test for paired data and $p < 0.05$ was chosen as a significant threshold.

Results: 4460 points of comparison were obtained. The mean difference in cardiac output measurements (NICO-CCO) was -0.06 L.min-1 with a 95% confidence interval between +2.32 and -2.45 L.min-1 (figure 1). However, there was a significant correlation between the two techniques ($p<0.001$; $r^2 = 0.5$). Large variabilities between and within patients were found.

Figure 1: correlation between both methods of cardiac output measure showed with Bland and Altmann method



Discussion: A significant correlation between the two techniques exists however the inter and intra-patient variabilities is rather high with mainly an underestimation of the cardiac output.

1. Crit Care Med 1997; 25: 675-83.

1007

Anesthesiology 2002; 96:A341
October 14, 2002, 9:00:00 AM - 11:00:00 AM, Orange County Convention Center, Room C

Intraoperative PCO_2 and Tissue Oxygenation

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Outcomes Research Institute and Dept. of Anesthesiology, University of Louisville, Louisville, Kentucky

Introduction: Wound infections are common and serious surgical complications. Oxidative killing by neutrophils is the primary defense against surgical pathogens and increasing intraoperative tissue oxygen tension markedly reduces the risk of such infections. We hypothesized that since moderate hypercapnia improves cardiac output and peripheral tissue perfusion, it woud increase tissue oxygenation intraoperatively compared to normocapnia.

Methods: General anesthesia was induced with propofol and maintained with sevoflurane in 40% oxygen in 20 ASA I-II patients undergoing abdominal surgery. $PaCO_2$ was randomly assigned to 30 (hypocapnia) or 45 (hypercapnia) mmHg intraoperatively. A subcutaneous tonometer, inserted into each subject's lateral upper arm, continuously monitored tissue oxygen, and a cerebral oximeter probe (INVOS), positioned on the forehead, monitored regional cerebral oxygen saturation. Target PCO_2 concentrations were obtained by eliminating soda lime from the anesthesia circuit and altering the respiratory rate between 11 and 15 breaths/min at a constant tidal volume of 10 ml/kg. Cardiac output was monitored continuously by a noninvasive system (NICO). Normally distributed data were analyzed with two-tailed, unpaired t-tests; Wilcoxon-Mann-Whitney Rank Sum tests were used if data were not normally distributed. $P<0.05$ was significant.

Results: Demographics, morphometrics, and confounding factors were similar between the groups. The hypercapnia group had higher cardiac index, cerebral oxygen saturation, and subcutaneous tissue oxygen values (Table 1). The arterial to end-tidal PCO_2 gradient averaged 3 ± 3 mmHg.

Hemodynamics and Tissue Oxygenation as a Function of Target End-Tidal PCO_2

Randomized $ETCO_2$ (mmHg)	30 (n=11)	45 (n=9)	*P*
MAP (mmHg)	85±10	82±7	0.447
HR (beats/min)	74±13	80±20	0.442
Cardiac Index ($L.min^{-1}.m^{-2}$)	2.8±0.7	3.5±0.6	0.064
Skin Blood Flow (U)	57.1±22.3	64.0±10.8	0.468
Cerebral Oxygen Saturation (%)	55±4	68±9	0.038*
Subcutaneous Tissue Oxygen (mmHg)	63±14	89±19	0.014*

Data presented as means±SDs. *Calculated with the Wilcoxon-Mann-Whitney Rank Sum tests.

Conclusion: Intraoperative hypercapnia increased subcutaneous tissue oxygen tension. Such an increase has the potential to halve the incidence of wound infections. We conclude that mild to moderate intraoperative hypercapnia is likely to improve resistance to surgical wound infections.

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Anesthesiology 2002; 96:A585
October 14, 2002, 2:00:00 PM - 3:30:00 PM, Orange County Convention Center, Room 224 A

Comparison of Non-Invasive, Semi-Invasive and Invasive Techniques of Cardiac Output Measurement under Different Haemodynamic Conditions in a Pig Model

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The aim of this study was the simultaneous evaluation of different methods of cardiac output measurement. Therefore we compared pulmonary artery thermodilution, trans-pulmonary thermodilution (PiCCO), a trans-oesophageal echo-Doppler probe (HemoSonic100) and partial CO2 - rebreathing technique, based on the Fick-principle (NICO-monitor) against a perivascular transit-time flow probe, placed around the ascending aorta as reference method.

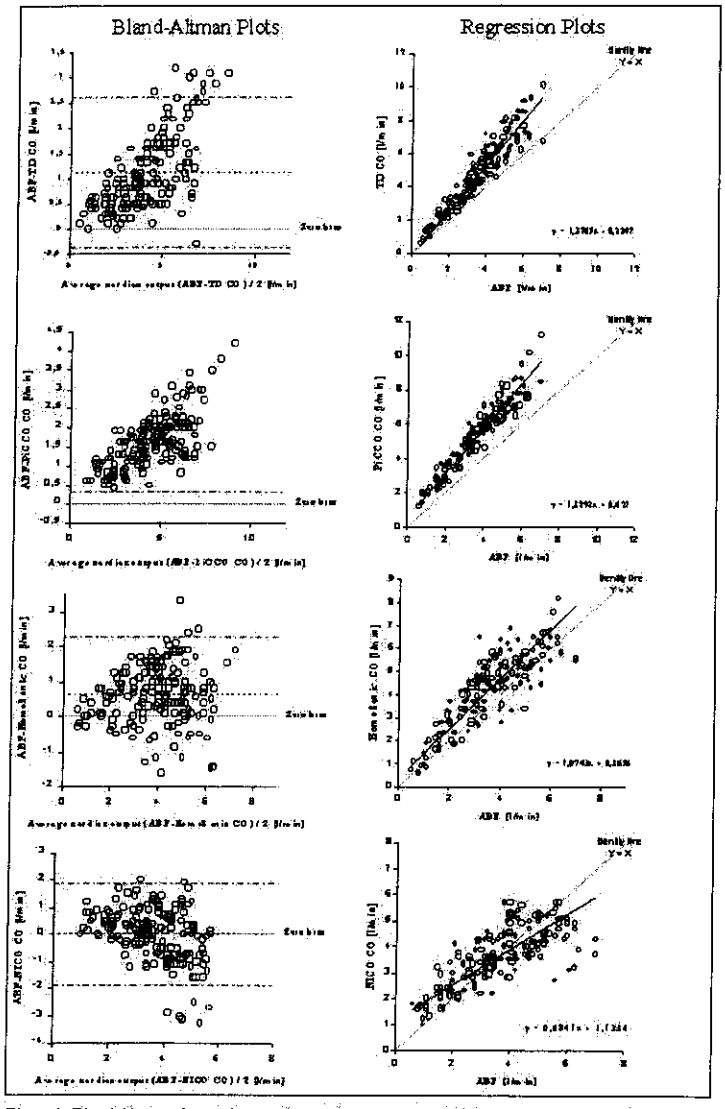

Figure 1: Bland-Altman plots and regression plots of comparison of invasive, semi-invasive and non invasive methods of cardiac output measurement against aortic blood flow. TD-thermodilution cardiac output, PiCCO™-transpulmonary thermodilution cardiac output, HemoSonic™-transesophageal doppler cardiac output, NICO™-non-invasive cardiac output by partial CO_2 rebreathing, ABF-aortic blood flow in ascendent aorta

After obtaining approval from the Local Ethics Committee on Animal Research, the investigations were conducted in 4 anaesthetized pigs. A thoracotomy and positioning of the peri-aortic flow probe was followed by the placement of a pulmonary artery catheter, a PiCCO"-catheter (femoral artery), the trans-oesophageal probe and the connection of the rebreathing loop. Different hemodynamic situations were obtained by application of catecholamines and induction of a hypovolemic shock. To compare the agreement between the concurrent measurements Bland-Altman statistics [1] and linear regression were used.

A total of 177 paired cardiac output measurements were carried out at a reference cardiac output between 0.5 to 6.4 l/min. The correlation coefficients of pulmonary artery and transpulmonary thermodilution against reference were 0.95 and 0.96. Analogous 0.85 and 0.75 for trans-oesophageal doppler and partial rebreathing technique. The Bland-Altman plot showed, that 95 % of the measurements lie within the mean ± 1.96 standard deviation (SD) range.

The results show a good comparability of the different methods. While the thermodilution techniques show a more reliable response to acute cardiac output changes, echo-doppler technique and partial CO2 - rebreathing distinguish by a less invasive application.

In conclusion, our animal model study showed that semi- and non-invasive methods of cardiac output measurement are useful and reliable. If the limitations and advantages of the different methods are considered, there may be clear alternatives to pulmonary artery based monitoring in a majority of clinical situations.

[1] Bland JM, Altman DG: Lancet (1986), 8: 307-310

1009

Anesthesiology 2002; 96:A236
October 14, 2002, 2:00:00 PM - 4:00:00 PM, Orange County Convention Center, Room D

Evolution of Intra Pulmonary Shunt during Coronary Artery Bypass: Comparison between Surgery with and without CBP

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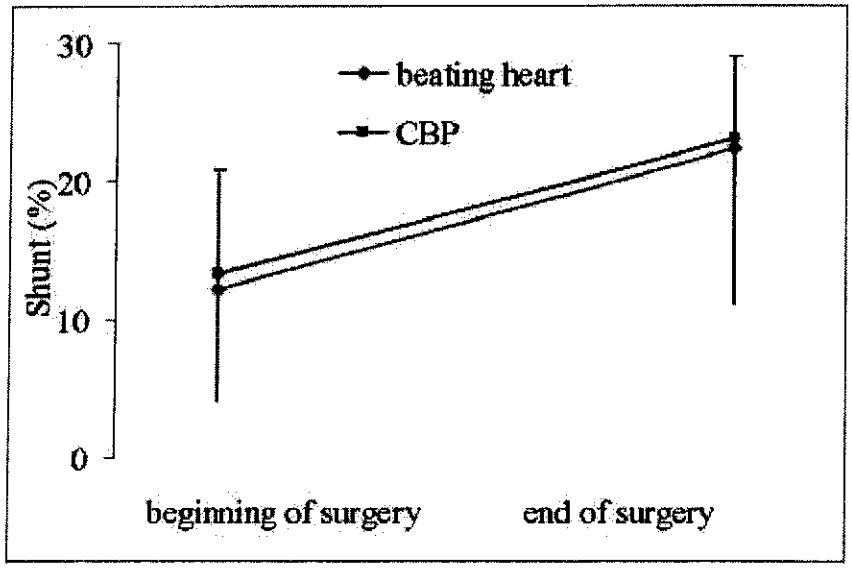
Anesthesiology, CHRU, Brest, France.

Introduction: Postoperative hypoxemia is frequent in cardiac surgery[1]. It is often in relation with an increase of the intra pulmonary shunt after pulmonary artery exclusion. The role of the CPB in the increase of the shunt is not clear, but can be evaluated with a comparison of the shunt between patients operated on coronary bypass with and without CBP. The aim of this prospective study was to compare intra pulmonary shunt between patients operated with or without CBP.

Materials and methods: The inclusion criteria was the need for invasive hemodynamic monitoring with a Swan Ganz catheter. Anesthesia was done with propofol, remifentanil, and cisatracurium. Intra pulmonary shunt was calculated at the beginning (before starting the CBP or heart luxation) and at the end of the procedure (after CBP or heart luxation removing). Data were compared with a split-splot anova design. $P < 0.05$ was chosen as a significant threshold.

Results: After ethical committee agreement and informed consent, 20 consecutive patients operated on coronary artery bypass were prospectively included. No significant difference was found between both groups for intra pulmonary shunt at the beginning and the end of the procedure.

Figure 1: evolution of the intra pulmonary shunt between patients operated with and without CBP



Conclusion: It has been postulated that the CBP plays a major role in the induction of intra pulmonary shunt due to the pulmonary collapsus during the exclusion of the pulmonary circulation. Our results shows that the intra pulmonary shunt is similarly increased at the end of the surgery in patients operated with or without CBP. Devices using an estimation of the shunt for the measurement of cardiac output (NICO) must take into account such an increase in the calibration procedure in patients operated with or without CBP.

1. J Cardiothorac Vasc Anesth. 2000 Oct;14(5):506-13.

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A-134

Cardiac output monitoring with partial carbon dioxide rebreathing system during one-lung ventilation

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Background and goal of study: $NICO_2$ (Novametrix Medical System Inc, Wallingford CT) is a non-invasive cardiac output monitor based on CO_2 Fick equation. This study was designed to compare measurements of cardiac output (CO) using this partial CO_2 rebreathing system and pulsed thermodilution during one-lung ventilation (OLV) and the goal was to assess the agreement of CO determinations using $NICO_2$ during OLV.

Materials and methods: After IRB approval and written informed consent, 5 patients scheduled for descending thoracic aorta graft replacement were enrolled in this study. Under local anesthesia, pulmonary artery catheter was placed and CO measurement was started by pulsed thermodilution using Baxter Vigilance Monitor (Baxter Healthcare Corporation, Irvine, CA). Then patient was anesthetized with 1–2% sevoflurane and fentanyl 20 $\mu g\,kg^{-1}$ and intubated with double lumen tube following vecuronium 1.2 $mg\,kg^{-1}$ IV. Graft replacement was done through left thoracotomy with the aid of OLV. Hemodynamic parameters and CO measurements using $NICO_2$ and Baxter Vigilance were simultaneously stored every 3 minutes. Data was compared (1) before thoracotomy (TT) with two-lung ventilation (TLV), (2) after TT with TLV, (3) OLV without aortic cross-clamping (AXC), and (4) OLV with AXC and partial CPB. Bland-Altman analysis and regression analysis were used to compare the two methods.

Results and discussions: Count (n), bias, precision (1SD) and correlation coefficient (r) are shown in table:

	n	Bias ($L\,min^{-1}$)	Precision ($L\,min^{-1}$)	r
Before TT with TLB	78	0.51	1.04	0.52
After TT with TLV	183	0.22	0.97	0.29
OLV without AXC	113	−0.06	0.84	0.85
OLV with AXC	81	0.64	0.63	0.81

Conclusion: During one-lung ventilation, the results show good agreement between $NICO_2$ measurements and Baxter Vigilance measurements. Even though this is a small cohort study, $NICO_2$ will be a good cardiac output monitor for surgery requiring one-lung ventilation.

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esophageal echocardiography (TEE) [2]. In this study we investigated whether transesophageal echocardiography is a noninvasive method for bedside assessment of hepatic venous blood flow in clinical practice.

Patients and Methods: Thirteen anesthetized and ventilated critically ill patients in whom hepato-splanchnic blood flow was augmented by a dobutamine infusion were studied.

Hepatic venous blood flow values were derived with TEE using the following calculations: Diameter (d) and velocity time integral (VTI) of all three hepatic veins were determined by TEE, heart rate (HR) was derived from ECG and flow subsequently calculated as $Q = \pi\,(d/2)^2\ 0.57\ \text{VTI}\ \text{HR}$ [2]. These values were compared with hepato-splanchnic blood flow (Qspl) measurements using a primed (12 mg) continuous (0.5 mg/min) infusion of indocyanine green with hepatic venous sampling as described before in detail [1]. Parameters were determined at baseline as well as after modulating splanchnic blood flow by the infusion of dobutamine.

Results: A significant increase in splanchnic blood flow could be determined with TEE (438 [387–555] vs 559 [495–709] ml/min/m^2) as well as using the ICG-method (889 [370–2285] vs 1098 [684–3479] ml/min/m^2). The Spearman correlation coefficient between both methods, however, was 0.77 at baseline and 0.63 after dobutamine-infusion.

Conclusion: The values of splanchnic blood flow determined by the two different methods had a great variance. TEE, hence, does not seem to offer a noninvasive approach for monitoring changes in hepato-splanchnic blood flow in critically ill patients.

References:

1. *Cardiovasc Res* 1995, **30**:106-112.
2. *Intensive Care Med* 2001, **27**:580-585.

P195 Assessment of the agreement between cardiac output measured by thermal filament continuous thermodilution (CCO) and noninvasive partial CO_2 rebreathing (NICO) with particular reference to $ETCO_2$ levels

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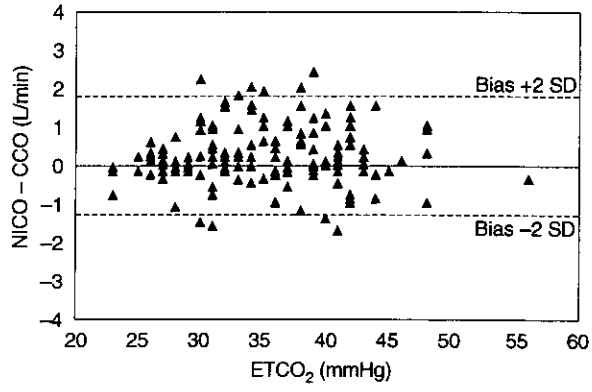
Introduction: Cardiac output (CO) is an important hemodynamic parameter and its continuous measurement has the potential to enable early recognition of hemodynamic trends and provide earlier therapeutic response. NICO is a new noninvasive cardiopulmonary monitor that provides an alternative to invasive CCO for measurement of CO. NICO uses a differential form of the Fick equation (change in CO_2 excretion and end-tidal CO_2, in response to a brief period of partial rebreathing) to provide noninvasive estimates of CO [1]. The accuracy and reliability of NICO as a function of the end-tidal CO_2 ($ETCO_2$) levels of the patient has not been studied. The purpose of this study was to determine if $ETCO_2$ levels affect the degree of agreement between NICO and CCO.

Methods: Matched sets of CO measurements from NICO (Novametrix Medical Systems, Wallingford, CT, USA) and CCO (Vigilance, Baxter-Edwards, Irvine, CA, USA) were collected in 25 patients undergoing elective cardiac surgery. The NICO sensor (consists of on-airway flow sensor, mainstream CO_2 sensor, adjustable dead space tubing, and a pneumatic valve) was attached between the endotracheal tube and the breathing circuit of the patient. The two measures, NICO and CCO were assessed for agreement by using methods proposed by Bland and Altman at different levels of $ETCO_2$.

Results: One hundred and fifty-four data points were obtained indicating variations in the difference of cardiac output compared with the variations of $ETCO_2$ of the patient. The range for CCO measures was 2.0–8.4 l/min and for NICO measures 2.5–8.3 l/min. The mean bias in CO between the two techniques for the entire protocol was 0.24 l/min and the precision (1 SD) was 0.77 l/min. The difference in CO was independent of the $ETCO_2$ levels of the patient (Fig.).

Figure



Difference in Cardiac Output (NICO-CCO) and $ETCO_2$.

Conclusion: The agreement between the NICO and CCO is clinically acceptable and is unaffected by $ETCO_2$.

Reference:

1. Haryadi DG, *et al.*: **Partial CO_2 rebreathing indirect Fick technique for non-invasive measurement of cardiac output.** *J Clin Monit* 2000, **16**:361-374.

P196 Comparison of cardiac output (CO) measurement before and after cardiopulmonary bypass: bolus thermodilution (TDco) and noninvasive partial CO_2 rebreathing (NICO)

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Introduction: NICO is a noninvasive cardiopulmonary monitor that provides an alternative to invasive TDco for measurement of CO. NICO uses a differential form of the Fick equation (change in CO_2 excretion and end-tidal CO_2, in response to a brief period of partial rebreathing) to provide noninvasive estimates of the CO [1]. The objective of this study was to compare the degree of agreement in

measurements of CO using NICO and TDco, at predetermined intervals in patients undergoing coronary artery bypass graft surgery (CABG).

Methods: Matched sets of CO measurements from a standard PA Catheter and NICO (Novametrix Medical Systems Inc, Wallingford, CT, USA, software version 4.2) were collected in 10 patients (age 35–62 years, weight 32–68 kg) undergoing elective CABG. Measurements were made at predetermined intervals during the surgery (during pre-cardiopulmonary bypass and post-cardiopulmonary bypass; chest wall open and closed). The NICO circuit was attached between the endotracheal tube and the breathing circuit of the patient. An average of three consecutive bolus (10 ml) TDco measurements made during end-expiration was compared with corresponding NICO measurements. Bland–Altman analysis was performed to compare the degree of agreement between the two methods.

Results: Bias, precision (1 standard deviation), and limits of agreement between the NICO and TDco during pre-CPB vs post CPB are shown in the Table.

Conclusion: The overall agreement between NICO and TDco was −0.03 (bias) and ± 0.80 (precision) l/min. There was no statistical difference in the CO measured by the two techniques neither during pre-CPB nor during post-CPB ($P < 0.01$) with the chest open or closed. The degree of agreement between NICO and TDco is within the recommended value [2] for NICO to be a clinically acceptable method for CO measurement during CABG.

Table

Study phase	Bias (l/min)	Precision (l/min), 1 SD deviation	Limits of agreement (bias ± 2 × SD)
Pre-bypass (chest closed)	+0.25	0.59	−0.93 to 1.43
Pre-bypass (chest open)	+0.10	0.81	−1.53 to 1.73
Post-bypass (chest open)	−0.31	0.92	−2.15 to 1.54
Post-bypass (chest closed)	−0.23	0.68	−1.58 to 1.13

References:

1. *J Clin Monit* 2000, **16**:361-374.
2. *J Clin Monit* 1999, **15**:85-91.

P197 Monitoring of intrathoracic blood volume in early septic patients: its correlation with survival

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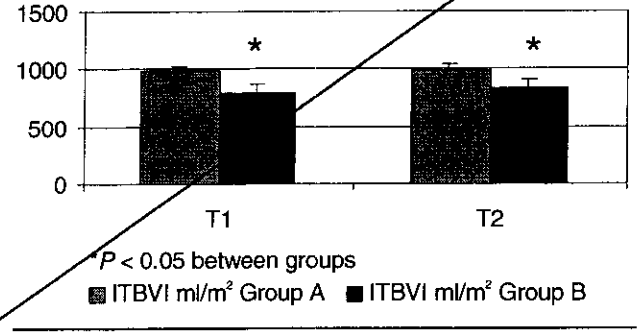
Introduction: Early goal directed therapy improves survival in sepsis, trough optimisation of contractility, oxygen balance and correction of fluids deficit [1]. Aim of the study is to investigate whether optimisation of ITBV (intrathoracic blood volume) an index of preload, could be a therapeutic end point in early sepsis, as previously demonstrated in burns patients [2].

Methods: Sixty septic patients (Bone criteria) were monitored with a central vein catheter and an artery femoral catheter connected to a fiberoptic system (Cold Z-02; Pulsion Medizintechnic) Patients were submitted to a fluid management protocol to obtain MAP ≥ 75 mm/Hg, maintaining ITBVI 800–1000 ml/m² and EVLWI < 7.5 ml/kg. At T0 (basal) and after 24 (T1), 48 (T2) 72 (T3) and 96 hours (T4) main volumetric, hemodynamic data were studied. ANOVA test was used to compare changes over time. A Fisher test was used to compare categorical data.

Results: Thirty-two patients survived (Group A) and 28 died at 28 days (Group B). ITBVI was higher in Group A than Group B at T1 and T2 (Fig. 1). And ITBVI > 800 ml/m² at T1 and T2 was predictive of survival.

Comment: (1) ITBVI improves earlier in survivors then non survivors during a reanimation period. (2) This improvement has a predictive value. (3) Optimisation of ITBVI during early sepsis should be evaluated in further trials.

Figure 1



References:

1. *N Engl J Med* 2001, **345**:1368-1377.
2. *J Trauma* 2000, **48**:728-734.

Table

	ITBVI > 800 ml/m²	95% CI
P	0.02	
Sensitivity	0.44	0.25–0.66
Specificity	0.84	0.67–0.94
RR	1.97	1.188–3.288
Positive predictive value	0.70	0.44–0.89
Negative predictive value	0.64	0.48–0.78

Monitoring of Pulmonary Capillary Blood Flow and Alveolar Dead Space Using the Combined Methods of Volumetric Capnography and "Partial CO_2 Rebreathing" ($NiCO_2$)

B. ALLARIA

Data available in all operating theaters and intensive care units make it possible to obtain important information about the adequacy of the ventilation perfusion ratio (V/Q). This ratio, which is normally 0.8, decreases and increases in two specific conditions. It decreases in the case of poorly ventilated but perfused alveoli (increased shunt QS/QT) and it increases with well-ventilated but poorly perfused alveoli (increased alveolar dead space $V_{D\,ALV}$). In both of these cases, it is difficult for the pulmonary capillary to eliminate CO_2, in the first case due to inadequate ventilation and in the second because of inadequate perfusion. Thus, arterial CO_2 (p_aCO_2) increases and alveolar pCO_2 (p_{et} CO_2 of traditional capnography) decreases in both situations.

In every case in which the V/Q ratio is altered, $p_{ET}CO_2$ – which is normally equal to p_aCO_2 or shifts by no more than 5 mmHg – becomes significantly lower, and thus the $p_aCO_2 - p_{ET}CO_2$ gradient increases.

Therefore, the availability of two simple values (p_aCO_2 and $p_{ET}CO_2$) makes it possible to detect an alteration in the V/Q ratio.

$$\Delta\ CO2 = paCO_2 - p_{ET}CO_2 = 0 - 5\ mmHg$$

If $\Delta CO_2 > 5$ mg, we can suspect an alteration in the V/Q ratio.

However, $\ddot{A}CO_2$ increases both in the case of shunt increase (reduced V/Q) and in the case of reduced perfusion with increased $V_{D\,ALV}$ (increased V/Q).

In order to proceed with a diagnosis, we need two sets of information: (1) pulmonary capillary blood flow (PCBF) and (2) the volume of the alveolar dead space ($V_{D\,ALV}$).

Today, monitoring alveolar dead space is relatively simple using volumetric capnography. The instrument that performs this has been available for a number of years (CO_2SMOPlus), and it essentially uses a flow sensor and a capnograph

to plot $P_{ET}CO_2$ against tidal volume (V_T), creating the curve illustrated in Fig. 1.

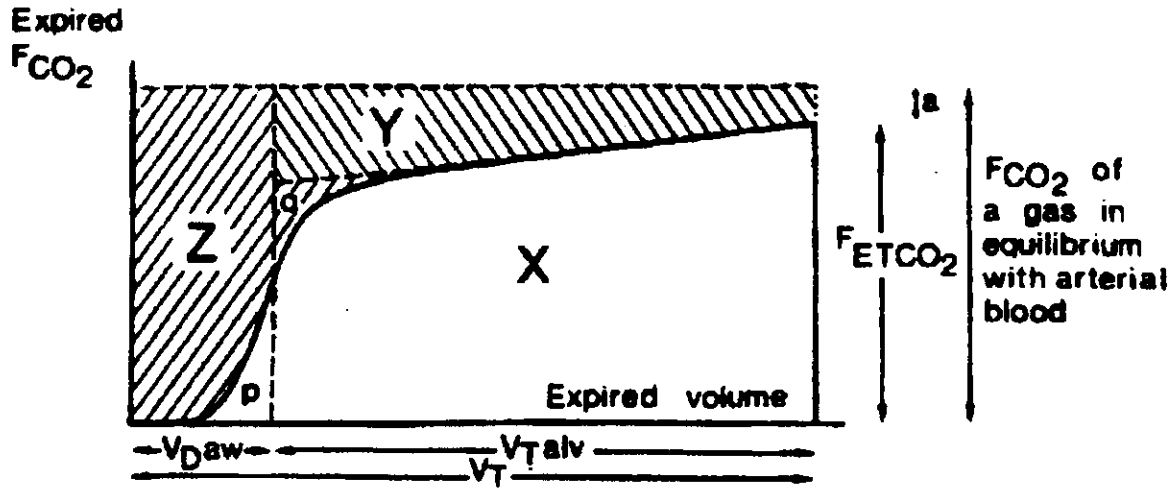


Fig. 1. Use of flow sensor and capnograph to plot $P_{ET}CO_2$ against tidal volume (V_T). x = Volume of expired CO_2, y = Vd alv, z = Vd aw, a = Δ CO_2

Consequently, by using this instrument we can obtain some information we need: the volume of the alveolar dead space ($V_{D\,ALV}$). Nevertheless, even with this information it is not always easy to detect whether an alteration in the V/Q ratio (and thus an increase in ÄCO₂ that, as we have indicated, is strictly correlated) is linked solely to an increase in dead space, or if there is a concomitant deficiency in alveolar ventilation. As shown in Fig. 1, volumetric capnography also makes it possible to monitor alveolar ventilation ($V_{T\,ALV}$), which is essentially the difference between V_T and $V_{D\,ALV}$: $V_{T\,ALV} = V_T - V_{D\,ALV}$.

For example, if we use increasing positive end-expiratory pressure (PEEP) values in acute respiratory distress syndrome (ARDS) to recruit alveoli, we may run the risk of disturbing alveolar perfusion, increasing the dead space, and diminishing effective alveolar ventilation. Here, what we mean by effective alveolar ventilation is not the type that simply recruits alveoli but the type that, in addition to recruiting them, also furnishes correct aeration.

As a result, when using volumetric capnography the PEEP that is best suited to the patient is the one that, at an equivalent V_t, will permit the best alveolar ventilation with the lowest $V_{D\,ALV}$.

However, it is widely known in both intensive care and in the operating theater that, in addition to information on aeration, it is also essential to have information on circulation. Here again, what interests us is not cardiac output in a broader sense but the quantity of blood per minute that has participated in aeration, thereby eliminating CO_2 and becoming rich in O_2. By using thermodi-

lution, we can state that this blood quantity corresponds to cardiac output (COTD) less the amount that does not participate in aeration (venous admixture = VA).

The cardiac output that participates in aeration (or non-shunted pulmonary capillary blood flow = NS PCBF) is thus

$$\mathbf{NS\ PCBF = CO_{TD} - VA}$$

Since optimized artificial ventilation permits alveolar recruitment, it should reduce the shunted pulmonary capillary blood flow and thus improve NS PCBF. However, artificial ventilation, particularly with high PEEP levels, can diminish venous return and thus lead to an overall reduction in pulmonary capillary blood flow. As a result, it is always difficult to know if the ventilation technique that has been selected will make NS PCBF better or worse.

Therefore, it is important to have a monitoring technique that can keep NS PCBF under control. Moreover, NS PCBF monitoring would also make it possible to avoid the frequent calculation of DO_2 that, because it expresses not only cardiac output but also the O_2 content of the blood, is the general parameter that best allows us to monitor the possibility of oxygenating the body. A very incisive study published recently in *Critical Care Medicine* [1] has in fact demonstrated a strong correlation between NS PCBF and DO_2 in pigs with induced ARDS.

Since NS PCBF is the part of the cardiac output that participates in aeration, it is difficult to imagine that it would not be correlated with DO_2. To date, however, NS PCBF was difficult to gauge without using a Swan Ganz catheter and even when it was used, the formula

$$\mathbf{NS\ PCBF = CO_{TD} - VA}$$

was debatable because of the difficulty in obtaining an accurate measurement of the VA.

Volumetric capnography has contributed significantly to solving this problem, making it possible to measure VCO_2 (area x in Fig. 1), as we have seen above. This has allowed measurement of pulmonary capillary blood flow with the Fick method, using the variations in VCO_2 and $EtCO_2$ during rebreathing [2].

This method is based on the assumption that PCBF can be measured in ventilation without rebreathing and with rebreathing, according to the following formulae:

$$\mathbf{Q\ PCBF} = \frac{\mathbf{VCO_2\ non\ rebr.}}{\mathbf{CVCO_2\ non\ rebr. - C_aCO_2\ non\ rebr.}} \qquad \mathbf{(1)}$$

$$\text{Q PCBF} = \frac{\mathbf{VCO_2\,rebr.}}{\mathbf{CVCO_2\,rebr. - C_aCO_2\,rebr.}} \quad (2)$$

in which VCO_2 is the elimination of CO_2/min and $CVCO_2$ is the concentration of CO_2 in the arterial part of the alveolar capillary.

Assuming that PCBF remains constant during measurement, equations **(1)** and **(2)** can be combined as follows:

$$\text{QPCBF} = \frac{\mathbf{VCO_2\,non\,rebr.- VCO_2\,rebr.}}{\mathbf{(CVCO_2\,non\,rebr. - C_aCO_2\,non\,rebr.) - (CVCO_2\,rebr.- C_aCO_2\,rebr.)}} \quad (3)$$

The large quantity of CO_2 in the venous compartment allows us to assume that $CVCO_2$ remains constant with or without rebreathing over a short period of time.

We can thus eliminate the terms $CVCO_2$ - $CVCO_2$ and transform equation **(3)** as follows:

$$\text{Q PCBF} = \frac{\mathbf{VCO_2\,non\,rebr.- VCO_2\,rebr.}}{\mathbf{(C_aCO_2\,rebr. - C_aCO_2\,non\,rebr.)}} = \frac{\Delta VCO_2}{\Delta C_aCO_2} + \quad (4)$$

The technological development of the volumetric capnograph, which already permits the measurement of VCO_2 (CO_2SMOPlus), has led to a new instrument, the $NICO_2$. In addition to the potential offered by the previous device, this new instrument also makes it possible to plot $P_{ET}CO_2$ versus TV during rebreathing periods inserted automatically through a valve and a circuit, as shown in Fig. 2, thereby measuring ÄVCO_2 according to formula **(4)**.

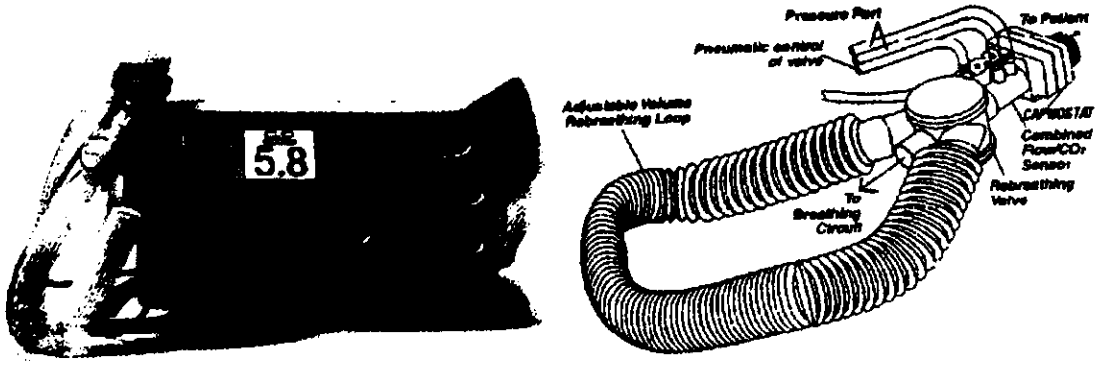


Fig.2. The $NICO_2$ device (non-invasive cardiac output) with the circuit for "partial rebreathing"

C_aCO_2 is calculated by measuring the $P_{ET}CO_2$, which is assumed as the equivalent of P_aCO_2, and the following formula is applied:

$$\mathbf{C_aCO_2 = [6.957\ (Hg) + 94.864] \times log.[1 + 0.1933\ P_aCO_2]} \quad \mathbf{(5)}$$

Given that, as we have stated repeatedly, $p_{ET}CO_2$ can also differ consistently from $p_{ET}CO_2$ in respiratory distress and hypovolemia, periodically it is useful to input the real p_aCO_2 value as assessed via hemogas analysis, in order to correct the unmeasured value.

The final formula is given below:

$$\mathbf{Q\ PCBF = \frac{\Delta VCO_2}{\Delta P_{ET}CO_2}}$$

The $NICO_2$ device thus measures the cardiac output component that participates in aeration, or in other words the parameter that we referred to above as

NS PCBF (non-shunted pulmonary capillary blood flow)

It is easy to see that when these data are available, it is then possible to arrive at the traditional value of cardiac output, adding the shunt value (QS/QT). In order to do this, this instrument uses a Nunn diagram that constructs the iso-shunt curves by plotting FiO_2 (x axis) versus P_aO_2 (y axis) replaced by SpO_2.

Based on our experience, the QS/QT value calculated using the Nunn diagram, is sufficiently correct if the shunt value is not high, but it is underestimated when it is important, as often occurs in severe cases of ARDS. It must be pointed out that if we use the $NICO_2$ device to evaluate cardiac output in routine situations (e.g., general anesthesia), the problem of high shunt values generally does not arise. On the other hand, if we use it to manage the artificial ventilation of the critical patient, the added value of this instrument lies mainly in the fact that it both measures NS PCBF and monitors $V_{D\ ALV}$, rather than in the opportunity it offers to measure cardiac output values non-invasively.

By allowing NS PCBF and $V_{D\ ALV}$ to be measured directly at the patient's bedside, the $NICO_2$ device offers us a new and noteworthy way of optimizing artificial ventilation in critical patients. While this is undoubtedly the most-interesting aspect of this new technique, the possibility it also offers for the non-invasive monitoring of cardiac output is equally welcome.

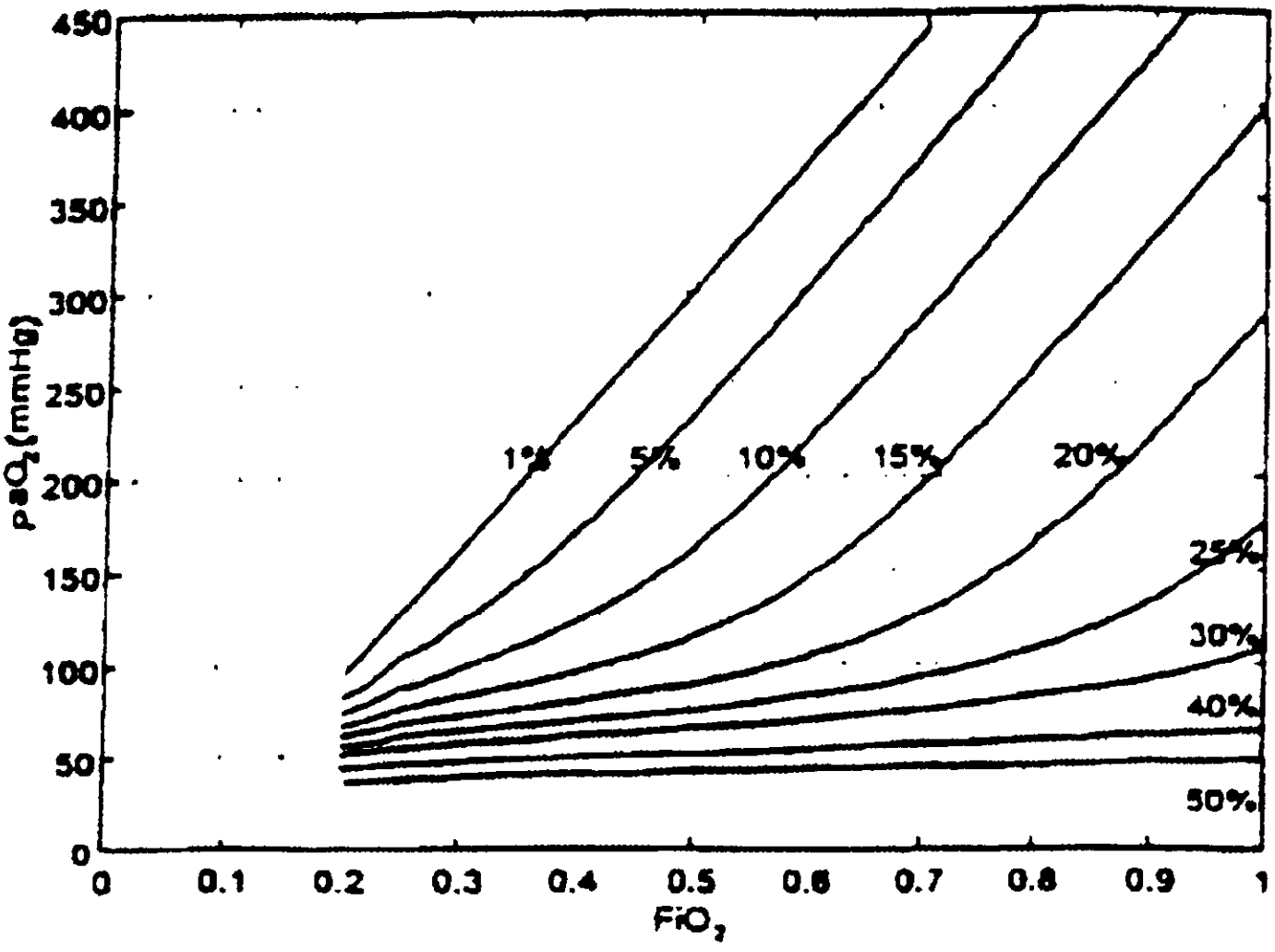


Fig. 3. Nunn diagram for evaluating the intrapulmonary shunt

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2. Jaffe MB (1999) Partial CO_2 rebreathing cardiac output. Operating principles of the NICO system. J Clin Monit Comp 15: 287
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Capnography and Cardiac Output Determination

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Since gas transfer across the alveolar capillary wall does not depend on active transport, the lung may be used as an aerotonometer, allowing the alveolar gas to equilibrate with the mixed venous blood. The analysis of this alveolar gas provides an indirect method for measuring mixed venous carbon dioxide tension ($pvCO_2$). The equilibration method, using a bag containing a high concentration of carbon dioxide in oxygen, has been shown to accurately measure oxygenated $pvCO_2$ and application of this method has led to the development of the non-invasive determination of cardiac output (CO) by the CO_2 rebreathing. Several studies have demonstrated the validity of this indirect Fick method in healthy subjects, in patients with cardiac dysfunction, in patients with obstructive airway disease, and in patients receiving mechanical ventilation [1-5].

Since the introduction to critical care of the balloon-directed thermistor-tipped pulmonary artery catheter in the 1970s [6], thermodilution CO measurements (TDCO) have been available at the bedside. Although inaccuracies of the method are known, it became the clinical "gold standard". However, soon after the introduction of the catheterization of the pulmonary artery, concerns about catheter safety appeared [7, 8], and some physicians recommended a moratorium in Swan Catheter catheter use [9-11].

Different approaches to non-invasive critical care monitoring have been suggested. Analyses of exhaled CO_2 and rebreathing techniques have been tested in the past for CO determination in the critical care setting. A close correlation was found between the rebreathing technique using arterial pCO_2 and the TD method in a variety of critically ill patients [2-5]. Unfortunately, the rebreathing method for CO determination was technically difficult and time consuming, factors that limited the routine use in the critical care arena. In order to reduce the technical burden of this method, the partial rebreathing technique for CO measurement (PRCO) has been developed (Non-Invasive Cardiac Output, NICO, Novametrix). PRCO technique allows non-invasive CO determination using the indirect Fick principle. PRCO may be performed automat-

ically by inducing a periodic cyclic and transient increase of the instrumental dead space [12, 13].

A recent study was designed to assess the accuracy of a new device (NICO, *Novametrix*) to measure CO by using the PRCO method in mechanically ventilated critically ill patients (see Appendix), and to assess the hemodynamic effect of the transient $paCO_2$ increase induced by the PRCO method during the CO measurement.

Villagra et al. [14] studied 29 mechanically ventilated patients with a TD catheter in place. They measured CO simultaneously with the PRCO and TD method (TDCO), by delivering two 10 ml iced DW5% bolus during the 50-s rebreathing period. Up to four sets of CO measurements were performed in each patient, allowing at least 2 h between measurements. Unstable CO_2 readings were excluded. We also performed three TDCO measurements 1 minute before and after the PRCO period. Hemodynamic parameters were obtained 1 min before, during, and 1 min after the PRCO period. Variables were compared by one-way ANOVA. The simultaneous TD and PRCO measurements were compared by a concordance analysis. Villagra et al. [14] performed 101 CO measurements; 22 were discarded due to unstable CO_2 elimination. The bias of 79 measurements eligible for analysis was -0.35 ± 1.62 l/min and the 95% limits of agreement ranged from –3.51 l/min to 2.82 l/min. Considering CO variations at high CO values clinically less relevant, these authors performed the analysis only for CO of less than 7 l/min, and the bias was -0.07 ± 0.93 l/min and the 95% limits of agreement ranged from –1.90 l/min to 1.75 l/min. No changes in CO, heart rate, systemic or pulmonary pressures were observed before, during, or after the PRCO measurement. Although NICO cannot replace the pulmonary artery catheter, it offers an instantaneous, reasonably accurate, and totally non-invasive estimate of CO. The transient increase in $paCO_2$ caused during the rebreathing period does not induce significant changes in CO or hemodynamics.

A strong limitation of research in this field is the lack of a true gold standard. Clinical use has confirmed TDCO at this place, but limitations of the method are well known [15-19]. However, as a "clinical gold standard" TDCO provides information to physicians for medical decision-making. When evaluating another method, the new one must provide similar information in similar situations. In this scenario, lack of agreement between both methods does not describe which is correct and which is false. A comparison of CO measured by rebreathing techniques and TD is shown in Table 1. Differences between rebreathing methods and TDCO could also be explained by how far is the real CO from the measured value using either technique.

Clinicians must be alert to potential problems with CO_2 rebreathing techni-

Table 1. Comparison of cardiac output (CO) measured by two methods

	CO reference method	CO CO_2 rebreath	R value	Bias	Agreement
Franciosa [1]	5.9 ±1.6	5.5 ± 1.7	0.95	-	-
Davis et al. [3]	3.7 ± 1.3	3.6 ± 1.2	0.93	-	-
Mahler					
ARRD 1985	4.3 ± 0.9	3.4 ± 0.8	0.70	-	-
Blanch et al. [4]	5.5 ± 1.5	5.6 ± 1.5	0.91	0.12	1.85/-1.65
Neviere et al. [2]	-	-	0.96	-0.06	0.55/0.55
van Heerden et al. [5]	5.4 ± 1.6	4.7 ± 1.5	0.70	0.8	4.9/-3.3

que for CO measurement. Selection of the initial CO_2 concentration for the rebreathing bag might be important. Since the difference between $pvCO_2$ and arterial pCO_2 is only 6 mmHg, the estimate of $pvCO_2$ obtained after rebreathing from a bag containing a known concentration of CO_2 should be accurate. PRCO by itself measures the non-shunted blood portion of the cardiac output and the non-invasive method of shunt estimation is an adaptation of Nunn's iso-shunt plots [12]. Because high intrapulmonary shunt is quite common in critically ill patients further studies are needed to assess the accuracy of the PRCO method in patients with acute lung injury receiving mechanical ventilation. During the rebreathing period, elevation in minute ventilation induced by the increment of instrumental dead space during NICO measurement could have added thermal noise and might affect TDCO reproducibility [20, 21]. Finally, the CO_2-hemoglobin dissociation curve is linear only at values of pCO_2 above 30 mmHg (Table 2).

In summary, the PRCO method offers an instantaneous, reasonably accurate, and totally non-invasive estimate of CO in critically ill patients. NICO may have a place in intensive care unit provided that patients are not breathing spontaneously and not needing the measurement of pulmonary artery pressures.

Table 2. Potential problems with CO_2 rebreathing technique for CO measurement

- Selection of the initial CO_2 concentration for the rebreathing bag
- $pvCO_2$ and $paCO_2$ difference is only 6 mmHg
- The estimate of arterial pCO_2 (end-tidal pCO_2)
- Intrapulmonary shunted blood is not measured.
- Rebreathing maneuver to obtain a plateau can alter CO
- CO_2-hemoglobin dissociation curve is linear only at values of pCO_2 above 30 mmHg

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Appendix (adapted from reference 12)

The original indirect Fick equation

$$CO = \frac{VCO_2}{CvCO_2 - CaCO_2}$$

is rearranged in a different mode

$$CO = \frac{VCO_{2N}}{CvCO_{2N} - CaCO_{2N}} = \frac{VCO_{2R}}{CvCO_{2R} - CaCO_{2R}}$$

or

$$CO = \frac{DVCO_{2N} - DVCO_{2R}}{(CvCO_{2N} - CaCO2N) - (CvCO_{2R} - CaCO_{2R})}$$

where "N" means non rebreathing and "R" means rebreathing period. It is assumed that there is no change in cardiac output between the partial rebreathing period and the non-rebreathing period. As mixed venous CO_2 content (CvCO2) does not change during rebreathing, the equation could be rewritten as:

$$CO = \frac{\Delta VCO_2}{\Delta CaCO_2} \quad \frac{\Delta VCO_2}{SX\Delta PETCO_2}$$

The last can be used to measure non-shunted pulmonary capillary blood flow. By adding shunted flow, CO can be calculated.

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Reference: Anesthesiology 2001; 95:A538

Effect of Ventilatory Settings on Accuracy of Cardiac Output Measurement Using Partial CO_2 Rebreathing.

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Recently a new device has been developed to measure cardiac output non-invasively using partial CO_2 rebreathing. Because this technique utilizes CO_2 rebreathing, we suspected that ventilatory settings such as tidal volume and ventilatory mode would affect its accuracy: we conducted this study to investigate which parameters affect the accuracy of the measurement.

We enrolled twenty-five adult post-cardiac surgery patients. When they were paralyzed, we applied six ventilatory settings in random order: volume controlled ventilation with inspired tidal volumes of 12 ml/kg or 6 ml/kg; pressure controlled ventilation with the same ranges of tidal volume; pure inspired oxygen; and high positive end-expiratory pressure. Then we challenged maximum or minimum length of rebreathing loop with tidal volume set at 12 ml/kg. After establishing steady-state conditions (15 min), we measured cardiac output using CO_2 rebreathing and thermodilution. Finally, we repeated the measurements during pressure support ventilation, when the patients had restored spontaneous breathing. The correlation between two methods was evaluated with linear regression and bias analysis.

When tidal volume was set at 12 ml/kg, cardiac output with the CO_2 rebreathing technique correlated well with that measured by thermodilution ($y = 1.02x$, $R^2 = 0.40$; bias, 0.28 L/min; and limits of agreement, -0.78 to +2.34 L/min), regardless of ventilatory mode, oxygen concentration, or positive end-expiratory pressure. However, at a lower tidal volume of 6 ml/kg, the CO_2 rebreathing technique underestimated cardiac output compared with thermodilution. When the loop was fully retracted, the CO_2 rebreathing technique overestimated cardiac output.

In conclusion, although cardiac output was underreported at small tidal volume values, cardiac output measured by the CO_2 rebreathing technique correlates well with that measured by the thermodilution method.

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Reference: Anesthesiology 2001; 95:A535

Evaluation of Partial CO_2 Rebreathing Cardiac Output Using a One Minute "Stat Mode" Measurement Cycle

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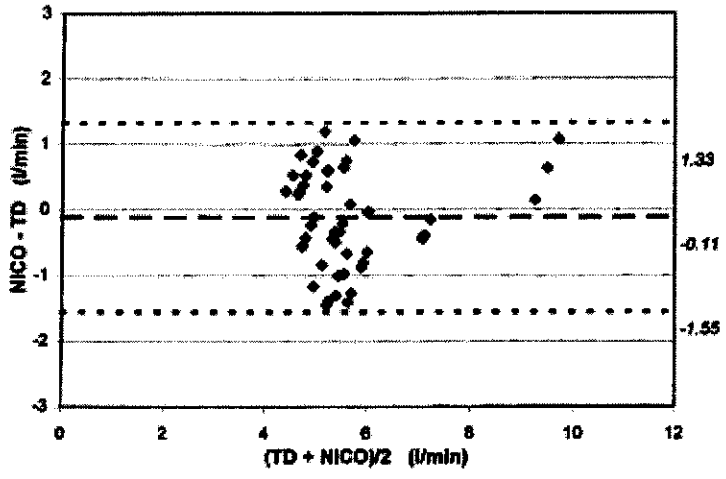
Introduction: Partial CO_2 rebreathing cardiac output measurement uses a differential form of the Fick equation to calculate cardiac output non-invasively. Traditional methods require baseline, rebreathing and recovery periods that last at total of at least 3 minutes in order to complete a cardiac output measurement. We have tested a modified system that has only two states (rebreathing and recovery) and can perform a complete measurement in 1 minute. This modification allows more frequent measurements and more robust performance in the presence of signal corruption.

Methods: A standard partial rebreathing based monitor (**$NICO_2$, Novametrix Medical Systems, Wallingford, CT**) was modified such that rebreathing occurred for 30 seconds during every minute of use. Data was collected using the modified monitor in 10 surgical intensive care unit patients who were recovering from thoracic surgery. Periodic thermal dilution cardiac output measurements were taken during the course of data collection. Cardiac output was calculated using the data from the modified monitor and was filtered using algorithms that weighted results based on the quality of the input signals. Each minute, a new cardiac output was calculated and compared to a corresponding average thermal dilution measurement when it was available.

Results: A total of 53 comparisons were made in 10 ICU patients. The average difference between the modified rebreathing and thermal dilution was -0.11 L/min. The standard deviation of the differences was 0.72 L/min. The Bland-Altman plot below shows limits of agreement to be between -1.55 and 1.33 L/min.



Discussion: These preliminary results indicate that partial rebreathing cardiac output measurements can be taken much more frequently than previously thought. Long baseline and recovery periods that are used in traditional partial rebreathing measurements are not needed. This method may allow for quicker responses to changes in cardiac output. Another advantage of a shorter measurement cycle is that corrupted cycles can be discarded without seriously compromising data availability.

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Reference: Anesthesiology 2001; 95:A399

Hypercapnia Improves Tissue Oxygenation

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Background: Surgical wound infections are common and serious complications.[1] Factors that increase intraoperative tissue oxygen tension markedly reduce the risk of surgical wound infections.[2] Primary determinants of tissue oxygen availability are arterial oxygen tension, cardiac output, and perfusion. Arterial carbon dioxide tension (PaCO2)appears as another factor to influence tissue oxygenation and perfusion. Hypocapnia shifts the oxyhemoglobin curve leftwards, and restricts oxygen off-loading at tissue level. In contrast, hypercapnia improves cardiac output, decreases systemic vascular resistance and oxygen extraction.[3] We therefore tested the hypothesis that peripheral tissue oxygenation and cerebral oxygen saturation increase as a function of PaCO2 in anesthetized humans.

Methods: With IRB approval and informed consent, we studied 10 ASA I, healthy volunteers aged 27 ± 5 yr (mean ± SD); 7 were men. Exclusion criteria were use of vasoactive or α2-agonist drugs, obesity, and smoking. Anesthesia was induced with propofol and maintained with sevoflurane in 30% oxygen. A subcutaneous tonometer was inserted into each subjects lateral upper arm for continuous tissue oxygen monitoring (PsqO2). A cerebral oximeter (INVOS 3100 Somanetics, Troy, Michigan, U.S.A.) probe was positioned on the forehead to monitor regional cerebral oxygen saturation (ScO2). PaCO2 was then adjusted to 20, 30, 40, 50 or 60 mmHg in a random order. Target PCO2 concentrations were obtained by eliminating soda-lime from the anesthesia circuit and altering the respiratory rate (RR) between 11 and 15 breaths/min at a constant tidal volume of 10 ml/kg. **Cardiac output was monitored continuously by a noninvasive system (NICO, Novametrix Medical System Inc, Wallingford, Connecticut, U.S.A.)**Outcome parameters including tissue oxygen tension, cerebral oxygen saturation, and cardiac index (CI) were recorded as well as confounding factors including mean arterial pressure, heart rate, core temperature, and arterial blood gas analyses. Confounding variables were analyzed by repeated-measures ANOVA. Major outcome variables were first averaged at each target PCO2 concentration; linear regression was then used to determine the relation between each variable and measured PCO2.

Results: Potential confounding factors did not differ significantly within the groups. Per protocol, PaCO2 and pH differed significantly at each tested carbon dioxide concentration. Subcutaneous oxygen tension, cerebral oxygen saturation, and cardiac index were linearly related to PaCO2 (r2:0.995, 0.942, 0.989 respectively).

Target PaCO2 (mmHg)	20	30	40	50	60
Measured PaCO2 (mmHg)	24 ± 2	33 ± 1	42 ± 2	51 ± 1	60 ± 2
pH	7.57 ± 0.04	7.50 ± 0.02	7.43 ± 0.04	7.37 ± 0.03	7.31 ± 0.02
RR (breaths/min)	15 ± 1	13 ± 1	13 ± 2	11 ± 1	11 ± 1
MAP (mmHg)	71 ± 4	69 ± 4	70 ± 5	70 ± 4	70 ± 6
HR (beats/min)	79 ± 11	77 ± 9	79 ± 10	82 ± 8	82 ± 10
SpO2 (%)	98.9 ± 1.3	98.9 ± 1.2	98.8 ± 1.0	98.9 ± 1.2	98.7 ± 1.1
PaO2 (mmHg)	178± 21	179± 19	175± 21	183± 21	179± 21
PsqO2 (mmHg)	52± 10	58± 11	65± 15	74± 12	82± 19
ScO2 (%)	68± 11	69± 14	79± 9	83± 10	85± 8
CI (L/min/m2)	2.7± 0.4	2.9± 0.4	3.2± 0.5	3.6± 0.7	3.9± 0.2

Conclusion: Our results indicate that increasing arterial carbon dioxide partial pressure within acceptable clinical range augments tissue oxygen tension by 15-20 mmHg. This difference is clinically important and will markedly reduce the risk of infection.[2] We concluded that permitted mild hypercarbia during anesthesia is likely to improve resistance to surgical wound infections.

References: 1. N Engl J Med 2000;342:161-7, **2.** Arch Surg 1997;132:997-1005, **3.** Crit Care Med 2000;28:360-5.

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Reference: Anesthesiology 2001; 95:A993

Changes in Onset Time of Rocuronium Are Related to Changes in Cardiac Output Produced by Ephedrine and Esmolol

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Background: Ephedrine (Eph) administered before rocuronium (R) was shown (1, 2) to reduce the onset of neuromuscular blockade (by 26% and 22% respectively) while Esmolol (Es) increased it by 26%. The 30 second prolongation in onset produced by esmolol could increase the time during which the patient is at risk for aspiration of gastric contents, eliminating one of the advantages of rocuronium. The mechanism behind the interaction between R and Eph or Es presumably depends on cardiac output (CO) and circulation time changes, which are increased after ephedrine and decreased after esmolol. The **NICO®(Non-Invasive Cardiac Output)** monitor from **Novametrix Medical Systems Inc** measures CO based on changes in respiratory CO_2 concentration caused by a brief period of rebreathing. The measurement of CO is accomplished by interpreting the data collected by proprietary sensors that measure flow, airway pressure and CO_2 concentration, and then combining these signals to calculate CO_2 elimination. Using these variables, a technique known as Fick partial rebreathing is applied to calculate CO.

Aim: To evaluate if changes in CO (measured by NICO) can explain the findings in the onset time of R produced by Es and Eph.

Methods: Following IRB approval and patient's informed consent, fifteen, ASA I and II patients (out of the 33 patients planned to take part in the study) were included in the study. All were induced with fentanyl 2 μg/kg, propofol 2 mg/kg and succinylcholine (Sux)1 mg/kg. After recovery from Sux the first CO was measured. The patients were then prospectively randomized to receive either 70 μg/kg of Eph (N =6), 0.5 mg/kg Es (N = 4) or placebo (P) (N=5), 30 sec. prior to administration of 0.6 mg/kg of rocuronium. Patients at risk for aspiration, with possible difficult intubation or ASA III -IV were excluded. Neuromuscular function was assessed by stimulating the ulnar nerve at the wrist, using surface electrodes with train-of-four monitoring (TOF) supramaximal square wave impulses of 0.2-s duration administered at 2 Hz every 10 s using a battery-operated stimulator (Constant Current Peripheral Nerve Stimulator - Fisher & Paykel- Health Care NS 252). The resulting force of contraction of the adductor pollicis brevis muscle was measured and recorded continuously using a force transducer. Onset time of R was defined as the time from the end of its injection to disappearance of all four twitches of the TOF. Noninvasive blood pressure (BP), and heart rate (HR) were recorded at one minute intervals, starting with the administration of fentanyl at the start of induction of anesthesia and up to 15 minutes. CO was recorded at 3 minutes intervals for 15 minutes. Data were analyzed using a repeated-measure ANOVA followed by Dunnett's t-test. When significant an unpaired t test was performed between groups. Results are reported as means±SDs; $P < 0.01$ was considered statistically significant.

Results: There were no differences in demographic data, mean arterial pressure and HR between the three groups. Cardiac output increased by 31% ($p<0.01$) in the Eph group compared to the other two groups and decreased by 12% in Es. The onset time of R was significantly shorter ($p<0.01$) in the E group when compared to the P and Es groups (46.3 sec vs. 84.3 sec and 97.2 sec respectively).

Conclusions: The results confirm our initial hypothesis that changes in CO are responsible for the changes in onset time of rocuronium pretreated with Es or Eph.

References: 1. Munoz HR et al. Anesth Analg 1997; 85:437-40.
2. Szmuk P et al. Anesth Analg 2000; 90:1217-9.

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Reference: Anesthesiology 2001; 95:A537

Clinical Evaluation of Non-Invasive Partial CO_2 Rebreathing Cardiac Output in Patients Undergoing Aortic Reconstruction Surgery

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Introduction: The accuracy and clinical utility of the partial CO_2 rebreathing method for non-invasive cardiac output measurements has been reported (1, 2). Changes in CO_2 elimination and end-tidal CO_2 in response to a brief rebreathing period are used to calculate cardiac output (3). The method relies on a stable CO_2 production and a constant gradient in $ETCO_2$-$PaCO_2$ during the measurements. Therefore, in patients undergoing aortic reconstruction surgery the dynamic changes in CO_2 production during ischemia and reperfusion may affect the accuracy of this method. We designed a study to compare partial CO_2 rebreathing cardiac output measurements with bolus thermodilution and continuous thermodilution cardiac output measurements in patients undergoing aortic reconstruction surgery.

Methods: With IRB approval and informed consent, 18 patients undergoing aortic reconstruction due to infrarenal abdominal aortic aneurysm were enrolled in this study. Cardiac output was continuously monitored with both partial CO_2 rebreathing method (**NICO monitor®, Novametrix Medical Systems**) and thermodilution (CCO,Vigilance®, Baxter Healthcare). Additionally, bolus thermodilution cardiac output (TDco) measurements were made during the study at the following predetermined intervals: (1) Anesthetic induction (Preop), (2) During aortic cross-clamp (XC), (3) reperfusion of unilateral iliac artery (Declamp) and (4) During peritoneal closure (Endop). These data were expressed as cardiac index (CI) and compared using Bland-Altman analysis.

Results: Thirteen male and five female patients were enrolled in the study (age = 71±10 years). The bias and precision (1SD) between TDco and NICO, as well as TDco and CCO, are summarized in the Table. NICO underestimated cardiac output measurements when compared with TDco measurements. On the contrary, CCO overestimated cardiac output measurements when compared with TDco measurements. The bias between NICO and TDco was within acceptable range before cross clamping but increased following reperfusion of the unilateral iliac artery. However, the precision was comparable for both NICO and CCO throughout the study period.

Data were indexed with body surface area (L/min/sqm) and expressed as bias±precision.

	Preop	XC	Declamp	Endop
NICO®	-0.44±0.54	-0.46±0.55	-0.72±0.63	-0.67±0.47
CCO	0.01±0.56	0.22±0.61	0.21±0.59	0.33±0.54

Discussion: The preliminary results indicate that the NICO® monitor underestimates cardiac output following reperfusion of the ipsilateral iliac artery in patients undergoing aortic reconstruction surgery. The reason of this finding in the small study population remains unclear but we speculate that the dynamic changes in CO_2 production and changes in pulmonary circulation (4), both triggered by reperfusion, may have contributed to this observed difference.

References: (1) Anesthesiol 2000:93;A323.
(2) Anesthesiol 2000:93;A589.
(3) Crit Care Med 1997:25;675.
(4) Anesthesiol 1995:85;1026.

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Reference: Anesthesiology 2001; 95:A539

Performance of a Partial CO_2 Rebreathing System with Shorter Rebreathing Periods

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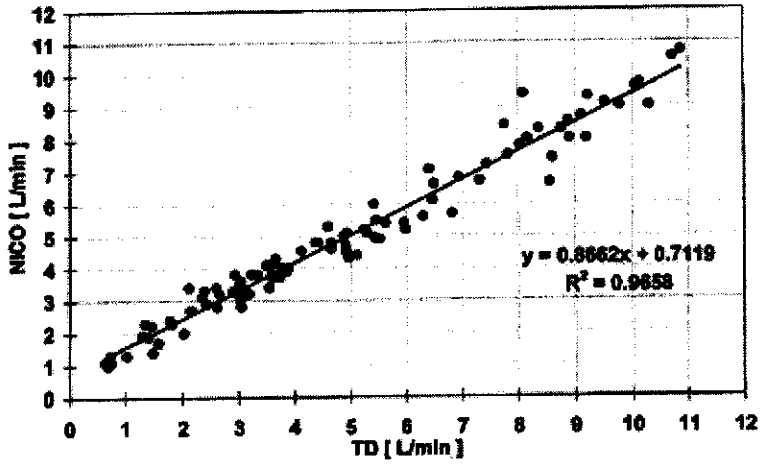
Introduction: A partial rebreathing non-invasive cardiac output monitor (**$NICO_2$, Novametrix Medical Systems, Inc., Wallingford, CT**) presently uses 50 seconds of partial rebreathing within a three-minute measurement cycle to calculate cardiac output. It would be desirable to shorten the rebreathing period to improve patient comfort and response time of the monitor. A shortened cycle could be repeated more frequently, thereby improving the reliability of the measurements and providing better support for clinical decisions. In this study, the $NICO_2$ monitor was altered so that the investigational rebreathing period lasted only 30 seconds within a one-minute measurement cycle. Three cycles were analyzed together for each cardiac output estimation. Corresponding cardiac output estimations from the modified $NICO_2$ and thermodilution were compared in five mechanically ventilated dogs.

Materials and Method: Five mongrel dogs (25.75kg - 42.4 kg) were induced with tiletamine HCL and zolazepam HCL, then intubated and mechanically ventilated. Anesthesia was maintained with halothane or isoflurane. A DualTherm (B. Braun, Bethlehem, PA) pulmonary artery catheter was placed for thermodilution cardiac output measurements. The sensor for the $NICO_2$ non-invasive cardiac output monitor was attached between the endo-tracheal tube and the breathing circuit wye piece. Data from the monitor was continuously recorded on a computer for subsequent analysis. Rebreathing and non-rebreathing periods were set to be 30 seconds each. Cardiac output changes were initiated with dobutamine, halothane, and xylazine. Thermodilution cardiac output measurements (iced saline, 10 ml) were made in triplicate every 10 minutes and at various times during the respiratory cycle.

Results: The correlation coefficient for the linear regression between $NICO_2$ and thermodilution cardiac output measurements was $r^2 = 0.966$ (n = 96). Bland-Altman comparisons showed a bias of 0.059 L/min and a standard deviation ($NICO_2$-TD) of 0.58 L/min.



Discussion: Cardiac output estimations based on a shorter rebreathing period correlated well with thermodilution in this animal study. With further algorithm refinements and clinical testing in patients, it may be possible to reduce the measurement period from three minutes to one minute. The increase in frequency of cardiac output measurements using the $NICO_2$ could help make earlier clinical decisions during episodes of hemodynamic instability. The more robust nature of the modified algorithm may also be useful for noninvasively monitoring cardiac output of spontaneously breathing patients.

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Reference: Anesthesiology 2001; 95:A574

Fick Partial Rebreathing CO_2 Cardiac Output: Is There Clinical Agreement with Intraoperative Transesophageal Echocardiography?

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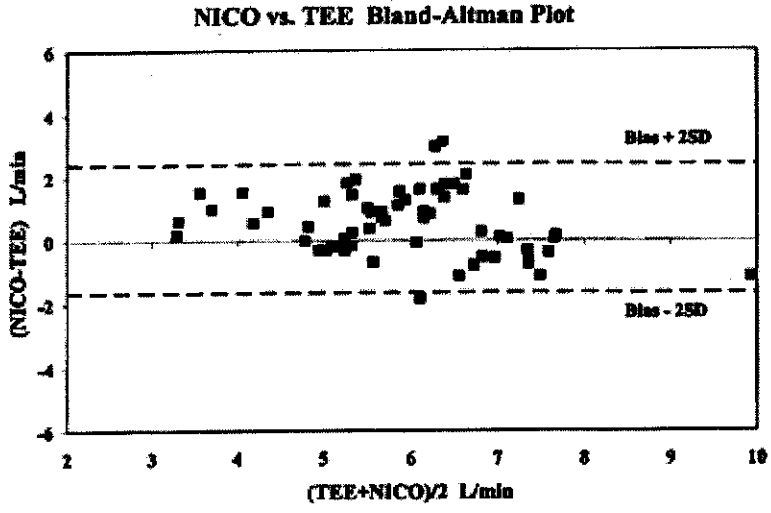
Introduction: By using partial rebreathing of carbon dioxide, the **NICO monitor (Novametrix Medical Systems, Wallingford, CT)** provides a fast, simple and non-invasive method of Fick cardiac output (CO) determination. Version 4.0 of this device uses a rebreathing period of 50 seconds and from measurements of changes in both CO_2 elimination and end-tidal CO_2, provides CO updates every 3 minutes. Non-invasive measurements of CO using a partial CO_2 rebreathing technique is particularly promising for intraoperative application. To assess the intraoperative performance of the NICO, we designed a clinical evaluation study to compare CO measurements obtained by NICO to those obtained by transesophageal echocardiography(TEE).

Methods: After IRB approval and written informed consent, matched sets of CO measurements from the NICO and TEE (SONOS 5500, Hewlett Packard, Andover, MA) were collected in intubated, mechanically ventilated surgical patients. Matched sets of CO measurements from the two techniques were collected at specific time periods per protocol. Preselected periods included post-incision, aortic cross-clamp, reaming, inotropic infusion, etc. Fick CO determination was performed with the NICO "FAST" mode which avoids algorhythmic averaging of COs from sequential rebreathing cycles. TEE CO was determined using multiplane continuous wave Doppler measurements of ascending aortic flow (transgastric longitudinal view) and planimetry of 2-D aortic valve area (midesophageal shortaxis view). Doppler spectral data was recorded on SVHS tape and analyzed off-line by experienced echocardiographers who were blinded to the NICO data. TEE determinations were compared to the NICO CO using Bland-Altman analysis. Statistical comparison of means was performed using Student's T-test with a $p<0.05$ considered significant.

Results: A total of 113 matched CO measurements were obtained from 17 of the 21 enrolled patients. Data analysis was not performed on 2 patients due to alterations in ventilation, in 1 patient due to sub-optimal TEE imaging and in 1 patient due to corrupted CO_2 signal. TEE cardiac outputs ranged from 2.8 to 10.5 (mean=5.6) L/m and NICO cardiac outputs ranged from 3.4 to 9.6 (mean=6.0) L/m. There was no statistical difference between the mean CO of the two techniques. Bland-Altman analysis resulted in a mean difference of 0.39 L/m (p=ns) and a standard deviation of the differences of 1.01 L/m.



Discussion: These data show the NICO device produces little systematic error in CO determinations. The standard deviation of the differences of 1.0 L/m demonstrates that the two techniques are not always in agreement. However, clinical CO techniques have inherent variability with a 15% variation currently regarded as clinically acceptable. (Ref 1) Therefore, we conclude that the degree of agreement between NICO and TEE demonstrated in this study is within clinically acceptable limits.

Reference: 1. Critchley LAH, Critchley JAJH. A meta-analysis of bias and precision statistics to compare cardiac output measurement techniques. J of Clin Monit 1999; 15:85-91.

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Reference: Anesthesiology 2001; 95:A572

Cardiac Output Measurement before and after Cardiopulmonary Bypass (CPB) during Coronary Artery Bypass Graft (CABG): Is Thermodilution Any Better Than Noninvasive Partial CO_2 Rebreathing

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Introduction: The noninvasive cardiac output monitor (**$NICO_2$; Novametrix Medical Systems, Inc**) is a new alternative to bolus (TDCO) and continuous thermodilution cardiac output (CCO) for measurement of CO. $NICO_2$ uses a differential form of the Fick equation to determine CO (1). The ratio of the change in CO_2 excretion and end-tidal CO_2, in response to a brief period of partial rebreathing provides a noninvasive estimate of the CO (2,3). The aim of this study was to compare measurements of CO using the $NICO_2$, pulmonary artery (PA) catheter (TDCO and CCO), with direct aortic flow using an ultrasonic flow probe (UFP) during the pre-cardiopulmonary bypass (CPB) vs post-CPB periods during CABG.

Methods: After anesthetic induction, matched sets of CO measurements from $NICO_2$, PA catheter (TDCO and CCO), and UFP were collected in 68 consenting adults undergoing elective CABG. All patients had a $NICO_2$ circuit attached between the endotracheal tube and the breathing circuit; a PA catheter (Baxter Healthcare Corporation, Irvine, CA); and an UFP (Transonic, Inc) placed directly on the ascending aorta and used for the reference CO. An average of 3 consecutive (10 ml 20 °C saline) TDCO measurements made during end-expiration was compared with corresponding CCO, NICO "FAST" mode, and UFP measurements. Bland -Altman analysis was performed to compare the agreement between the different methods.

Results: Bias and precision between the different methods in the pre-CPB vs post CPB are shown in the table. Conclusion: In the pre-CPB period, the accuracy was similar for all three techniques compared to the UFP. In the post-CPB, the tendency was for NICO to underestimate CO and for TDCO and CCO to overestimate it. CCO showed a lower precision during both periods. $NICO_2$ offers a good alternative to invasive CO measurement during CABG.

	Pre-CPB			Post-CPB		
	Bias	**Precision**	**Data points**	**Bias**	**Precision**	**Data Points**
TDCO vs UFP	0.18	1.01	99	0.35	1.39	32
CCO vs UFP	0.29	1.40	103	0.36	1.96	31
NICO vs UFP	0.04	1.07	108	-0.46	1.06	32

References: (1) J Clin Monit Comput 1999; 15:85.
(2) IEEE Trans BME 1988; 35:9.
(3) Intensive Care Med 1991; 17(2):98.

2001 ASA Meeting Abstracts.

Published by Lippincott Williams & Wilkins.

1032

Reference: Anesthesiology 2001; 95:A536

Can NICO® be used in the Intensive Care Unit on Patients with Mixed Ventilation Patterns and Low Cardiac Outputs?

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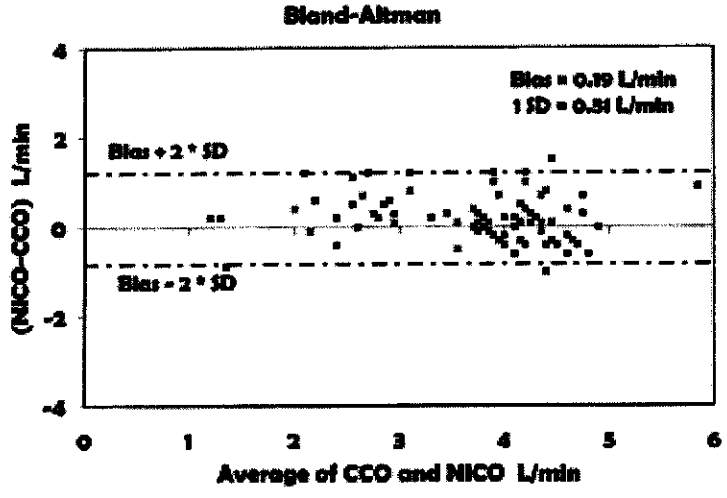
Introduction: NICO® is a non-invasive cardiac output monitor based on the partial CO_2 rebreathing indirect Fick technique. The ratio of the change in end-tidal CO_2 ($ETCO_2$) and CO_2 excretion (VCO_2), in response to a 50-second period of rebreathing is used to calculate cardiac output. The accuracy of the NICO monitor has been reported to be clinically acceptable in the operating room under stable ventilation patterns and a wide range of cardiac outputs. We have designed a study protocol to evaluate the performance of the NICO monitor in intensive care unit patients under a wide range of mixed ventilation patterns (changing respiratory pressure, volume, and flow characteristics) and low cardiac outputs.

Methods: Patients in the intensive care unit on mixed ventilation patterns (breathing spontaneously with mechanical ventilation support) and low cardiac outputs (cardiogenic shock, sepsis and/or multi-organ dysfunction) were identified as eligible to be enrolled in the study protocol. Invasive cardiac output measurements were recorded from a continuous thermodilution monitor (CCO, Baxter-Vigilance, Irvine, CA, U.S.A.) and used as the comparison standard. The cardiac output from the **NICO monitor (Novametrix Medical Systems, Wallingford, CT, U.S.A.)** was recorded at predetermined intervals during the study protocol. Matched pairs of NICO and CCO cardiac output measurements were compared using Bland-Altman analysis.

Results: Matched pairs (n = 88) of CCO (Range = 0.9 to 6.3 L/min) and NICO (Range = 1.1 to 5.4 L/min) cardiac output measurements were recorded in five patients. There was no statistical difference in the mean cardiac output measured using the CCO (3.59 ± 0.98 L/min) and NICO (3.77 ± 0.91 L/min). The Pearson correlation coefficient between CCO and NICO was 0.86. Bland-Altman analysis resulted in a bias of -0.28 L/min with a precision (1 SD) of 0.51 L/min.



Conclusions: In patients in the intensive care unit, with mixed ventilation patterns and low cardiac outputs, the NICO has so far shown to be a clinically acceptable method for measurement of cardiac output despite the wide range of ventilator modes, respiratory pressure, volume and flow adjustments. The ease of use, minimal set up time, cost effectiveness and mainly the safety of NICO when compared with invasive procedures makes it a good alternative for continuous cardiac output monitoring.

2001 ASA Meeting Abstracts.

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Reference: Anesthesiology 2001; 95:A534

Can NICO® Detect Changes in Thermodilution Cardiac Output?

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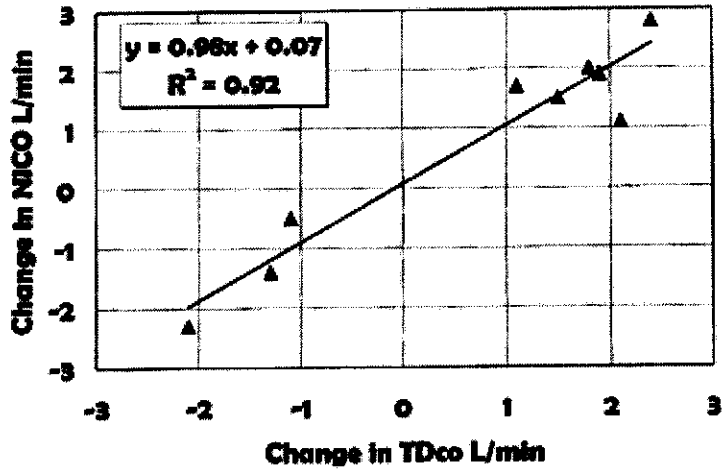
Introduction: The clinical usefulness of any cardiac output monitoring system lies in its ability to detect acute changes in cardiac output. NICO is a relatively new noninvasive cardiac output monitor based on indirect Fick partial CO_2 rebreathing. We have designed a study protocol to investigate if true changes in cardiac output during cardiac surgery, as detected by the bolus thermodilution technique, are reflected in changes in NICO measurements.

Methods: After anesthetic induction, adult patients undergoing elective cardiac surgery were monitored with **NICO® (Novametrix Medical Systems, U.S.A.)** and a pulmonary artery catheter. The NICO sensor was attached between the endotracheal tube and the breathing circuit. The NICO monitor measured pulmonary capillary blood flow based on the ratio of the corresponding changes in CO_2 elimination and $ETCO_2$ imposed by a 50-seconds rebreathing maneuver. Cardiac output was calculated from pulmonary blood flow by correcting for shunt (estimated from SpO_2 and FiO_2). An average of 3 consecutive (10 ml room temperature saline) bolus thermodilution measurements made during end-expiration, at fixed time intervals during surgery, was compared with corresponding NICO measurements. The difference between consecutive thermodilution and NICO measurements was calculated. To accommodate for the inherent variability in each of the measurements, changes in bolus thermodilution cardiac output greater than 1 L/min were considered significant to be included in the data analysis.

Results: Twenty-five matched pairs of consecutive changes in cardiac output measurements were recorded in four patients undergoing elective cardiac surgery. Nine of the twenty-five matched pairs met the criteria of a difference greater than 1 L/min in thermodilution cardiac output to be included in the data analysis. The figure below shows the relationship between changes in thermodilution and NICO cardiac output measurements. The regression analysis resulted in a r^2 of 0.92 ($y=0.98x+0.07$). Students t-test revealed no statistical difference in the mean of the difference in the two measurements.



Discussion: In this preliminary study the changes in the bolus thermodilution cardiac output were reflected in corresponding changes in NICO measurements. If this finding holds good in a larger patient population that will be enrolled in this study, then the NICO monitor would provide a good alternative to invasive CO measurements during cardiac surgery.

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Reference: Anesthesiology 2001; 95:A573

Performance of NICO Partial CO_2 Rebreathing Cardiac Output Monitor during Acute Intraoperative Changes in Cardiac Output

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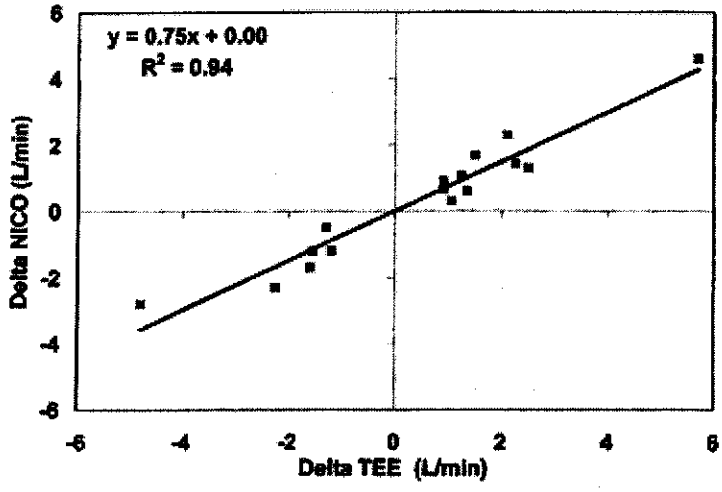
Introduction: Detection of acute changes in cardiac performance and tracking response to therapy are critically important to intraoperative cardiac output (CO) monitoring. NICO is a commercially available non-invasive cardiac output monitor that is based on the Fick partial CO_2 rebreathing technique. Changes in CO_2 elimination and end-tidal CO_2 in response to a brief rebreathing period are used to calculate cardiac output. The NICO monitor has shown promise in clinical and animal studies. However, its ability to detect and track large changes in cardiac output has not been evaluated. Consequently we undertook a study which evaluates the performance of NICO during acute changes in cardiac output as compared with transesophageal echocardiography (TEE).

Methods: Following an IRB approved protocol and written informed consent, matched pairs of **NICO (Novametrix Medical Systems, Wallingford, CT)** and TEE (SONOS 5500, Hewlett Packard, Andover, MA) data were collected in 21 intubated, mechanically ventilated surgical patients. Data was collected during dobutamine stress protocol and/or at predetermined surgical events selected to capture hemodynamic fluctuations. TEE CO was calculated by the Doppler method with ascending aortic flow measured in the transgastric longitudinal view and aortic valve orifice area calculated from the mid-esophophageal short axis view. Doppler CO analysis was performed off-line by echocardiographers blinded to the NICO CO determinations. For data analysis, an acute change in CO was defined as an alteration in TEE CO exceeding 20% (Delta TEE). Corresponding changes in NICO CO (Delta NICO) were calculated for each acute change in TEE CO. Statistical analysis included Student's T test comparing the mean absolute value in Delta NICO to Delta TEE and regression analysis. A p value less than 0.05 was considered significant.

Results: 21 patients were enrolled into the study. 16 alterations in CO exceeding 20% were observed in 13 patients. 8 patients did not demonstrate the predetermined threshold of 20% for CO change. The four quandrant graph illustrates the relationship between Delta NICO and Delta TEE. In all cases NICO correctly detected the direction of the acute change in TEE CO with data clustered in the upper right and lower left quandrants. Regression analysis reveals an intercept of 0.0, a slope of 0.75, and an r-squared 0.94. Student's T test showed no significant difference between the magnitude of the mean delta TEE and the mean delta NICO.



Discussion: This study protocol captured 16 acute changes in CO and demonstrated the NICO to reliably track these events. Although there was no significant difference between the magnitude of Delta NICO and Delta TEE, the slope of the regression line suggests that NICO underestimates the magnitude of CO changes. These preliminary data suggest that partial rebreathing CO_2 Fick provides accurate detection of acute intraoperative changes in CO.

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P-9174

COMPARISON OF PARTIAL CO_2 REBREATHING FICK TECHNIQUE WITH INVASIVE BOLUS THERMODILATION TECHNIQUE DURING CABG SURGERY

Primary Author: **PINAR DURAK, M.D.**

Co-Authors:

Tugba Han Yilmaz, M.D. **Tulga Ulus, M.D.**
Ozcan Erdemli, M.D.

Turkiye Yuksek Ihtisas Hospital – Ankara, Turkey

The aim of this study is to determine whether invasive and non invasive cardiac output measurements are in good agreement during different stages of cardiopulmonary bypass. After the institutional approval and patient consent, 8 patients undergoing elective cardiac surgery were studied. The hemodynamic parameters were correlated with invasive bolus thermodilution technique after induction and after protamin infusion. Statistical analysis were performed by paired t thest. We found no difference between invasive and non invasive cardiac output parameters after induction and after protamin infusion. Therefore we concluded that there is a strong correlation of good agreement between invasive CO technique and non invasive CO during open cardiac surgery conditions.

Reference: *Postgraduate Assembly in Anesthesiology* New York, Dec 9-13, 2000.

1036

P-9173

THE DETERMINATION OF VCO_2 MEASUREMENTS DURING CABG USING NON INVASIVE CARDIAC OUTPUT TECHNIQUE (NICO)

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NICO provided critical information by measuring vital parameters as CO_2 elimination. With this method the CO is proportional to the change in CO_2 elimination divided by the resulting change in end tidal CO_2. After the institutional approval and patient consent, the NICO system was tested in 20 patients undergoing cardiac surgery in T.Y.I.H. Statistical analysis were performed by ANOVA test. Patients were anesthetized by 10 ug/kg fentanyl, 0.1 mg/kg pancuronium, 0.1 mg/kg midazolam and mild hypothermia was used. Online VCO_2 measurements were performed throughout the operation with NICO. There were no statistical differences in VCO_2 measurements before and early after perfusion. Therefore, we concluded that stable VCO_2 measurements during CABG surgery indicated that the metabolic function, perfusion and oxygenation was adequate.

Reference: *Postgraduate Assembly in Anesthesiology* New York, Dec 9-13, 2000.

P-9172

COMPARISON OF HEMODYNAMIC PARAMETERS DURING CABG SURGERY WITH RECURONIUM BROMIDE AND PANCURONIUM BROMIDE BY USING NON INVASIVE METHOD OF CARDIAC OUTPUT

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The aim of this study is to measure the hemodynamic effects of rocuronium bromide and pancuronium bromide with non invasive cardiac output which also measures the ventilation parameters. After getting the patient consent, 20 patients were studied. In Group P: 0.1 mg/kg pancuronium bromide was used with moderate dose fentanyl with 0.1 mg/kg midazolam for induction and 0.03 mg/kg pancuronium bromide was used for maintenance. In Group R: 0.15 mg/kg rocuronium bromide was used for induction and as for maintenance 0.5 mg/kg/h rocuronium bromide was used. The parameters were measured by non invasive rebreathing technique. Statistical analysis was performed by ANOVA test. In Group P: the HR was significantly higher after induction and m Alv was statistically higher after heparin infusion ($p<0.05$). In Group R: stroke volume (SV) after heparin infusion and pulmonary capillary blood flow (PCBF) after protamin infusion was statistically higher than Group P ($p<0.05$). As a result we concluded that hemodynamic and ventilation profile of rocuronium bromide infusion is acceptable for patients with cardiovascular disease.

Reference: *Postgraduate Assembly in Anesthesiology* New York, Dec 9-13, 2000.

1038

P-9133

EVALUATION OF PARTIAL REBREATHING CARDIAC OUTPUT MEASUREMENT IN THE ICU

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Co-Authors:
Dinesh G. Haryadi, Ph.D. **Kai Kuck, Ph.D.**

University of Utah – Salt Lake City, Utah

The partial rebreathing system ($NICO_2$, Novametrix Medical Systems) was used to monitor cardiac output continuously in 6 intensive care unit patients. Periodic thermal dilution (TD) cardiac output measurements were made in triplicate using 10ml bolus injections of room temperature saline. The average thermal dilution measurement was compared against the $NICO_2$. A total of 45 measurements were used for comparison. The average different ($NICO_2$ —TD) was 0.44 with a standard deviation of 0.84 L/min. Regression analysis gave a correlation coefficient of r=0.91. Cardiac output values ranged from 3.4 to 9.6 liters per minute.

Reference: *Postgraduate Assembly in Anesthesiology* New York, Dec 9-13, 2000.

1039

P-9114

COMPARISON OF NONINVASIVE CARDIAC OUTPUT USING A PARTIAL CO2 REBREATHING SYSTEM WITH BOLUS THERMODILUTION DURING HEMORRHAGIC SHOCK

Primary Author: PATRICK SEIGNE, F.F.A.R.C.S.I.

Co-Authors:

Carrie Sims, M.D.
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Juan Carlos Poyana, M.D.
Michael Menconi, Ph.D.
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Ten domestic male pigs (25-30kgs) were hemorrhaged to a MAP of 40mmHg for 1 hour and resuscitated. Cardiac outputs for both techniques were recorded simultaneously at 5 time points: baseline, shock, end-shock, resuscitation and recovery. A total of 62 comparisons were made with CO ranging from 1.1 to 5.3 litres/minute. Paired t test analysis showed no significant difference between thermodilution and partial CO2 rebreathing measurements ($p<0.01$) with a linear regression coefficient ® of 0.8. Bland-Altman analysis resulted in a bias of –0.17L/min with a precision of .78L/min (1 so). The results from this animal study show good agreement between thermodilution and partial CO2 rebreathing CO measurements during low flow states.

Reference: *Postgraduate Assembly in Anesthesiology* New York, Dec 9-13, 2000.

1040

Measurement of Cardiac Output in the Intensive Care Unit (ICU) after Coronary Artery Bypass Grafting (CABG): Comparison of Pulmonary Artery Catheter and Noninvasive Partial CO_2 Rebreathing ($NICO_2$)

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Department of Anesthesiology, University of Florida College of Medicine & Veterans Affairs Medical Center, Gainesville, Florida, U.S.

Introduction: Noninvasive partial CO_2 rebreathing ($NICO_2$; Novametrix Medical Systems, Inc.) is a new alternative to thermodilution (TDCO) and continuous cardiac output (CCO) techniques for measurement of cardiac output (CO). This study was designed to compare CO measurements using the $NICO_2$ and PA catheter (TDCO and CCO) in the ICU after CABG. $NICO_2$ uses a differential form of the Fick equation to calculate CO (1). The ratio of the change in CO_2 excretion and end-tidal CO_2, in response to a brief period of partial rebreathing, provides a noninvasive estimate of the CO (2,3).

Methods: After undergoing CABG, 20 consenting adults admitted to the ICU were monitored with $NICO_2$ and a PA catheter. The $NICO_2$ sensor was attached between the endotracheal tube and the breathing circuit. An average of 3 consecutive (10 ml 20°C saline) TDCO measurements was compared with corresponding CCO and $NICO_2$ measurements. Bland-Altman analysis was performed to compare the agreement between the different methods.

Results: Precision and bias between the different methods are shown in the table.

	Bias L/min	Precision (1 SD) L/min	Corr. Coeff (r)	Count (n)
TDCO, NICO	-0.19	0.91	0.83	68
TDCO, CCO	-0.22	1.25	0.71	68
NICO, CCO	-0.04	1.35	0.68	71

Conclusion: Comparable accuracy between CO values was obtained with the $NICO_2$, CCO, and TDCO. $NICO_2$ showed a higher precision than CCO when compared to TDCO (0.91 L/min vs. 1.25 L/min). Our data suggest that this noninvasive technique ($NICO_2$) offers a good alternative to invasive CO measurement after CABG in patients in the ICU.

Reference:

1. J Clin Monit Comput 1999;15:85
2. IEEE Trans on BME 1988;35:9
3. Intensive Care Med 1991;17(2):98

Reference: Anesthesiology, ASA-2000, A-590.

1044

Comparison of Alternative Methods for Intraoperative Cardiac Output Determination: Fick Partial Rebreathing CO_2 & Transesophogeal Echocardiography

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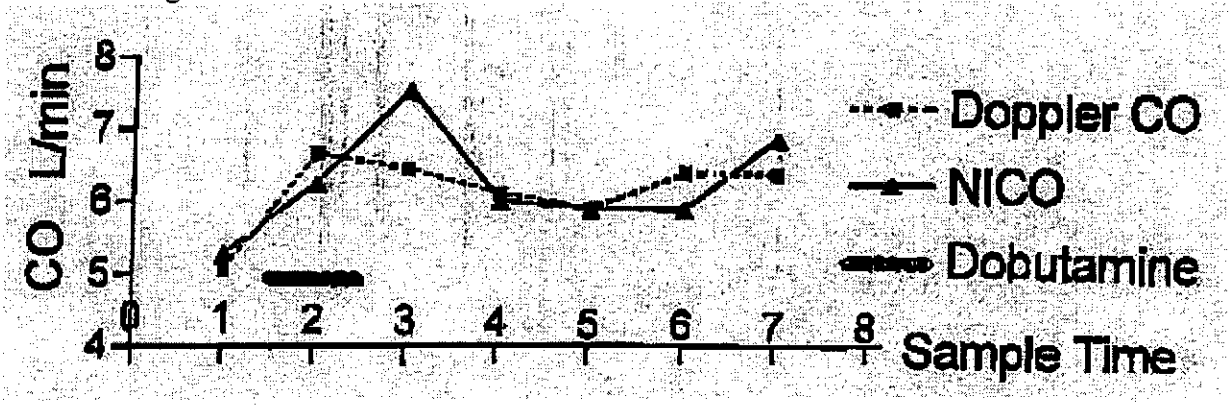
Introduction: The Fick partial CO_2 rebreathing method employed by the $NICO_2$ device (Novametrix Medical Systems, Wallingford, CT) provides a non-invasive measure of cardiac output (CO). The applicability of this technique in anesthetized patients undergoing major vascular and other non-cardiac surgeries has not been well examined. Further, this technique has not been previously compared to another less invasive alternative to pulmonary artery catheterization, transesophageal echocardiography (TEE). The goal of this study was to assess the agreement of CO determinations using the $NICO_2$ technology to those obtained by TEE.

Methods: After IRB approval and written informed consent, matched sets of CO measurements from the $NICO_2$ and TEE (SONOS 5500, Hewlett Packard, Andover, MA) were collected in intubated, mechanically ventilated patients undergoing non-cardiac surgery. The matched sets of CO measurements from the two techniques were collected at specific time periods per protocol. Preselected periods included postincision, aortic crossclamp, reaming, inotropic infusion, etc. to capture periods of hemodynamic fluctuation. Fick CO determination utilizes a 3 minute rebreathing cycle and the $NICO_2$ "FAST" mode which avoids algorhythmic averaging of COs from sequential rebreathing cycles. TEE CO was determined using multiplane continuous wave Doppler measurements of ascending aortic flow (transgastric longitudinal view) and planimetry of 2-D aortic valve area (midesophageal shortaxis view). A TEE CO measurement was obtained at the onset and completion of each $NICO_2$ rebreathing cycle. The mean of two TEE determinations was compared to the $NICO_2$ CO using bias analysis.

Results: 31 data points from 8 enrolled patients were examined. Bias analysis revealed a mean difference between $NICO_2$ and TEE CO determinations of 0.20 L/min and a standard deviation (SD) of the differences of 0.92 L/min. On a percentage basis, this represents a mean bias of 3.3% and a SD of 16.3%. The figure below illustrates a case example of the performance of the two CO devices in a patient receiving a dobutamine infusion.



Discussion: These data show that the $NICO_2$ device produces little systematic error in CO determinations, however the SD of the differences suggest important disparities between its measurements and those of the Doppler approach. Additional data from this ongoing investigation will clarify the clinical utility of this promising application of the Fick technique.

Abstract summary: Disparities shown between these methods warrant further study of a promising application of the Fick technique.

Reference: Anesthesiology, ASA-2000, A-589.

1042

CO_2 Rebreathing Cardiac Output Technique Does Not Increase Heart Rate

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Introduction: The noninvasive partial rebreathing method uses a form of the CO_2 Fick equation to measure cardiac output. During the measurement, the arterial CO_2 content rises, and this induced change is used together with the amount of CO_2 produced to calculate the cardiac output. A potential issue related to the partial rebreathing method was raised that the elevated levels of CO_2 might lead to a higher cardiac output, largely due to an increase in heart rate. This critique was based on earlier work by Eger et al.[1] which states that the cardiac output was raised, mostly by an increase in heart rate, when CO_2 levels were elevated during six-minute intervals. We tested whether there was an observed change in the heart rate of patients undergoing partial CO_2 rebreathing cardiac output measurements in the OR and in the ICU.

Methods: The partial rebreathing cardiac output monitor ($NICO_2$, Novametrix Medical Systems) was used continuously on 93 patients in the OR and ICU. Each $NICO_2$ measurement cycle lasts 3 minutes, and is comprised of a 60 second baseline period, a 50 second rebreathing period, and a 70 second recovery period. Each cycle was subdivided into 30 six-second intervals. We compared the heart rate measured during the baseline intervals to the heart rate measured during the different intervals of the rebreathing cycle. Care was taken to control for possible underlying trends in the heart rate, as well as for a possible delay in the response of the heart rate to elevated CO_2 levels.

Results: A total of 5142 rebreathing cycles from 50 patients in the OR and 43 patients in the ICU were examined. In the OR, an average increase in $etCO_2$ of 5.1 mmHg had a corresponding average decrease in the heart rate of 0.24 beats/min. The standard deviations were 3.0 mmHg for $etCO_2$ and 5.5 beats/min for heart rate. In the ICU, an average increase of 7.8 mmHg in $etCO_2$ levels corresponded to a heart rate decrease of 0.34 beats/min, with standard deviations of 3.1 mmHg and 6.8 beats/min, respectively.

Discussion:. We compared baseline heart rates to rebreathing time periods and other periods throughout the cycle to examine whether the heart rate was changed, but did not find statistically significant differences. The $etCO_2$ was elevated in our method for 50 seconds, while in the literature, $etCO_2$ was elevated for six minutes. During the shorter time period of rebreathing used by $NICO_2$ we did not observe a difference in heart rate caused by increases in $etCO_2$ and have concluded that the concerns related to the possible increases in heart rate do not affect $NICO_2$ performance.

Reference:

1. Eger, EI: Cardiovascular Effects of Carbon Dioxide in Man. Anesthesiology, 41:345-349, 1974.

Abstract summary: Short rebreathing periods for measuring cardiac output do not affect heart rate. Thus, $NICO_2$ performance is not altered by changes in HR initiated by rebreathing.

Reference: Anesthesiology, ASA-2000, A-588.

1043

Accuracy of Partial Rebreathing Cardiac Output during Mixed-Breathing

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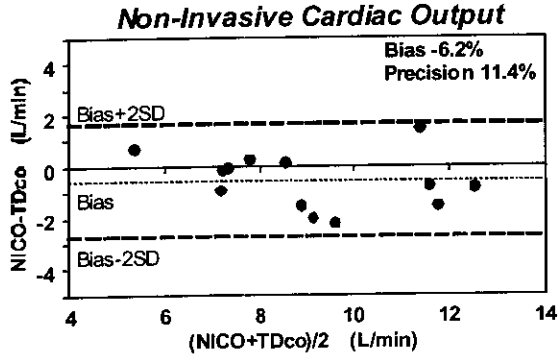
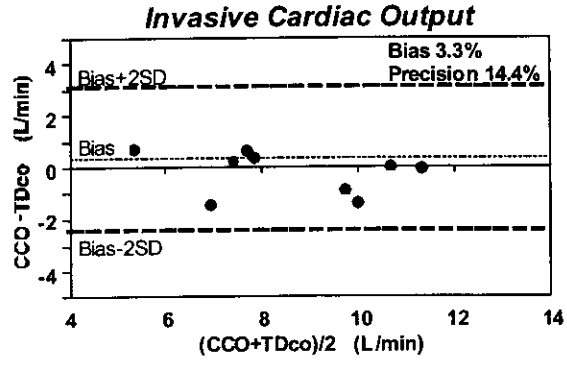
Introduction: We previously showed that the partial CO_2 rebreathing technique accurately determines cardiac output during controlled ventilation in anesthetized subjects.[1] This study evaluates a new algorithm that extends this non-invasive and cost effective method to spontaneous and assisted modes of ventilation. We compared non-invasive measurements with bolus thermodilution and continuous (pulsed) thermodilution measurements.

Methods: With IRB approval, informed consent was obtained and data was collected from 6 intensive care patients on ventilator support. Every patient had a preexisting pulmonary artery catheter, with cardiac output being measured by bolus thermodilution and continuous (pulsed) thermodilution using a Baxter Vigilance Monitor (Baxter Healthcare Corporation, Irvine, CA). During the 3-hour study period, continuous non-invasive cardiac output measurements were additionally obtained with a NICO monitor (Novametrix Medical Systems, Wallingford, CT). This system continuously measures airway flow, pressure, and CO_2 concentration. It controls a rebreathing valve, placed between the ET tube and the Y-piece of the breathing circuit, which introduces approximately 150cc of deadspace for 50 seconds every 3 minutes. This causes a transient rise in end-tidal CO_2 (2-5 mmHg) and a commensurate decrease in VCO_2. A non-invasive estimate of pulmonary blood flow is achieved by tracking CO_2 concentration and elimination. Cardiac output is calculated from pulmonary blood flow by correcting for shunt (estimated from SpO_2).

Results: The non-invasive rebreathing technique (NICO) had a bias and precision of -0.59 ± 1.09 L/min when compared to bolus thermodilution (TDco) (left Bland-Altman plot). The continuous thermodilution technique (CCO) had a bias and precision of 0.32 ± 1.37 L/min when compared to bolus thermodilution (right Bland-Altman plot).





Discussion: The results demonstrate that $NICO_2$ is as accurate as invasive continuous (pulsed) thermodilution, over a wide range of cardiac outputs (5 to 13 L/min), when each is compared with bolus thermodilution. The bias and precision values were higher than those previously reported for anesthetized patients; this is probably due to the large range of cardiac outputs in this patient population. These results validate the use of non-invasive cardiac output monitoring in ICU patients on mixed spontaneous-assisted modes of ventilator support.

Reference: 1. Anesthesiology 91:A474, 1999.

Abstract summary: During mixed spontaneous-assisted ventilator support, cardiac outputs determined non-invasively by $NICO_2$ were as accurate as those determined by invasive pulsed thermodilution.

Reference: Anesthesiology, ASA-2000, A-428.

1044

Mixed Venous CO_2 Does Not Need to Remain Constant During CO_2 Rebreathing Cardiac Output Measurements

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Introduction: The Fick method to determine cardiac output relies on arterial and mixed venous blood gasses, making the technique invasive and cumbersome. Using CO_2 Fick instead of O_2 Fick allows estimation of the arterial CO_2 content from noninvasive end-tidal CO_2. By letting the patient rebreathe all or part of the previously exhaled CO_2, the CO_2 Fick equation can be used without knowing mixed venous CO_2 content. However, conventional total or partial CO_2 rebreathing methods rely on the assumption that mixed venous CO_2 does not change during the measurement period, which might be on the order of two to three minutes long. This assumption may not hold true, unless ventilation is optimally adjusted to have CO_2 elimination exactly match metabolic CO_2 production. We have developed a more general form of the Fick equation, which allows noninvasive CO_2 Fick cardiac output determinations, even if mixed venous CO_2 content does change during the measurement period. We have studied the cardiac output estimation error of conventional CO_2 Fick methods in the face of changing mixed venous CO_2 concentrations and compared it to our new method.

Methods: Following an IACUC approved protocol, six mongrel dogs (26-36 kg) were induced using Telazol, intubated, and maintained on halothane. Mechanical ventilation was adjusted to maintain endtidal CO_2 concentrations between 35 and 40 mmHg. Cardiac output was changed using halothane and dobutamine. Thermodilution measurements (Dualtherm, B. Braun) based on three 10 ml boluses of iced saline, randomized with respect to the respiratory cycle were performed about every 10 minutes. The collected data was later used to calculate both the conventional CO_2 Fick cardiac output and our new improved CO_2 Fick cardiac output method. Performance was assessed on the basis of linear regression and Bland-Altman.

Results: When comparing the new and the old method in 252 measurements, both bias and precision improved substantially (see table for details).

	Improved CO_2 Fick Rebreathing	Conventional CO_2 Fick Rebreathing
Number of Samples	252	252
Avg (TD-NICO) [L/min]	-0.42	-0.78
SD (TD-NICO) [L/min]	0.79	0.90
Correlation r	0.96	0.95

Discussion:. The CO_2 Fick technique allows noninvasive and automated estimation of cardiac output. A new more general CO_2 Fick method, which does not rely on mixed venous CO_2 content staying constant during the measurement period shows improved estimation bias and accuracy compared to the conventional method.

Abstract summary: A new CO_2 rebreathing method to estimate cardiac output does not require constant venous CO_2 and improves estimation bias and precision.

Reference: Anesthesiology, ASA-2000, A-331.

1045

Clinical Evaluation of $NICO_2$ in ICU Patients

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Introduction: $NICO_2$ is a noninvasive cardiac output monitor based on partial CO_2 rebreathing technique. It uses the ratio of the change in end-tidal CO_2 and CO_2 excretion (VCO_2), in response to a brief 50-second period of rebreathing to calculate cardiac output. We have previously shown that the accuracy of this method is acceptable for use in OR patients where stable ventilation is predominant. To extend the applications of $NICO_2$ to ICU patients, we made modifications in signal processing in order to calculate cardiac output in patients breathing spontaneously with mechanical support (mixed ventilation). In this study we evaluated the clinical performance of a modified version of $NICO_2$ in ICU patients on mixed ventilation

Methods: Hospital IRB approval was obtained for the study and data was collected in 40 ICU patients who were spontaneously breathing with mechanical support. The $NICO_2$ sensor was connected in the breathing circuit between the patient's endotracheal tube and the ventilator wye. A modified version of the partial rebreathing system ($NICO_2$, Novametrix Medical Systems) was used to monitor continuous cardiac output. An average of three consecutive thermodilution cardiac output (TDco) measurements made at regular intervals were compared using Bland-Altman analysis with corresponding $NICO_2$ measurements.

Results: A total of 234 comparisons were made with cardiac output ranging from 2.41 to 11.00 L/min. Bland-Altman analysis resulted in a bias of -0.28 L/min with a precision (1SD) of 0.98 L/min. The correlation coefficient between $NICO_2$ and TDco measurements was 0.84.

Discussion: Results indicate that $NICO_2$ may be a clinically acceptable method for measurement of cardiac output in ICU patients. Improvements in signal processing have made it possible to extend applications of $NICO_2$ from OR patients on controlled mechanical ventilation to ICU patients with mixed ventilation. The ease of use, minimal set up time, and cost effectiveness of $NICO_2$ when compared with invasive procedures makes it a good alternative technique for noninvasive continuous cardiac output monitoring.

Abstract summary: $NICO_2$ is a noninvasive cardiac output monitor based on partial CO_2 rebreathing. We evaluated $NICO_2$ in 40 ICU patients. Bias = -0.28 L/m, Precision = 0.98 L/m.

Reference: Anesthesiology, ASA-2000, A-328.

1046

Noninvasive Cardiac Output Using Partial CO_2 Rebreathing vs. Direct Aortic Flow Measurements During Off Pump Coronary Artery Bypass Grafting (OPCABG)

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Introduction: Intraoperative determinations of cardiac output (CO) guide hemodynamic management of patients (1). This study was designed to compare measurements of CO using a noninvasive partial CO_2 rebreathing system ($NICO_2$; Novametrix Medical Systems, Inc) and an ultrasonic flow probe (UFP; Transonic, Inc) during OPCABG. $NICO_2$ uses a differential form of the Fick equation to calculate CO. The ratio of the change in end-tidal CO_2 and CO_2 excretion, in response to a brief period of rebreathing provides a noninvasive estimate of the CO (2,3).

Methods: After anesthetic induction, 13 consenting adults undergoing elective OPCABG had a $NICO_2$ circuit attached between the endotracheal tube and the breathing circuit. A UFP was placed on the ascending aorta and used for the reference CO. During different periods of coronary artery grafting, CO was measured by $NICO_2$ and UFP. Statistical analysis was performed with two-way ANOVA and Bland-Altman.

Results: A total of 25 simultaneous measurements were made. Agreement between methods resulted in a bias of -0.07 L/min with a precision (1 SD)+/-0.63.

Conclusion: Correlation between CO obtained with $NICO_2$ and directly measured aortic blood flow is equivalent to that from traditional invasive thermodilution measurement (4). Our data suggests this noninvasive technique offers a good noninvasive alternative to thermodilution CO during OPCABG.

Reference:

1. J Clin Monit Comput 1999;15:85
2. IEEE Trans on BME 1988;35:9
3. Intensive Care Med 1991;17(2):98
4. Crit Care Med 1999;27(12):A77

Reference: Anesthesiology, ASA-2000, A-323.

1047

MEASUREMENT OF CARDIAC OUTPUT DURING CORONARY ARTERY BYPASS GRAFTING (CABG): COMPARISON OF PULMONARY ARTERY CATHETER, NONINVASIVE PARTIAL CO_2 REBREATHING, AND DIRECT AORTIC FLOW

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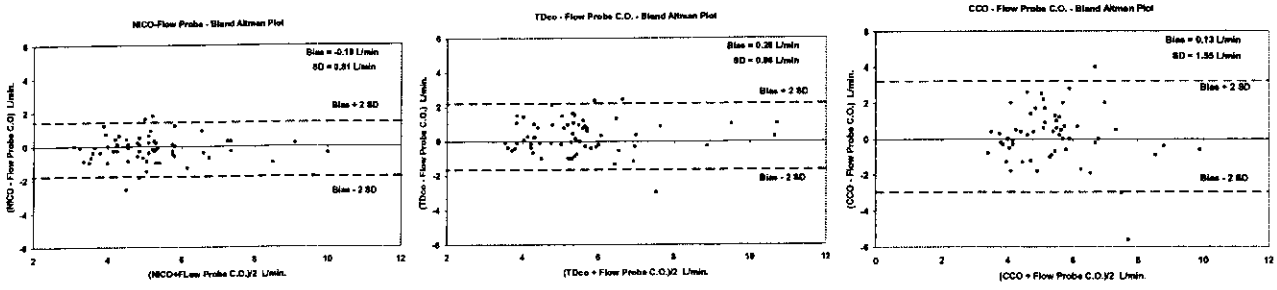
Nikolaus Gravenstein, MD; Emilio B. Lobato, MD

Departments of Anesthesiology and Cardiovascular Surgery, University of Florida College of Medicine and Veterans Affairs Medical Center, Gainesville, Florida

Introduction: Noninvasive partial CO_2 rebreathing (NICO; Novametrix Medical Systems, Inc) is a new alternative to thermodilution (TDCO) and continuous cardiac output (CCO) for measurement of CO. This study was designed to compare measurements of CO using the NICO, PA catheter (TDCO and CCO), and an ultrasonic flow probe (UFP; Transonic, Inc) during CABG surgery. NICO uses a differential form of the Fick equation to calculate CO (1). The ratio of the change in CO_2 excretion and end-tidal CO_2, in response to a brief period of partial rebreathing, provides a noninvasive estimate of the CO (2,3).
Methods: After anesthetic induction, 34 consenting adults undergoing elective coronary artery bypass grafting (CABG) were monitored with NICO and a PA catheter. The NICO circuit was attached between the endotracheal tube and the breathing circuit. An average of 3 consecutive (10 ml 20° C saline) TDCO measurements made during end-expiration was compared with corresponding CCO and NICO measurements. A UFP was placed on the ascending aorta and used for the reference CO. CO was measured before and after cardiopulmonary bypass (CPB) by TDCO, CCO, NICO, and UFP. Bland-Altman analysis was performed to compare the agreement between the different methods for measurement of CO.
Results: The agreement between NICO, TDCO and CCO, and UFP CO for all subjects at all time points is shown in the Bland-Altman plots. Measurements were made pre CPB (149) and post CPB (42). Precision and bias between the different methods are shown in the table.

	Bias ± SD
NICO-Flow Probe	-0.19 ± 0.81
CCO, Flow Probe	+0.13 ± 1.55
TDCO, Flow Probe	+0.28 ± 0.96



Discussion: There was a comparable precision between CO values obtained with the NICO, TDCO, and directly measured aortic blood flow. CCO showed a lower precision when compared to UFP CO. Our data suggest that this noninvasive technique offers a good alternative to invasive CO measurement during CABG.

References: (1) J Clin Monit Comput 1999; 15:85 (2) IEEE Trans on BME 1988; 35:9 (3) Intensive Care Med 1991;17(2):98

Reference: *Anesthesia & Analgesia*, April 2000; V90(4S); SCA87.

1048

CARDIAC OUTPUT MEASUREMENT DURING OFF PUMP CORONARY ARTERY BYPASS GRAFTING (OPCABG): COMPARISON OF FOUR METHODS

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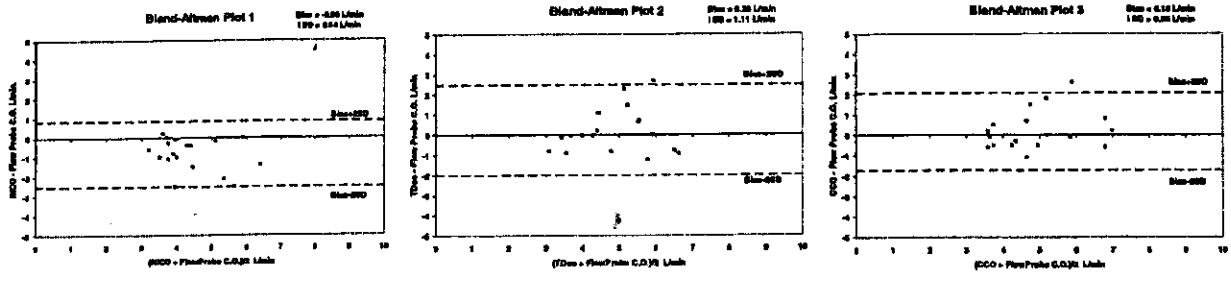
Departments of Anesthesiology and Cardiovascular Surgery, University of Florida College of Medicine and Veterans Affairs Medical Center, Gainesville, Florida

Introduction: Intraoperative determinations of cardiac output (CO) guide hemodynamic management of many patients (1). This study was designed to compare measurements of CO using a noninvasive partial CO_2 rebreathing system (NICO; Novametrix Medical Systems, Inc), thermodilution (TDCO), continuous cardiac output (CCO), and an ultrasonic flow probe (UFP; Transonic, Inc) during OPCABG. NICO uses a differential form of the Fick equation to calculate CO. The ratio of the change in CO_2 excretion and end-tidal CO_2, in response to a brief period of partial rebreathing, provides a noninvasive estimate of the CO (2,3).

Methods: After anesthetic induction, 8 consenting adults undergoing elective OPCABG with a pulmonary artery (PA) catheter had a NICO circuit attached between the endotracheal tube and the breathing circuit. A UFP was placed on the ascending aorta and used for the reference CO. During different periods of coronary artery grafting, CO was measured by NICO, CCO, TDCO, and UFP. Bland-Altman analysis was used to compare the agreement between the different methods for measurement of CO.

Results: The agreement between NICO CO, CCO, TDCO, and UFP CO for all subjects at all time points is shown in the Bland-Altman plots. A total of 19 simultaneous measurements were made with UFP and 32 with CCO, TDCO, and NICO. Precision and bias between the different methods are shown in the table.

	Bias ± SD
NICO-Probe	-0.83 ± 0.84
CCO-Probe	0.18 ± 0.95
TDCO-Probe	0.25 ±1.12



Discussion: In this small series the tendency was for NICO to underestimate CO. The SD (precision) was similar for all techniques compared to the UFP. If this observation holds in a larger population, NICO with an offset to correct the apparent bias offers a good alternative to invasive techniques to determine CO during OPCABG.

References: (1) J Clin Monit Comput 1999; 15:85 (2) IEEE Trans on BME 1988; 35:9 (3) Intensive Care Med 1991;17(2):98

PARTIAL REBREATHING FOR CARDIAC OUTPUT (CO) DETERMINATION DOES NOT ALTER CO DURING THE MEASUREMENT.

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Monitoring errors may be due to variations in the measured variable induced by the equipment itself. Changes in $PaCO_2$ alter vascular resistance and CO. During measurements of CO by the partial rebreathing method (PRCO), $PaCO_2$ may transiently increase, but it is not known whether CO can be affected. The objective was to assess the bias caused by transient elevations of $PaCO_2$ during CO determination using the PRCO method. **Methods**: In 15 patients, we performed thermodilution CO (TdCO) measurements one minute before (Pre PRCO), during PRCO and one minute after (Post PRCO) a PRCO with the NICO system (Novametrix). In each patient, up to 4 sets of measurements separated 2 hours in between were evaluated. Before (Pre), during and after the PRCO maneuver, hemodynamics and end-tidal CO_2 ($PetCO_2$) were recorded. One way ANOVA was used to compare measurements. Data are showed as mean ±SD. **Results**: 42 sets of measurements were taken. $PetCO_2$ increased from 32 ±4.8 to 39 ±5.5 Hg ($p<0.0001$). Hemodynamic variables remained unchanged:

	Pre-PRCO	During-PRCO	Post-PRCO	p
TdCO	5.6 ± 2.5	5.7 ± 2.5	5.8 ± 2.4	0.96
HR ($b.min^{-1}$)	94 ± 20	95 ± 20	94 ± 30	0.94
MAP (mmHg)	77 ± 12	76 ± 13	77 ±1 4	0.98
MPAP (mmHg)	29 ± 7	30 ± 8	29 ± 8	0.94

HR: heart rate; MAP: mean arterial pressure; MPAP: mean pulmonary artery pressure.

Conclusion: The transient increase in $PaCO_2$ caused by the PRCO period does not induce changes in CO and hemodynamics. PRCO measurements appear not biased by the partial rebreathing maneuver. *Funded by Fundació Parc Tauli and Novametrix.*

Reference: American Journal of Respiratory and Critical Care Medicine, 2000, 161(3):A395.

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frequency of manipulation was averaged for the two radiologists.
Results: 248 [34%] of the 730 were deemed acceptable, requiring no manipulation. Barring individual preferences of overall density and contrast, the images were manipulated for optimizing for mediastinum in 361[50%], and optimizing for lung parenchyma in 339[46%]. Ninety-three [13%] were overexposed with irreversible loss pulmonary detail; 9[1.2%] were underpenetrated with irretrievable mediastinal detail. **Conclusion:** PACS offers the added advantage over conventional radiography of imag manipulation to optimize diagnostic yield. The availability of a user-friendly and instantaneous manipulation makes image optimization quick and easy: 50% percent we manipulated for the lung parenchyma and 46% manipulated for the mediastinum. Only third of the CRs were accepted as submitted, requiring no image manipulation.

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EVALUATION OF THE NON-INVASIVE PARTIAL REBREATHING METHOD FOR CARDIAC OUTPUT MEASUREMENT IN CRITICAL CARE.

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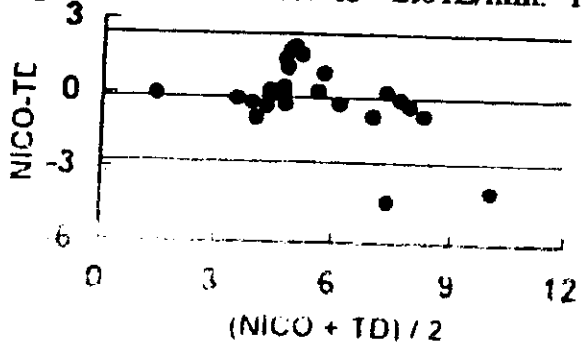
The thermodilution (TD) method is the gold standard for monitoring cardiac output (CO) in critical care. However, great concern exits on the safety of TD catheters. The CO_2 rebreathing technique allows non-invasive CO determination using the indirect Fick principle. We assessed the accuracy of the NICO system (Novametrix) to measure CO by using the CO_2 partial rebreathing method in mechanically ventilated patients. **Methods**: We measured simultaneously CO with NICO and TD in 15 critically ill patients in assist-control ventilation. Two 10ml iced DW5% boluses were randomly delivered during the respiratory cycle within the 50-s rebreathing period. The average of both TD measurements was compared with simultaneous NICO measurement. Up to 4 CO measurements were performed in each patient. We reject CO measurements in which the NICO was unable to found a "stable CO_2" period. The agreement between TD and NICO was assessed by a concordance analysis. **Results**: 42 sets of CO measurements were attempted, but 14 of them (33%) were rejected due to unstable CO_2. The remaining 28 sets of CO showed a bias of -0.14L/min and a 95% limits of agreement from -2.89 to +2.61L/min. Two sets of CO measurement (outliers) accounted for half of the estimated agreement. Excluding these 2 outliers, the bias was 0.19L/min and 95% limits of agreement were -1.39 and +1.77L/min. **Conclusions**: The non invasive partial CO_2 rebreathing technique may be a useful non-invasive method to determine CO in critically ill patients



Funded by Fundació P. Tauli and Novametrix

1051

Cardiac output by CO2-rebreathing technique

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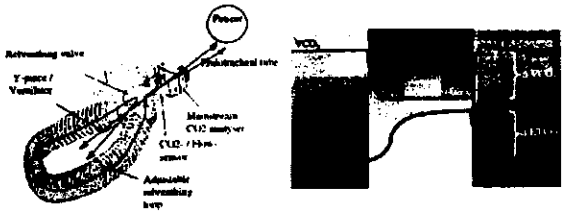
Background

Monitoring and optimizing hemodynamics is essential in high risk surgical and critically ill patients. Since the use of the pulmonary artery catheter lately has been questioned, new and less invasive methods are needed. Gedeon and co-workers described in 1984 a method for calculation of cardiac output, based on the Fick principle and partial CO_2-rebreathing technique (1). This system has now been developed for clinical use ($NICO_2$, Novametrix Medical Systems Inc., Connecticut, USA).

We have evaluated this new device and compared it to cardiac output obtained by thermodilution technique.

The partial CO_2-rebreathing technique

$NICO_2$ measures CO_2, volume and flow. Carbon dioxide production (VCO_2) is calculated from the area under the CO_2 - flow curve, breath by breath. Every three minutes an extra dead space is added automatically and gives 50 seconds of partial CO_2-rebreathing. The differences in CO_2 elimination and in end-tidal CO_2 between the normal and the rebreathing situations are used to calculate cardiac output using the Fick principle.



According to Fick's equation cardiac output based on oxygen is

$$C.O. = VO_2 / (CaO_2 - CvO_2)$$

and analogously for carbon dioxide

$$C.O. = VCO_2 / (CvCO_2 - CaCO_2)$$

Based on the assumption that cardiac output is stable during the whole measurement cycle, cardiac output can be expressed as

$$C.O. = VCO_2nr / (CvCO_2 - CaCO_2nr)$$

during normal, non-rebreathing conditions and

$$C.O. = VCO_2re / (CvCO_2 - CaCO_2re)$$

during the rebreathing period when the extra dead space is connected. If the assumption is made, that the period of rebreathing is short enough not to change mixed venous carbon dioxide content the two equations can be subtracted from each other to form a differential Fick's equation.

$$C.O. = \Delta VCO_2 / \Delta CaCO_2$$

If the alveolar-arterial carbon dioxide tension difference is equal during non-rebreathing and rebreathing conditions the arterial CO_2 content can be calculated from the end tidal CO_2 value using the equation for the CO_2-dissociation curve.

$C.O. = (VCO_2nr - VCO_2re) / (ETCO_2re - ETCO_2nr) * CO_2$-dissociation curve

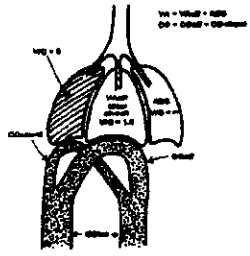
$$C.O. = \frac{\Delta\, VCO_2}{\Delta\, ETCO_2} * CO_2\text{-dissociation coefficient}$$

Shunt

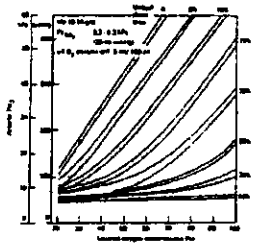
This measured flow will only represent the blood flow through ventilated parts of the lungs (C.O.eff), the pulmonary capillary blood flow. To get the total cardiac output the shunt fraction is added, calculated by the standard shunt formula

$$Qs/Qt = (CcapO_2 - CaO_2) / (CcapO_2 - CvO_2)$$

using SpO_2 and an assumed arterial-mixed venous oxygen content difference of 50 ml/l (2). Entering values for FiO_2 and arterial blood gas values makes it possible to further enhance the calculation of shunt.



The effective cardiac output, COeff, is measured by the $NICO_2$ apparatus



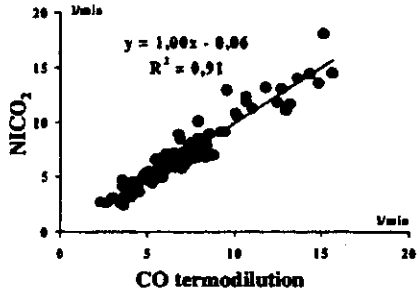
The iso-shunt diagram is used to estimate shunt flow, which is added to the effective cardiac ouput to obtain total cardiac output

Patients and methods

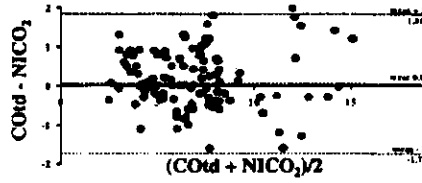
13 patients, on volume controlled ventilation (PEEP between 4 and 18 cm H_2O) and with pulmonary artery catheter, were studied perioperatively (liver transplantation (6), aortic surgery (4)) or in the ICU (3). Cardiac output was measured by thermodilution and with the rebreathing technique: $NICO_2$. The inspiratory and expiratory fractions of O_2 and CO_2 were analysed as well as mixed venous and arterial blood. Shunt was calculated by the standard shunt equation and compared to the estimated shunt of the $NICO_2$.

Results

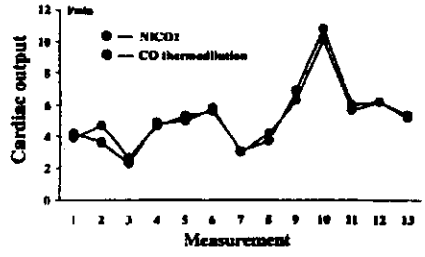
113 paired measurements of cardiac output were obtained over a wide range of flows (2.3-15.7 l/min). Linear regression analysis showed a good agreement between the two methods (R^2=0,91). The mean difference was 0,06 l/min and the SD 0,9 l/min. Cardiac output measured by $NICO_2$ is somewhat lower than that measured by thermodilution technique, probably due to an underestimation of the shunt. The correlation between shunted blood flow estimated by $NICO_2$ and the shunt calculated by the shunt formula is poor (R^2=0,32). Improved shunt estimation could further increase the reliability of this non invasive technique for cardiac output determination.



Correlation between thermodilution measurements and the CO_2 rebreathing technique



Bland-Altman plot showing the close correlation over a wide range of cardiac output values



Rebreathing cardiac output and thermodilution cardiac output during an aortic aneurysm operation

Conclusion

Pro

- Non-invasive
- Quick to set up and easy to handle
- Good correlation with standard methods
- Follows well marked hemodynamic changes
- Reliable results even with large shunt or alveolar dead space
- Little influenced by PEEP or humidity
- Monitors other parameters such as VEO$_2$ and dissolved gases

Con

- Intubation is necessary
- Sedated patients in volume controlled ventilation
- Somewhat complicated theoretical principle
- Inexact shunt calculation
- Unreliable values during manipulation of the drainage or if the patient makes ventilatory efforts

References:
1. Gedeon *Clin. Physiol.* 1985;5:49-58
2. Nunn *Applied Respiratory Physiology* 4th Ed. 1993

1052

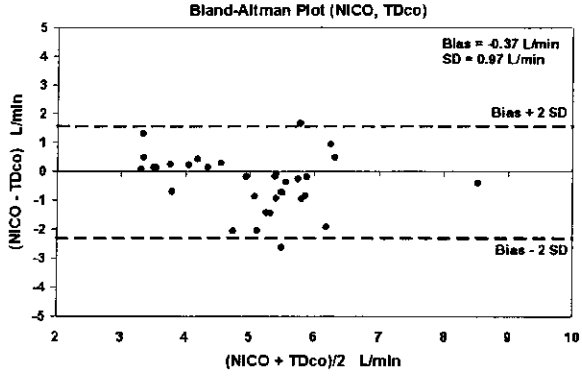
Comparison of noninvasive determination of cardiac output (CO) using a partial CO_2 rebreathing system with thermodilution during cardiac surgery

Monica Botero, MD, Kurt Briesacher, MD, David Kirby, MD, Nikolaus Gravenstein, MD, P. Hess, MD, Emilio B. Lobato, MD.
University of Florida College of Medicine

Introduction: Noninvasive partial CO_2 rebreathing (NICO; Novametrix Medical Systems, Inc) is a new alternative to thermodilution (TD) for measurement of CO. This study was designed to compare CO measurements using the NICO and bolus thermodilution. NICO uses a differential form of the Fick equation to calculate CO. The ratio of the change in end-tidal CO_2 and CO_2 excretion, in response to a brief period of partial rebreathing, provides a non-invasive estimate of the CO (1,2).

Methods: After anesthetic induction, 14 consenting adults undergoing elective coronary artery bypass grafting were instrumented with NICO and a PA catheter. The NICO circuit was attached between the endotracheal tube and the breathing circuit. An average of 3 consecutive (10 ml 20^0C saline) TD CO measurements made during end-expiration was compared with corresponding NICO measurements. Statistical analysis was performed with Bland-Altman and two-way ANOVA. A $p<0.05$ was considered significant.

Results: The correlation's between NICO CO and TD CO for all subjects at all time points are shown in the Figure. A total of 33 measurements were performed. Agreement between methods resulted in a bias of -0.37 L/min with a precision (1 SD) of +/- 0.97 L/min, r=0.7.



Conclusion: CO values obtained with NICO and TD CO correlated well as confirmed by applying the Critchley analysis (3). Our data show the NICO noninvasive technique offers an alternative to invasive CO measurements.

References: (1) IEEE Trans on BME 1988; 35:9
(2) Intensive Care Med 1991; 17(2):98
(3) J Clin Monit Comput 1999; 15:85

Reference: Anesthesia & Analgesia, 2000; V90(2S); S32
Also presented at International Anesthesia Research Society (IARS) 74th Clinical and Scientific Congress, March 10-14, 2000, Hawaii

1053

Comparison of noninvasive cardiac output using a partial CO_2 rebreathing system with direct aortic flow measurements during cardiac surgery

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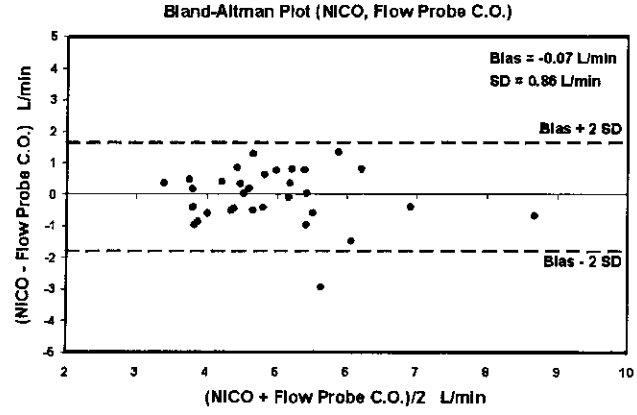
Introduction: Intraoperative determinations of cardiac output (CO) guide hemodynamic management of many patients (1). This study was designed to compare measurements of CO using a noninvasive partial CO2 rebreathing system (NICO; Novametrix Medical Systems, Inc) and an ultrasonic flow probe (UFP; Transonic, Inc). NICO uses a differential form of the Fick equation to calculate CO. The ratio of the change in end-tidal CO2 and CO2 excretion, in response to a brief period of partial rebreathing, provides a noninvasive estimate of the CO (2,3).

Methods: After anesthetic induction, 14 consenting adults undergoing elective coronary artery bypass grafting (CABG) had a NICO circuit attached between the endotracheal tube and the breathing circuit. A UFP was placed on the ascending aorta and used for the reference CO. During steady state conditions, CO was measured by NICO and UFP. Statistical analysis was performed with two-way ANOVA and Bland-Altman plots. A $p<0.05$ was considered significant.

Results: The correlations between NICO CO and UFP CO for all subjects at all time points are shown in the Bland-Altman plot. A total of 33 measurements were performed. Agreement between methods resulted in a bias of -0.07 L/min with a precision (1 SD) of ± 0.86 L/min and a correlation coefficient of 0.72.



Conclusion: There was a significant correlation between CO values obtained with the NICO device and directly measured aortic blood flow. Our data show that this noninvasive technique offers a good alternative to invasive CO measurement.

References: (1) J Clin Monit Comput 1999; 15:85
(2) IEEE Trans on BME 1988; 35:9
(3) Intensive Care Med 1991;17(2):98

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$NICO_2$ – Fick Partial CO_2 Rebreathing Noninvasive Cardiac Output

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FICK METHOD FOR MEASUREMENT OF CARDIAC OUTPUT:

The first known technique for measuring cardiac output in humans is based on the theoretical principle enunciated by Adolf Fick in 1870, who never actually made the measurement himself. The Fick principle states that over a given time period, the quantity of a gas such as O_2 or CO_2 entering or leaving the lungs is equal to the quantity of the gas taken up or expelled by the blood flowing in the pulmonary capillaries. The Fick technique for measurement of cardiac output has long been a standard by which other methods of determining cardiac output have been compared. However, the practical application of the Fick technique in a clinical setting is limited due to technical issues involved in accurate metabolic gas measurements and the need for invasive arterial and mixed venous blood gas measurements. To eliminate the need for invasive blood gas samples, indirect Fick methods known as rebreathing techniques have been developed[1,2,3]. Total rebreathing techniques use estimates of arterial and mixed venous CO_2 contents obtained from measurements of end-tidal CO_2 partial pressure ($ETCO_2$) made at the mouth during normal breathing and rebreathing maneuvers[4]. With total rebreathing, the patient inhales his or her own exhaled gas from a bag attached at the mouth. During the total rebreathing maneuver, no CO_2 is eliminated from the lungs and the concentration of exhaled CO_2 approaches the mixed venous concentration, allowing it to be estimated non-invasively from respiratory gas measurements. $ETCO_2$ is used as a non-invasive estimate of the arterial CO_2 concentration. Even though the total CO_2 rebreathing technique allows noninvasive cardiac output estimation based on routinely obtained respiratory gas measurements, the compliant rebreathing bag and the need for patient co-operation makes it impractical for use in mechanically ventilated patients.

$NICO_2$ – FICK PARTIAL CO_2 REBREATHING NONINVASIVE CARDIAC OUPUT

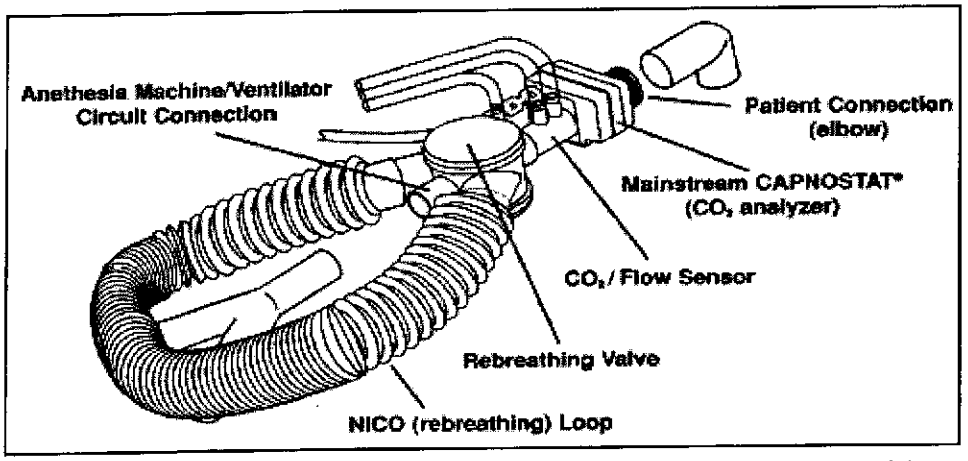

FIGURE 1. $NICO_2$ Sensor assembly consists of a mainstream CO_2 sensor, differential pressure flow sensor, and a rebreathing loop connected to the pneumatic rebreathing valve.

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The partial rebreathing technique, which is used by the $NICO_2$ monitor, employs a differential form of the Fick method for non-invasive measurement of cardiac output. This technique was first described by Gedeon et. al.[5] and later expanded upon by Capek and Roy[6]. With partial rebreathing, a change in VCO_2 (exhaled volumetric CO_2) and an associated change in $ETCO_2$, in response to a change in ventilation, is used in the Fick calculation. $NICO_2$ accomplishes the required change in ventilation by using the rebreathing valve and $NICO_2$ rebreathing loop illustrated in Figure 1 as part of the $NICO_2$ sensor. By temporarily adding a rebreathing volume to the breathing circuit, the patient inhales only a portion of the exhaled gases. The resulting changes in VCO_2 and $ETCO_2$ are used to calculate cardiac output. The $NICO_2$ monitor uses Novametrix proprietary sensors for mainstream CO_2 and respi-

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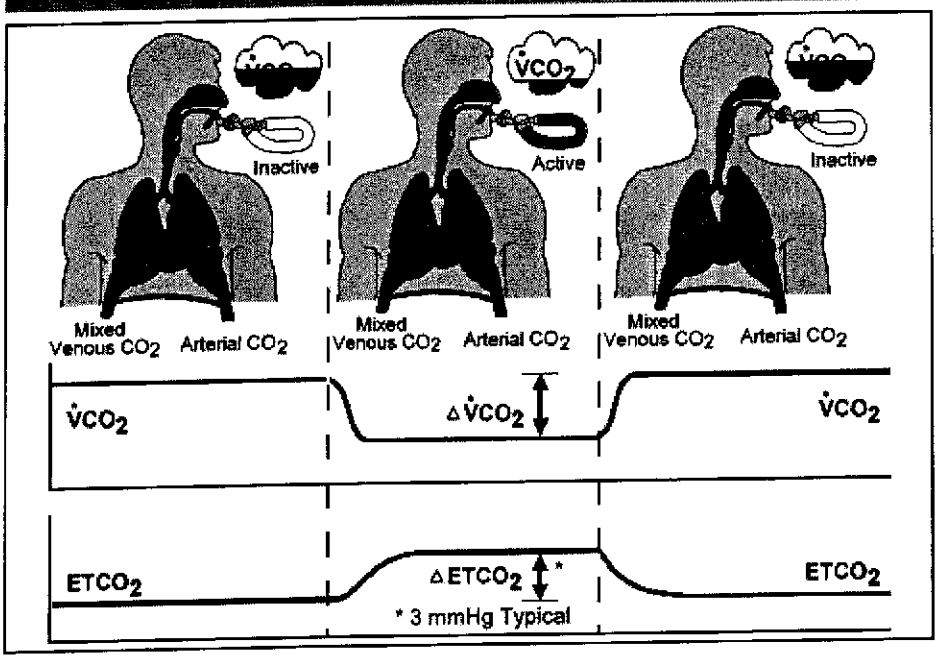

FIGURE 2. NICO Timing Diagram (3 minute cycle)

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ratory flow monitoring capabilities. VCO_2 is calculated as the product of the integrated flow and CO_2 signals.

Every three minutes (see Figure 2), the patient's inhaled and exhaled gases are diverted through the $NICO_2$ loop for 50 seconds by the rebreathing valve, preventing normal volumes of CO_2 from being eliminated. As a result, the CO_2 elimination decreases and the concentration of CO_2 in the pulmonary artery ($CaCO_2$) increases.

The equation for differential Fick partial rebreathing cardiac output is:

$$C.O. = \frac{[\ \dot{V}CO_{2N} - \dot{V}CO_{2R}\ ]}{[\ CaCO_{2R} - CaCO_{2N}\ ]}$$

Where VCO_{2N} and VCO_{2R} are the volumetric CO_2 elimination during normal and rebreathing periods, respectively, and $CaCO_{2N}$ and $CaCO_{2R}$ are the arterial CO_2 concentrations during normal and rebreathing periods, respectively. The preceding equation can also be written as:

$$C.O. = \frac{[\ \Delta\dot{V}CO_2\ ]}{[\ \Delta CaCO_2\ ]}$$

Where delta-VCO_2 and delta-$CaCO_2$ represent the changes in VCO_2 and $CaCO_2$ between normal and rebreathing periods. The change in $CaCO_2$ is reflected in and measured by the change in $ETCO_2$. See http://www.nico2.com/library/techreview/tr_fullmath2.htm for a more detailed mathematical explanation.

It has been shown that mixed venous CO_2 concentration does not change significantly throughout the 50 second rebreathing period[6], thus the terms associated with mixed venous CO_2 concentration cancel out and are not shown in the above equation. This permits cardiac output calculations based entirely on non-invasively monitored physiologic signals. The NI-CO_2 implementation of the partial rebreathing method is automated, providing cardiac output determinations on a real-time and continual basis.[7,8]

When CO_2 concentration is measured indirectly via the breath as $NICO_2$ does, the Fick method considers only that portion of the cardiac output that participates in gas exchange, or the pulmonary capillary blood flow. By estimating the amount of blood flow bypassing the lung (shunt flow) and adding that amount to the equation above, the indirect Fick method accurately reflects the total cardiac output.[8] The $NICO_2$ monitor corrects for shunt using oxygen saturation derived from pulse oximetry and a user entered value for inspired O_2 concentration.

CLINICAL VALIDATION

When evaluating newer methods of cardiac output monitoring, bolus thermodilution cardiac output measurements are routinely used as the comparison standard. The limited reproducibility of thermodilution hampers evaluation of new cardiac output devices.[9,10] Recently, in a multi-modality cardiac output study using ultrasonic flow probe placed on the ascending aorta of cardiac surgery patients researchers at the University of Florida, Gainesville have shown that the precision of NI-CO_2 (1 SD = 0.81 L/min) is better when

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compared with bolus thermodilution (1 SD = 0.96 L/min) and Continuous Cardiac Output (1 SD = 1.55 L/min)[11]. The accuracy and precision of $NICO_2$ has also been demonstrated in a number of other clinical studies to be within acceptable clinical limits over a wide range of cardiac outputs.[12-16]

DISCUSSION

The partial rebreathing technique for measurement of cardiac output is non-invasive, easy to use, automated and continual, not technique dependent and is based on the accepted Fick principle. It can be easily implemented and integrated with standard respiratory gas monitoring already available in most patients in the critical care environment. The small increase in end-tidal CO_2 associated with partial rebreathing is not harmful and can be easily tolerated by the patient. $NICO_2$ is not indicated for use in patients with severe lung pathology. $NICO_2$ in its present implementation can be used on patients who are mechanically ventilated (can be total mechanical ventilation or mixed breathing with spontaneous breaths). Future firmware upgrades will allow the user to use $NICO_2$ with a facemask or mouthpiece in spontaneously breathing patients. The per patient cost of the $NICO_2$ sensor and set-up time are much less than that associated with the use of a PA catheter. We expect that this technique may allow cardiac output monitoring in all patients in the OR and ICU, not only in which PA catheterization is not indicated (required or worth the risk), thus allowing a wide patient population to benefit from improved hemodynamic (cardiac) monitoring and management. The simplicity of use and the additional respiratory parameters available with $NICO_2$ offers advantages over other noninvasive cardiac output techniques.

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Call for Abstracts

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This meeting will provide a forum for the discussion and advancement of the application of simulators in clinical medicine and other health sciences. Although the meeting is being held cooperatively with STA, the meeting is by no means limited to anesthesia applications. Abstracts from the allied health specialties, emergency medicine, surgery, radiology, medicine and others are highly encouraged. The Medical Simulation Meeting will be of interest to those individuals working in the scientific development of simulation technology, as well as

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REBREATHING USED FOR CARDIAC OUTPUT MONITORING DOES NOT INCREASE HEART RATE

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Salt Lake City, UT 84132

Abstract

The partial rebreathing method for cardiac output determination produces short periods of elevated arterial CO_2 content. Because previous work had shown that elevated $etCO_2$ levels increased cardiac output, mostly due to heart rate increases, a concern was raised that the rebreathing periods could be inducing an elevated heart rate. This could also raise the cardiac output (CO), since CO = (Heart Rate) X (Stroke Volume). We studied 93 patients in the OR and the ICU who had undergone a total of 5142 partial rebreathing measurements by the $NICO_2$ monitor (Novametrix Medical Systems) to determine whether the heart rate was raised, even if transiently, during the monitored period. Our conclusion was that the rebreathing periods caused no detectable change in the heart rate.

Introduction

Cardiac output is a clinically important variable although it remains difficult to measure, since it is based on many interrelated factors and can vary even with respiration. Information about the level of cardiac output describes the general health of the heart and cardiovascular system and can be used by physicians to guide care, especially in critical care situations. Cardiac output is monitored clinically in about 1,000,000 patients each year with the bolus thermodilution technique.[1] The thermodilution method, in which a bolus of cold saline is injected through a pulmonary artery (PA) catheter directly into the heart, is currently the most widely used and clinically accepted standard for measurement of cardiac output.[2,3]. Unfortunately, the costs associated with placement of a PA catheter are high. Because it is associated with considerable morbidity and mortality, [4-6] not all patients in whom cardiac output monitoring would be valuable can be monitored by thermodilution.

A reliable method for measuring cardiac output non-invasively is desirable, especially for those patients who are at risk for peri-operative cardiac morbidity but in whom the risk-benefit ratio does not justify invasive monitoring. Non-invasive methods are also more desirable because they can be less costly and can require less set up time. A number of non-invasive methods have been introduced for clinical use, including transthoracic bioimpedance, esophageal Doppler, transesophageal echocardiography, and $NICO_2$ partial rebreathing.

The $NICO_2$ method is based on a version of the Fick equation and produces intermittent periods of elevated arterial CO_2 content. The difference in endtidal (or end-expiratory) CO_2 levels between the rebreathing and normal periods is approximately 5 mmHg. It is during this period of elevated arterial CO_2 levels that the appropriate variables for the cardiac output calculation are generated. A concern was raised that since the CO_2 levels were being elevated for the measurement, the cardiac output may have been raised by the measurement technique itself. This concern was related to previous work, including that of Eger[20], which stated that cardiac output was raised, mostly due to increased heart rate, when the $etCO_2$ was raised stepwise in six-minute increments.

To address this issue, we monitored 93 subjects in the OR and the ICU who underwent $NICO_2$ non-invasive cardiac output monitoring to see if we could observe a difference in the heart rate attributable to the elevated CO_2 levels.

Partial Rebreathing Non-invasive Cardiac Output Technology ($NICO_2$)

Our lab has developed a non-invasive CO_2 rebreathing system to measure cardiac output from the respiratory measurements of intubated patients.[7,8] The $NICO_2$ technology has been approved by the FDA and is commercially available for use in hospitals to monitor mechanically ventilated patients. Clinical studies have shown that the $NICO_2$ system performs well in intubated, mechanically ventilated patients. [25, 26]

The method is based on a principle described by Adolf Fick in 1870.[9] Fick postulated that the quantity of a gas such as O_2 or CO_2 entering or leaving the lungs is equal to the quantity of the gas expelled or taken up by the blood as it flows through the pulmonary capillaries and participates

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in gas exchange. (Figure 1).

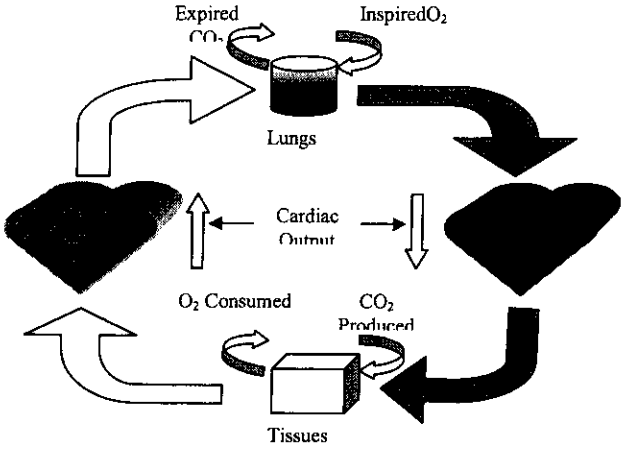

Figure 1: Circulation and gas exchange[27]

That is, a mass balance equation can be used to describe how cardiac output is related to gas exchange. The conventional Fick technique based on O_2 has long been a standard by which other methods of determining cardiac output have been evaluated:

$$\dot{Q} = \frac{\dot{V}_{O_2\ consumed}}{C_{aO_2} - C_{\bar{v}O_2}}, \qquad \dot{V}_{O_2} \qquad (1)$$

where $\dot{Q}$ is cardiac output (liters/minute), *consumed* is the amount of O_2 consumed by tissue metabolism (liters/minute), and C_{vO_2} is the mixed venous O_2 concentration of the blood (blood flowing into the lungs in % volume) and C_{aO2} is the arterial O_2 concentration of blood flowing from the lungs (%volume).

Unfortunately, in its original form, the Fick method is an invasive method requiring catheterization to determine the blood gas concentrations (c_{vO2}, c_{aO2})and V_{CO2}. The original Fick equation can be modified to require only non-invasively measured variables[21-24]. This is done by expressing the Fick principle in terms of alveolar (A) instead of arterial (a) blood gas concentrations and by measuring CO_2 elimination rather than O_2 uptake:

$$\frac{\dot{Q}_{PCBF}}{\dot{Q}} = \frac{\dot{V}_{CO_2\ \ produced}}{C_{\bar{v}CO_2} - C_{ACO_2}}, \qquad (2)$$

where $_{PCBF}$ is the pulmonary capillary blood flow (the part of the cardiac output actually participating in the gas exchange), V_{CO2} is the volume of CO_2 excreted by the lungs per minute and C_{ACO2} and C_{VCO2} are the alveolar and mixed venous CO_2 contents, $\dot{Q}$ respectively.

Cardiac output can be calculated from $_{PCBF}$ by estimating the fraction of cardiac output bypassing the lung (shunt fraction).

The alveolar CO_2 concentration can be determined non-invasively by monitoring the endtidal CO_2 partial pressure in the expired gas and relating it to the blood concentration through a CO_2 dissociation curve. Before inserting the values in the Fick equation, the non-invasive measurements of CO_2 elimination and C_{ACO2} must be corrected. There are two reasons for this correction. First, the lung retains some gas, even after complete expiration (functional residual capacity). Second, some regions of the lung do not participate in the gas exchange (deadspace). The $NICO_2$ algorithm can compensate for these effects.

To eliminate the need to know mixed venous CO_2 content, we use a partial rebreathing technique. A pneumatically driven valve temporarily adds a serial dead space to the circuit so that the patient inhales a portion of the previously exhaled CO_2.[8,10,11] Partial rebreathing does not require patient cooperation and has only a small impact on ventilation. The arterial CO_2 content rises in response to this change in ventilation, and this induced change is used together with the amount of CO_2 produced to calculate cardiac output.

The $NICO_2$ system estimates shunt fraction based on blood oxygen saturation (SpO_2) data from the non-invasive pulse oximeter and on concentration of inspired oxygen (FiO_2). The limited accuracy of pulse oximetry measurements of SpO_2 (1-2%) and the steepness of the oxygen tension-saturation curve (especially for SpO_2 > 95%) may lead to inaccuracies in the estimates of non-invasive shunt fraction. In most cases, the shunt fraction is very small, so even a large relative error in the estimate of shunt fraction leads to a small error in cardiac output. An accuracy of up to ± 20% in the estimation of shunt fraction is sufficient to ensure that the error in the estimation of cardiac output is less than ±5%.[12]

Clinical studies have shown that the non-invasive cardiac output $NICO_2$ system performs well in intubated, mechanically ventilated patients, in whom regular breathing patterns and the good seal of the endotracheal tube provide optimal conditions for the $NICO_2$ system. A MEDLINE search compared the $NICO_2$ technique with bioimpedance and Doppler methods. Bias and precision statistics were used to determine limits of agreement with thermodilution (two standard deviations of the difference from thermodilution / mean cardiac output) for each method. The proposed $NICO_2$ system showed better limits of agreement (± 28%) than either impedance (± 37%) or

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Doppler(± 65%).[13-19]

The $NICO_2$ valve assembly

The $NICO_2$ valve assembly (Figure 2) is connected between the patient's breathing circuit (at the Y-piece) and the patient's endotracheal tube. The $NICO_2$ monitor controls the operation of the pneumatic valve by application of positive pressure. In its default position, the pneumatic valve causes gas from the breathing circuit to bypass the adjustable deadspace. When actuated, the pneumatic valve places the adjustable deadspace (150-450 ml) serially in the breathing circuit between the Y piece of the breathing circuit and the endotracheal tube connected to the patient. This causes the patient to rebreathe a portion of previously exhaled CO_2. The increase in inhaled CO_2 due to rebreathing causes a reduction in the CO_2 volume eliminated from the lung (decrease in VCO_2) and a corresponding increase in alveolar and arterial CO_2 tension (increase in P_{ACO2} and P_{etCO2}).

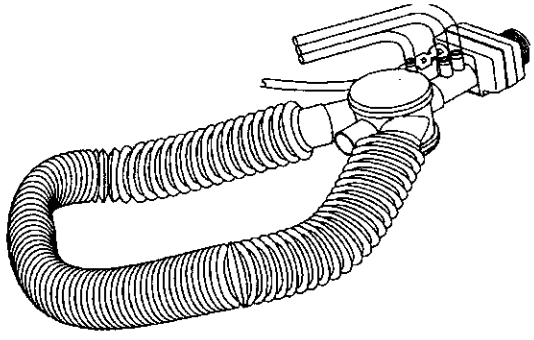

Figure 2: The $NICO_2$ valve assembly (Novametrix Medical Systems)

The Rebreathing Cycle

Each $NICO_2$ measurement cycle lasts 3 minutes, and is comprised of a 60 second baseline period, a 50 second rebreathing period, and a 70 second recovery period. The resulting changes in VCO_2 and $PetCO_2$ are shown in Figure 3. The flow and CO_2 signals are sampled at 100 Hz with a resolution of 0.1 L/min for flow and 0.1 mmHg for PCO_2. The $NICO_2$ monitor computes and displays VCO_2 and $PetCO_2$ data on a breath-to-breath basis. Baseline values for VCO_2 and $PetCO_2$ are calculated as the average of a group of samples taken 27 seconds before the start of the rebreathing process. During rebreathing, values for VCO_2 and $PetCO_2$ are calculated as the average of the samples taken from 25 to 50 seconds into the rebreathing period.

The changes in $PetCO_2$ and VCO_2 are then used to calculate that part of the cardiac output that participates in gas exchange (pulmonary capillary blood flow (Q_{PCBF})). The percentage of cardiac output bypassing the lung (shunt fraction) is determined based on Nunn's iso-shunt plots from the inspired O_2 fraction (FiO_2) values and the average blood oxygen saturation values (SpO_2), determined non-invasively by a pulse oximeter. Cardiac output is then calculated from Q_{PCBF} and shunt fraction.

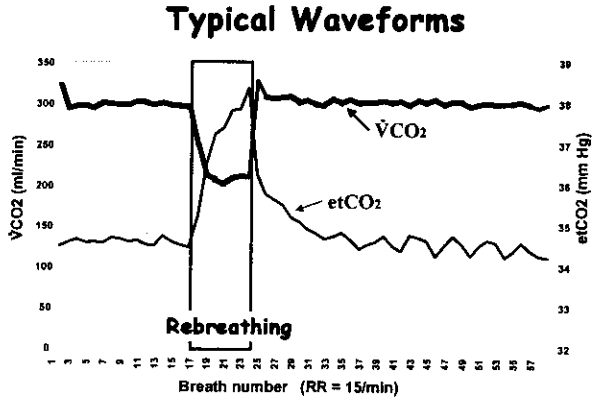

Figure 3: Typical change in carbon dioxide elimination and end-tidal CO_2 during the rebreathing cycle.

Methods

Data Collection:

The partial rebreathing cardiac monitor (NICO2, Novametrix Medical Systems) was used continuously on 93 patients in the OR (n = 50) and the ICU (n = 43). Each of the patients was intubated and mechanically ventilated throughout the measurement period. Patients in the OR were fully anesthetized under general anesthesia, while those in the ICU were less deeply anesthetized as they recovered from surgery. During each of the cases, the information about the $etCO_2$ and heart rate was automatically stored on a laptop for later analysis.

Data Analysis:

Theoretically, the response of the heart rate to the elevated $etCO_2$ levels could differ according to how deeply anesthetized the patient is, and therefore the OR and ICU sample groups were analyzed separately.

Each recorded three minute rebreathing cycle was subdivided into 30 six-second intervals. The heart rate and $etCO_2$ levels recorded during the baseline interval (I_0) were compared to levels before, during, and after the 50 second rebreathing period. For each cycle, differences in the heart rate and $etCO_2$ were calculated for $I_{During\ or\ After} - I_0$ and $I_0 - I_{Before}$, where Δt (seconds) between intervals = T_{DA0} and T_{0B}, respectively. To account for the possibility of underlying trends in the heart rate, the Δt between the intervals being compared was set to be equal ($T_{DA0} = T_{0B}$). Thus, for each cycle, there were two resultant ΔHR and $\Delta etCO_2$ values with respect to baseline (I_0). If the rebreathing were causing a change in the heart rate, one would expect to see a difference in HR for $I_{During\ or\ After} - I_0$ but not for $I_0 - I_{Before}$.

This process of generating values for ΔHR and $\Delta etCO_2$ was repeated for Δt's from 14 to 60 seconds while the I_0 was held constant so that the entire 3 minute cycle period was evaluated. This was done to check whether there was a delay in the response of the heart rate to elevated CO_2 levels such that it occurred after rebreathing was completed.

To test whether the differences measured were significantly different, a second part of the evaluation was necessary. The same data was again evaluated with the procedure outlined above, but all intervals occurred during the baseline (non-rebreathing) period. This set of data was considered to be the control data which describes the inherent variation in the respiratory signals and heart rate during non-rebreathing periods. The student's t-test was used to determine whether the sample and control values were significantly different from one another for each set of Δt's where $T_{DA0sample} = T_{DA0control}$ and $T_{0Bsample} = T_{0Bcontrol}$. Standard deviations, averages, and averages of differences were also calculated.

Results

A total of 5142 measurement cycles from 50 patients in the OR and 43 patients in the ICU were examined. In the OR, an average increase in $etCO_2$ of 5.1 mmHg had a corresponding average decrease in the heart rate of 0.24 beats/min. The standard deviations were 3.0 mmHg for $etCO_2$ and 5.5 beats/min for heart rate. The sample and control groups were found to be statistically different ($p < 0.05$) from each other for $etCO_2$ but not for HR.

In the ICU, and average increase of 7.8 mmHg in $etCO_2$ levels corresponded to a heart rate decrease of 0.34 beats/min, with standard deviations of 3.1 mmHg and 6.8 beats/min, respectively.

Discussion

We compared baseline heart rates to rebreathing time periods and other periods throughout the cycle to examine whether the heart rate was changed, but did not find statistically significant differences (at a 0.05 significance level). The variability in the heart rate was so large that the standard deviation was much larger than any observed differences in heart rate. This is an important point clinically, as some doctors are under the impression that elevated etCO2 levels produced by the NICO2 could increase HR.

We observed that the heart rate actually decreased by less than one beat per minute, but this value was so small compared to the variability that there is really no change. This is in contradiction to the results found in the literature. One explanation for this contradiction could be that the $etCO_2$ was elevated in our method for only 50 seconds, while in the literature, $etCO_2$ was elevated for six minutes. During the shorter time period of rebreathing used by $NICO_2$ we did not observe a difference in heart rate caused by increases in $etCO_2$ and have concluded that the concerns related to the possible increases in heart rate do not affect $NICO_2$ performance.

It was somewhat surprising that the HR did not change in the ICU patients. This could have been due to remaining effects of anesthesia or because there is really no induced change during a short partial rebreathing period. This issue should be tested further in spontaneously breathing, awake subjects.

Acknowledgements

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	Differential temperature, minutes post induction				
	30	45	60	50	90
Non-rebreathing	3.5 ± 1.7	4.6 ± 1.6	5.0 ± 1.8	5.2 ± 2.0	5.1 ± 2.0
Pediatric circle	3.7 ± 1.5	4.5 ± 1.6	4.9 ± 1.6	5.2 ± 1.6	5.3 ± 1.7

at the base of the heart. Temperatures recorded immediately post induction were used to determine differential temperature at 30, 45, 60, 75 and 90 minutes post induction throughout the surgical procedure. Animals were placed on circulating warm water blankets during surgery. Data were expressed $X \pm SD$.

Results. There was no significant difference in heat loss between the two devices at any time interval.

Discussion. Although breathing a warmed and humidified gas will reduce caloric expenditure needed to humidify and heat the inspired gas, the magnitude of thermal conservation was not great enough to detect in this study. To prevent or reduce hypothermia, warming devices such as thermostatically controlled, forced warm air blowers may be needed.

SYSTEMATIC ERROR ANALYSIS OF THE PARTIAL REBREATHING METHOD FOR NON-INVASIVE CARDIAC OUTPUT

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Summary. **Studies of the effect of systematic errors on noninvasive cardiac output calculated using the partial rebreathing method [1, 2] have not been previously published. This cardiac output method, which uses the differential CO_2 Fick equation and a form of the CO_2 dissociation curve that includes hemoglobin, has been analyzed from both theoretical and measurement viewpoints. This analysis has shown theoretically a low sensitivity to errors in hemoglobin and that reasonable measurement errors in flow and CO_2 has no clinically significant effect on the reported cardiac output values.**

Methods. Cardiac output (Q) can be calculated as shown in the Equations below:

$$Q = \frac{VCO_2(NR) - VCO_2(R)}{CaCO_2(R) - CACO_2(NR)}$$

$$CaCO_2 = (6.96 \cdot Hb + 94.9) \cdot Log(1 + 0.19 \cdot PaCO_2)$$

where VCO_2 is the carbon dioxide elimination (ml/min), $CaCO_2$ is the CO_2 arterial content values (ml CO_2/ml blood), Hb is hemoglobin (g/dl) and $PaCO_2$ is a measure of the alveolar partial pressure of CO_2; R and NR refer to whether the values were measured during rebreathing or normal modes (non-rebreathing).

Theoretical systematic error – An expression for the systematic error in cardiac output $(Q_m-Q_t)/Q_t$ (where m = measured and t = true value) as a function of the variables in the above equations has been derived using previously published methodologies [3]. Since the systematic error during the adjacent non-rebreathing and rebreathing time intervals are the same for both VCO_2 and $PaCO_2$ these terms cancel. The resulting systematic error is due only to the errors due to differences between the measured and actual hemoglobin.

Systematic errors in measured parameters – Simulations of measurement errors and its effect on cardiac output was performed with sample waveforms using flow calculated from differential pressure and CO_2 from the ratio of absorption of CO_2 and a reference channel. Errors in gain representing improper calibration and offsets representing improper zeroing of 2 LPM and 2 torr for flow (i.e. differential pressure) and CO_2, respectively were introduced and the resulting differences between expected and calculated cardiac output recorded.

Results. Theoretical systematic error – Hemoglobin measurement errors of 0.5 g/dl, typical of clinical instruments such as co-oximeters, result in cardiac output estimation errors of less than 2% for Hb values greater than 10 g/dl. Large errors such as 2 g/dl in Hb may contribute approximately a 7% error in cardiac output at a Hb value of 14 g/dl.

Systematic error in measured parameters – Gain and offset errors due to improper calibration and zeroing in CO_2 and flow produce errors smaller than 5% in cardiac output.

Conclusions. This analysis indicates that systematic errors in hemoglobin and in the basic measurements of flow and CO_2 has no clinically significant effect on the reported cardiac output values.

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INTERACTIVE, WEB-BASED, EDUCATIONAL SIMULATION OF AN ANESTHESIA MACHINE

Sem Lampotang, *Walter Dobbins, Michael L Good, Nikolaus Gravenstein, Dietrich Gravenstein, Department of Anesthesiology, University of Florida, Gainesville, FL, U.S.A.*

Summary. **We implemented an interactive, Web-based simulation of the flow of oxygen, nitrous oxide, carbon dioxide and volatile anesthetics in an anesthesia machine to help our residents learn how an anesthesia machine functions. The simulation is implemented using Director 7.0, a multi-media authoring software package for producing Web-based animations. Using the Shockwave 7 Web player, the animation can be viewed at the University of Florida, Department of Anesthesiology, URL: http://www.anest.ufl.edu/tds**

Introduction. The inner workings of an anesthesia machine, a "familiar" piece of equipment used daily by anesthesiologists, remains somewhat of a mystery for some. Specifically, how adjustment of anesthesia machine controls affects gas flow remains an area where residents can benefit from learning tools that exploit the latest Internet technology. Understanding how an anesthesia machine works internally is difficult because the gas molecules are invisible and cannot be traced

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EVALUATION OF A MODIFIED PARTIAL REBREATHING CARDIAC OUTPUT SYSTEM FOR USE IN THE ICU

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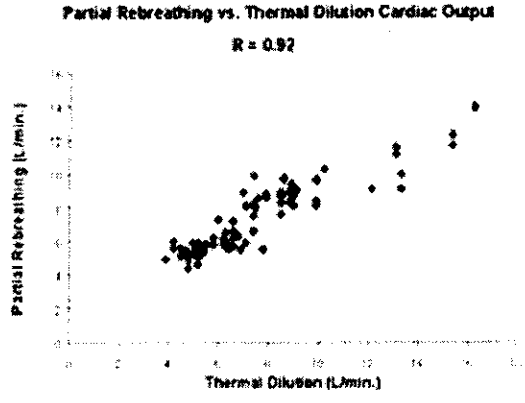
CRITICAL CARE MEDICINE 1999;27:A86

Abstract 221
Introduction: Partial rebreathing cardiac output measurements are calculated from changes in end tidal CO_2 and CO_2 excretion in response to addition of dead space to the breathing circuit. Accurate assessment of these changes requires stable ventilation during the rebreathing cycle. Mixed mechanical and spontaneous ventilation causes variability in the CO_2 signals making cardiac output measurement difficult. We have developed a modified system that filters the signals, making cardiac output measurement possible during mixed ventilation. **Methods:** 89 paired measurements were made using partial rebreathing (NICO2, Novametrix Medical Systems) and thermodilution in 10 ICU patients. During periods of mixed ventilation, end-tidal CO_2 and CO_2 production data were stored and processed by our algorithm to calculate cardiac output. **Results:** Linear regression resulted in a correlation of 0.92. The bias and standard deviation, as a percent of cardiac output, were 0.4% and 15% respectively. The algorithm rejected 6.7% of the data because of low signal quality. **Discussion:** Through improvements in signal processing and modifications to the basic algorithm, partial rebreathing can be used to measure cardiac output during mixed spontaneous and mechanical ventilation



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Partial CO_2 Rebreathing Cardiac Output Performs Well During Mixed Ventilation

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INTRODUCTION

The $NICO_2$ monitor (Novametrix, CT) uses the partial Fick CO_2 rebreathing method to monitor cardiac output noninvasively. Irregular respiration during spontaneous or mixed ventilation poses a special challenge to this method. We evaluated a modified algorithm to address this challenge.

MATERIAL AND METHODS

Anesthesia was induced in three mongrel dogs (21.9 kg-29.3 kg). Following intubation anesthesia was maintained using halothane or isoflurane. After initial mechanical ventilation, ventilation was switched to SIMV. Cardiac output was changed using inhalational anesthetics, beta-blocking agents, and dobutamine to cover a range from 3.1 to 9.2 L/min. Every three minutes the $NICO_2$ monitor switched a deadspace of 200-400 mL into the breathing circuit. Endtidal CO_2 and CO_2 production data were collected automatically through the $NICO_2$ monitor and a laptop computer. Every 10 minutes, thermodilution (Dualtherm, B. Braun, PA) cardiac output was determined from three 10 ml bolus injections of iced saline. Instead of using the standard partial rebreathing Fick equations used in the $NICO_2$ monitor, a digital filtering technique was used to estimate cardiac output from the CO_2 signals.

RESULTS

The linear regression between the modified $NICO_2$ cardiac output (mNICO) and thermodilution (TD) results in a correlation of r=0.92 (n=16) and a relationship of mNICO = 1.1 x TD - 1.25 L/min. The precision (SD of mNICO-TD) was 0.93 L/min. The modified filters reduced the frequency of mNICO determination from one every three minutes to one every nine and a half minutes.

DISCUSSION

The results suggest that the $NICO_2$ algorithm can be modified to provide clinically useful noninvasive cardiac output estimations even in the presence of severe respiratory variability. The reduced frequency of $NICO_2$ estimations ($3min^{-1}$ to $9.5min^{-1}$) is probably acceptable in the ICU where mixed ventilation mostly occurs. Future work will address estimation accuracy and frequency of measurements.

Reference: *Crit Care Med* 1999, 27(12, Suppl.):220.

1065

EQUIPMENT, MONITORING AND ENGINEERING TECHNOLOGY

A558

TITLE: EVALUATION OF A DUAL DIAPHRAGM VALVE FOR PARTIAL REBREATHING CARDIAC OUTPUT
AUTHOR: Michael B. Jaffe PhD
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Introduction: A pneumatically controlled dual diaphragm valve that is used with a non-invasive cardiac output monitor, based upon the partial rebreathing CO2 Fick method, has been evaluated on the bench and clinically.

Methods: Resistance: The pressure drop in both inspiratory and expiratory directions (using static flows from 5 to 80 LPM) was measured across a 7.0 and 8.0 ET tubes with and without the CO2/flow sensor/valve assembly in both non-rebreathing and rebreathing modes. Effect on Flow - The change in inspiratory flow rate (due to changes in inlet conditions) was measured. Performance under 'pressure' - The valve assembly in normal, rebreathing and disconnect modes was tested with PEEP as high as 50 cmH2O and PIP up to 110 cm H2O. The FiCO2, and VCO2 inspired values and capnogram were monitored to indicate rebreathing.

Results: Resistance: The added inspiratory and expiratory pressure drop of the valve and sensor relative to the 7.0 and 8.0 ET with an elbow is <2 and 1 cmH2O at 60 LPM, respectively. Effect on Flow: The ,percent difference between the normal and rebreathing modes for both inspiratory and expiratory flow is less than 1% at all flow rates tested. Performance under 'pressure': The addition of large swings in peak and baseline pressures did not cause rebreathing to occur during normal and disconnect modes nor change the amount of rebreathing during rebreathing mode .

Discussion: The sensor/valve adds a small and clinically acceptable amount of resistance and deadspace (< 32ml in normal mode) to the breathing circuit. The valve has performed reliably on the bench and on over 200 patients.

A559

TITLE: NON-STEADY STATE COMPUTER MODEL: HOW DOES DECREASED CARDIAC OUTPUT DECREASE PULM VCO2 & VO2?
AUTHOR: Peter H. Breen MD, FRCPC David H Chien, BSc
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INTRODUCTION: In a previous study (1), a decrease in cardiac output (QT) decreased pulm CO2 elimination (VCO2) by increasing dead space and by decreasing pulm CO2 delivery. We reasoned that, by the same mechanisms, decreased QT will decrease pulm VO2 uptake. However, compared with CO2, the decrease in VO2 will be less sustained because tissue O2 stores are 100 fold less. To test these hypotheses, we developed a computer model of non-steady state gas kinetics.

METHODS: The components of the numerical analysis are arterial and venous blood, peripheral tissues (O2 consumption and CO2 production), and lung. Lung is divided into 5 units, with alveolar ventilation/perfusion (VA/Q) ratios of 0 (shunt), 0.1, 1 (normal), 10, and infinity (alv dead space). For each unit, equations describe gas exchange between inspired gas and venous blood, using O2/CO2 blood dissociation curves. Initial values came from a separate steady-state model (2). Then, at every time increment, gas exchange components interact and update overall O2/CO2 stores and transport.

RESULTS: The perturbation decreased QT from 5 to 2.5 L/min and diverted 17% of total ventilation to the high VA/Q (=10) unit. Within a few sec, VCO2 decreased from 240 to 177 ml/min, which recovered little after 2 min of reduced QT. At onset of decreased QT, a similar decrease in VO2 occurred (300 to 203 ml/min), which mostly recovered to baseline by 2 min.

DISCUSSION: During sustained decreased QT, pulm VCO2 remains depressed but VO2 recovers to baseline because tissue O2 stores are a hundred fold less than CO2. High VA/Q units (reduced pulm blood pressure) contained high PO2, which increased end-tidal PO2 relative to arterial PO2. Thus, non-steady state measurements of pulm VO2 and VCO2 may non-invasively detect the magnitude and time course of a QT decrease. REFERENCES: 1. Anesth Analg 86:S544, 1998. 2. Anesth Analg 88:S409. 1999 SUPPORT: NIH HL-42637.

A560

TITLE: EVALUATION OF THE NICO2 PARTIAL CO2 RE-BREATHING CARDIAC OUTPUT MONITOR IN SPONTANEOUSLY BREATHING ANIMALS
AUTHOR: Kai Kuck Dipl. Ing. Joseph A. Orr, Ph.D.; Dinesh G. Haryadi, M.S.; Scott McJames, B.S.
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Introduction: The partial re-breathing cardiac output measurement has been tested and found effective in mechanically ventilated patients. This method assumes respiratory stability during a brief change in effective ventilation. We tested the accuracy of the partial re-breathing method in spontaneously breathing animals.

Methods: Four mongrel dogs were intubated and anesthetized using inhaled anesthetic and fentanyl. Cardiac output was measured using a pulmonary artery catheter (Dual-Therm, B. Braun) and a partial re-breathing non-invasive cardiac output system (NICO2, Novametrix Medical Systems, Wallingford, CT). The animals were allowed to breath spontaneously and cardiac output was raised using a continuous infusion of dobutamine. Comparisons between the two methods of cardiac output measurement were recorded

Results: The average difference was 0.11 L/min with a standard deviation of the difference was 0.61 L/min. Regression analysis showed a correlation of r= 0.97.

Discussion: The NICO2 system agreed well with the thermodilution over a wide range of cardiac output measurements. During the 50-second re-breathing period, there was no evidence of re-circulation or increase in respiratory effort due to inspired CO2. Further testing is needed to determine the usefulness of the NICO2 system in non-intubated patients breathing through a mouthpiece or mask.

A561

TITLE: ARTERIAL PULSE WAVE ANALYSIS IN OPERATING THEATRE - VALIDATION OF A NEW TECHNIQUE FOR LESS INVASIVE CONTINUOUS CARDIAC OUTPUT MONITORING
AUTHOR: A. Falthauser MD J. Braun, MD; J. Hoitz, MD; L. Lampl, MD
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Background: For early detection of hemodynamic changes a continuous cardiac output monitoring during the perioperative period is needed. We validated a less invasive technique for continuous cardiac output monitoring (PiCCO, Pulsion Medical Systems) based on beat to beat analysis of the area under the systolic part of the arterial pulse wave form (PCCO), using the relation of the systolic area and stroke volume.

Method: In a prospective study 38 patients (classified ASA III, NYHA I-III) undergoing larger urologic intervention were monitored. After standardized induction of general anesthesia a common central venous line and an arterial thermodilution catheter with lumen for arterial pressure monitoring were administered.

Initial transcardiopulmonary thermodilution (COTDa) with a 10 ml iced NaCl 0,9% bolus served for calibrating the system for PCCO monitoring. CO was modulated by hemodilution, volume load, application of catecholamines and surgical intervention. COTDa served as reference method. 380 trippled measurements were taken.

Statistic evaluation was done with Bland-Altman plot, regression and variation analysis.

Results: Bland-Altman: PCCO-COTDa = -0,10±0,82 l/min

Linear Regression: PCCO = COTDa*0,9+0,31; r = 0,96

Discussion: This new easy-to-handle and inexpensive method provides continuous CO-monitoring. Correlation to clinical standard procedures is very good. The technique shows good reproducability and works reliable without calibration for the perioperative period. Due to its low invasiveness and short reaction time compared to semicontinuous CCO-techniques this method has the potential to become a clinical routine method.

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EQUIPMENT, MONITORING AND ENGINEERING TECHNOLOGY

A550

TITLE: CO2 PRODUCTION IS NOT A GOOD SURROGATE CARDIAC OUTPUT INDICATOR

AUTHOR: Kai Kuck Dipl.-Ing. Joseph A. Orr, Ph.D.; Dinesh G. Haryadi, M.S.; Scott McJames, B.S.; Dwayne R. Westenskow, Ph.D.
AFFILIATION: University of Utah, Salt Lake City, UT

INTRODUCTION: Monitoring of CO2 production (VCO2) has been proposed as a noninvasive and continuous surrogate measure for cardiac output (CO). According to the Fick principle VCO2 should be proportional to cardiac output, with the inverse of the difference between mixed venous and arterial CO2 content being the proportionality factor. We compared VCO2 to thermodilution cardiac output over a wide range of cardiac outputs in a controlled animal lab setting.

MATERIAL AND METHODS: Six mongrel dogs were intubated, mechanically ventilated, and maintained on halothane. CO was changed using halothane and dobutamine. Thermodilution (TDCO) measurements (Dual-Therm, B. Braun) based on three 10 ml bolusses of iced saline were performed every 10 minutes. Every 3 minutes a 16 second average of VCO2 (CO2SMO+, Novametrix, CT) was calculated for comparison to thermodilution. Linear regression was performed to compare VCO2 to TDCO.

RESULTS: A total of 245 data points were collected with thermodilution cardiac output ranging from 0.6 to 8.9 L/min. Linear regression coefficients r 2 for data from individual animals were 0.88, 0.86, 0.83, 0.59, 0.42, and 0.32, respectively (n=53, 16, 15, 56, 71, and 37). Linear slopes (ml/min VCO2)/(l/min TDCO) ranged from 5.0 to 19.0. Linear correlation of pooled data was poor at r 2=0.21.

DISCUSSION: VCO2 is not a reliable absolute indicator of cardiac output. It may work as a cardiac output trend indicator in some, but not all individuals.

A551

TITLE: A COMPARISON OF OSCILLOMETRIC BLOOD PRESSURE MEASUREMENT FROM THE UPPER ARM AND HAND

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Introduction. The oscillometric method of blood pressure measurement has been applied at numerous anatomical sites including the upper arm, forearm, wrist, finger, ankle, calf, and thigh. The hand may be an alternative, convenient site for measuring blood pressure in situations where upper arm measurement is problematic, e.g. in the obese patient. The Tuff Glove(tm) (CAS Medical Systems, Inc.) is an inflatable half-mitten designed for use in measuring oscillometric blood pressure from the hand. We compared hand blood pressure measured with the Tuff Glove(tm) to upper arm blood pressure in adult and pediatric volunteers.

Methods. After IRB approval and informed consent, blood pressure measurements were made in the seated position with the hand and upper arm cuffs maintained at the level of the heart. Hand blood pressure was measured using an appropriately-sized Tuff Glove(tm). Upper arm blood pressure was measured using an appropriately-sized arm cuff. A CAS model #9300 blood pressure monitor was used for all measurements. In each volunteer, 2 or 3 sets of measurements were recorded from each arm.

Results. A total of 83 volunteers, 47 female and 36 male were studied. A total of 344 measurement cycles were completed. Subjects ranged in age from 9 to 79. The bias (upper arm minus hand) and precision for systolic, diastolic and mean pressures was -1.9 ± 12.2, 2.9 ± 10.9, and 0.3 ± 11.0 mmHg respectively. Correlation between hand and arm measurements was 0.76, 0.62, and 0.67 for systolic, diastolic and mean pressures respectively.

Conclusions. The bias for each parameter, i.e. systolic, diastolic and mean, was small, suggesting there are no inherent mechanical problems with measuring oscillometric blood pressure from the hand. The variability observed may be due to measurement error inherent to the oscillometric method. Non-simultaneous measurements may also have contributed to variability. Oscillometric blood pressure measurement from the hand is a useful alternative to upper arm measurement.

A552

TITLE: CLINICAL EVALUATION OF THE NICO CARDIAC OUTPUT MONITOR IN PATIENTS UNDERGOING ORTHOTOPIC LIVER TRANSPLANTATION

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Introduction: A non-invasive cardiac output (CO) monitor based on a partial rebreathing CO2 Fick technique was recently approved by the FDA (NICO, Novametrix). No human data are available on performance during high CO states. Patients undergoing orthotopic liver transplantaion (OLT) typically have high CO. We compared the bias and precision of the NICO to thermodilution (TD) CO during OLT.

Methods: Patients had pulmonary artery catheters inserted as part of their routine monitoring. Anesthetic management was directed according to normal clinical indicators. At times during the proecedure when TD CO was measured (usually at least in triplicate at the beginning of expiration), the simultaneous NICO CO was recorded. Differences between the CO techniques were evaluated following the methodology of Bland and Altman. Data are shown as mean (SD) in units of L/min.

Results: Two patients were monitored with a total of 16 CO determinations (TD CO range 9.0 - 14.1 L/min). The NICO CO was 12.4 (1.9) while the TD CO was 12.0 (1.6). The bias between NICO and the average CO was 0.17 and the precision (SD of the bias) was 0.85. Differences between the NICO and average CO fell within the bias ± 2 x precision.

Discussion: The NICO demonstrates adequate accuracy in patients undergoing liver transplantation during high cardiac output states. Use of the NICO technique may represent an advantage over TD CO in that the CO is automatically and continually updated . However, use of the NICO will not eliminate the need for pulmonary artery catheterization during OLT.

A553

TITLE: PERIPHERALLY INSERTED CENTRAL VENOUS CATHETERS (PICC) CAN REFLECT THE CENTRAL VENOUS PRESSURE (CVP): A LABORATORY AND CLINICAL PATIENT STUDY

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Introduction: The use of a PICC line to measure the CVP would obviate the risks and costs of the centrally inserted CVP catheter. Currently, no study is available on the accuracy of a PICC line for CVP measurement.

Method: An initial laboratory study showed a.) passive hydrostatic pressure equilibration across a PICC line to require up to 60 minutes. However, the resistance of the PICC line could be overcome with a standard invasive pressure transducer that infuses a volume of saline at 3 ml/hour; b.) with the PICC line open to atmosphere, infusion of 3 ml/hour created a constant backpressure of 3 mmHg (95% CI 2.9-4.1) and equilibration occurred in seconds. After institutional approval and informed consent from patients in the Intensive Care Unit who had both types of catheters in situ (for clinical reasons), we compared pairs of simultaneous CVP measurements (from PICC lines and centrally inserted CVP catheters).

Results: Individual CVP measurements ranged from 1-32 mmHg. The average of 77 CVP measurements (12 patients) was 11±7 mmHg. (mean ± standard deviation) for the centrally inserted catheters and 12±7 for the PICC lines. The CVP measurements by the 2 techniques had a high degree of correlation (R2=0.88, p<0.01 least squares regression). The bias (PICC larger) was 1±3 mmHg. (p<0.001, Bland and Altman statistical method).

Conclusion: Our results demonstrate that PICC lines can be used to follow CVP trends in a clinical setting but only when used with a pressure infusion device to overcome the natural resistance of the PICC line.

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EQUIPMENT, MONITORING AND ENGINEERING TECHNOLOGY

A542

TITLE: INTRAOPERATIVE ESTIMATION OF CARDIAC OUTPUT FROM PULSED DOPPLER RECORDING OF PULMONARY VENOUS FLOW USING TRANSESOPHAGEAL ECHOCARDIOGRAPHY

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INTRODUCTION: We are unaware of any report evaluating whether cardiac output (CO) can be estimated from pulmonary venous flow (PVF). This study was designed to assess the agreement of CO estimated from pulsed Doppler recording of PVF (DCO) to that measured using thermodilution technique (TCO).

METHODS: After institutional approval and written informed consent, we studied 12 patients undergoing cardiovascular surgery (ages 56 - 77 yr.). Transesophageal echocardiography probe (21369A; Hewlett-Packard, MA) was positioned to obtain the view of a left upper pulmonary vein. PVF recording and TCO measurements were simultaneously performed 2 to 4 times in each patient. From PVF tracings, we measured time-velocity integrals of systolic (TVI-S), early diastolic (TVI-D), and reversal (TVI-R) waves, and RR interval. Heart rate (HR) and minute distance (MD) (cm/min) were calculated as follows: HR = 60/RR interval; MD = (TVI-S + TVI-D - TVI-R) x HR. Linear regression analysis was performed between TCO and MD. From the equation of a regression line, DCO was calculated. Agreement between DCO and TCO was evaluated by plotting the difference against the mean value on the 2 measurements (Bland-Altman plots). Paired Student's t test was used to compare the mean difference with zero, and $P<0.05$ was considered to be significant. Data were expressed as mean ± SD.

RESULTS: In 12 patients, 31 measurements were performed. PVF were recorded clearly in all epochs. There was a good correlation between MD and TCO ($r = 0.86$, $p < 0.0001$, $y = 0.002x + 1.662$). TCO (y) was 4.5±1.3 L/min (2.1 to 7.5 L/min), with close agreement with DCO (x) calculated from MD ($y = 1.07x - 0.12$, -CO =0.20±0.63 L/min, P =NS).

CONCLUSIONS: Despite ignoring the pulmonary vein cross-sectional area, this alternative method for intraoperative measurement of CO seems to be reliable, useful, and highly successful.

A543

TITLE: VALIDATION OF NOVEL INDICATOR/DILUTION METHOD FOR CARDIAC OUTPUT MEASUREMENT USING A METABOLIZABLE AMMONIUM SOLUTION INJECTATE IN SWINE

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INTRODUCTION. A novel technique of measuring cardiac output (CO) using a metabolizable indicator based on monitoring ammonia dilution of a constant rate right atrial infusion was initially examined in a swine model.

METHODS. The protocol was approved by institutional Animal Care and Use Committee. Following ketamine premedication swine were anesthe-tized with isoflurane. Ventilation was controlled via a tracheostomy. A thermodilution cardiac output (TDCO) PA catheter and a femoral arterial (FA) line were placed. TDCO were measured in triplicate (10ml 5°C) immediately prior to and following a 0.1 ml/sec constant rate infusion for 38 sec of 30 or 60 mmol/L of buffered ammonium chloride. Ammonia concentrations were monitored by obtaining blood samples from the PA port prior to the infusion and beginning 12 seconds after initiation of the infusion. CO was varied utilizing deep inhalation anesthesia, fluid, and dopamine. Ammonia assays (Vitros colorimetric AMON kit —Johnson & Johnson, Rochester, NY.) were immediately iced, centrifuged, and quickly measured with 6 replicates of each sample. Arterial/mixed venous blood gases and hematocrit/hemoglobin were also monitored. Ammonia dilution CO (NH3CO) was calculated based upon the measured change in plasma ammonia concentration (corrected for recirculation effect) resulting from a known rate of ammonium infusion.

RESULTS. Six swine (22.7 - 29.5 kg) were studied. CO varied from 0.9 to 8.6 L/min. 41 NH3CO measurements were made. Compared to TDCO the NH3CO yielded a bias of +0.02 and precision (± 2 std dev) of 0.78 L/min. There was no observed dependence identified with the level of hematocrit/hemoglobin concentration.

CONCLUSION. NH3CO provides an accurate estimate of TDCO and appears to be insensitive to hematocrit/hemoglobin concentration. NH3CO may provide benefits over TDCO due to the lack of noise in the monitored parameter that can limit TDCO measurements.

A544

TITLE: PARTIAL CO2 REBREATHING INDIRECT FICK TECHNIQUE FOR NON-INVASIVE MEASUREMENT OF CARDIAC OUTPUT

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OBJECTIVE: Evaluation in animals of a noninvasive cardiac output monitoring system (NICO2, Novametrix Medical Systems, Wallingford CT) based on partial CO2 rebreathing indirect Fick technique.

METHODS: The partial rebreathing technique employs a differential form of the Fick equation for calculating cardiac output (Qt) noninvasively. Changes in the CO2 elimination rate and in partial pressure of end-tidal CO2 in response to a brief change in effective ventilation (by adding serial dead space to the breathing circuit) are used to measure pulmonary capillary blood flow (Qpcbf). A noninvasive estimate of intrapulmonary shunt fraction (Qs/Qt) based on oxygen saturation from pulse oximetry and inspired oxygen fraction is used to compute cardiac output [$Qt = Qpcbf/(1 - Qs/Qt)$]. The performance of the NICO system was compared with iced-injectate bolus thermodilution cardiac output (TDco) measurements in 6 dogs (n=246, TDco range = 0.60 - 8.87 L/min). Qt was varied using dobutamine, halothane and clamping of the inferior vena cava.

RESULTS: The average difference between measurements made with the two devices was -0.07 L/min. The standard deviation of the difference was 0.7 L/min. Correlation was $r = 0.94$.

CONCLUSION: The NICO is simple to use, automated, and is based on the well accepted Fick principle. The results of this study show that NICO performed as well, and in some cases better, than other currently available noninvasive cardiac output techniques.

A545

TITLE: PERIPHERAL VENOUS PRESSURE PREDICTS CENTRAL VENOUS PRESSURE IN THE POST-ANESTHESIA CARE UNIT

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The incidence of pneumothorax, arterial puncture and infection associated with CVP line placement may rise exponentially if less than ideal anatomical or technical circumstances exist. The use of peripheral venous pressure (PVP) monitoring in lieu of CVP in special subsets of patients may decrease these risks and associated costs. Data on whether PVP predicts CVP after surgery are sparse.

Methods: Fifty spontaneously ventilating patients following non-cardiac surgery were studied. All patients had indwelling peripheral venous and CVP lines. Both transducers were zeroed at the phlebostatic axis (mid-axillary line and 4th intercostal space). If typical sinusoidal wave forms were not seen on PVP tracings, the patient was excluded from the study (n=3). Following a 2 min. stabilization period, readings were made on a strip chart recorder. PVP and CVP data were pooled within commonly used clinical criteria of low (0-5), medium (6-12) and high (>12) CVP (mmHg) to determine the degree of agreement between these measurements.

Results: PVP and CVP data were 7 +/- 4 mmHg and 5 +/- 4 mmHg, respectively. PVPwas consistently greater than CVP by 2 mmHg using Bland-Altman plots(not shown). PVP correlated highly to CVP ($y=1.7+0.9XPVP$, $r=.88$) (Figure). CVP and PVP corrected(PVP-2) pooled data showed an overall high degree of agreement in the low (81%), medium (64%) and high (50%) ranges (Table). No patient with a low PVP had a high CVP, and conversely, no patient with a high PVP had a low CVP.

Conclusions: In adults who have an adequate sinusoidal PVP tracing, PVP predicts CVP non-invasively using common clinical ranges of right atrial pressure in the PACU.

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A474

TITLE: CLINICAL ACCURACY OF A NEW NON-INVASIVE CARDIAC OUTPUT MONITOR

AUTHOR: Robert G Loeb MD Elizabeth A Brown, RN; James A DiNardo, MD; Joseph A Orr, PhD; Rich C Watt, MSEE

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INTRODUCTION: This study evaluates the clinical accuracy of a new non-invasive cardiac output monitor, compared with invasive bolus and continuous thermodilution.

METHODS: With IRB approval, informed consent was obtained and data collected from 12 patients during and after cardiac surgery. After induction of anesthesia a pulmonary artery catheter was placed; invasive cardiac output was measured by bolus thermodilution (triplicate determinations, 10cc room temperature injectate) and continuous (pulsed) thermodilution using a Baxter Vigilance Monitor (Baxter Healthcare Corporation, Irvine, CA). Continuous non-invasive cardiac output measurements were obtained from a Novametrix NICO monitor (Novametrix Medical Systems, Wallingford, CT). This system continuously measures airway flow, pressure, and CO2 concentration. It controls a rebreathing valve placed between the ET tube and the Y-piece of the breathing circuit which introduces approximately 150cc of deadspace for 50 seconds every 3 minutes. An estimate of pulmonary blood flow is achieved by tracking the CO2 concentration and elimination. Cardiac output is calculated by correcting for shunt.

RESULTS: The NICO technique had a bias and precision of -0.19 ± 1.16 when compared to bolus thermodilution. The CCO technique had a bias and precision of 0.28 ± 0.75.

DISCUSSION: Bolus thermodilution has long been considered the only practical and reliable method of clinical cardiac output monitoring. A recent innovation uses pulsed energy to achieve nearly continuous thermodilution monitoring. Although this technique is continuous and easier to use, it still requires pulmonary artery catheterization and is therefore used in only a small percentage of anesthetic procedures. The Novametrix NICO monitor is a new, non-invasive, device that provides automatic, continual cardiac output determinations in ventilated patients. We found that it had adequate precision and accuracy, similar to that of invasive continuous thermodilution.

A475

TITLE: COMPARISON OF THREE DIFFERENT TECHNOLOGIES OF MEASURING CARDIAC OUTPUT (CO) IN PATIENTS UNDERGOING OPEN HEART SURGERY

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INTRODUCTION: A recently developed novel lithium indicator dilution technology (LIDCO) for the measurement of CO is quick to set up and avoids pulmonary artery catheterisation (1). The aim of our study was to compare LIDCO with two different thermal based systems to obtain CO in patients undergoing coronary artery bypass grafting (CABG).

METHODS: After informed consent 17 patients scheduled for CABG were studied at three predefined points (A: pre cardiopulmonary bypass, B: 10 min after bypass, C: 10 min after chest closure). In each case LIDCO, bolus CO (BCO) and continuous CO (CCO) were determined simultaneously. Statistical analysis was performed by linear regression and Bland-Altman plots.

RESULTS: LIDCO on x-axis: r2 range 0.67 to 0.79 BCO, 0.44 to 0.79 CCO. BCO on x-axis: r2 range 0.53 to 0.8 LIDCO, 0.35 to 0.41 CCO. CCO on x-axis: r2 range 0.0482 to 0.5 BCO. BCO generally overestimated CO compared to LIDCO -0.99 to -1.49 l/min and CCO -0.41 to -1.22l/min. Limits of agreement for LIDCO compared to the thermal methods: 1.28 to 2.48 l/min and between the two thermal methods 2.38 to 2.76 l/min.

CONCLUSIONS: The higher correlation and the better agreement seen between LIDCO and either thermodilution system strongly suggests that it is the more precise estimate of CO in patients undergoing CABG. These findings confirm earlier work (2).

REFERENCES: 1)Critical Care Medicine 25:1798-1800, 1997; 2)British J of Anaesth 79:770-775, 1997

A476

TITLE: GRAPHIC ANESTHESIA DISPLAY ENHANCES SITUATION AWARENESS DURING HYPOVOLEMIA

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An anesthesia information display was designed specifically for visually representing cardiovascular physiology.1 We tested the display using a full-body patient simulator with two cardiovascular scenarios and two using pulmonary scenarios. We expected improved performance for the cardiovascular scenarios, but poorer performance for the pulmonary scenarios.

Methods: Twelve residents and faculty members from the Department of Anesthesiology participated as volunteers in the evaluation. They each observed four 10-minute scenarios, two using a traditional display and two using the new display. The simulation was frozen every 2.5 minutes and a set of questions asked to assess situation awareness.

Results: During hypovolemia, questions asking about whether variables were high, normal or low were more often answered correctly with the graphic display (63%) than with the traditional display (46%). Questions asked about the overall status of the patient were also answered more correctly with the graphic display (63%) than with the traditional display (42%).

Conclusions: During hypovolemia, situation awareness improved when using a graphic display designed to show cardiovascular physiology. The number of correct answers to high/low/normal and status questions was higher with the graphic display than with the traditional display. Arrhythmia and bronchospasm were seen better with the traditional display. From this study we learn the importance of keeping the traditional ECG waveform and some digital values on a new display.

References:

Blike G. T. Anesthesiology, 1997, V87, No3A, Sep A458.

A477

TITLE: HYPOTHERMIA PREVENTS INCREASE OF GASTRIC REGIONAL CO2 DURING CARDIOPULMONARY BYPASS

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AFFILIATION: University of Mississippi School of Medicine, Jackson, Mississippi USA

INTRODUCTION: Ischemic gastrointestinal complications of cardiac surgery are uncommon, but significant, sources of perioperative morbidity and mortality. It has been suggested that early detection of and intervention in mucosal hypoperfusion during cardiopulmonary bypass (CPB) may improve outcome (1). We investigated the utility of air gastric tonometry measurement of regional CO2 (rCO2) as a reflection of perfusion during CPB.

METHODS: Following approval of the institutional review board and informed consent, 10 patients undergoing cadriac surgery had 16Fr. gastric tonometers placed in the stomach following induction of anesthesia. The tonometers utilized a 10cc air-filled balloon to measure rCO2 every 10 minutes. The process was controlled by the TONOCAP device (Datex, Finland). rCO2 and temperature were recorded at the start of CPB, at the nadir of cooling, at the start of rewarming, just before separation from CPB, and folowing protamine administration. Data were analyzed using ANOVA and Dunnett's test for comparison between groups.

RESULTS: rCO2 did not increase during cooling on CPB. rCO2 increased only during rewarming and following CPB.

DISCUSSION: We observed an increase in rCO2 only during rewarming on CPB. Hypothermia appears to prevent increase in rCO2. This is in contradiction to a previous study which demonstrated an increase in rCO2 during CPB, regardless of temperature (2). The TONOCAP functions well under the rapidly changing conditions of CPB and is a useful monitor of mesenteric perfusion. 1) Crit Care Med 21:S55-68, 1993. 2) Anasthesiol Intensivmed Notfallmed Schmerather 33:S85-90, 1998.

1069

Comparison of Non-Invasive, Partial Rebreathing Cardiac Output with Invasive Bolus and Continuous Thermodilution

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Summary: We compared the accuracy of a new non-invasive cardiac output technique (partial CO_2 rebreathing) with an invasive continuous cardiac output technique (pulsed thermodilution), using bolus thermodilution as the standard. In twenty one patients, studied during and after cardiac surgery, the accuracy of the two techniques was similar.

Introduction: A reliable non-invasive cardiac output monitor could enhance patient safety and reduce risk. This study evaluates a new non-invasive method of cardiac output measurement based on partial rebreathing and a differential form of the CO_2 Fick equation. We compared this technique with bolus thermodilution and continuous (pulsed) thermodilution.

Methods: With Human Subjects Committee approval, informed consent was obtained and data collected from 21 human subjects during and after cardiac surgery. After induction of anesthesia, a pulmonary artery catheter was placed; invasive cardiac output was measured by bolus thermodilution and continuous (pulsed) thermodilution using a Baxter Vigilance Monitor (Baxter Healthcare Corporation, Irvine, CA). Continuous non-invasive cardiac output measurements were obtained using a prototype device (Novametrix Medical Systems, Wallingford, CT). This system continuously measures airway flow, pressure, and CO_2 concentration. It controls a rebreathing valve, placed between the ET tube and the Y-piece of the breathing circuit, which introduces approximately 150cc of deadspace for 50 seconds every 3 minutes. This causes a transient rise in End Tidal CO_2 (2-5 mmHg) and a commensurate decrease in VCO_2. A non-invasive estimate of pulmonary blood flow is achieved by tracking CO_2 concentration and elimination. Cardiac output is calculated from pulmonary blood flow by correcting for shunt (estimated from SpO_2).

Results: The non-invasive rebreathing technique (left scatter plot) yields a bias and precision of 0.11 $\pm$ 0.95 when compared to bolus thermodilution. The continuous thermodilution technique (right scatter plot) yields a bias and precision of -0.36 $\pm$ 1.00.

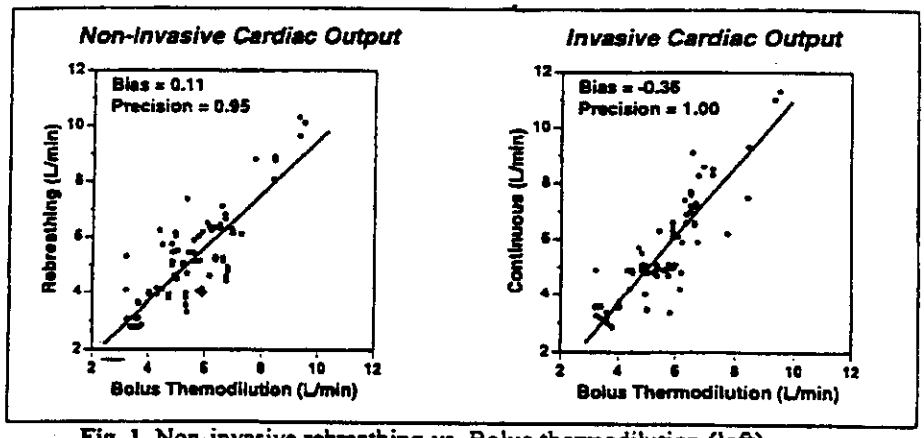

Fig. 1. Non-invasive rebreathing vs. Bolus thermodilution (left) and Continuous thermodilution vs. Bolus thermodilution (right)

Discussion: Bolus thermodilution measurements have long been considered the only practical and reliable method of clinical cardiac output monitoring. A recent innovation uses pulsed energy to achieve continuous thermodilution monitoring. Although this technique is continuous and easier to use, it still requires pulmonary artery catheterization and is therefore used in only a small percentage of anesthetic procedures. A reliable, inexpensive, and non-invasive (low risk) cardiac output monitor could enhance patient care during most anesthetic procedures. We evaluated a new non-invasive rebreathing technique for determining cardiac output. It compared favorably to continuous thermodilution when evaluated against conventional bolus measurements.

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INFLUENCE OF ERROR IN ESTIMATION OF INTRAPULMONARY SHUNT ON THE MEASUREMENT OF CARDIAC OUTPUT USING REBREATHING TECHNIQUES

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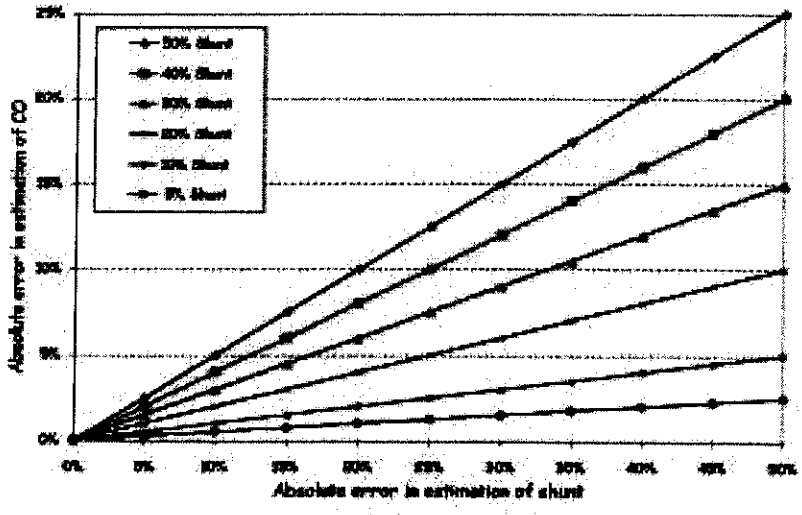
SUMMARY: Rebreathing cardiac output (RBco) techniques typically measure pulmonary capillary blood flow (PCBF) and use an invasive or noninvasive estimate of intrapulmonary shunt (Qs) to compute cardiac output (CO). We studied the effect of inaccuracy in the measurement of Qs on measurement of RBco. The results indicate an accuracy of ± 20% in the estimation of Qs is sufficient to ensure that the error in the estimation of CO is less than ± 5%, even under conditions of 25% Qs.

Introduction: Advances in technology have now enabled us to implement an automatic partial CO_2 rebreathing technique for near continuous measurement of CO in operating rooms and intensive care units on mechanically ventilated patients.[1-3] RBco techniques typically measure PCBF and use an estimate of Qs to compute CO (RBco=PCBF+Qs). Measurement of Qs involves calculation of arterial and mixed venous oxygen contents. When mixed venous blood samples are not readily available, oxygen tension-based indices such as alveolar to arterial oxygen tension differences ($P[A-a]O_2$), arterial oxygen tension to alveolar oxygen tension ratio (PaO_2/PAO_2), PaO_2 to FiO_2 ratio (PaO_2/FiO_2) and respiratory index (RI) are widely utilized to reflect on Qs. Noninvasive methods of estimating Qs based upon oxygen saturation from pulse oximetry (SpO_2) and FiO_2 measurements can also be used in conjunction with iso-shunt plots[4] to estimate Qs. We studied the effect of inaccuracy in the measurement of Qs on measurement of RBco.

Methods: After IACUC approval, oleic acid pulmonary injury (true Qs = 39 ± 12 %, mean ± 1SD, n=34) was created in four mongrel dogs to study the reliability of invasive versus noninvasive estimates of Qs. Using a model of pulmonary circulation[4], the absolute error in the estimation of CO was calculated for different absolute values of error (0 to 50%, in steps of 5%) in the estimation Qs for given values of Qs (5 to 50%).

Results: The noninvasive estimates of Qs compared well with invasive estimates of shunt. Including the noninvasive Qs estimates in the calculation of RBco improved the bias from -1.37 L/min to +0.02 L/min. The error relationship was found to be linear (see Figure). Under conditions of high Qs (=50%), an error of ±20% in the measurement of Qs shunt leads to an error of ±10% in the calculation of cardiac output. Under normal conditions (Qs = 5-10%), an error of ±20% in the measurement of Qs leads to an error of less than ±2% in the calculation of CO.



Discussion: Errors introduced in the calculation of Rbco, from inaccuracy in the estimation of Qs, is within the range of the confidence interval of the standard it is usually compared to (bolus thermodilution). As long as Qs is taken into consideration while computing RBco the error introduced by the inaccuracy in estimation of Qs is not significant.

References:

1. Anesth Analg, 1998;86,SCA53.
2. Anesthesiology, 1998, 89(3A)A534.
3. Anesthesiology, 1998, 89(3A)A542.
4. JF Nunn, Applied Respiratory Physiology, Butterworth-HeinemannLtd, Oxford. 1993.

Reference: *Journal of Clinical Monitoring and Computing* 1999, 15 (3-4):256-57.

1071

CLINICAL EVALUATION OF PARTIAL CO_2 REBREATHING FICK TECHNIQUE FOR NONINVASIVE MEASUREMENT OF CARDIAC OUPUT

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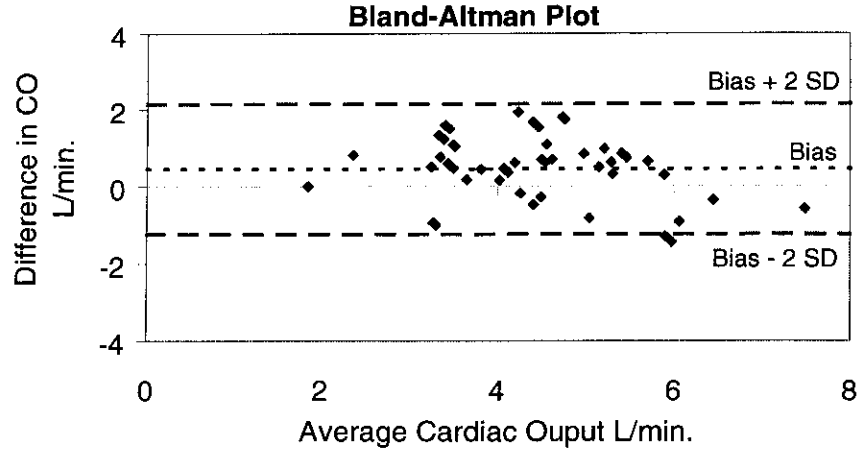
SUMMARY: Advances in technology have enabled us to implement an automatic partial CO_2 rebreathing technique for near continuous noninvasive measurement of cardiac output (CO) in mechanically ventilated patients. Results from comparing a prototype system with standard bolus thermodilution in patients undergoing cardiac surgery indicate good agreement between the two methods of CO measurement.

Introduction: The partial CO_2 rebreathing technique uses a differential form of the Fick equation to calculate cardiac output (CO). The ratio of the change in end-tidal CO_2 and the change in CO_2 excretion, in response to a brief period of rebreathing, gives a non-invasive estimate of the CO. In patients undergoing cardiac surgery we tested a prototype of the system that included improved signal processing algorithms, a noninvasive estimation of intrapulmonary shunt, and a disposable dead space adapter.

Methods: After IRB approval and patient consent the system was tested in ten patients (5 Male, 5 Female, Age 56-80 Years) undergoing cardiac surgery. End-tidal CO_2 was measured using a mainstream CO_2 analyzer and a disposable pneumotachograph (COSMO®, Novametrix Medical Systems, Wallingford, CT). CO_2 production was calculated for each breath as the integral of the flow and CO_2 concentration. Actuation of a pneumatic valve under computer control resulted in breathing circuit changes, which increased airway dead space by 120 ml, thereby causing partial rebreathing of exhaled gas. The valve was actuated for 50 seconds once every 3 minutes. Changes in CO_2 excretion and $etCO_2$ were used to calculate the partial CO_2 rebreathing CO using the differential Fick equation. Noninvasive estimates of shunt from SpO_2 and FiO_2 measurements were used to correct for intrapulmonary shunts. An average of three consecutive thermodilution cardiac output (TDco) measurements, made during end expiration, were compared with corresponding partial CO_2 rebreathing cardiac output measurements. Measurements made during the first 45 minutes after bypass were discarded since thermal noise can make the TDco measurement unreliable.

Results: A total of 48 comparisons were made with CO ranging from 1.85 to 7.78 L/min. Bland-Altman analysis resulted in a bias of 0.46 L/min with a precision (1SD) of ±0.85 L/min.



Discussion: Results indicate that the improvements in signal processing algorithms and the use of a noninvasive estimation of shunt help improve the agreement between partial CO_2 rebreathing CO measurements and TDco measurements. The partial CO_2 rebreathing system is completely automatic and can provide frequent, nearly continuous measurements of CO. The partial CO2 rebreathing technique may be a clinically acceptable method for measurement of CO.

Reference: Journal of Clinical Monitoring and Computing 1999, 15 (3-4):255-56.

1072

PERFORMANCE OF A NEW 'REBREATHING' VALVE FOR NON-INVASIVE CARDIAC OUTPUT ESTIMATION

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Summary: A new double diagraphm rebreathing valve (2.4x2.7x2.9in) used with a new non-invasive cardiac output monitor (Novametrix Medical Systems) has been evaluated in terms of resistance, dead space, effects on measured flow and bench performance with a ventilator. The monitor computes a non-invasive estimate of cardiac output using the partial rebreathing method (1). With this method cardiac output is calculated as the ratio of the change in CO_2 elimination and end-tidal CO_2, in response to a brief period of re-breathing.

Methods:

Resistance: The pressure drop in both inspiratory and expiratory directions (using static flows from 5 to 80 LPM) was measured by a Timeter RT-200 connected across a 7.0 ET tube with and without the CO_2/flow sensor/valve assembly in both normal (i.e. no rebreathing) and rebreathing modes.

DeadSpace: The deadspace of the valve and sensor assembly was estimated dimensionally and by measuring the increase in Fowlers deadspace with the sensor and valve in-circuit vs out of circuit.

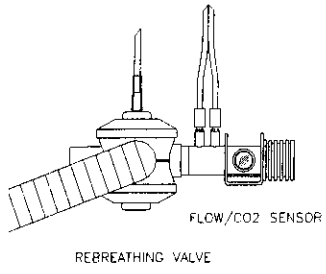
Effect on Flow Measurements – The change in inspiratory flow rate (due to changes in inlet conditions) was measured by the monitor's flow sensor. A static flow ranging from 5 to 80 LPM was adjusted using a Timeter RT-200 connected to the outlet of the CO_2/flow sensor and valve assembly.

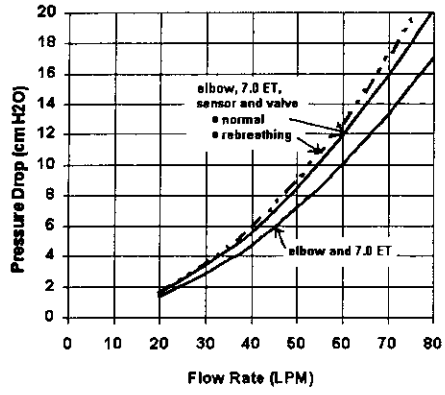
Performance under 'pressure' – The valve assembly in normal, rebreathing and disconnect (i.e control line disconnected from monitor) modes was tested with a Siemens 300 ventilator and low compliance (5 ml/cmH_2O) static test lung. The ventilator was varied over a range of PEEP (0-50 cmH_2O), PIP (up to 110 cm H_2O), and I:E ratio values under different ventilatory modes. The $FiCO_2$, and VCO_2 inspired values and capnogram were monitored as an indication of rebreathing.

Results:

Resistance: The inspiratory resistance of the valve and sensor relative to the 7.0 ET with elbow is shown.

DeadSpace – The deadspace of the sensor/valve assembly as measured in normal mode was 32 ml.





Effect on Flow - The percent difference between the normal and rebreathing modes for both inspiratory and expiratory flow less than 1% at all flow rates.

Performance under 'pressure' – Under all conditions tested, the valve performance did not change (ie. No rebreathing under normal and disconnect modes and no change in rebreathing during rebreathing mode).

Discussion:

The flow/CO_2 sensor/valve adds a small and clinically acceptable amount of deadspace and resistance to the breathing circuit. The valve performs reliably under a wide range of ventilator settings and its presence does not alter the flow measurement used to estimate cardiac output.

References:

(1) Capek, JM and Roy, RJ, IEEE Trans BME, 1988, p 653-661.

Reference: Journal of Clinical Monitoring and Computing 1999, 15 (3-4):239.

1073

RELIABILITY OF INVASIVE VERSUS NONINVASIVE INDICES IN REFLECTING INTRAPULMONARY SHUNT

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Introduction: Measurement of intrapulmonary shunt (Qs/Qt) is widely used as a standard for monitoring disturbances of pulmonary oxygen transfer in critically ill patients[1,2]. It involves calculation of arterial and mixed venous oxygen contents. When mixed venous blood samples are not readily available, oxygen tension-based indices such as alveolar to arterial oxygen tension differences ($P[A\text{-}a]O_2$), arterial oxygen tension to alveolar oxygen tension ratio (PaO_2/PAO_2), PaO_2 to FiO_2 ratio (PaO_2/FiO_2) and respiratory index (RI) are widely utilized to reflect on Qs/Qt. Noninvasive methods of estimating Qs/Qt based upon oxygen saturation from pulse oximetry (SpO_2) and FiO_2 measurements can also be used in conjunction with iso-shunt plots[3] to estimate Qs/Qt. We studied the reliability of invasive versus the noninvasive indices of Qs/Qt.

Methods: With IACUC approval, anesthesia was induced in four mongrel dogs with ketamine and maintained with halothane/pancuronium/O2. Each animal was instrumented with a pulmonary artery thermodilution catheter and an arterial line. After obtaining baseline measurements, a pulmonary capillary leak was created by a bolus infusion of oleic acid (0.08 ml/Kg) into the right atrium. Serial arterial and venous blood gases and TDco measurements were made once every 20 minutes until the PaO_2 decreased to one third of its baseline value when FiO_2 was 100%. The true Qs/Qt obtained from arterial and mixed venous blood gas measurements were compared with invasive and noninvasive indices of Qs/Qt.

Results: The oleic acid pulmonary injury produced a true Qs/Qt of 39 ± 12 % (mean ± 1SD) (n=34). The table shows how well each of the indices performed.

Predictor	r
$RI = P[A\text{-}a]O_2/PaO_2$	0.60
$[CcO_2\text{-}CaO_2]/[3.5+(CcO_2\text{-}CaO_2)]$	0.93
PaO_2/PAO_2	-0.83
$PaO_2/FiO2$	-0.83
$P[A\text{-}a]O_2$	0.83
Iso-shunt plot (SpO_2, FiO_2)	0.85

Conclusion: Even though there is no real substitute for mixed venous oxygen content in the estimation of Qs/Qt, the noninvasive estimates compares well with the invasive estimate of shunt.

References:

1. Dean MJ, et al., Crit Care Med, 13(12):1029-1033, 1985.
2. Cane RD, et al., Crit Care Med, 16(12):1243-1245, 1988.
3. Nunn JF. Applied Respiratory Physiology. 4th Ed, Butterworth Ltd, Oxford, 1993.

Reference: Crit Care Med 1999, 27(1, Suppl.):A116.

1074

EVALUATION OF PARTIAL RE-BREATHING CARDIAC OUTPUT MEASUREMENT IN ANIMALS

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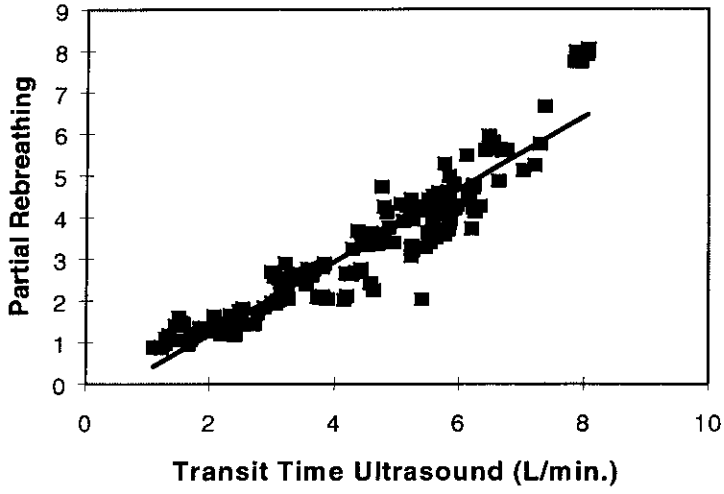
Summary: The partial CO_2 rebreathing method of non-invasive cardiac output measurement was tested. The system uses algorithms to compensate for intra-pulmonary shunt and changes in end-tidal alveolar CO_2 partial pressure differences.

Introduction: The non-invasive partial rebreathing method uses a differential form of the CO_2 Fick equation to calculate cardiac output. The ratio of change in end-tidal CO_2 and CO_2 excretion, in response to a brief period of re-breathing, gives a non-invasive estimate of cardiac output. This method assumes that the difference between end-tidal and arterial CO_2 content does not change during re-breathing. We have developed a partial re-breathing algorithm based on a two-compartment lung model which corrects the measurement when this assumption is false. This computer model compensates for the changing end-tidal to arterial CO_2 gradient during partial rebreathing.

Methods: The mathematical model separates the alveoli into completely perfused and non-perfused regions. End-tidal CO_2 concentration is the weighted sum of the two regions. Gas concentration in the un-perfused region is a slowly changing version of the inspired concentration, which can be calculated from the capnogram and airway flow signals. Partial rebreathing cardiac output calculations are made using the perfused alveolar CO_2 content as estimated by the computer model.

Five mongrel dogs, anesthetized with halothane were instrumented with a transit time ultrasonic flowmeter (Transonic Systems, Ithaca NY) placed directly around the pulmonary artery. Cardiac output was raised and lowered using a continuous infusion of epinephrine and dobutamine and was lowered using increased inhaled concentration of halothane. Average cardiac output measurements from the invasive and non-invasive devices were compared and recorded every 10 minutes.

Results: The figure below shows partial re-breathing cardiac output estimates versus the invasive ultrasound



measurements. Regression analysis gives a correlation of r= 0.94 with a slope of 0.86 and an offset of 0.51 L/min. Shunt correction based on arterial blood gas data improved the slope and offset to 1.04 and –0.78 respectively. The average error was –1.1 and standard deviation of the error was 0.62 L/min, N = 176.

Discussion: The two compartment model seems to take into account the effects of alveolar dead-space on the end-tidal CO_2 measurements in the differential Fick equation. The rebreathing method does not measure shunted blood, thus, partial rebreathing will under estimate cardiac output. The partial rebreathing system is completely automatic and can give continuous measurements.

Reference: Crit Care Med 1999, 27(1, Suppl.):A114.

1075

ARTERIAL BLOOD GAS MEASUREMENTS IMPROVE NONINVASIVE CARDIAC OUTPUT ESTIMATES FROM PARTIAL CO_2 REBREATHING FICK TECHNIQUE

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Introduction: The partial CO_2 rebreathing Fick technique in combination with FiO_2 monitoring and pulse oximetry can be extended to provide noninvasive and near continuous cardiac output measurements (NICO). The estimation of intrapulmonary shunt fraction needed for this method may be improved by intermittent arterial blood gas measurements, but at the cost of rendering the method more cumbersome and invasive. We measured the improvement in NICO performance when blood gas measurements are taken into consideration.

Methods: After obtaining IRB approval and informed patient consent, NICO data was collected at four hospitals during mostly cardiovascular bypass surgeries in 42 patients (30-85 yrs, 46-141 kg) and post-operatively in the ICU. Deadspace for rebreathing was added to the breathing circuit for fifty seconds every three minutes. A modified CO_2SMO Plus! respiratory monitor (#Novametrix, Wallingford, CT) provided breath-to-breath endtidal CO_2, CO_2 production, and SpO_2 values, which were stored for later analysis on a laptop computer. Blood gases, FiO_2, and thermodilution cardiac outputs were obtained as dictated by clinical routine. After rejecting artifacts, pulmonary capillary blood flow was estimated using the CO_2 Fick method. This was used to estimate cardiac output after estimating the shunt fraction based on an algorithm suggested by Nunn[1]. One pass through the data was made using the recorded blood gases and FiO_2 values as inputs to the shunt fraction algorithm, and another pass using default values. NICO performance was evaluated against thermodilution cardiac output using linear regression and Bland-Altman statistics.

Results:

Blood Gases	n	r	Bias (Mean Error)	Precision (SD of Error)
Yes	132	0.82	0.34 l/min	0.88 l/min
No	134	0.78	0.69 l/min	0.94 l/min

Conclusion: As expected, considering blood gases in the NICO algorithm does improve NICO performance, however to a relatively small degree. NICO may be completely noninvasive and still deliver clinically useful cardiac output estimations.

[1] Nunn JF. Nunn's Applied Respiratory Physiology, 4th Ed, Butterworth Ltd, Oxford, 1993

Reference: Crit Care Med 1999, 27(1, Suppl.):A109.

1076

Anesthesiology
V89, No 3A, Sep 1998

A544

TITLE: NONINVASIVE CARDIAC OUTPUT DETERMINATION UTILIZING THE METHOD OF PARTIAL CO2 RE-BREATHING. A COMPARISON WITH CONTINUOUS AND BOLUS THERMO-DILUTION CARDIAC OUTPUT.

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AFFILIATION: Department of Anesthesiology,
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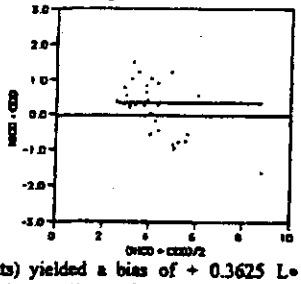
Introduction. The development of a noninvasive monitor to measure cardiac output (NICO) has been a long desired goal. A system that utilizes application of the Fick method with CO2 has been developed. The equipment uses standard capnometry and flow sensors to determine CO_2 production and end-tidal CO_2 without and during rebreathing episodes to calculate pulmonary capillary blood flow (PCBF). PCBF is then converted to cardiac output following a correction for the pulmonary shunt, which is derived from F_IO_2 and SpO_2 data.

Methods. Following IRB approval and informed consent, NICO monitoring was performed utilizing a modified Novametrix CO_2SMO Plus!™ respiratory parameter monitoring system (Novametrix, Medical Systems, Inc, Wallingford, CT). Cardiac output was also determined via the Abbott QVue™ (Abbott Laboratories, N. Chicago, IL) continuous cardiac output (CCO) and at intervals (average of triplicate measures) utilizing 10 ml room temperature normal saline injectate via a closed injection set for thermodilution boluses (TDCO) using the same Abbott QVue™ system.

Results. Bland-Altman plot of the NICO vs. CCO (n=48



measurements) yielded a bias of + 0.3625 L• min^{-1} and a precision (± 2σ or 95% confidence interval) of -1.08 – +1.80 L• min^{-1}. NICO vs. TDCO yielded a bias of + 0.26 L• min^{-1} and a precision of -1.75 – +2.28 L• min^{-1}. Precision between the individual determinations of the triplicate TDCO was ± 1.15 L• min^{-1}.

Discussion. The noninvasive NICO system tested provided measures of cardiac output that was similar to those provided by the invasive CCO and TDCO systems.

Reference:

JM Capek and RJ Roy, IEEE Trans BME, 1988, p 653-661.

1077

Anesthesiology
V89, No 3A, Sep 1998

ENGINEERING TECHNOLOGY

A542

Evaluation of Partial Re-breathing Cardiac Output Measurement During Surgery

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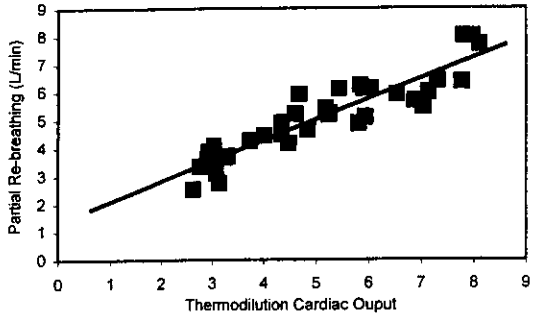
Introduction: Partial re-breathing is a non-invasive method of measuring cardiac output. The method is based on a differential form of the CO_2 Fick equation. The relative change in VCO_2 and $etCO_2$ in response to addition of dead space to the breathing circuit is used to measure cardiac output. Because partial re-breathing does not measure the shunted blood flow, our system used periodic arterial blood gas data to compensate for shunted blood flow.
Methods: After IRB approval and patient consent the system was tested in 10 patients (8 male, 2 female, age 33-78 years) undergoing cardiac surgery. End-tidal CO_2 was measured using a combination mainstream CO_2 analyzer and pneumotachograph (COSMO+, Novametrix Medical Systems, Wallingford CT). CO_2 production was calculated as the integral of the flow and CO_2 signal. Every 3 minutes, a pneumatic valve was actuated for 50 seconds causing 120 ml of dead space to be added to the breathing circuit. The resulting changes in VCO_2 and $etCO_2$ were used to calculate cardiac output.

An average of three consecutive thermodilution cardiac output (TDco) measurements made during end-expiration were compared with corresponding partial CO_2 re-breathing cardiac output measurements. Measurements made during the first 45 minutes after bypass were discarded since thermal noise can make the TDco measurement unreliable.
Results: A total of 36 cardiac output comparisons were made ranging from 2.63 to 8.1 L/min. Bland –Altman analysis resulted in a bias of 0.02 and confidence interval (bias ± 2σ) of –1.40 to 1.45 L/min. Regression analysis gives an r=0.92.



Discussion: The partial re-breathing method gives clinically useful cardiac output measurements during cardiac surgery. We selected cardiac surgery cases because PA catheters were in place to allow comparison with thermodilution cardiac output measurements. Because this method is non-invasive and completely automatic, we expect that it may allow cardiac output monitoring in any general anesthetic in which PA catheterization is not indicated.

A543

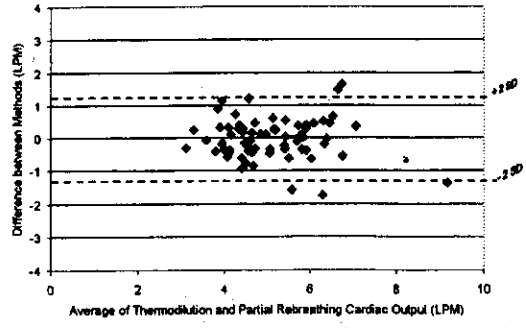
Title: CLINICAL EVALUATION OF A NEW NONINVASIVE METHOD OF CARDIAC OUTPUT MEASUREMENT– PRELIMINARY RESULTS IN CABG PATIENTS

Authors: Louis Guzzi MD*, Michael B Jaffe PhD*** and Joseph A Orr PhD**
Affiliations: *Dept. Anesth., Florida Hospital, Orlando, FL, **Dept. Anesth., University of Utah, Salt Lake City, UT 84132

Introduction: The opportunity to measure cardiac output non-invasively has applications in emergency, transport and critical care medicine. We have been evaluating in the OR a unique noninvasive method of cardiac output measurement which uses a differential form of the CO_2 Fick equation and is known as the non-invasive partial rebreathing method.(1) The ratio of the change in CO_2 elimination and CO_2 content, in response to the brief addition of dead space, corrected for shunt provides a non-invasive estimate of cardiac output. We have compared this new method in CABG patients during pre-bypass against the currently accepted technique of bolus thermodilution.

Methods: Following IRB approval and written informed consent, 27 mechanically ventilated patients undergoing CABG procedures (n=27, age 63 ±11 years) with a PA catheter were studied. A combined flow/CO_2 sensor and a computer controlled rebreathing valve was positioned between the ET tube of the patient and Y piece of the breathing circuit. The sensors and valving were connected to a prototype non-invasive cardiac output monitor*** which performed the data acquisition, valve control and calculation and display of cardiac output. Approximately 150-200 cc of volume was added to the breathing circuit every 3 minutes for approx. 50 seconds causing nominally a 3-5 mmHg rise in $etCO_2$ and 50-75 ml/min decrease in VCO_2. Bolus thermodilution (10 ml at room temp.) was performed in triplicate or greater if the variability between measurements was judged to be excessive by the attending anesthesiologist.

Results: Partial rebreathing cardiac output values were chosen to be within 5 minutes of bolus thermodilution determinations (n=69).Overall bias and precision is -0.01±0.62 LPM and r=0.85.



Conclusions: The present study shows that partial rebreathing cardiac output is a viable clinical method of cardiac output measurement in this patient group. Using this method, noninvasive cardiac output measurement may be a viable alternative to more invasive methods that have a significant risk of morbidity.

References:
(1) Capek, JM and RJ Roy, IEEE Trans BME, 1988, p 653-661.

Study supported by ***Novametrix Medical Systems, Inc.

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A536

TITLE: Comparison of a New Non-Invasive Cardiac Output Technique with Invasive Bolus and Continuous Thermodilution

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Background: A reliable non-invasive cardiac output monitor could enhance patient safety and reduce risk. This study evaluates a new non-invasive method of cardiac output measurement based on partial rebreathing and a differential form of the CO_2 Fick equation. We compared this technique with bolus thermodilution and continuous (pulsed) thermodilution.

Methods: With Human Subjects Committee approval, informed consent was obtained and data collected from 5 human subjects during and after cardiac surgery. After induction of anesthesia a pulmonary artery catheter was placed; invasive cardiac output was measured by bolus thermodilution and continuous (pulsed) thermodilution using a Baxter Vigilance Monitor (Baxter Healthcare Corporation, Irvine, CA). Continuous non-invasive cardiac output measurements were obtained using a prototype device (Novametrix Medical Systems, Wallingford, CT). This system continuously measures airway flow, pressure, and CO_2 concentration. It controls a rebreathing valve placed between the ET tube and the Y piece of the breathing circuit which introduces approximately 150cc of deadspace for 50 seconds every 3 minutes. This causes a transient rise in End Tidal CO_2 (2-5 mmHg) and a commensurate decrease in VCO_2. A non-invasive estimate of pulmonary blood flow is achieved by tracking the CO_2 concentration and elimination. Cardiac output is calculated from pulmonary blood flow by correcting for shunt (estimated from SpO_2).

Results: The non-invasive rebreathing technique (left scatter plot) yields a bias and precision of 0.20 ± 0.79 when compared to bolus thermodilution. The continuous thermodilution technique (right scatter plot) yields a bias and precision of -0.22 ± 1.19.

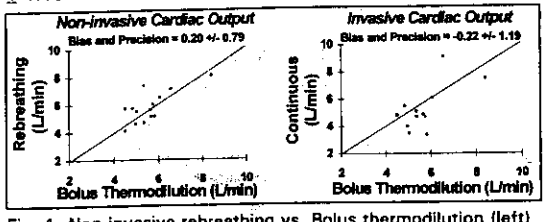

Fig. 1. Non-invasive rebreathing vs. Bolus thermodilution (left) and Continuous thermodilution vs. Bolus thermodilution (right)

Discussion: Bolus thermodilution measurements have long been considered the only practical and reliable method of clinical cardiac output monitoring. A recent innovation uses pulsed energy to achieve continuous thermodilution monitoring. Although this technique is continuous and easier to use, it still requires pulmonary artery catheterization and is therefore used in only a small percentage of anesthetic procedures. A reliable, inexpensive, and non-invasive (low risk) cardiac output monitor could enhance patient care during most anesthetic procedures. We evaluated a new non-invasive rebreathing technique for determining cardiac output. It compared favorably to continuous thermodilution when evaluated against conventional bolus measurements.

A537

TITLE: EVALUATION OF A MODEL FOR PERIOPERATIVE HEAT EXCHANGE

AUTORS: A. Bräuer MD[1], W. Weyland MD[1], M.J.M. English MD[2], H. Sander[1]. A. Timmermann MD[1] U. Braun MD[1]

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It is only possible to avoid perioperative hypothermia when heat exchange between the body surface and the environment can be controlled. Non-evaporative environmental heat exchange can be described as follows:

$$Q/A = h\,\Delta T$$

Q/A=Heat flux per area [W m^{-2}]
h=Heat exchange coefficient [W m^{-2} °C^{-1}]
ΔT=Temperature gradient between environment and surface [°C]

To allow a systematic analysis of this process we constructed and evaluated a copper model of the human body. This model consists of six tubes painted matte-black to simulate the emissivity of the human skin. Two tubes serve as arms, two as legs, one as the head and one as the trunk. The exposed surface is 1.98 m^2. A hot-water mattress is bonded to the undersurface of the copper tubes to set the surface temperature and to transport heat. Heat flux and the surface temperature are measured with calibrated heat flux transducers (HFTs)(Concept Engineering, USA).

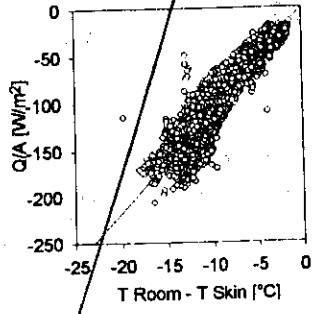
The present study was designed to determine whether the combined heat exchange coefficient for radiation and convection (h_{RC}) of the model correlates well with the h_{RC} of volunteers.

Determination of the h_{RC} of the model: HFTs were placed on the following points: Forehead, chest, abdomen, upper arm, forearm, hand dorsal, thigh anterior, anterior leg and foot of the model. Room temperature was set to 22°C. Surface temperature of the model was set between 22°C and 38°C. The h_{RC} was determined with a linear regression analysis as the slope of the temperature gradient between room and surface of the model versus the measured heat flux.

Determination of h_{RC} of volunteers: With informed consent and approval by the local ethics committee we studied five minimally clothed volunteers in a climate chamber. Initial chamber temperature was set to 29°C and was lowered slowly to 10°C. The h_{RC} was determined exactly as described above.

Results: The h_{RC} of the model was 10.9 W m^{-2} °C^{-1}, r^2 0.81, n=1200; and of the volunteers 10.9 W m^{-2} °C^{-1}, r^2 0.87, n=6137. (fig. 1).

Interpretation: The h_{RC} values of the volunteers are in accordance with the values given in literature ranging between 9.7 W m^{-2} °C^{-1} (1) und 10.2 W m^{-2} °C^{-1} (2). The excellent correlation between the volunteers and the model will allow the model to be used for standardized studies of perioperative heat exchange.



References: (1) English MJM et al. (1990) J Trauma 30, 422-425 (2) Clark RP, Edholm OG (1985): Man and his thermal environment. Edward Arnold Ltd., London

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Anesthesiology
V89, No 3A, Sep 1998

ENGINEERING TECHNOLOGY

A534

Title: EVALUATION OF A PARTIAL CO_2 REBREATHING FICK TECHNIQUE FOR MEASUREMENT OF CARDIAC OUTPUT

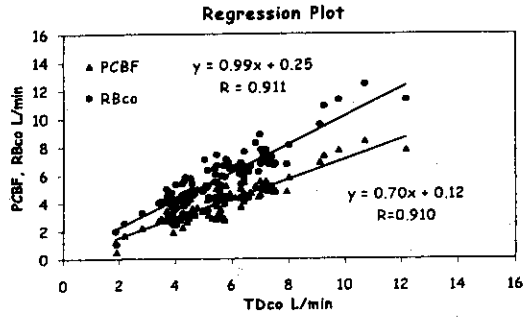
Authors: Dinesh G. Haryadi MS., Joseph A. Orr, Ph.D., Kai Kuck Dipl. Ing., Scott McJames BS., Dwayne R. Westenskow Ph.D.

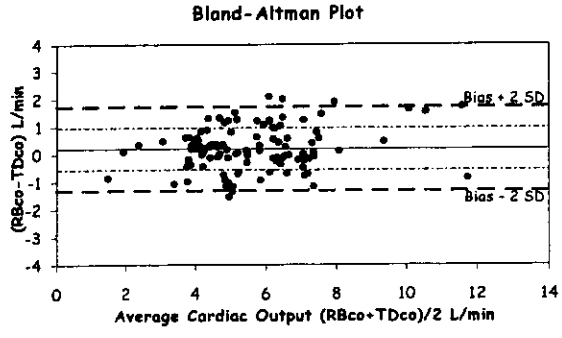
Affiliation: Depts. of Anesthesiology and Bioengineering
University of Utah, Salt Lake City, UT 84132.

Introduction: The noninvasive partial CO_2 rebreathing technique uses a differential form of the Fick equation to calculate cardiac output. The ratio of the change in CO_2 production (VCO_2) and end-tidal CO_2 ($etCO_2$), in response to a brief period of rebreathing, is used to calculate pulmonary capillary blood flow (PCBF). We used periodic blood gas measurements to estimate intrapulmonary shunt blood flow (Qs) and compute total cardiac output (RBco = PCBF + Qs).

Methods: After IACUC approval, four dogs (23-35 kg) were anesthetized with isoflurane and mechanically ventilated. End-tidal CO_2 and VCO_2 was measured using a mainstream CO_2 analyzer and a disposable pneumotachograph (COSMO®, Novametrix Medical Systems, Wallingford, CT). A pneumatic valve was actuated for 50 seconds once every 3 minutes causing 120 ml of dead space to be added to the breathing circuit. The resulting changes in VCO_2 and etCO2 were used to calculate RBco. Cardiac output was varied by manipulating contractility (dobutamine and halothane). Thermodilution CO (TDco) was measured using 10ml iced 5% dextrose (DualTherm®, B. Braun Medical Inc., Bethlehem, PA) and the average of three sequential measurements, phased randomly with respect to respiration, were recorded as TDco. Paired t-test and Bland-Altman statistics were used to compare the degree of agreement between concurrent measurements of TDco and RBco.

Results: Paired t-test analysis revealed no significant ($p<0.01$) difference between RBco and TDco measurements (n=115, Range =1.9 to 12.2 L/min). The overall difference between RBco and TDco was 0.21 ± 0.76 (bias±1SD) L/min. The linear regression coefficient (r) was 0.91.





Discussion: The results from the animal study show good agreement between TDco and RBco measurements. The standard deviation of the difference in the two techniques (0.76 L/min) is comparable to other noninvasive cardiac output technologies. The partial CO_2 rebreathing system is completely automatic and can provide frequent, nearly continuous measurements of cardiac output.

A535

TITLE: INFLUENCE OF PULMONARY EDEMA ON NONINVASIVE MEASUREMENTS OF CARDIAC OUTPUT USING PARTIAL CO_2 REBREATHING IN A CANINE MODEL

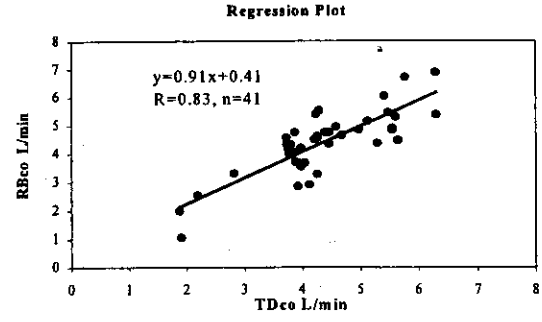
AUTH: KB Johnson, MD, DG Haryadi, MS, JA Orr, PhD, S McJames, BS, K Kuck, Dipl-Ing, DR Westenskow, PhD

AFFIL: Department of Anesthesiology, University of Utah, Salt Lake City, Utah 84132.

INTRODUCTION: Noninvasive measurements of cardiac output (CO) using a partial CO_2 rebreathing technique have been found to correlate well with conventional methods of measuring CO[1]. Since this technique measures the non-shunted pulmonary capillary blood flow (PCBF), it needs a noninvasive estimate of shunted blood flow (Qs) (from inspired oxygen concentration (FiO_2) and pulse oximetry (SpO_2)) to compute cardiac output (CO = PCBF + Qs). We set out to determine how pulmonary edema would influence measurements of partial rebreathing CO (RBco) in a canine model of oleic acid respiratory failure.

METHODS: With IACUC approval, four mongrel dogs were studied. All animals were given a ketamine induction and maintained with halothane/pancuronium/O_2. Each animal was instrumented with a pulmonary artery thermodilution (TD) catheter, an arterial line, and a RBco ventilator circuit (Novametrix Medical Systems, Wallingford, CT). After obtaining baseline measurements, a pulmonary capillary leak was created by a bolus infusion of oleic acid (0.08 ml/kg) into the right atrium. Serial arterial and venous blood gases, TDco and RBco measurements were made once every 20 minutes until the arterial pO_2 decreased to one third of the baseline values when FiO_2 was 100%.

RESULTS: (1) The oleic acid pulmonary injury produced an intrapulmonary shunt of 39 ± 12% (mean ± 1SD).
(2) A comparison of CO measurements (n = 41) using the RBco and the TDco techniques before, during and after the pulmonary injury revealed an R value of 0.83. RBco tracked changes in CO.
(3) Bland-Altman analysis resulted in a bias of +0.02 L/min and precision (1SD) of 0.65 L/min.



CONCLUSIONS: In this animal study, the pulmonary shunt developed during severe pulmonary edema did not appear to adversely influence the accuracy of CO measurements using the partial CO_2 rebreathing technique. The use of periodic arterial blood gas values may improve the estimation of Qs thus improving measurements of RBco.

REFERENCE: (1) Orr JA, et al., J Clin Monit., 1996; 12:464.

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PARTIAL CO_2 REBREATHING FICK TECHNIQUE FOR NONINVASIVE MEASUREMENT OF CARDIAC OUTPUT

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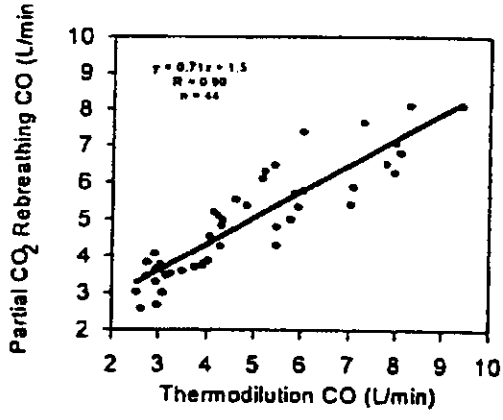
Introduction: The noninvasive partial CO_2 rebreathing technique uses a differential form of the Fick equation to calculate cardiac output (CO). The ratio of the change in end-tidal CO_2 and CO_2 excretion, in response to a brief period of rebreathing, gives a non-invasive estimate of the CO.[1,2] The method assumes that the difference between end-tidal and arterial CO_2 content does not change during rebreathing. We have developed a partial CO_2 rebreathing algorithm based on a two-compartment lung model, which minimizes error in estimation of CO when this assumption is not true. This model compensates for the changing end-tidal to arterial CO_2 gradient during partial rebreathing.

Methods: After IRB approval and patient consent the system was tested in seven patients (6 Male, 1 Female, Age 47-78 Years) undergoing cardiac surgery. End-tidal CO_2 was measured using a mainstream CO_2 analyzer and a disposable pneumotachograph (COSMO®, Novametrix Medical Systems, Wallingford, CT). CO_2 production was calculated as the integral of the flow and CO_2 signals over the entire breath. Actuation of a pneumatic valve under computer control resulted in breathing circuit changes, which increased airway dead space by 120 ml thereby causing partial rebreathing of exhaled gas. The valve was actuated for 50 seconds once every 3 minutes. Changes in CO_2 excretion and $etCO_2$ were used to calculate the partial CO_2 rebreathing CO using the differential Fick equation.

An average of three consecutive thermodilution cardiac output (TDco) measurements made during end expiration were compared with corresponding partial CO_2 rebreathing cardiac output measurements. Measurements made during the first 45 minutes after bypass were discarded since thermal noise can make the TDco measurement unreliable[3].



Results: A total of 44 comparisons were made with CO ranging from 2.5 to 9.4 L/min. Regression analysis gives an r = 0.90 with a slope of 0.71 and an offset of 1.49 L/min. Bland-Altman analysis resulted in a bias of 0.07 L/min with a precision (1SD) of ±0.85 L/min.

Discussion: The results suggest that partial CO_2 rebreathing technique may be a clinically acceptable method for measurement of CO. Observed differences between the two techniques may have resulted from intrapulmonary shunts. The partial CO_2 rebreathing system is completely automatic and can provide frequent, nearly continuous measurements of CO.

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EVALUATION OF PARTIAL RE-BREATHING CARDIAC OUTPUT MEASUREMENT IN ANIMALS

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Introduction: The non-invasive partial re-breathing method uses a differential form of the CO_2 Fick equation to calculate cardiac output. The ratio of the change in end-tidal CO_2 and CO2 excretion, in response to a brief period of re-breathing, gives a non-invasive estimate of cardiac output. This method assumes that the difference between end-tidal and arterial CO_2 content does not change during re-breathing. This assumption may be false and can lead to errors. We have developed a partial re-breathing algorithm based on a two-compartment lung model. This computer model compensates for the changing end-tidal to arterial CO_2 gradient during partial re-breathing.

Methods: The mathematical model separates the alveoli into completely perfused and non-perfused regions. End-tidal CO_2 concentration is the weighted sum of the two regions. Gas concentration in the un-perfused region is a slowly changing version of the inspired concentration, which can be calculated from the capnogram and airway flow signals. Partial re-breathing cardiac output calculations are made using the perfused alveolar CO_2 content as estimated by the computer model.

Six mongrel dogs, anesthetized with halothane were instrumented with a transit time ultrasonic flowmeter (Transonic Systems, Ithaca NY) placed directly around the pulmonary artery. Cardiac output was raised and lowered using a continuous infusion of epinephrine and dobutamine and was lowered using increased inhaled concentration of halothane. Average cardiac output measurements from the invasive and non-invasive devices were compared and recorded every 10 minutes.

Results: Regression analysis gives a correlation of r= 0.94 with a slope of 0.86 and an offset of 0.51 L/min. Shunt correction based on arterial blood gas data improved the slope and offset to 1.04 and –0.78 respectively. Without shunt correction, the average error was –1.1 and standard deviation of the error was 0.62 L/min, N = 176.

Discussion: The two-compartment model seems to take into account the effects of alveolar dead-space on the end-tidal CO_2 measurements in the differential Fick equation. The re-breathing method does not measure shunted blood, thus, partial re-breathing will under estimate cardiac output. The partial re-breathing system is completely automatic and can give continuous measurements.

Supported by: Novametrix Medical Systems and NIH 1R43 HL57031

Reference: Abstract # 25, Joint Meeting of Society for Technology in Anesthesia & Rochester Simulator Symposium, January 14-17, 1998, Tucson, Arizona.

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A NON-INVASIVE CARDIAC OUTPUT SYSTEM USING THE PARTIAL RE BREATHING FICK METHOD

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Summary. **The CO_2 partial re breathing method of Fick cardiac output was tested in 5 animals. The system is automatic and non-invasive. The system was accurate when compared with thermodilution.**

Introduction. Traditionally, the Fick method of measuring cardiac output requires blood gas values for arterial and mixed venous blood. The partial re breathing method allows computation of a differential version of the Fick equation which does not require any direct blood gas measurements.

Methods. The partial re breathing technique uses the change in CO_2 production (VCO_2) and end tidal CO_2 in response to a brief sudden change in ventilation. The change in CO_2 production divded by the change in CO_2 content of arterial blood, as estimated from end-tidal CO_2, equals pulmonary capillary blood flow. The method assumes that venous CO_2 levels remain constant during the 30 second measurement.

The system was tested in five anesthetized swine (45–60 kg) End-tidal CO_2 was measured using on-airway CO_2 system and a disposable pneumotach (Novametrix Medical Systems, Wallingford, CT), CO_2 production was calculated as the integral of the flow and CO_2 signals over the entire breath. A pneumatic valve under computer control increased airway dead space by 120 ml, thereby causing partial re-breathing of exhaled gas and effectively decreasing ventilation. The valve was acuated for 30 seconds every 4 minutes. Changes in VCO_2 and $etCO_2$ in response to actuation of the valve were used to calculate the differential Fick equation.

Average thermodilution cardiac output measurements were taken every 10 minutes and compared with corresponding partial re breathing cardiac output measurements. The outputs of both measurements were filtered using a 5 point average filter. Signals containing artifact were removed automatically using experimentally determined logic rules.

Results. A total of 272 comparisons were made with cardiac outputs ranging from 1.8 to 13.5 L/min. The figures below shows an X-Y plot of the data (R = 0.92, SEE = 0.96) and an example plot of cardiac output versus time for both thermodilution (sold diamonds) and re breathing cardiac output (empty boxes).

Discussion. As with all Fick based techniques, this technique does not measure pulmonary shunts. This difference may have led so some of the error in the measurements. It is expected that cycle times may be decreased to allow more frequent measurements.

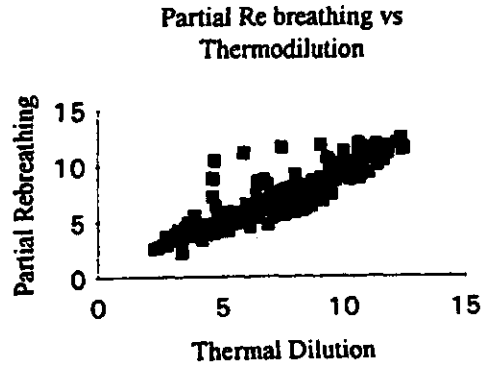

Fig 1.

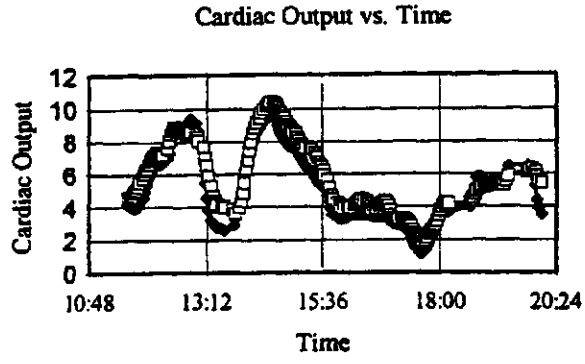

Fig 2.

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CARDIAC OUTPUT (OTHER PARTIAL REBREATHING)

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A new method for noninvasive bedside determination of pulmonary blood flow

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Abstract—*A method is presented for determining the pulmonary blood flow from measurements of the time-averaged end-tidal pCO_2 and the CO_2 output.*

The novel technique is based on a formula that is derived from Fick's principle in such a way that it allows a direct calculation of the lung perfusion from simultaneously measured changes in end-tidal pCO_2 and CO_2 output.

These changes are induced by altering the ventilation pattern of the patient for short (30 s) periods of time. Different ways of doing this are discussed and it is shown that a bidirectional change in ventilation, involving hyper- and hypoventilation patterns, most adequately corresponds to the formula derived.

The method has been validated by comparison with cardiac output data obtained by thermodilution. Forty-two measurements were performed during mechanical ventilation on five dogs and six patients with essentially healthy lungs. Lung perfusion was in the range 0·4–6·5 l/min. We found that $Q_{CO_2} = 0{\cdot}97\,Q_{thermo}$ with a s.d. = 18%. The reproducibility of individual measurements was better than 0·3 l/min.

Keywords—*Carbon dioxide, CO_2 output, End tidal pCO_2, Hyperventilation, Hypoventilation, Pulmonary blood flow*

1 Introduction

FICK's principle applied to the O_2 uptake in the lung provides a standard method for measuring the systemic cardiac output. While this technique gives reliable results, it has to be performed with direct measurement of the mixed venous O_2 content and thus requires cardiac catheterisation. To avoid this drawback, noninvasive techniques have been described, applying Fick's principle instead to the CO_2 elimination in the lung. Two approaches for estimating the mixed venous CO_2 content are in current use. Either a rebreathing procedure is employed or the estimation relies on an analysis of a single-breath CO_2 partial pressure recording (CAMPBELL, HOWELL, 1962; COLLIER, 1956; DEFARES, 1958; HLASTALA *et al.*, 1972; KIM *et al.*, 1966; FARHI *et al.*, 1976).

Common to many of these CO_2 methods is the fact that the arterial and the mixed venous CO_2 content are established by separate procedures. Therefore, systematic errors in each procedure cumulate when calculating the arteriovenous difference $C(a-\bar{v})_{CO_2}$. This is unfortunate since $C(a-\bar{v})_{CO_2}$ is usually small and thus the error in the cardiac output becomes large. As an example, for a difference between mixed venous

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and arterial pCO_2 of about 0·8 kPa (6 mm Hg), an error of only ~0·13 kPa (1 mm Hg) in the individual blood gas estimates may result in 25% error in the cardiac output value.

Another problem associated with previous methods is that they involve rather intricate experimental setups and require time-consuming evaluation of the measured data. Furthermore, the equipment has sometimes to be adjusted to the patient for optimal performance and patient cooperation is frequently assumed. All this makes it difficult, if not impossible, to use present noninvasive techniques for patients on mechanical ventilators.

The aim of this work is to provide a method for determining lung perfusion that is truly simple to carry out and yields the result immediately from a simple calculation or a nomograph. The ambition is to provide a means for online routine measurements especially on mechanically-ventilated patients who do not necessarily have healthy lungs.

2 Theory

2.1 *Background*

KNOWLES *et al.* (1960) have presented a potentially accurate way of obtaining the arteriovenous difference in pCO_2. They measured the change in alveolar pCO_2, P_{ACO_2} for different breath-holding times. These experiments, yielding $\frac{d}{dt}(P_{ACO_2})$, were repeated with different CO_2 concentrations in the inspired gas, thereby changing the P_{ACO_2} working point. The plot $\frac{d}{dt}(P_{ACO_2})$ vs P_{ACO_2} turned out to be a straight line, in accordance with the results of DUBOIS and coworkers (1952). This line has the equation

$$\frac{dP_A}{dt} = \text{constant} \times \frac{\dot{Q}}{V_A} \times (P_{\bar{v}} - P_A) \quad . \quad . \quad . \quad (1)$$

where $P_{\bar{v}}$ is the mean oxygenated mixed venous CO_2 tension, $\dot{Q}$ is the cardiac output and V_A is the equivalent alveolar lung volume. In eqn. 1 and in the following, the subscript 'CO_2' is omitted and all quantities are assumed to refer to carbon dioxide.

As seen from eqn. 1 $P_{\bar{v}}$ can be obtained from the intercept of the straight line with the P_A-axis, where $dP_A/dt = 0$. Although the value of the constant in eqn. 1 can also be calculated, the equivalent volume is an unknown quantity and therefore the lung perfusion cannot be obtained in this way. The present method is an extension of the ideas on which the work of KNOWLES *et al.* is based (GEDEON, 1977; GEDEON, 1979). The problem with the unknown equivalent lung volume encountered by KNOWLES *et al.* is circumvented by measuring the CO_2 output (that is $\frac{d}{dt}(V_A \times P_A)$) instead of the rate of change in P_A with time (that is $\frac{d}{dt}P_A$). Furthermore, to adapt the method to easy clinical use, the $P_{\bar{v}}$ working point is altered by a properly performed change in the ventilation pattern instead of adding CO_2 to the inspired gas.

2.2 *Derivation of a formula for the pulmonary blood flow* $\dot{Q}$

Consider Fick's equation for the CO_2 balance in the lung

$$\dot{V} = \dot{Q} \times (C_{\bar{v}} - C_a) \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where $C_{\bar{v}}$ and C_a stand for the mixed venous and the arterial CO_2 content, and $\dot{V}$ is the CO_2 output. Eqn. 2 can be rewritten by making use of the CO_2 dissociation curve, that is, the content C vs the partial pressure P relation

$$C = C(P) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

Eqn. 2 becomes

$$\dot{V} = \dot{Q} \times S \times (P_{\bar{v}} - P_a) \quad . \quad . \quad . \quad . \quad . \quad (4)$$

where S is the slope of the dissociation curve evaluated in between the arterial and the mixed venous CO_2 tensions

$$S = \left(\frac{dC}{dP}\right) \quad \text{at} \quad P = \frac{P_{\bar{v}} + P_a}{2} \quad . \quad . \quad . \quad . \quad (5)$$

$P_{\bar{v}}$ and P_a are the mean oxygenated mixed venous and the arterial CO_2 tensions, respectively (KNOWLES *et al.*, 1960).

Using the mathematical expression given by eqn. 14 in Appendix 1 for the dissociation curve, we may calculate directly the difference in CO_2 content for the partial pressures $P_{\bar{v}} = 6·133$ kPA (46 mm Hg) and $P_a = 5·333$ kPa (40 mm Hg). The value obtained is 2·839 vol%. Calculating the same quantity from the partial pressure difference multiplied by the slope factor S (according to eqn. 4) gives 2·840 vol%. Thus eqn. 4 is a very good approximation of eqn. 2.

We now consider a sudden change $dP_a = P_{a1} - P_{a2}$ in the arterial tension. It is here assumed that mixed venous pCO_2 has the same value for the two arterial tensions P_{a1} and P_{a2}.

The immediate change in CO_2 output $d\dot{V}$ is obtained by differentiating eqn. 4

$$d\dot{V} = -\dot{Q} \times S \times dP_a \quad . \quad . \quad . \quad . \quad . \quad (6)$$

where S is assumed to be unaffected by the small change in P_a. Since S is a slowly varying function of P, this approximation is accurate for most practical purposes.

The two most important advantages of using eqn. 6 instead of eqn. 4 to calculate $\dot{Q}$ are immediately apparent.

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Firstly, P_t no longer appears explicitly in eqn. 6. It is only in the evaluation of the slope factor S that P_t must be considered. The impact of this property of eqn. 6 on the accuracy of the calculation of $\dot{Q}$ is considerable. As an example, an uncertainty in the estimated value of P_t of about 0·53 kPa (4 mm Hg) will give an error of only about 6% in $\dot{Q}$. This error comes from the change in the factor S in eqn. 6 as a result of the error in P_t. The calculation is based on the formulae given in Appendix 1.

Second, only changes and not absolute values of $\dot{V}$ and P_a are to be measured accurately. This puts less stringent requirements on the absolute calibration of the CO_2-concentration recording equipment. More important, it admits an indirect measurement of P_a and thereby allows for a noninvasive procedure. To see this we may write P_a in the form

$$P_a = P_{ET} + E \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

where P_{ET} denotes the end tidal CO_2 partial pressure and E is simply an unknown quantity which in general has positive values. Rewriting eqn. 7 in the form

$$E = (P_a - P_A) + (P_A - P_{ET}) \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

one can interpret E, the difference between end tidal and arterial CO_2 tension, as a sum of the $(a-A)$ difference (first term eqn. 8) due to regions having a $\dot{V}/\dot{Q}$-distribution corresponding to ventilation perfusion ratio $\ll 1$ and the $(A-ET)$ difference (second term in eqn. 8) due to the alveolar dead space with ventilation perfusion ratio $\gg 1$ and the mixing conditions of the alveolar gas.

Assuming that the previously mentioned change in P_a is achieved without affecting E, it follows that

$$dP_a = dP_{ET} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (9)$$

How to ascertain the validity of the assumptions made above will be discussed below.

According to eqn. 9 we can replace dP_a in eqn. 6 by dP_{ET} and we can also eliminate P_a in eqn. 5 by using eqn. 7. This gives us a formula with parameters that can be measured in a noninvasive way.

$$\dot{Q} = -\frac{1}{S} \times \frac{d\dot{V}}{dP_{ET}} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (10)$$

Although the slope of the dissociation curve S is a slowly varying function of the CO_2 parameters, we refrain from assuming that it is a constant. Details of the calculation of a more general form of S will be found in Appendix 1. The final result is

$$\dot{Q} = -\left(\frac{1}{K_0} + \frac{1}{K_1}\left(P_{ET} + E - \dot{V} \times \tfrac{1}{2} \times \frac{dP_{ET}}{d\dot{V}}\right)\right)\frac{d\dot{V}}{dP_{ET}} \quad . \quad . \quad . \quad . \quad . \quad (11)$$

where K_0 and K_1 are constants determined by the dissociation curve. In Appendix 1 it is shown that $K_0 = 0{\cdot}332$ and $K_1 = 0{\cdot}228$ may be used for all practical purposes.

For E the value of 0·53 kPa (~4 mm Hg) is chosen somewhat arbitrarily. However, using this value in eqn. 11, any clinically observed value between 0–1·06 kPa (0–8 mm Hg) will give, as before, less than 6% error in $\dot{Q}$. Thus a broad range of end tidal-arterial pCO_2 differences can be accounted for.

A nomogram-like technique can be developed to eliminate the need to calculate $\dot{Q}$ from eqn. 11. A simple geometrical construction and a special graduated arc are all that is needed to obtain the lung perfusion in this case. The graphical procedure is explained in Appendix 2.

3 Realisation

Turning to the question of how to produce a change in P_a without affecting P_t and E, it should be remembered that eqn. 11 is derived without any specific assumption about the method chosen. One obvious way is to add CO_2 to the inspired gas. Measurements of P_{ET} and $\dot{V}$ made before the effect of recirculation is observed on P_t could be used to calculate the pulmonary blood flow. One advantage of this technique would be that large changes in P_a and $\dot{V}$ are easily achieved. On the other hand the measured $\dot{V}$ has to be corrected for the added CO_2, which could be a considerable source of error. Moreover, special equipment would be required to perform these measurements.

In this work we have used another approach that can be readily applied in a clinical setting. The basic idea is to change the length of the pause between inspiration and expiration but to keep the tidal volume, the inspiratory and the expiratory time constant. The example shown in Fig. 1 demonstrates

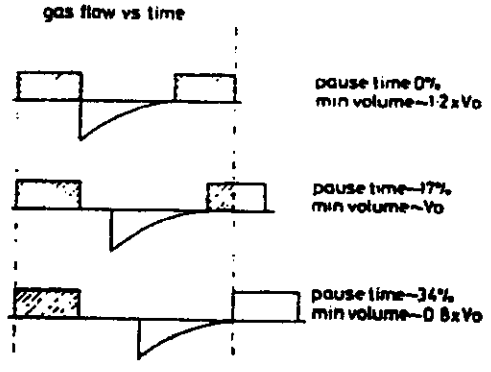

Fig. 1 Illustration of how a variation in the pause time gives changes in the minute volume although the tidal volume, the inspiratory and the expiratory times remain the same. The area under the flow vs time curve corresponds to the volume delivered

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that this scheme is equivalent to changing the minute volume and will therefore bring about rapid changes in P_{ET} and $\dot{V}$. The pause time between inspiration and expiration can be regarded as a very short, mandatory breath-holding period. Therefore one may say that the ventilatory change suggested to produce the changes in P_{ET} and $\dot{V}$ amounts to a repeated, well controlled breath-holding procedure of short duration that can be implemented using existing respiratory equipment. Since the expiratory time is kept constant, P_{ET} values are recorded at comparable points on the alveolar plateau even in a case when the CO_2 partial pressure vs time curve does not level off at the end of the expiration. Since the tidal volume is not changed, the peak pressure in the lung remains the same and the mean intrathoracic pressure is also almost unaffected. The change in this parameter may be estimated to be about 7% of the peak pressure value for +50% change in minute volume. The maintenance of constant pressure conditions is important since, if the pressure in the lung was allowed to alter from one ventilation pattern to another, adverse effects could result, such as a change in the cardiac output or in the equivalent alveolar volume.

A change from a steady-state ventilation pattern to a hyperventilation pattern such as from minute volume $\dot{V}_0$ to $1{\cdot}2\dot{V}_0$, shown in Fig. 1, is in accordance with the rules discussed above. The difference between arterial and end tidal pCO_2 will not be significantly affected and thus our assumption on which eqn. 9 is based is expected to be valid. The most obvious way to perform a lung-perfusion measurement would therefore be to use the two CO_2-parameter values observed for the steady-state ventilation pattern together with the two CO_2 values obtained after a short period of hyperventilation to calculate $\dot{Q}$ from eqn. 11. However, in order not to violate the other of our two assumptions, namely that mixed venous pCO_2 has the same value when recording the CO_2 data of the two ventilation settings, the hyperventilation period must be short enough compared with the system's recirculation time. Recirculation due to hyperventilation tends to lower the $P_{\bar{v}}$ value, which would lead to falsely low values for the calculated lung perfusion.

To minimise the effect of recirculation, a procedure involving a hyperventilation period followed by a hypoventilation period (see pattern with minute volume $0{\cdot}8\dot{V}_0$ in Fig. 1) appears more attractive. Such a bidirectional deviation from steady state is an advantage in that mixed venous pCO_2 tends to return to the same value at the end of the hypoventilation period as it had at the end of the hyperventilation period. This value may now differ from the initial steady state $\overline{P_{\bar{v}}}$ and the calculation of $\dot{Q}$ is therefore based on the CO_2 parameters of the hyper- and the hypoventilation settings, while the steady state CO_2 values are not used.

Recirculation will primarily affect the measured change in P_{ET}. Therefore one can say, in general, that for large changes in P_{ET} (that is, for low values for the lung perfusion) our method is more accurate than for small changes in P_{ET} (large perfusion values).

We have measured $\dot{Q}$ both by the steady-state hyperventilation approach and by the hyper-hypoventilation procedure described above. Changes in pause time corresponding to minute volume changes from 20% up to 100% of the basal value have been implemented.

4 Application of the method

All measurements were carried out using a ventilator (Siemens–Elema Servo Ventilator 900 B) and a CO_2 analyser (a slightly modified Siemens-Elema CO_2 Analyzer 930). The ventilator can be set to give predetermined inspiratory and pause-time fractions. Thus different ventilator settings, for instance such as those shown in Fig. 1, could be realised. A small deviation from the constant inspiration time condition had to be accepted in some cases. The electronic ventilator provides instantaneous expiratory flow monitoring at a.t.p.s. conditions and the fast response (response time 6 ms) CO_2 analyser measures the CO_2 partial pressure with no time delay close to the airway opening (at a point between the patient and the Y-piece). Connecting these two pieces of equipment together allows a direct multiplication of the flow curve with the partial pressure curve which, after integration with respect to time, yields the tidal CO_2 output. Thus for each breath one has the tidal output and the end tidal value (which is defined as the maximal partial pressure value during expiration). With a slight modification of the standard CO_2 analyser one can get a display of the time-averaged CO_2 output (expressed in ml/min) and the corresponding time-averaged P_{E1} (in kPa). The averages are taken by analogue electronic circuitry with a 90% response in about 20 s. The averaged values are displayed and updated every breath.

Reference measurements of cardiac output were done, using a thermodilution computer (Instrumentation Laboratories 701), in five dogs (19–34 kg weight) during thiopental anaesthesia, and in six patients during neuroleptanaesthesia prior to coronary bypass surgery. The thermodilution data were recorded as the mean of three consecutive measurements. In dogs, cardiac output usually decreased slowly with time during the measurements. To obtain a greater range in cardiac output, some dogs were also subjected to stepwise controlled bleeding. The data were taken using the ventilation patterns discussed before.

The length of the hyperventilation was always 30 s, while the hypoventilation period lasted 25–40 s. We found that the exact time was best calculated as $\sim 1{\cdot}8 \times T$. T, a measure of the recirculation time, was estimated from the time required before the rise in the CO_2 output started to level off after the onset of

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hyperventilation. In general the hypoventilation period lasted ~25 s in dogs and ~35 s in patients. It should be noted here that in the case of a left to right shunt, the shunted flow recirculates in about 10 s and will not significantly contribute to the lung perfusion value obtained with the present technique.

5 Results and discussion

Fig. 2 shows the measured time course of P_{ET} and $\dot{V}$ in a patient with a decrease in pause time corresponding to a 25% increase in minute volume. $\dot{Q}$ was measured by thermodilution to 3·6 l/min. Using this value and evaluating the slope of the CO_2 dissociation curve at $P = P_{ET}$, the time course of P_a can be calculated from Fick's equation and the measured P_{ET}, $\dot{V}$ data. The result, shown by the dashed line in Fig. 2, agrees with the blood gas values shown by the crosses. Plotting P_{ET} vs $\dot{V}$ in a diagram, the point (P_{ET}, $\dot{V}$) moves in time as shown in Fig. 3. Calculating the lung perfusion using the steady state point at $t = 0$ and the hyperventilation points at $t = 30$ s, 60 s, 90 s and 120 s, we get $\dot{Q} = 3{\cdot}70$, 3·55, 3·55 and 3·40 l/min, respectively.

Despite the lowering of the value with time, an effect which is due to recirculation, good agreement with the thermodilution value of 3·6 l/min is observed over a considerable time interval.

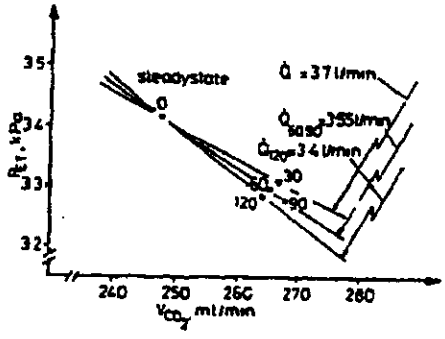

Fig. 3 P_{ET} vs $\dot{V}$ diagram showing how the point (P_{ET}, $\dot{V}$) moves in time, according to the measurements shown in Fig. 2. The $\dot{Q}$-values obtained with the steady state point and the different hyperventilation points are indicated (see also Fig. 6)

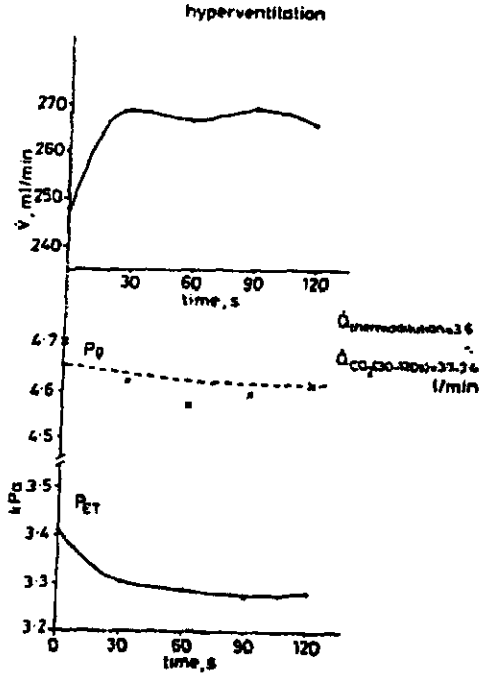

Fig. 2 Time course of $\dot{V}$, P_{ET} and P_a subsequent to a 25% increase in minute volume. Dashed line shows the expected course of oxygenated P_a as calculated from the $\dot{V}$ and P_{ET} data. Crosses represent blood gas P_a measurements. For a detailed discussion see the text

Fig. 4 shows typical tracings of P_{ET} and $\dot{V}$ when a hyperventilation setting is followed by a hypoventilation setting as described above. Note the overshoot (in the hyperventilation step) and the undershoot (in the hypoventilation step) of the CO_2 output curve. This phenomenon is in part due to the contribution from the lung tissue stores as they unload and load CO_2, respectively. The lung tissue quickly equilibrates with the new P_{ET} level (FARHI *et al.*, 1976) and, as seen in Fig. 4, will have a negligible effect on the changes in $\dot{V}$ and P_{ET} as measured at the end of the

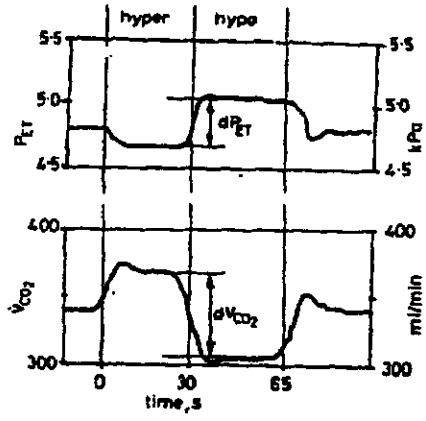

Fig. 4 Typical P_{ET} and $\dot{V}_{CO_2}$ vs time tracings for a 30 s hyperventilation period followed by a 35 s hypoventilation period. The quantities dP_{ET} and $d\dot{V}_{CO_2}$ defined in the figure yield the lung perfusion according to eqn. 10

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ventilation periods. The ratio $d\dot{V}/dP_{ET}$ obtained from a tracing such as the one in Fig. 4 is, according to eqn. 10, proportional to the lung perfusion.

Fig. 5 summarises the results obtained when comparing the noninvasive CO_2 method to thermodilution determinations ($\dot{Q}_{thermo}$) of cardiac output.

We find $\dot{Q}_{CO_2} = 0{\cdot}97 \cdot \dot{Q}_{thermo}$ with a standard deviation of 18%. (Disregarding the six points obtained from a 100% increase in ventilation, the standard deviation of the material is 15%.) The standard deviation is 20% for the dogs and 8% for the patients. An individual measurement could be reproduced within 0·3 l/min.

The present method is based on three major assumptions:

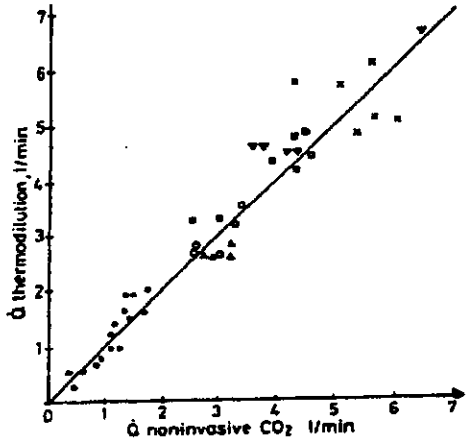

Fig. 5 Comparison between thermodilution measurements of cardiac output and the noninvasive CO_2 method. Line of identity is shown for comparison. The percentage values given below refer to the change in minute volume

Dogs:
- ▲ *steady state and 50% hyperventilation.*
- X *steady state and 100% hyperventilation.*
- ▼ *50% hyperventilation and 50% hypoventilation.*
- ■ *20% hyperventilation and 20% hypoventilation.*
- ● *20% hyperventilation and 20% hypoventilation.*

Human subjects:
- ○ *steady state and 50% hyperventilation*

(i) the patient is in steady state at the beginning of the measurement.
Since the determination of lung perfusion affects the blood gas equilibrium, steady state conditions have to be awaited between each measurement. In our experience the measurements can be repeated at an interval of ~15 min.

(ii) The changes that are induced in the CO_2 parameters P_{ET} and $\dot{V}$ must be implemented with a minimum of perturbation of the end tidal to arterial pCO_2 difference (E in eqn. 7). According to Fig. 5, the method used in this work although not necessarily the optimal one fulfills this requirement quite well.

(iii) The effect of recirculation on P_i is minimised for instance by a bidirectional change in ventilation, relative to the basal condition.

In addition it is important to note, when comparing results of the present method to other techniques for measuring cardiac output, that left to right shunts and anatomic right to left shunts (regions with $\dot{V}/\dot{Q} = 0$) will not be properly accounted for with the noninvasive technique.

On the other hand, since only relative changes and no accurate absolute values for the end-capillary or alveolar pCO_2 are needed in calculating the lung perfusion, it is expected that the present method is applicable to lungs in disease (the clinical validation of this claim is outside the scope of this paper). Together with the fact that the method is very simple to apply, especially in patients on mechanical ventilators, this makes our approach potentially quite attractive for clinical diagnostic purposes.

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Appendix 1

The CO_2 dissociation curve

The dissociation curve describes the relation between the CO_2 content of oxygenated blood C (in the units volume % or ml s.t.p.d./ml) and the partial pressure of CO_2, P. The slope of the dissociation curve S is the derivative of C with respect to P. Thus, evaluated between the arterial and the mixed venous points, the slope can be obtained according to eqns. 5 and 7 as

$$S = \left(\frac{dC(P)}{dP}\right) \quad \text{for} \quad P = \frac{P_v - P_{ET} - E}{2}$$

where the relation between C and P, here denoted by $C(P)$, is specified below. Since, according to eqns. 4, 6 and 7 (see also Fig. 6),

$$\frac{P_{ET1} - P_{ET2}}{\dot{V}_1 - \dot{V}_2} = \frac{P_v - E - P_{ET1}}{-\dot{V}_1} \qquad (12)$$

we find

$$P = \left(\frac{P_{ET1} - P_{ET2}}{\dot{V}_2 - \dot{V}_1}\right) \times \dot{V}_1 \times \frac{1}{2} + P_{ET1} - E \qquad (13)$$

To derive a formula for S, the dissociation curve has to be given a mathematical form. It is easy to verify that

$$C(P) = K_1 \times \ln(1 + K_2 P) \qquad (14)$$

with $K_1 = 0{\cdot}228$ and $K_2 = 1{\cdot}45$, fits an oxygenated CO_2 dissociation curve very well over a wide range. P must be expressed in the unit kPa, where

$$1\,\text{kPa} = 7{\cdot}5\,\text{mm Hg} = 10\,\text{cm}\,H_2O\,.$$

Comparing the above mathematical formula for instance to the measurements of CHRISTIANSEN, DOUGLAS and HALDANE (1914) we find less than 2 vol. % error in C everywhere from $pCO_2 = 0$ to $pCO_2 = 10$ kPa (75 mm Hg). The displacement of the dissociation curve due to various blood parameters does not constitute a major problem here since only the slope of the curve enters the calculations. The slope is a slowly changing function of P, and since the physiological range is rather limited, the function given by eqn. 14, although by no means a unique representation, is quite adequate (KLAUSEN, 1965). Calculating S according to eqn. 5 from eqn. 14 gives

$$S = \frac{K_1 \times K_2}{1 + K_2 P}$$

where P is given by eqn. 13. This gives finally

$$\frac{1}{S} = \frac{1}{K_u} + \frac{1}{K_1}\left(P_{ET1} + E - \frac{1}{2}\dot{V}\left(\frac{P_{ET1} - P_{ET2}}{\dot{V}_1 - \dot{V}_2}\right)\right) \qquad (15)$$

where $K_u = K_1 K_2 = 0{\cdot}332$ and $K_1 = 0{\cdot}228$.

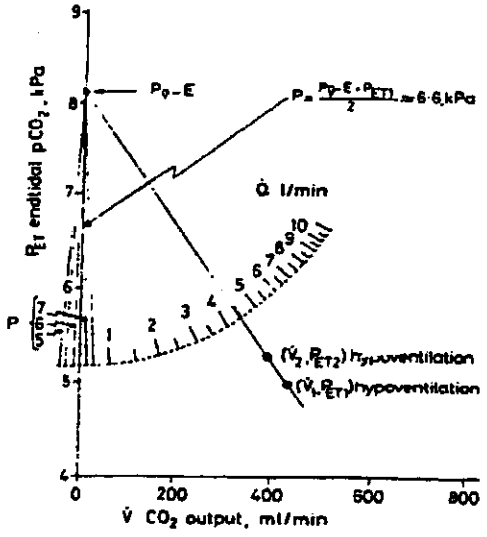

Fig. 6 End tidal pCO_2 vs CO_2 output. Simultaneously measured values of these parameters corresponding to hyper- and hypoventilation are represented by the two points. The straight line through these points intercepts the P_{ET}-axis at the value $P_v - E$, where P_v is the mean oxygenated mixed venous CO_2 tension and E is the unknown difference between arterial and end tidal pCO_2. As explained in Appendix 2, the graduated arc is centred on the P_v point and the base line designated by 6·6 is aligned along the P_{ET}-axis. The straight line then indicates the pulmonary blood flow of 4·45 l/min on the scale. Since by definition (see eqn. 7) $P_{ET} = P_v - E$, the difference between the extrapolated $P_v - E$ and $P_{ET} = P_v - E$ is always $P_v - P_v$ irrespective of the value of E. Therefore the lung perfusion obtained is not sensitive to the precise value of E

Appendix 2

Graphical evaluation

Consider a coordinate system for end tidal pCO_2, P_{ET} vs CO_2 output $\dot{V}$ as shown in Fig. 6. The measured values $(\dot{V}_1, P_{ET1})$ and $(\dot{V}_2, P_{ET2})$ appear here as two points. The intersection of a straight line drawn through these two points with the P_{ET}-axis gives the value $P_v - E$ (see eqns. 4 and 7). Now as seen from eqn. 10 the slope of the line would be proportional to the inverse of $\dot{Q}$ if the dissociation curve were linear, that is if S were a constant. The actual curvature of the dissociation curve can be taken into account to the first order by a small rotation of the line around the $P_v - E$ point. In practice, a number of base lines are given on the graduated

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arr Each base line is labelled with the P-value for which the slope of the dissociation curve is evaluated. When the base line with the proper value is aligned along the P_{ET}-axis and the centre of the arc is positioned on the $P_{\bar{v}}$-point, the straight line connecting the measured points will directly indicate the pulmonary blood flow value on the scale. In the example shown in Fig. 6, $P_{ET} = 5{\cdot}0$kPa, $P_{\bar{v}} - E$ is extrapolated to 8·2 kPa, and thus according to eqn. 5 the slope is to be taken at the mean of these two values: $P = 0{\cdot}5(8{\cdot}2 + 5{\cdot}0) = 6{\cdot}6$ kPa. Aligning the arc so that the $P = 6{\cdot}6$ base line coincides with the P_{ET}-axis, one reads $\dot{Q} = 4{\cdot}45$ l/min on the scale. This is to be compared to $\dot{Q} = 4{\cdot}37$ l/min computed from eqn. 11. In general the accuracy of the graphical method is typically 2–3% compared to calculated values.

Also when using the graphical representation it is easy to demonstrate why the present method based on eqn. 6 is insensitive to the errors inherent in noninvasive procedures based on measurements of P_{ET}. One sees that the unknown difference E between end tidal and arterial pCO_2 also appears in the extrapolated value of the mixed venous pCO_2. Mathematically, E will cancel out when taking the arteriovenous difference; and graphically, the line in Fig. 6 will be shifted up and down as E varies, but its slope will not be changed. It is only when taking into account the curvature of the dissociation curve that a small error is introduced because of the uncertainty in the value of E.

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Noninvasive Measurement of Cardiac Output Using Partial CO_2 Rebreathing

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Abstract—A noninvasive algorithm for estimating cardiac output has been developed and tested in dogs. The technique is based on a differential form of the CO_2 Fick equation applied during normal ventilation and a 30 s period of partial rebreathing using additional deadspace. Using the Fick equation in a differential form eliminates the need to estimate mixed venous pCO_2, also the sensitivity of the cardiac output estimate to changes in the alveolar deadspace fraction is greatly reduced. The procedure is fully automated, requires minimal staff supervision, and provides cardiac output estimates every 3 1/2 min. Estimates of cardiac output when compared to thermodilution yielded a correlation coefficient of 0.92 with a linear regression slope of 0.92 (n = 451). Temporary increases in alveolar deadspace did not significantly alter this relationship. Cardiac output estimates obtained during periods of increased pulmonary shunt due to oleic acid infusion yielded a correlation coefficient of 0.90 with a linear regression slope of 0.92 when compared to direct thermodilution measurements.

INTRODUCTION

CARDIAC output is normally measured using invasive techniques: thermodilution, dye dilution, and direct Fick procedures. These techniques involve morbidity and mortality risks and limitations on the duration and frequency of measurement. The development of an accurate and easily implemented noninvasive technique for the measurement of cardiac output would avoid many of the drawbacks of the invasive techniques.

This paper presents a method for estimating pulmonary capillary blood flow (PCBF) in mechanically ventilated subjects, based on changes in respiratory CO_2 concentrations caused by a 30 s period of partial rebreathing. The technique is easily implemented by intermittently activating additional deadspace between the subject and any ventilator. The procedure is fully automated, requires minimal staff supervision, and provides PCBF estimates every 3 1/2 min. The technique can be performed over long periods without intervention, allowing clinicians to monitor the recovery of intubated patients without the need for right heart catheterization.

The direct Fick equation, when applied to the CO_2 balance in the lungs, takes the form

$$\dot{Q} = \frac{\dot{V}_{CO_2}}{(C_{\bar{v}CO_2} - C_{aCO_2})} \quad (1)$$

where

$\dot{V}_{CO_2}$ = rate of carbon dioxide elimination
$C_{\bar{v}CO_2}$ = mixed venous CO_2 blood concentration
C_{aCO_2} = arterial CO_2 blood concentration
$\dot{Q}$ = pulmonary capillary blood flow.

Since $C_{\bar{v}CO_2}$ and C_{aCO_2} represent CO_2 concentrations in blood, direct application of (1) requires invasive sampling of both arterial and mixed venous whole blood, the latter of which requires right heart catheterization.

In an attempt to provide noninvasive estimates of pulmonary capillary blood flow, previous investigators have used measurements of respiratory CO_2 concentrations to estimate arterial and mixed venous gas concentrations. Since CO_2 diffuses rapidly in the lungs, arterial pCO_2 levels can be estimated from measurements of end-tidal pCO_2, if compensation is made for the effects of alveolar deadspace. Estimation of mixed venous pCO_2 has followed three different lines of development: breath-holding techniques [1]–[4], single-breath techniques [5]–[7], and rebreathing techniques [8]–[12].

In 1980, Gedeon *et al.* [13] proposed a formula relating PCBF to the ratio of changes in CO_2 elimination and end-trial CO_2 partial pressure created by a sudden change in minute ventilation. By using a differential form of the Fick equation the need to estimate mixed venous pCO_2 was eliminated, provided appropriate end-tidal CO_2 points were selected where the mixed venous concentration was exactly equal.

This procedure was quite sensitive to the selection of the time interval between measurements. However, the concept of using a differential measurement was novel. We have used the differential measurement concept, corrected for the presence of alveolar deadspace and variations in the slope of the CO_2 dissociation curve, and created a partial rebreathing ventilatory maneuver which does not require an accurate interval between measurements. Although Gedeon used a 10–15 min recovery time between measurements, which may be necessary using the hyperventilation–hypoventilation maneuver employed, we

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have found that the approach we used requires only a 3 min recovery period. Algorithms have also been incorporated to automate the procedure, reduce the effects of noise in the measured data, and to compensate for the response characteristics of the measurement equipment.

Theory

A brief period (30 s) of partial rebreathing using additional deadspace will cause a change in arterial CO_2 and a change in CO_2 elimination, but as will be shown little or no change in mixed venous CO_2. Assuming that cardiac output $\dot{Q}$ does not change during this 30 s interval, the Fick equation of (1) can be rewritten in the differential form of (2):

$$\dot{Q} = \frac{-(\dot{V}_2 - \dot{V}_1)}{C_{a_2} - C_{a_1}} = \frac{-\Delta \dot{V}}{\Delta C_a} \tag{2}$$

where the subscript 1 indicates before and the subscript 2 indicates either the conclusion or during the partial rebreathing maneuver.

Since the CO_2 dissociation curve is nearly linear over the small range of changes between C_{a_1} and C_{a_2}, (2) can be rewritten using a mathematical expression for the slope (S) of the CO_2 dissociation curve.

$$\dot{Q} = \frac{-\Delta \dot{V}}{S \Delta P_a} \tag{3}$$

where

$\Delta P_a = P_{a_2} - P_{a_1}$
$\Delta \dot{V}$ = ml CO_2/min
ΔP, P = mm Hg
S = ml CO_2/liter blood/mm Hg.

McHardy (14) described the slope of the CO_2 dissociation at a constant CO_2 partial pressure (40 mm Hg) as a function of the hemoglobin concentration:

$$\Delta CO_2(30 - 60) = 0.448[\text{Hb}] + 6.3$$

or

$$S = 0.0149[\text{Hb}] + 0.21 \quad (\text{ml } CO_2/100 \text{ ml blood/mm Hg}). \tag{4}$$

However, using the original data presented by Peters [15], this slope was recalculated as

$$S = 0.154[\text{Hb}] + 2.1 \quad (\text{ml } CO_2/\text{liter blood/mm Hg}). \tag{5}$$

Gedeon expressed the CO_2 content (C) as a function of CO_2 partial pressure, producing a mathematical expression for the CO_2 dissociation curve

$$[C(P)] = K_1 \ln (1 + .1933P) \tag{6}$$

where

(C) = ml CO_2/L blood
K_1 = dimensionless constant.

The slope of the dissociation curve is found by differentiating (6) to produce

$$S = \frac{0.1933K_1}{1 + 0.1933P} \text{ (ml } CO_2/\text{L blood/mm Hg)} \tag{7}$$

The constant K_1, which shifts the dissociation curve, is primarily affected by hemoglobin concentration and less so by the bicarbonate concentration. For our analysis, the bicarbonate effect has been neglected.

If (5) and (7) are equated at a CO_2 partial pressure of 40 mm Hg, then an expression for K_1 can be found:

$$K_1 = 6.957[\text{Hb}] + 94.864. \tag{8}$$

Substituting this expression for K_1 into (7) yields the form which was used for slope determination:

$$S = \frac{1.34[\text{Hb}] + 18.34}{1 + 0.193P}. \tag{9}$$

For a noninvasive measurement, end-tidal CO_2 can be substituted for arterial CO_2 provided a correction is made for alveolar deadspace. The relationship between arterial and end-tidal CO_2 can be derived from the alveolar deadspace (10), as shown in [16]:

$$P_a = P_{ET}\left(\frac{V_T}{V_T - V_{DALV}}\right) = KP_{ET} \tag{10}$$

where

V_T = tidal volume (ml)
V_{DALV} = alveolar deadspace (ml)
$K = V_T/(V_T - V_{DALV})$.

Since it is reasonable to assume that the alveolar deadspace fraction (V_{DALV}/V_T) remains constant during the 30 s partial rebreathing maneuver, it follows that

$$\Delta P_a = K \Delta P_{ET} \tag{11}$$

where

$$\Delta P_{ET} = P_{ET_2} - P_{ET_1}.$$

If an average $P = K(P_{ET_2} + P_{ET_1}/2)$ is used in (9) and then (9) and (11) substituted into (3), a final expression for $\dot{Q}$ can be obtained, as shown in (12):

$$\dot{Q} = \frac{-\Delta \dot{V}(1 + 0.097K(P_{ET_1} + P_{ET_2}))}{(1.34[\text{Hb}] + 18.34)K\Delta P_{ET}}. \tag{12}$$

The use of (12) can be best understood by examining Fig. 4 which shows an expanded view of CO_2 elimination and end-tidal CO_2 during a 30 s rebreathing period. The values $\dot{V}_1$ and P_{ET_1} are averaged baseline values prior to rebreathing. The values $\dot{V}_2$ and P_{ET_2} are averaged plateau values towards the end of the rebreathing period. The values $\Delta \dot{V}$ and ΔP_{ET} are the difference values. The value of K can be obtained by (10) using simultaneous values of arterial and end-tidal CO_2. However, as will be shown in the "Results section," the value of PCBF is relatively

insensitive to values of K, allowing an approximation for K to be made in the absence of an arterial blood sample.

As will be pointed out in the "Discussion," a reasonably accurate value of hemoglobin should be obtained.

Methods

A block diagram of the experimental system used in the animal experiments is shown in Fig. 1. A mass spectrometer (AIMT Medspect II, St. Louis, MO) was used to measure airway CO_2 concentrations at the subject's endotracheal tube via a 4 ft cannula with an in-line moisture filter. A heated pneumotachometer (Fleisch) and differential pressure transducer (Validyne MP45-1, Northridge, CA) were used to measure instantaneous airway flow. Analog output signals from both the mass spectrometer and the pneumotachometer were sampled at 40 Hz (MINC PDP-11, Digital Equipment Corp., Maynard, MA). Breath-by-breath determinations of respiratory rate, tidal volume, CO_2 elimination, and end-tidal CO_2 were calculated and displayed on a graphics terminal (VT-105, Digital Equipment Corp., Maynard, MA). A three-way valve (ASCO 8300A81U, 120 vac 1/4 in) was used to temporarily introduce an additional 170 ml of deadspace tubing into the ventilation circuit. The valve was controlled by the D/A output of the computer through a single transistor power amplifier.

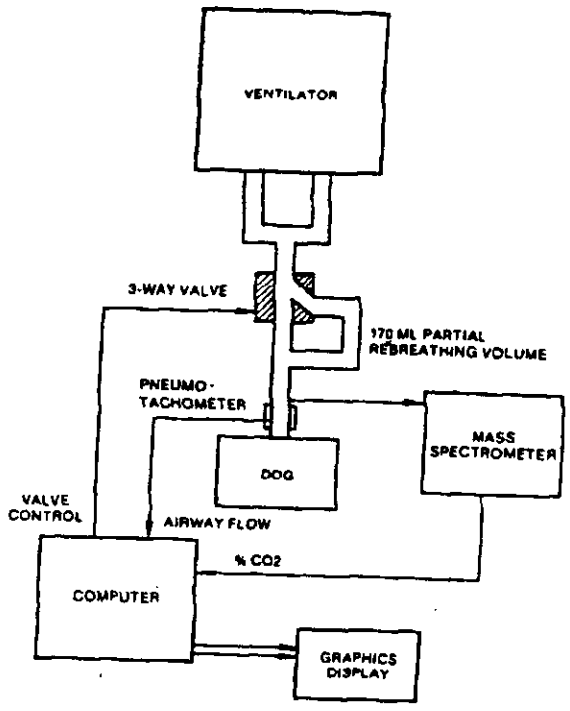

Fig. 1. System block diagram.

The rate of CO_2 elimination was calculated on a breath-by-breath basis by integrating the product of airway flow and the fractional concentration of CO_2. Compensation for the time delay and response time of the CO_2 measurement device, relative to the airway flow transducer, was performed as described by Noguchi *et al.* [17]. Briefly, the input to the measurement device is calculated by the equation

$$x(t) = y(t + D) + T\,dy(t + D)/dt \qquad (13)$$

where $x(t)$ is the input to the measurement device, D is the delay time, T is the time constant, and $y(t)$ is the measured output.

Later versions of this technique have eliminated this need for compensation by using an in-line capnograph (Siemens 930) instead of the mass spectrometer.

End-tidal pCO_2 was determined on a breath-by-breath basis using a peak detection algorithm which stored the maximum value of the transient CO_2 signal for each breath.

PCBF estimates were calculated using (12), and displayed by the computer. Baseline CO_2 elimination and end-tidal pCO_2 levels were determined at the conclusion of the normal ventilation period as the output of a 15 breath running average filter. Data outliers were removed by passing the data through two boxcar filters in which the past 1 min of $\dot{V}_{CO_2}$ and P_{ET} values are averaged and both standard deviations calculated. A new data point is introduced into the first in-first out filter and a new average and standard deviation calculated. If the new SD is greater than 1.10 (user determined) times the old SD, then the new data point is discarded. CO_2 elimination and end-tidal pCO_2 levels during rebreathing were determined as the average values calculated during the rebreathing period, excluding the first breath. A similar outlier routine was used during the rebreathing period.

Approval by the Institute Animal Care Committee was obtained prior to animal experimentation. 16 mongrel dogs weighing between 20 and 30 kg were anesthetized using pentobarbital sodium (25 mg/kg IV), intubated, and placed on a volume controlled ventilator (Siemens 900C) using room air. Supplemental injections of 50–100 mg of anesthetic were administered as needed throughout the experiment. Dogs were paralyzed with tubocurarine chloride (0.5 mg/kg) or pancuronium bromide (0.1 mg/kg) when necessary to limit respiratory effort. Isotonic saline was administered intravenously at approximately 100 ml/h and the dogs were kept warm with a heating pad. A Swan-Ganz catheter (Edwards, 7F) was placed percutaneously into an external jugular vein and advanced into the pulmonary artery. An arterial line was placed percutaneously into a femoral artery. Arterial pressure, central venous pressure, and pulmonary artery pressures were monitored continuously (Mennen Horizon). Thermal dilution cardiac output determinations were performed in triplicate using a cardiac output computer (Sorenson) and 7 cc of room temperature saline injections. Arterial and mixed venous blood gases were analyzed on a blood gas analyzer (Radiometer ABL2). At a tidal volume of 15 ml/kg, respiratory rate was adjusted to maintain an arterial pCO_2 of 40 mm Hg and sodium bicarbon-

ate was administered, as necessary, to regulate the arterial pH at 7.4.

The key assumption used in this technique is that mixed venous CO_2 does not change during the 30 s rebreathing period. This assumption was verified on a series of 20 trials on six dogs. The pulmonary artery pressure line was connected to an infusion/withdrawal pump (Harvard Apparatus 907). 20 s prior to the partial rebreathing maneuver, blood was withdrawn at 1 ml/s through a multiple serial stopcock arrangement from which ten 1 ml blood samples could be taken at 5 s intervals. Samples were then packed in ice and immediately analyzed on the blood gas analyzer. This was repeated during the 30 s partial rebreathing maneuver, providing a value of mixed venous pCO_2 every 5 s both before, during, and after partial rebreathing. End-tidal CO_2 was similarly measured, providing a comparison between the two measurements during partial rebreathing.

The PCBF measurement technique was tested by varying cardiac output, increasing alveolar deadspace, and inducing pulmonary edema. At the start of the monitoring period, normal ventilation was maintained for 3 1/2 min through the direct connection to the "Y" piece of the ventilator tubing. The computer then activated the three-way valve, causing an additional 170 ml of airway deadspace to be added. After 30 s of partial rebreathing the computer deactivated the valve, returning the ventilation circuit to normal, and estimated the PCBF. This procedure was repeated every 3 1/2 min. Measurements of cardiac output by the thermodilution were made in triplicate at approximately 10 min intervals.

Increases in cardiac output were initiated using intravenous infusion of dopamine (4–8 μg/kg/min). Decreases in cardiac output were initiated using incremental intravenous doses of propranolol (0.5 mg/dose).

Temporary increases in the alveolar deadspace fraction were created by occluding a branch of the pulmonary artery with the inflated balloon of the Swan-Ganz catheter. PCBF estimates by partial rebreathing were obtained before, during, and after the occlusion. Arterial blood gas analysis and end-tidal pCO_2 measurements were used to assess the changes in alveolar deadspace according to (10).

Three animals received incremental doses of oleic acid (0.05 ml/kg) to study the effects of pulmonary edema on the PCBF estimation algorithm. The stage of pulmonary edema was indirectly assessed through arterial blood gas analysis and a postmortem exam.

Results

The results of the comparisons between end-tidal CO_2 and mixed venous CO_2 are shown in Fig. 2. Mixed venous CO_2 did not change until after 30 s of partial rebreathing, whereas end-tidal CO_2 showed an exponential rise immediately upon rebreathing. This shows that the basic assumption that mixed venous CO_2 is constant during partial rebreathing is correct.

Comparison of thermodilution measured cardiac output

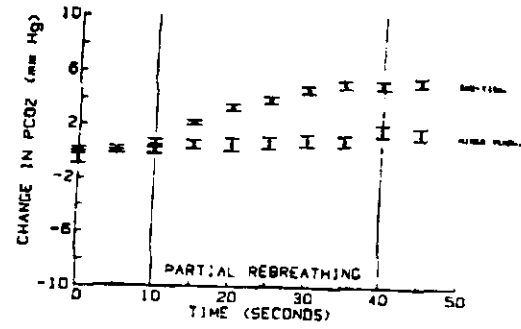

Fig. 2. End-tidal and mixed venous pCO_2 changes during partial rebreathing. Baseline pCO_2 levels were calculated as the average of samples taken during the preliminary normal ventilation period (0–10 s). Partial rebreathing (170 ml rebreathing volume) was maintained for 30 s (10–40 s). Ventilation was returned to normal at 40 s. Results shown as mean ± S.E.M. from 20 experiments on six dogs.

with PCBF estimates under conditions of time varying cardiac output show acceptable correlation. A sample of the end tidal pCO_2 and $\dot{V}_{CO_2}$ data obtained during a typical experiment is shown in Fig. 3. At t = 25 min, a dopamine infusion of 4 μg/kg/min was started, which was increased to 7 μg/kg/min at t = 35 min. At t = 75 min, the dopamine infusion was stopped and at t = 90 min, a 1 ml bolus of propranolol was slowly given. The information required for calculation of PCBF is contained in the pulses, each pulse representing the 30 s partial rebreathing maneuver. The recovery period is between each pulse. There are some noise spikes not within the 30 s interval but these do not affect the estimate. Noise spikes which occur within the 30 s interval are removed by the outlier processing routine. There is a sharp increase in $P_{ET_{CO_2}}$ and a similar sharp decrease in $\dot{V}_{CO_2}$ during this maneuver. During the change in cardiac output there is a change in the baselines of both measurements due to the increase in metabolic activity. However, it is the change from baseline that is used in this estimate. The absolute value of any measurement does not directly affect the result except in the determination of the slope of the CO_2 dissociation curve. An expanded view of one of these pulse pairs is shown in Fig. 4 showing the measurements necessary to make the PCBF estimate. The time course of both the thermodilution measurement and the PCBF estimate for this data set are shown in Fig. 5. As seen, there is acceptable agreement between these two different approaches.

The PCBF technique allows for an estimate to be made every 3 1/2 min, allowing 30 s for the partial rebreathing maneuver (inserting an additional 170 ml of deadspace in the ventilation circuit) and 3 min for the pCO_2 to return to normal values.

Linear regression was performed on 458 PCBF estimates compared to thermodilution measurements of cardiac output in 16 mongrel dogs, yielding a correlation coefficient of 0.92 about the regression line $y = 0.92x + 0.29$ (Fig. 6). Thermodilution measurements of cardiac output ranged from 1.5 to 7.0 l/min and 87 percent of the PCBF estimates were within 20 percent of the corre-

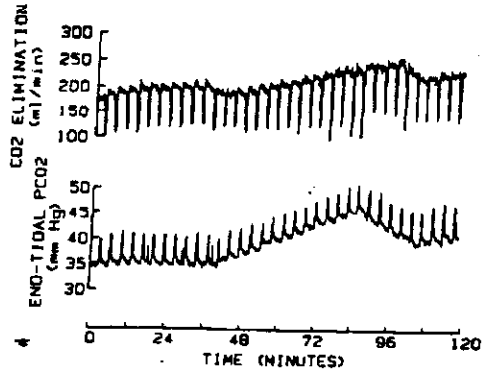

Fig. 3. End-tidal pCO_2 and CO_2 elimination data during a typical experiment. The periodic peaks in end-tidal pCO_2 and valleys in CO_2 elimination are caused by the partial rebreathing maneuvers.

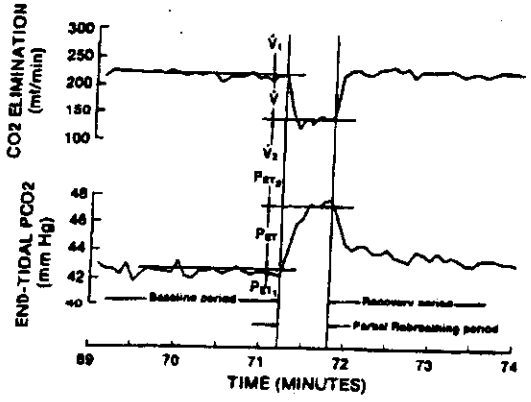

Fig. 4. End-tidal pCO_2 and CO_2 elimination data from one period of partial rebreathing. Partial rebreathing (170 ml) was maintained for 35 s (71.2–71.8 min). Tidal volume and respiratory rate were 400 ml and 15 breaths/min. Measurements of CO_2 elimination during normal ventilation (217 ml/min) and partial rebreathing (136 ml/min) and end-tidal pCO_2 during normal (42.4 mm Hg) and partial rebreathing (47.0 mm Hg) were used in (12) with [Hb] = 12.50 and K = 1.11 to provide a cardiac output estimate of 4.78 l/min. Cardiac output was measured by thermodilution to be 4.80 l/min.

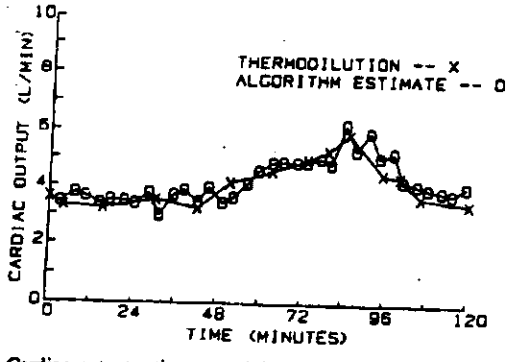

Fig. 5. Cardiac output estimates and thermodilution cardiac output during a typical experiment.

sponding thermodilution value. When thermodilution measurements of cardiac output were not made simultaneous with the estimates of PCBF, linear interpolation was used to obtain intermediate thermodilution values for comparison with the PCBF estimates. If the linear regression were to be forced through zero then a correlation coefficient of 0.91 would be obtained about the regression line $y = 1.00x$.

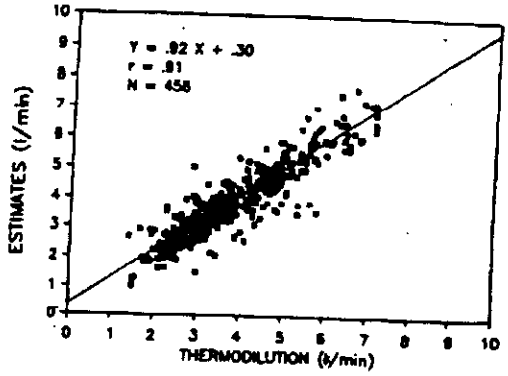

Fig. 6. Cardiac output estimates versus thermodilution cardiac output. Results of 458 determinations made in 16 mongrel dogs. Linear regression resulted in a correlation coefficient of 0.92 about the regression line $y = 0.92x + 0.29$, or a correlation coefficient of 0.91 about the regression line $y = 1.00x$.

TABLE I
COMPARISON OF AVERAGE RESULTS FOR EACH DOG

Dog	N	Average C.O. (ctm)	Average C.O. (est)	Average % Error	Average Absolute Error
1	21	5.71 ± .75	5.48 ± .65	0.00 ± .86	-.03 ± .67
2	34	4.01 ± .78	4.16 ± .76	6.44 ± 9.42	.15 ± .38
3	22	6.68 ± 1.10	5.12 ± 1.09	11.50 ± 14.7	.43 ± 59
4	9	2.28 ± .12	2.45 ± .16	7.80 ± 7.20	.18 ± .16
5	19	3.30 ± .42	3.09 ± .57	-6.40 ± 11.86	-.21 ± .40
6	88	3.64 ± .20	3.70 ± .41	1.09 ± 11.13	.06 ± .29
7	28	4.35 ± 1.10	4.50 ± 1.01	7.82 ± 26.29	.15 ± .37
8	20	3.43 ± .20	3.46 ± .35	0.93 ± 7.70	.03 ± .27
9	30	2.61 ± .61	2.52 ± .78	-4.69 ± 15.91	-.09 ± .41
10	56	2.77 ± .54	2.76 ± .55	0.59 ± 14.96	-.01 ± .38
11	29	3.64 ± .86	3.35 ± .75	-4.97 ± 16.27	-.29 ± .72
12	33	3.22 ± .55	3.17 ± .53	-1.21 ± 10.05	-.04 ± .32
13	65	5.58 ± .89	5.50 ± .89	-1.15 ± 8.12	-.08 ± .45
14	37	3.62 ± .20	3.67 ± .41	1.26 ± 9.48	.05 ± .34
15	56	4.00 ± .63	3.94 ± .76	-0.32 ± 19.65	-.06 ± .68
16	19	2.62 ± .70	2.76 ± .79	4.87 ± 15.41	.12 ± .35
All	458	3.74 ± 1.21	3.75 ± 1.22	1.16 ± 15.28	.01 ± .51

Table I shows the complete list of data taken from individual dogs, showing the number of points per dog, the average ± standard deviation for both estimate and thermodilution cardiac outputs, the percent error ± standard deviation, and the absolute error ± standard deviation. Fig. 7 shows the distribution of errors as a percentage of the number of points.

Alveolar deadspace was increased by inflating the Swan-Ganz balloon. The PCBF estimates and thermodilution measurements of cardiac output obtained before the Swan-Ganz catheter balloon was inflated were not significantly different ($p < 0.05$) from those obtained after the balloon was deflated. The PCBF estimates obtained during the inflation period were significantly different ($p < 0.01$) from those obtained before and after inflation. The

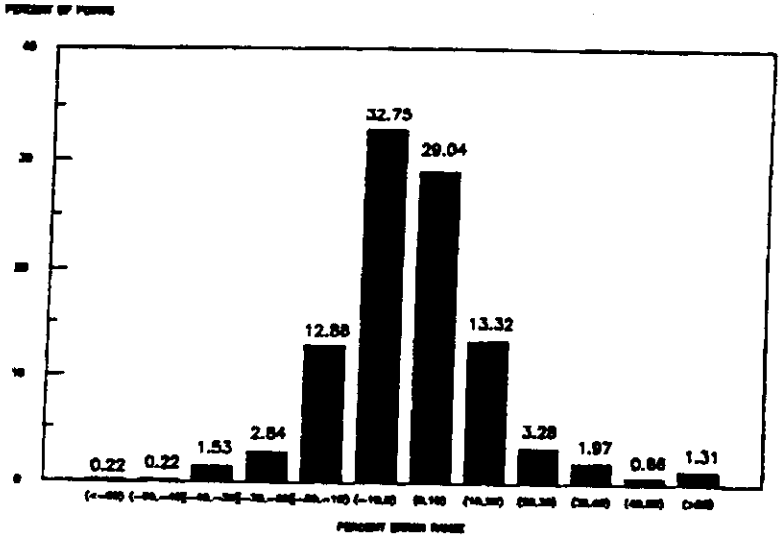

Fig. 7. Distribution of errors as a percentage of the number of points.

average PCBF estimate obtained during balloon inflation was 11.3 percent lower than the mean of the estimates obtained before and after the inflation period. The average alveolar deadspace fraction more than doubled from 0.14 to 0.37 and the average arterial to end-tidal pCO_2 gradient increased from 5.8 to 20.1 mm Hg during the inflation period.

This is in agreement with a mathematical sensitivity analysis of the estimate in cardiac output versus the factor K. Differentiating $\dot{Q}$ in (12) with respect to K, the sensitivity index $S = \partial\dot{Q}/\dot{Q}/\partial K/K$ can be found by the substitution of normal values for the variables. The sensitivity index S is found to be 0.11, meaning that a 100 percent change in the value of K (approximately a 500 percent change in alveolar deadspace) would cause only an 11 percent change in cardiac output. This means that the result is relatively insensitive to changes in alveolar deadspace.

One of the most surprising results of this study is the tracking of PCBF estimates with thermodilution cardiac output during oleic acid infusion. It is expected that there are large ventilation perfusion mismatches during this procedure. However, for the three dogs tested there was good correlation. One of these experiments is reproduced in Fig. 8. 56 PCBF estimates were compared to thermodilution measurements of cardiac output during this experiment in which oleic acid injections were used to create progressive stages of pulmonary edema. Despite a reduction in arterial pO_2 from 104.2 to 44.3 mm Hg and an increase in alveolar deadspace fraction from 0.16 to 0.39, indicating a deterioration of lung function, linear regression provided a correlation of 0.90 and regression slope of 0.92 between the PCBF estimates and direct thermodilution measurements of cardiac output. The only significant deviation occurred at approximately 80 s at which time an additional injection of oleic acid was given.

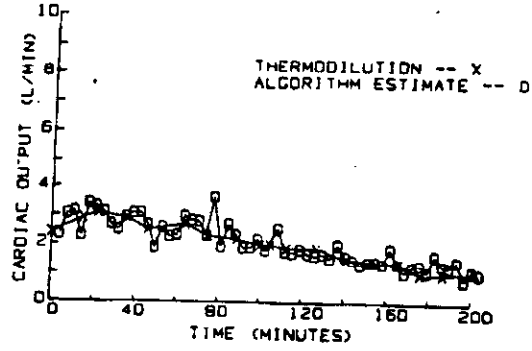

Fig. 8. Cardiac output estimates and thermodilution cardiac output during pulmonary edema. Injections of oleic acid were made at 45 min (0.75 ml), 75 min (0.75 ml), and 130 min (1.0 ml). Linear regression between the estimates of cardiac output and direct thermodilution measurements yielded the regression line $y = 0.92x + 0.22$, $r = 0.90$, $n = 56$.

Discussion

This paper describes a technique for estimating pulmonary capillary blood flow based on the differences in end-tidal pCO_2 and CO_2 elimination measured during normal ventilation and during a 30 s period of partial rebreathing. The computational equation used to estimate PCBF is different from other Fick techniques using CO_2 as the indicator in that the need to estimate mixed venous pCO_2 has been eliminated.

The most commonly used noninvasive technique to estimate mixed venous pCO_2 and PCBF is total rebreathing [8]–[12]. In this technique, alveolar pCO_2 rises toward an equilibrium value which is taken to represent mixed venous pCO_2. However, the determination of the equilibrium pCO_2 is corrupted by the continuous uptake of O_2 from the rebreathing bag resulting in what has been subsequently called "lung-bag volume shrinkage" [18], [19]. In addition, the maneuver creates temporary periods of

elevated, and at times severe hypercapnia, which limits its use. The partial rebreathing technique developed in this paper is similar to the total rebreathing technique except that the effects of lung-bag volume shrinkage are eliminated, and the changes in arterial pCO_2 are reduced by approximately half. This is accomplished by the brief (30 s) insertion of an additional fixed deadspace into the breathing circuit, causing rapid, temporary changes in pCO_2 and $\dot{V}_{CO_2}$. These changes are used to calculate the PCBF.

One of the major assumptions of the algorithm is the constancy of the mixed venous CO_2 content during the partial rebreathing period. The results shown in Fig. 2 support the assumption that for 30 s periods of partial rebreathing, the effects of recirculation on mixed venous pCO_2 are small when compared to the observed changes in end-tidal pCO_2. If the mixed venous CO_2 content does increase during partial rebreathing the CO_2 elimination and end-tidal pCO_2 would increase, leading to a low estimate of PCBF. Under conditions of elevated cardiac output, the recirculation time is often reduced; therefore, effects of recirculation would be expected to cause systematically low estimates of PCBF at high cardiac outputs. However, Figs. 5 and 6 indicate that for cardiac outputs as high as twice the resting level, there is no systematic error in the PCBF estimates.

Shortening the partial rebreathing period is one method of limiting the changes in the mixed venous CO_2 content. This may decrease the accuracy in determining the end-tidal pCO_2 and $\dot{V}_{CO_2}$ elimination levels during partial rebreathing. Increased error may arise since the end-tidal pCO_2 and $\dot{V}_{CO_2}$ elimination measurements taken on a breath-by-breath basis are corrupted by measurement noise and by variations in tidal volume and respiratory rate. To reduce the effects of breath-by-breath variations in the measured data, averages of the end-tidal pCO_2 and $\dot{V}_{CO_2}$ elimination were taken during the partial rebreathing period (excluding the first breath) and used in (12) to determine the PCBF estimate.

Another assumption of the algorithm is that the alveolar deadspace to tidal volume ratio is constant during the partial rebreathing period. Since tidal volume and respiratory rate change little during the partial rebreathing period, this assumption is valid unless the alveolar deadspace volume changes directly due to a change in the ventilation/perfusion distribution in the lungs. Limiting the duration of partial rebreathing maintains alveolar oxygen levels which minimizes the effects of hypoxic pulmonary vasoconstriction and bronchoconstriction. Changes in the distribution of ventilation and perfusion in the lung during partial rebreathing would therefore be small.

Sensitivity analysis demonstrates that if the alveolar deadspace fraction is greater than the assumed value of 0.10, then the algorithm will overestimate the PCBF. However, PCBF estimates obtained during temporary inflation of the Swan–Ganz catheter balloon were lower than those estimates obtained before and after the inflation. This decrease in estimated PCBF may reflect a reduction in cardiac output due to an increase in pulmonary vascular resistance. Other investigators using total rebreathing techniques experienced significant errors in estimating cardiac output when the arterial to end-tidal pCO_2 gradient exceeded 5 mm Hg [20]–[22]. In the present algorithm, estimates of PCBF were lowered by only 11.3 percent in the presence of arterial to end-tidal pCO_2 gradients as high as 28.0 mm Hg. The reduced sensitivity of the present technique to increased alveolar deadspace results from the use of end-tidal pCO_2 changes instead of absolute end-tidal pCO_2 values in the calculation of PCBF. Absolute values of end-tidal pCO_2 are needed only for the calculation of the slope of the CO_2 dissociation curve.

Other factors such as pH and temperature affect primarily the position of the dissociation curve but have little effect on the slope. Since it is the slope of the CO_2 dissociation curve that is used in the calculation of PCBF, only factors which affect the slope are of prime consideration. As discussed previously, a mathematical sensitivity analysis of the alveolar deadspace factor, K shows a sensitivity factor of 0.11 for this factor, indicating that the estimate for PCBF is relatively insensitive to this factor. Alternatively the value of hemoglobin (Hb) does have a significant influence on the slope of the dissociation curve. Performing a sensitivity analysis on (12), the sensitivity index $\partial Q/Q/\partial \mathrm{Hb}/\mathrm{Hb}$ using normal values for the variables is found to be 0.52. This means that a 30 percent change in Hb (a loss of 3–4 units of blood) will cause an error in PCBF estimate of 15 percent. This is a much more significant source of error than a change in alveolar deadspace. The two locations where this technique is likely to be used are in the operating room (OR) and the intensive care unit (ICU). In both of these sites, hemoglobin is usually tracked frequently, especially if a rapid blood loss is involved. However, this is a source for error which must be taken into consideration.

The PCBF estimates demonstrated a high correlation (0.90) with direct thermodilution measurements of cardiac output in the pulmonary edema experiment (Fig. 8). Since during periods of pulmonary edema large pulmonary shunts are typically measured, this result was not expected. Pulmonary shunt flow is that portion of the pulmonary blood flow that perfuses alveoli but does not undergo oxygen exchange with the ventilated region of the lung. Due to the different solubilities of carbon dioxide and oxygen, it is possible that the presence of edema fluid in the lungs affects oxygen exchange to a greater degree than carbon dioxide. Since the PCBF estimates agreed well with direct thermodilution measurements of cardiac output, our results suggest that regions of the lung that were unable to exchange oxygen were still capable of exchanging carbon dioxide even in the presence of a diffuse pulmonary shunt.

The effects of changes in the CO_2 lung tissue stores due to changes in alveolar pCO_2 have been neglected in the PCBF estimation algorithm. Changes in CO_2 lung stores,

as a result of the sudden increase in CO_2 partial pressures during partial rebreathing, result in a transiently low measurement of $\dot{V}_{CO_2}$ elimination made at the mouth when compared to the actual rate of elimination of CO_2 at the alveoli. This transient difference could result in an overestimation of the PCBF depending on the duration and magnitude of the difference. Hlastala *et al.* [23] calculated that 34 percent of a sudden change in alveolar CO_2 is reabsorbed by lung tissue, while Kim *et al.* [5], using a similar approach, determined that the lung tissue could only retain less than 1 percent of the change in CO_2.

The calculations of Hlastala *et al.* [23] were obtained assuming that the time constant of equilibration between alveolar pCO_2 and the CO_2 lung stores was zero. If this is the case, then the discrepancies between the CO_2 elimination measured at the mouth and the CO_2 elimination present at the alveoli will only be present as the alveolar pCO_2 is increasing. Since during partial rebreathing the end-tidal pCO_2 typically reaches its new steady state within 15 s, the effects of changes in CO_2 lung stores are reduced. If the equilibration time constant is greater than zero (Kim *et al.* [5] assumed an infinite time constant), the magnitude of the discrepancies will be reduced, but their duration increased.

It has been suggested by Breen and others [24]–[27] that changes in end-tidal CO_2 can be used to track changes in cardiac output. Referring back to (1), this suggestion will hold only if both the rate of CO_2 elimination ($\dot{V}$) and mixed venous CO_2 ($C_{\bar{v}}$) remain constant. Fig. 5 shows a rise in the baseline of both $\dot{V}$ and P_{ET} carbon dioxide during a rise in cardiac output induced by dopamine. Consequently, a technique which tracks only changes in end-tidal CO_2 will be incorrect.

Conclusions

The technique presented in this paper provides a semi-continuous method of noninvasively estimating cardiac output. Estimates (458) of cardiac output when compared to direct thermodilution measurements in 16 dogs yielded a correlation coefficient of 0.91 with a linear regression slope of 1.00. Temporary increases in alveolar deadspace did not significantly alter this relationship. The technique is simple to perform requiring measurements of end-tidal CO_2 and CO_2 elimination during both normal ventilation and during 30 s periods of partial rebreathing. A differential form of the Fick equation is used which requires only the difference in measurements, not the absolute values. This approach does not require the measurement of mixed venous CO_2 content, eliminating the major source of error in previous rebreathing techniques.

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Partial carbon dioxide rebreathing: A reliable technique for noninvasive measurement of nonshunted pulmonary capillary blood flow

Marcelo Gama de Abreu, MD, MSc; Michael Quintel, MD; Max Ragaller, MD; Detlev Michael Albrecht, MD

Objective: To determine the validity and clinical utility of the partial CO_2 rebreathing technique for measurement of nonshunted pulmonary capillary blood flow and cardiac output.

Design: Prospective, controlled animal laboratory investigation and clinical trial.

Settings: Animal research facility and intensive care unit of a university hospital.

Subjects: Fifteen adult sheep, weighing 58 to 78 kg.

Patients: Mechanically ventilated patients with different underlying diseases (n = 12) and with adult respiratory distress syndrome (ARDS) (n = 8).

Interventions: CO_2 elimination rate ($\dot{V}co_2$) was measured breath-by-breath with a system developed for the study and also by gas collection (validation procedure in patients with different underlying diseases). Partial CO_2 rebreathing maneuvers, cardiac output by thermodilution, and blood gas analysis were performed in sheep with lung atelectasis and in patients with ARDS.

Measurements and Main Results: The degree of correlation between $\dot{V}co_2$ measured with the system developed and gas collection was very good (r^2= .95, $p < .0001$), and bias and precision calculations (1 ± 9 mL/min) showed close agreement between methods. The overall degree of correlation between partial CO_2 rebreathing measurements and cardiac output was moderate (r^2 = .54, $p < .0001$), the noninvasive method tending to underestimate cardiac output, as shown by bias and precision calculations (–1.69 ± 1.90 L/min). In contrast, the overall degree of correlation between partial CO_2 rebreathing measurements and nonshunted pulmonary capillary blood flow was good (r^2 = .73, $p < .0001$). Bias and precision calculations (0.25 ± 0.83 L/min) showed a tendency for the partial CO_2 rebreathing technique to slightly overestimate pulmonary capillary blood flow. Variance differences between partial CO_2 rebreathing measurements and cardiac output could be mostly explained by intrapulmonary right-to-left shunt fraction (r^2 = .51, $p < .0001$).

Conclusions: Our results support the use of the system developed for breath-by-breath $\dot{V}co_2$ measurements. The lack of agreement between partial CO_2 rebreathing measurements and cardiac output was mostly explained by intrapulmonary right-to-left shunt, suggesting that this technique may not be appropriate for monitoring cardiac output in patients with increased venous admixture. In contrast, our results demonstrate that the partial CO_2 rebreathing technique is reliable for measurement of the effective nonshunted pulmonary capillary blood flow. This technique may prove useful to guide ventilatory therapy adjustments in an attempt to optimize nonshunted pulmonary capillary blood flow. (Crit Care Med 1997; 25:675–683)

KEY WORDS: cardiac output; pulmonary capillary blood flow; noninvasive measurement; gas collection; breath-by-breath analysis; partial CO_2 rebreathing; thermodilution; pulmonary artery catheter; lung atelectasis; adult respiratory distress syndrome

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Cardiac output represents one of the hemodynamic variables which best describes the adequacy of the macrocirculatory function. Invasive methods, such as the direct Fick principle and dilution of markers, have been widely used to measure cardiac output because of their accuracy and precision but require pulmonary artery catheterization, which can be hazardous to the patient (1–6). Among the noninvasive methods, the indirect Fick principle has received special attention because it is relatively easy to perform and is precise and accurate enough for clinical and research purposes (7). According to this principle, cardiac output can be calculated as the ratio between CO_2 elimination rate ($\dot{V}co_2$) and mixed venous-arterial CO_2 content difference ($C\bar{v}co_2$-$Caco_2$). While $Caco_2$ can be easily estimated from the end-tidal Pco_2 ($Petco_2$) when arterial end-tidal Pco_2 differences are neglectable, more complex maneuvers, such as total CO_2 rebreathing or analysis of single-breath, are required to estimate $C\bar{v}co_2$ noninvasively (7). These maneuvers have in common the transitory interruption of CO_2 elimination, which leads $Petco_2$ to increase progressively,

tending to reach the mixed venous P_{CO_2} ($P\bar{v}CO_2$), until pulmonary recirculation occurs. $P\bar{v}CO_2$ is finally converted to $C\bar{v}CO_2$ using standard dissociation curves.

More than a decade ago, Gedeon et al. (8) proposed a differential form of the CO_2 rebreathing technique which eliminates the need of estimating $C\bar{v}CO_2$. By means of a mathematical manipulation of the Fick equation, it can be demonstrated that cardiac output can be determined from simultaneous gradient changes in $\dot{V}CO_2$ and $CaCO_2$ (see Materials and Methods). Since this technique leads to lesser increases in $PaCO_2$, as observed in total rebreathing, does not require any special gas mixture, and can be repeated at intervals of 2 mins (9), it could find a broader use than traditional CO_2 rebreathing methods.

Recently, Capek and Roy (9) suggested that this noninvasive method is reliable for measurement of cardiac output even in the presence of ventilation/perfusion mismatching in the lungs, although it has been suggested that the partial CO_2 rebreathing technique should not be capable of measuring cardiac output in patients with pulmonary disease (8). Since only the amount of blood flowing through the well-ventilated alveolocapillary bed contributes significantly to the $\dot{V}CO_2$, and P_{ETCO_2} changes more closely reflect CO_2 content changes of the well-ventilated, well-perfused alveolocapillary bed, we hypothesized that the partial CO_2 rebreathing technique might be able to measure only the blood flow which effectively undergoes gas exchange, i.e., the nonshunted pulmonary capillary blood flow.

In the present study, we evaluated the reliability of the partial CO_2 rebreathing technique for measurement of nonshunted pulmonary capillary blood flow and whole cardiac output in mechanically ventilated sheep with lung atelectasis and patients with adult respiratory distress syndrome (ARDS). Following the implementation and validation of a breath-by-breath gas exchange measurement system, the accuracy and precision of this noninvasive method were determined for the variables investigated. Additionally, the influence of arterial end-tidal P_{CO_2} differences, ventilation/perfusion mismatching (quantified as intrapulmonary right-to-left shunt and physiologic deadspace), and pulmonary recirculation on the error of estimating cardiac output with the partial CO_2 rebreathing technique were investigated.

MATERIAL AND METHODS

Theoretical Background. The Fick equation for cardiac output using CO_2 is written as shown in Appendix 1, where $\dot{Q}$ is cardiac output, $\dot{V}CO_2$ is CO_2 elimination rate, $C\bar{v}CO_2$ is mixed venous CO_2 content, and $CaCO_2$ is arterial CO_2 content. Rewriting Equation *1* for both a nonrebreathing (NR) and a partial rebreathing period (R), we obtain Equations *2* and *3*, respectively (Appendix 1).

If we subtract Equation *3* from Equation *2* and rewrite the resulting equation, we obtain Equation *4* (Appendix 1).

If the mixed venous P_{CO_2} ($P\bar{v}CO_2$) remains unaltered during rebreathing, $C\bar{v}CO_2$ does not change and Equation *4* can be rewritten as shown in Equation *5* (Appendix 1), where $\dot{Q}_{reb}$ is blood flow measured by the partial CO_2 rebreathing technique. If $\dot{V}CO_2$ is represented in mL/min and CO_2 content in mL/100 mL, then $CaCO_2$ must be multiplied by 10 in order to obtain blood flow in L/min.

Implementation of the Gas Exchange Measurement System. In order to perform breath-by-breath gas exchange measurements, we built a system, as represented schematically in Figure 1. The system consisted of a mechanical ventilator (Servo 900C, Siemens-Elema, Solna, Sweden), from which internal flow sensors the air flow signal was obtained, a mainstream infrared CO_2 analyzer (CO_2-Analyzer 930, Siemens-Elema), which provided respiratory CO_2 fraction (F_{CO_2}) signal, a 16-bit analog-digital board (AT-MIO-16X, National Instruments, Austin, TX) and a microcomputer, for data acquisition and processing. F_{CO_2} and air flow signals were acquired over the entire respiratory cycle, i.e., during inspiration and expiration, with 60-Hz sampling frequency filtered with a triangular moving average filter (cut-off frequency at 12 Hz) to remove high-frequency noise from the signals, and processed off-line for calculating P_{ETCO_2}, and breath-by-breath $\dot{V}CO_2$, as represented in Equation *6* (Appendix 1), where V is air flow, F_{CO_2} is CO_2 fraction, and T is time interval of analysis. Data from the capnometer (F_{CO_2}) were corrected for its known oxygen error (10).

Adaptation for Partial CO_2 Rebreathing Measurements. The experimental setup for the noninvasive measurements by partial CO_2 rebreathing was pratically the same as used for validation of breath-by-breath $\dot{V}CO_2$. In order to perform the rebreathing maneuver, two low resistive, low deadspace three-way valves with a 200-mL tube were used, as shown in Figure 1.

The software was adapted to the measurement of P_{ETCO_2} and breath-by-breath $\dot{V}CO_2$ in three different periods.

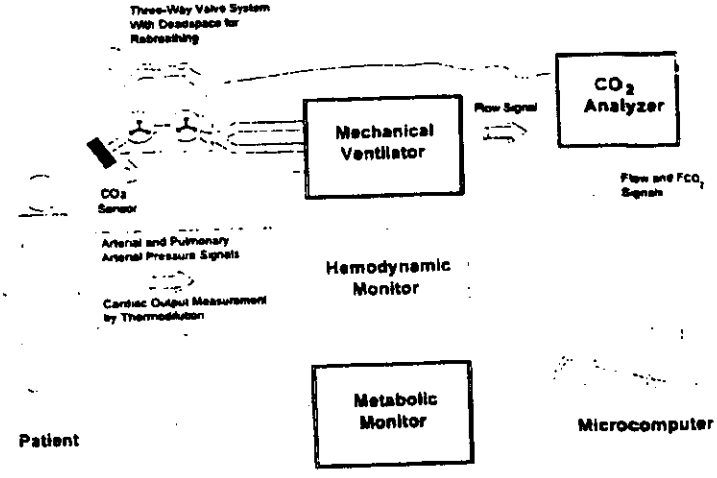

Figure 1. Schematic diagram of the experimental setup for validation of breath-by-breath CO_2 elimination rate and partial CO_2 rebreathing measurements. The devices in the boxes marked with *dashed lines* were used for the partial CO_2 rebreathing experiments only (see text).

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The first one took ~60 secs and was performed with a low deadspace circuit (nonrebreathing period). The second one took ~30 secs and was performed after switching the three-way valves. Thereby, 200 mL was added to the respiratory circuit (rebreathing period). Finally, the valves were switched to the original position until P_{ETCO_2} and $\dot{V}CO_2$ returned to control values (recuperation period).

Nonrebreathing $\dot{V}CO_2$ and P_{ETCO_2} were determined as the mean value of each respective variable during the 60-sec nonrebreathing period. Rebreathing $\dot{V}CO_2$ and P_{ETCO_2}, however, were determined as the mean values from the last 15 secs of the partial CO_2 rebreathing period to: a) exclude the transitory phase until a new plateau was achieved (defined as a difference of ≤1 torr [≤0.13 kPa] between consecutive P_{ETCO_2} measurements); and b) minimize the effects of the pulmonary recirculation (increase of the $P\bar{v}CO_2$) on the measurements. The $Paco_2$ between rebreathing and nonrebreathing periods was estimated using the equation proposed by McHardy (11), with appropriate corrections for hemoglobin concentration and oxygen saturation, and as represented in Equation *7* (Appendix 1), where Hb is hemoglobin concentration (g/dL), Sao_2 is the measured arterial hemoglobin saturation, and the symbols (NR) and (R) represent nonrebreathing and rebreathing periods, respectively; corrections for acid-base status were not required since blood pH was always in the range of 7.30 to 7.50.

Study Protocols. This study included three protocols, which were approved by the Institutional Review Board for patient measurements and the Animal Care Committee for animal measurements. Measurements in patients were performed after informed consent was obtained from a next-of-kin. Measurements in animals were performed in accordance with the Guide for the Care and Use of Laboratory Animals (National Institutes of Health).

Protocol for Validation of the Gas Exchange Measurement System. Breath-by-breath $\dot{V}CO_2$ measurements were performed on 12 intensive care patients who were naso- or orotracheally intubated, volume-control ventilated with 10 to 15 mL/kg of tidal volume and respiratory frequencies of 8 to 15 breaths/min, anesthetized with fentanyl (0.2 mg/hr) and midazolam (10 to 20 mg/hr), and paralyzed with pancuronium (4 mg/hr).

Gas collection (Deltatrac, Datex, Bremen, Germany) and breath-by-breath $\dot{V}CO_2$ measurements were performed for 10 mins and for 60 secs, respectively. The mean value of each method, in standard temperature, and pressure dry conditions, were used for comparison. Both the gas collection device and infrared CO_2 analyzer were calibrated with a gas mixture containing 5.15% CO_2 and 16% oxygen and nitrogen (calibration certificate from Messer Griesheim, Griesheim, Germany).

Protocol for Partial CO_2 Rebreathing Measurements in a Lung Atelectasis Group. Fifteen adult sheep, weighing 58 to 78 kg, were entered into a study of computer tomographic examination of lung atelectasis model. Additionally, they were used for this protocol during the stabilization period. They were anesthetized with ketamine (4 mg/kg/hr) and midazolam (0.1 mg/kg/hr) and paralyzed with pancuronium (0.1 mg/kg/hr). Following tracheostomy and tracheal intubation, animals were ventilated with an F_{IO_2} of 0.4, 1:2 inspiration/expiration ratio, and a positive end-expiratory pressure (PEEP) level of 5 cm H_2O. The minute volume was adjusted to maintain $Paco_2$ in the 35 to 45 torr (4.7 to 6 kPa) range. Hemodynamic monitoring was performed by means of a catheter placed in the right carotid artery and a pulmonary artery catheter with fiberoptic oximetry, which was placed through the right internal jugular vein. A continuous infusion of crystalloid solution was also maintained (10 mL/kg/hr) and the diuresis was monitored with a suprapubic urinary catheter.

Thirty minutes before measurements were taken, the animals' hemodynamics and gas exchange parameters were allowed to stabilize. Initially, arterial blood was sampled and assayed with a blood gas analyzer (ABL 520, Radiometer, Copenhagen, Denmark). The physiologic deadspace fraction (V_D/V_T) was determined according to the Bohr-Enghoff equation, as represented in equation *[8]* (Appendix 1), where P_{ECO_2} is mean-expiratory Pco_2.

Partial CO_2 rebreathing measurements were then performed in triplicate with the mean value being used for comparison. During a nonrebreathing period, mixed venous blood was sampled through the pulmonary artery catheter and nonrebreathing $P\bar{v}CO_2$ was determined with the blood gas analyzer. The pulmonary artery catheter was not flushed, and during the last 15 secs of one rebreathing maneuver, 4 mL of mixed venous blood was sampled and immediately assayed. Rebreathing $P\bar{v}CO_2$ was estimated after correcting for the amount of blood contained in the pulmonary artery catheter with nonrebreathing $P\bar{v}CO_2$ as represented by Equation *9* (Appendix 1), where Pco_2 (15 secs – 30 secs) is partial CO_2 pressure of the 4-mL mixed venous blood sampled between 15 and 30 secs of rebreathing, v_{cat} is blood volume contained in the pulmonary artery catheter, and NR and R represent nonrebreathing and rebreathing periods, respectively.

Cardiac output was measured invasively by the thermodilution method using the Sirecust Unit 1281 (Siemens, Erlangen, Germany). Measurements were performed three times with 10 mL 0.9% saline solution at 4°C. The mean value was used for comparison. Following 15 mins of ventilation with an F_{IO_2} of 1.0, arterial and mixed venous blood were sampled and intrapulmonary right-to-left shunt fraction ($\dot{Q}sp/\dot{Q}t$) was calculated according to Equations *10* to *14* (Appendix 1), where $Cc\dot{o}_2$ is capillary oxygen content, Cao_2 is arterial oxygen content, $C\bar{v}o_2$ is mixed venous oxygen content, Hb is hemoglobin, PB is barometric pressure, P_{H_2O} is water vapor pressure at 37°C, RQ is respiratory quotient, Sao_2 is arterial oxygen saturation, $S\bar{v}o_2$ is mixed venous oxygen saturation, and $P\bar{v}o_2$ is mixed venous Po_2.

Finally, computed tomography scanning of the thorax was performed. Pulmonary capillary blood flow by thermodilution ($\dot{Q}_{c,TD}$) was calculated as shown in Equation *15* (Appendix 1).

Protocol for Partial CO_2 Rebreathing Measurements in a Lung Injury Group. Eight patients with ARDS were investigated. They were naso- or orotracheally intubated, mechanically ventilated with 6 to 15 breaths/min respiratory frequency, 10 to 15 mL/kg tidal volume, 1:2 or 1:1 inspiration/expiration ratio, and 8 to 15 cm H_2O PEEP to maintain adequate arterial oxygenation. They were anesthetized with fentanyl (0.2 mg/hr) and midazolam

(10 to 20 mg/hr) and paralyzed with pancuronium (4 mg/hr). Invasive hemodynamic monitoring was performed by means of a catheter placed in the left or right radial artery and a pulmonary artery catheter with fiberoptic oximetry inserted through the right inominate vein or the right internal jugular vein. A diagnosis of ARDS was based on all of the following criteria: a) at least one commonly accepted risk factor for ARDS; b) Pao_2/Fio_2 <150 torr; c) new diffuse interstitial and/or alveolar infiltrates by chest radiograph; d) total static pulmonary compliance <50 mL/cm H_2O; and e) pulmonary artery occlusion pressure <18 mm Hg.

Partial CO_2 rebreathing, cardiac output, V_D/V_T, and intrapulmonary right-to-left shunt fraction measurements were performed in the same way as described for the sheep group. Blood gas analysis and invasive hemodynamic monitoring were performed with the same devices as previously described.

Statistics. The statistical analysis was performed according to the general guidelines proposed by Altman and Bland (12). Correlation between methods was assessed by linear regression analysis. Concordance between methods was determined by means of bias (mean difference of two methods) and precision (SD of the mean difference of two methods) calculations. A stepwise multiple linear regression analysis was performed using the difference between cardiac output and partial CO_2 rebreathing measurements as the dependent variable and intrapulmonary right-to-left shunt fraction, V_D/V_T, and arterial end-tidal P_{CO_2} difference as the independent variables. To ensure that the arterial end-tidal P_{CO_2} difference and V_D/V_T were not important covariants, a simple linear regression analysis was performed with these variables alone. The increase in $P\bar{v}CO_2$ due to pulmonary recirculation was tested with the paired Student's two-tailed *t*-test and the influence of this effect on the difference between cardiac output and partial CO_2 rebreathing measurements was also evaluated with simple linear regression in the sheep group. A $p < .05$ was considered statistically significant.

Table 1. Characteristics of patients investigated in the protocol for validation of a gas exchange measurement system

Pt.	Age	Gender	Underlying Disease
1	19	F	Multiple trauma
2	43	M	Head injury
3	55	M	Brain tumor
4	37	M	Aspiration of gastric contents
5	49	F	Hemorrhagic shock
6	68	M	Head injury
7	39	F	Acute pancreatitis
8	52	M	Multiple trauma
9	69	M	Pneumonia
10	61	F	Head injury
11	57	M	Hemorrhagic shock
12	48	M	Sepsis

Pt., patient.

RESULTS

Validation of the Gas Exchange Measurement System. Eight men and four women with mean age of 50 yrs (range 19 to 69) were studied. Demographic and clinical data of this group are presented in Table 1. The overall degree of correlation between breath-by-breath $\dot{V}co_2$ and $\dot{V}$ by the gas collection method was very good ($r^2 = 0.95$, $p < .0001$). All measurements obtained with the breath-by-breath method were situated within ±7.5% of the measurements obtained with gas collection (Fig. 2, *top*). Bias and precision calculations (1 ± 9 mL/min) also showed close agreement between methods (Fig. 2, *bottom*). The 95% confidence interval for the mean difference between methods ranged from +19 mL/min to −17 mL/min.

Partial CO_2 Rebreathing Measurements. Dorsal lung atelectasis as a consequence of prolonged supine position was confirmed qualitatively, by means of the visualization of opacification zones in computed tomography scans of the thorax of all sheep investigated. General characteristics of this group and the effective physiologic

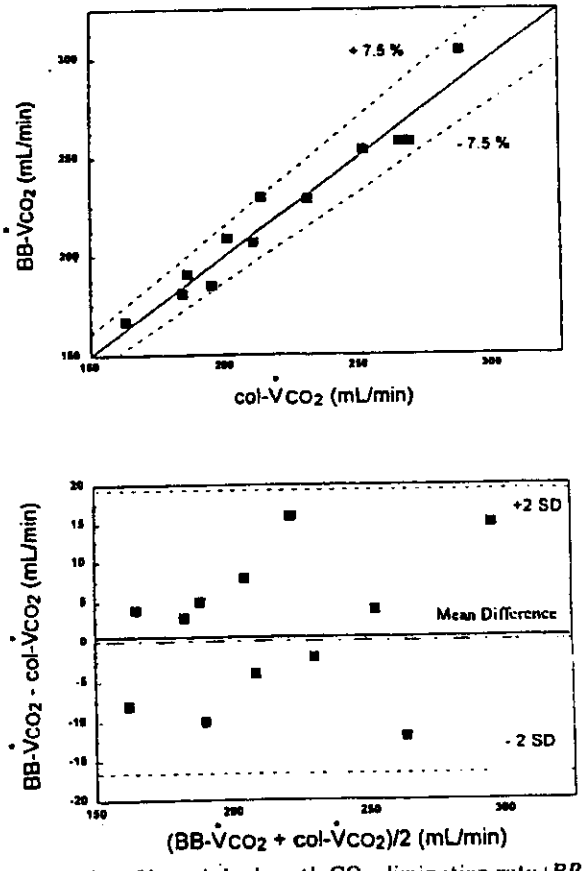

Figure 2. *Top:* Scatterplot of breath-by-breath CO_2 elimination rate ($BB\text{-}\dot{V}co_2$) measured with the system implemented (see text) against gas-collection CO_2 elimination rate ($col\text{-}\dot{V}co_2$), both in standard temperature and pressure, dry conditions. All data pairs fell within 7.5% of the identity line. *Bottom:* Difference in CO_2 elimination rate plotted against the average of the two techniques. *Solid line*, mean difference (1 mL/min); *dashed lines*, 95% confidence limits (±2 SD) for mean difference.

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derangement which resulted from atelectasis, as well as the increase in $P\bar{v}CO_2$ due to pulmonary recirculation, are shown in Table 2. Clinical and physiologic data of patients with ARDS who were also studied are presented in Table 3.

Figure 3 shows the time course of breath-by-breath $\dot{V}CO_2$ and P_{ETCO_2} in a typical measurement using partial CO_2 rebreathing. The decrease of the $\dot{V}CO_2$ in the rebreathing period was followed by the increase of the P_{ETCO_2}, which tended to achieve a new plateau about 15 secs after the beginning of the rebreathing period. Following the switching of the valves to the original position, $\dot{V}CO_2$ and P_{ETCO_2} returned to control values within −15 secs.

Partial CO_2 rebreathing measurements correlated only moderately with cardiac output ($r^2 = .54$, $p < .0001$). Only 43% (10 of 23) of the noninvasive measurements were within 20% of cardiac output values (Fig. 4, *top left panel*). Bias and precision calculations (−1.69 ± 1.90 L/min) showed a tendency for the partial CO_2 rebreathing technique to underestimate cardiac output (Fig. 4, *bottom left panel*). The 95% confidence interval for the mean difference between methods ranged from +2.11 L min to −5.79 L min.

The overall degree of correlation between partial CO_2 rebreathing measurements and nonshunted pulmonary capillary blood flow was good ($r^2 = .73$, $p < .0001$). Seventy-eight percent (18 of 23) of the noninvasive measurements fell within 20% of nonshunted pulmonary capillary blood flow values (Fig. 4, *top right panel*). Bias and precision calculations (0.24 ± 0.83 L/min) showed a tendency for the partial CO_2 rebreathing technique to slightly overestimate the nonshunted pulmonary capillary blood flow (Fig. 4, *right bottom panel*). The 95% confidence interval for the mean difference between methods ranged from +1.91 L min to −1.41 L/min.

Multiple regression analysis of possible sources of error which could account for the differences between the partial CO_2 rebreathing technique and thermodilution, with regard to the determination of cardiac output, showed that intrapulmonary right-to-left shunt fraction alone could explain most of the variance difference between methods ($r^2 = .51$, $p < .0001$). Inclusion of V_D/V_T ($r^2 = .60$, $p = .06$) and arterial end-tidal P_{CO_2} difference ($r^2 = .66$, $p = .24$) in the multiple regression model did not contribute significantly to explain variance differences between partial CO_2 rebreathing measurements and cardiac output. However, simple regression analysis showed that arterial end-tidal P_{CO_2} difference alone correlated with the differences between the noninvasive and the invasive method ($r^2 = .29$, $p < .005$), but not V_D/V_T ($p = .46$). The $P\bar{v}CO_2$ increased significantly ($p < .0001$) during the last 15 secs of partial CO_2 rebreathing as a consequence of the pulmonary recirculation, but influence of this effect could not be demonstrated by simple linear regression ($p = .76$).

Table 2. Characteristics of animals investigated in a protocol for partial CO_2 rebreathing measurements and possible sources of error accounting for differences between the partial CO_2 rebreathing technique and thermodilution for measurement of cardiac ouput

Sheep	Weight (kg)	$\dot{Q}sp/\dot{Q}t$ (%)	V_D/V_T (%)	$Paco_2-P_{ETCO_2}$ (torr)*	$\Delta P\bar{v}CO_2$ (torr)*
1	70	29.0	59.8	7.7	0.6
2	78	22.1	44.8	10.0	5.1
3	61	22.4	55.2	6.9	2.9
4	60	37.4	55.9	11.1	2.4
5	61	24.5	43.2	14.7	—
6	65	12.0	54.1	8.3	5.6
7	65	17.0	61.6	7.2	—
8	69	20.1	52.3	0.2	—
9	66	23.0	55.4	6.4	1.1
10	75	16.0	35.5	3.5	1.5
11	73	32.7	48.5	0.5	2.7
12	62	24.6	51.1	5.3	5.9
13	72	14.1	52.6	4.0	6.0
14	68	10.8	58.9	1.2	2.7
15	58	11.8	53.4	7.3†	5.6

$\dot{Q}sp/\dot{Q}t$, intrapulmonary right-to-left shunt fraction; V_D/V_T, physiologic deadspace; $Paco_2-P_{ETCO_2}$, arterial-end tidal CO_2 partial pressure difference; $P\bar{v}CO_2$, increase in mixed venous CO_2 partial pressure within 15 secs to 30 secs of rebreathing (see text).

*$p < .0001$ by Student's paired two-tailed t-test.

To convert torr to kPa, multiply the value by 0.1333.

Table 3. Characteristics of patients investigated in a protocol for partial CO_2 rebreathing measurements and possible sources of error accounting for differences between the partial CO_2 rebreathing technique and thermodilution for measurement of cardiac output

Patient	Age	Gender	Primary Cause of ARDS	$\dot{Q}sp/\dot{Q}t$ (%)	V_D/V_T (%)	$Paco_2-P_{ETCO_2}$ (torr)*
1	56	M	Aspiration of gastric contents	28.3	56.8	11.1
2	35	F	Acute pancreatitis	40.4	48.1	14.5
3	64	M	Multiple transfusions	36.6	50.9	12.5
4	43	F	Sepsis	30.1	54.2	8.5
5	56	F	Sepsis	29.0	55.7	13.8
6	74	F	Sepsis	35.6	63.6	17.6
7	52	F	Hemorrhagic shock	39.9	56.8	7.3
8	58	M	Sepsis	32.5	55.0	12.3

ARDS, adult respiratory distress syndrome; $\dot{Q}sp/\dot{Q}t$, intrapulmonary right-to-left shunt fraction; V_D/V_T, physiologic deadspace; $Paco_2-P_{ETCO_2}$, arterial-end tidal CO_2 partial pressure difference.

To convert torr to kPa, multiply the value by 0.1333.

DISCUSSION

Gas Exchange Measurements. As the accuracy of $\dot{V}CO_2$ measurement represents a limiting factor for determining cardiac output with CO_2 rebreathing techniques, standard air flow and FCO_2 measurements are usually required. However, the need for standard devices (e.g., mass spectrom-

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eters, Fleisch pneumotacographs) can make a potentially interesting technique prohibitive to the clinical practice. In view of this important limitation, we decided to work with air flow and F_{CO_2} signals obtained from the internal sensors of devices commonly used in most intensive care units. Therefore, the validation of the breath-by-breath gas exchange measurement with the system implemented was an obligatory step in our study.

Although all breath-by-breath $\dot{V}_{O_2}$ measurements were performed with a commercial apparatus which was elsewhere proven to be accurate and precise enough for both clinical and research purposes, the evaluation methods used by other investigators (13, 14) were slightly different from those presented in our study. In other works, the CO_2 transducer is normally connected directly to the Y piece of the ventilator tubing and the amount of rebreathed CO_2 is assumed to be zero. In our study, however, the amount of rebreathed CO_2 was also taken into account in the computation of breath-by-breath $\dot{V}_{CO_2}$.

Olsson et al. (13) compared a similar system of gas exchange measurement with the results of mass spectrometry and the Scholander apparatus and concluded that the 930 CO_2-Analyzer provides $\dot{V}_{CO_2}$ and P_{ETCO_2} measurements which are sufficiently

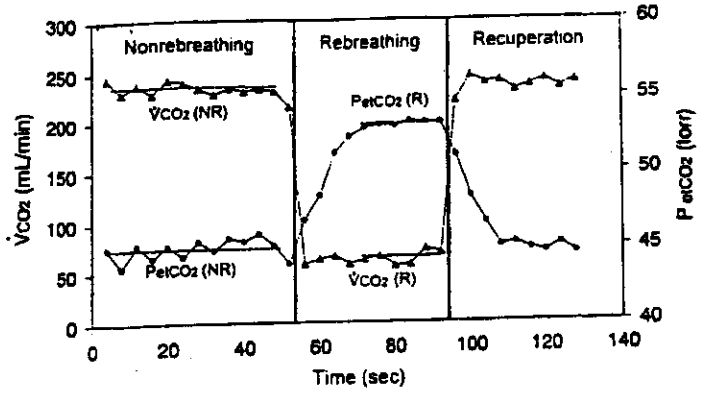

Figure 3. Breath-by-breath CO_2 elimination rate ($\dot{V}co_2$, *solid triangles*) and end-tidal Pco_2 (*Petco*$_2$, *solid circles*) during a typical measurement with the partial CO_2 rebreathing technique (nonrebreathing, rebreathing, and recuperation periods). $\dot{V}co_2(NR)$, $\dot{V}co_2$ during nonrebreathing; *Petco*$_2$*(NR)*, end-tidal Pco_2 during nonrebreathing; $\dot{V}co_2(R)$, $\dot{V}co_2$ during partial CO_2 rebreathing; *Petco*$_2$*(R)*, end-tidal Pco_2 during partial CO_2 rebreathing. CO_2 elimination rates in standard temperature and pressure, dry conditions. To convert torr to kPa, multiply the value by 0.1333.

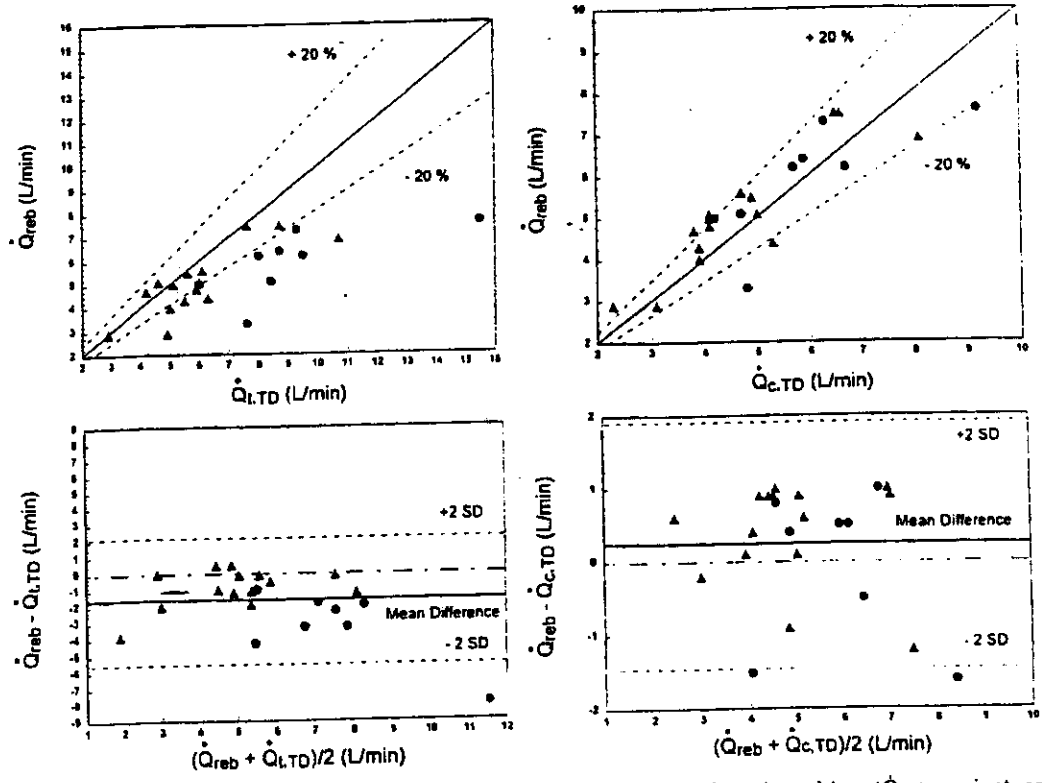

Figure 4. *Top left panel:* Scatterplot of cardiac output estimated by partial CO_2 rebreathing ($\dot{Q}_{reb}$) against cardiac ouptut by thermodilution ($\dot{Q}_{t,TD}$). Forty-three percent (10/23) of the data pairs fell within 20% of the identity line. *Bottom left panel:* Difference between and plotted against the average of the two techniques. *Solid line*, mean difference (−1.69 L/min); *dashed lines*, 95% confidence limits (±2 SD) for mean difference. *Top right panel:* Scatterplot of cardiac output estimated by partial CO_2 rebreathing ($\dot{Q}_{reb}$) against pulmonary capillary blood flow by thermodilution ($\dot{Q}_{c,TD}$). Seventy-eight percent (18/23) of the data pairs fell within 20% of the identity line. *Bottom right panel:* Difference between and plotted against the average of the two techniques. *Solid line*, mean difference (0.25 L/min); *dashed lines*, 95% confidence limits (±2 SD) for mean difference. *Solid triangles*, sheep (n = 15); *solid circles*, patients with adult respiratory distress syndrome (n = 8).

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accurate for research purposes. Accordingly, Bohrn et al. (14) demonstrated that $\dot{V}co_2$ could be determined with high precision with this infrared analyzer. Similar results were also reported by Damask et al. (15) when validating a lung model for simulation of gas exchange. The values obtained by those investigators (13–15) for $\dot{V}co_2$ with the 930 CO_2-Analyzer were situated within 7% of the reference. Our results are in agreement with those reports (13–15), supporting the adequacy of air flow and Fco_2 measurements, as well as the computer program routines, to calculate $\dot{V}co_2$. The accuracy of measurement obtained with this system is comparable with the accuracy one of the authors (M.G.A.) obtained using air flow measurements by Fleisch pneumotacographs placed at the endotracheal tube and Fco_2 by mass spectrometry in a previous work (16). Since the reliability of measurement does not depend on the geometry of the respiratory circuit or on the underlying disease (patients were used just as a CO_2 elimination source), our results also support the use of the system implemented for partial CO_2 rebreathing measurements.

Partial CO_2 Rebreathing Measurements. Total CO_2 rebreathing methods have been widely used for the estimation of cardiac output in both experimental and clinical situations and have proved to be reliable tools. As pointed out by Sackner (7), noninvasive methods based on the indirect Fick principle are particularly suitable for individuals without cardiorespiratory diseases, since they measure the effective nonshunted pulmonary capillary blood flow, which in the setting of normal respiratory function differs little from cardiac output (3% to 8%). In such individuals, the noninvasive estimation of the $Caco_2$ and $C\bar{v}co_2$ may be adequately performed because the $Petco_2$ provides a useful estimation for the $Paco_2$ in normal individuals under resting conditions (17), and the $P\bar{v}co_2$ can be mathematically calculated from the exponential increase of the $Petco_2$ during total CO_2 rebreathing maneuver.

In patients with cardiopulmonary diseases, however, the ventilation/perfusion mismatching in the lungs may lead to significant differences between $Petco_2$ and $Paco_2$ and also to unsatisfactory equilibrium of the lungs with the rebreathing system (18). Clausen et al. (19) reported that the total CO_2 rebreathing technique is not reliable for estimating cardiac output in middle-aged patients with coronary or pulmonary disease and Mahler et al. (18) also obtained very similar results in patients with obstructive airway disease. Despite these observations, some investigators (20–22) have shown concordance between total CO_2 rebreathing and invasive methods in severely ill patients. Franciosa (20) found close agreement between dye-dilution and total CO_2 rebreathing in patients with cardiac disease, but determined only poor correlation (r^2 = .026) in patients with pulmonary disease. This limitation was not observed by Davis et al. (21), who demonstrated that the CO_2 rebreathing method is reliable even in the setting of ARDS, provided that the $Paco_2$ is measured directly from arterial blood. More recently, Blanch et al. (22) confirmed this observation and proposed that the CO_2 rebreathing technique is reliable when measured, rather than estimated, $Paco_2$ is used to determine cardiac output. According to those authors (22), the use of the estimated $Paco_2$ leads to the underestimation of cardiac output in patients with respiratory insufficiency. These facts suggest that in the setting of ventilation/perfusion mismatching, the noninvasive estimation of the $P\bar{v}co_2$, although technically more complex, is more reliable than the noninvasive estimation of the $Paco_2$.

However, the partial CO_2 rebreathing technique has become interesting because it eliminates the need for estimating the $P\bar{v}co_2$, which in normal subjects represents the major source of error with the total CO_2 rebreathing technique (23–26). Gedeon et al. (8) reported that a model of the partial CO_2 rebreathing technique with alteration of minute volume leads to results that are comparable with thermodilution in dogs and in patients with coronary disease. More recently, Capek and Roy (9) suggested that a similar model of partial CO_2 rebreathing as used in our work (alteration of the apparatus deadspace) is a reliable method for estimating cardiac ouput in the setting of respiratory insufficiency in dogs. Our results are in disagreement with that work (9). According to our data, partial CO_2 rebreathing measurements correlate only moderately with cardiac output and underestimates it. Moreover, only 43% of the values obtained with the noninvasive technique were within 20% of cardiac output values, a level of agreement which decreases beyond the limits of acceptability for clinical and research purposes. In contrast, the degree of correlation between the partial CO_2 rebreathing measurements and nonshunted pulmonary capillary blood flow was good and comparable with the degree of correlation obtained by Steinhart et al. (27) with the much more accurate multiple inert gas technique (r^2 = .84, $p < .001$). Bias and precision were also good, with 78% of the values obtained with the noninvasive method falling within 20% of nonshunted pulmonary capillary blood flow values, which indicates a satisfactory level of agreement for clinical purposes.

According to our data, partial CO_2 rebreathing measurements correlate only moderately with cardiac output and underestimates it.

Since the degree of impairment of the respiratory function in the study by Capek and Roy (9) was not reported, we are not able to explain the disagreement between our studies on the basis of physiologic data. Nevertheless, according to Russell et al. (28), the thermodilution technique systematically overestimates cardiac output as determined by dye-dilution and, therefore, some positive bias may have been introduced in our study when measuring this variable. However, this phenomenon cannot explain our observation that the degree of respiratory impairment correlates with the difference between the noninvasive and invasive methods when measuring cardiac output.

According to our data, intrapulmonary right-to-left shunt explained most of the variance differences between

partial CO_2 rebreathing measurements and cardiac output, but an influence of the arterial end-tidal P_{CO_2} difference could not be excluded. The arterial end-tidal P_{CO_2} difference and intrapulmonary right-to-left shunt probably represented similar physiologic alterations in the groups studied in this work, as suggested by a statistically significant degree of correlation between these variables ($r^2 = .26$, $p < .01$). This finding is the reason why the arterial end-tidal P_{CO_2} difference was excluded in the multiple linear regression analysis and contributes to support the hypothesis that P_{ETCO_2} changes obtained with partial CO_2 rebreathing more closely reflect CO_2 content changes in the well-ventilated, well-perfused alveolocapillary bed than in the arterial bed. Consequently, blood flow measurements obtained from P_{ETCO_2} changes should agree more closely with the amount of blood flow undergoing gas exchange than with whole cardiac output. This hypothesis is supported by our results.

We also observed a lack of correlation between V_D/V_T and the differences between the noninvasive method and cardiac output. This finding is not altogether surprising since the respiratory impairment of the groups investigated was not primarily obstructive, and we were probably not able to detect errors resulting from poor equilibration of the rebreathing system with lung areas characterized by long time constants.

A final consideration is the effect of the pulmonary recirculation on the partial CO_2 rebreathing technique. Even though attempts were made to minimize this effect, increases in $P\bar{v}CO_2$ were observed during 15 to 30 secs of rebreathing. Although this phenomenon represents the violation of the assumption that $C\bar{v}CO_2$ does not change, its contribution to the differences between the partial CO_2 rebreathing technique and cardiac output could not be demonstrated in our study, confirming the observations of Gedeon et al. (8) and of Capek and Roy (9) that the pulmonary recirculation does not lead to important errors with this noninvasive method if the analysis of rebreathing is limited to 30 secs. Theoretically, it could be postulated that the pulmonary recirculation also leads to the increase of the expected CO_2 during the rebreathing period and that this effect compensates errors due to the increase of $C\bar{v}CO_2$ in the final computation of the noninvasive method.

In conclusion, partial CO_2 rebreathing is a noninvasive rebreathing technique which has major advantages in not requiring estimation of $C\bar{v}CO_2$ or the use of special gas mixtures. It requires a relatively simple intervention, namely, the sudden introduction of a deadspace in the respiratory circuit, and can be performed with devices normally used in most intensive care units. The lack of agreement between this noninvasive method and cardiac output was proportional to the intrapulmonary right-to-left shunt, indicating that this noninvasive technique is not appropriate for monitoring of cardiac output in patients with increased venous admixture. In contrast, agreement was good between the partial CO_2 rebreathing technique and the effective nonshunted pulmonary capillary blood flow, demonstrating that partial CO_2 rebreathing is a reliable method for measurement of this variable. This technique may be attractive when the placement of a pulmonary artery catheter is contraindicated (e.g., in certain burn patients, coagulopathies, congenital heart diseases), or for adjusting the ventilatory therapy in respiratory insufficiency (e.g., titration of PEEP and of inspiration/expiration ratio) to optmize the amount of nonshunted blood flow and, thereby, the oxygen delivery. Further studies are necessary to determine the value of this noninvasive technique as a guide for ventilatory therapy adjustments and its validity in the setting of predominantly obstructive airway disease.

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Appendix 1. Equations

$$\dot{Q} = \frac{\dot{V}co_2}{(C\bar{v}co_2 - Caco_2)} \qquad \text{Equation } 1$$

$$\dot{Q} \times (C\bar{v}co_2[NR] - Caco_2[NR]) = \dot{V}co_2(NR) \qquad \text{Equation } 2$$

$$\dot{Q} \times (C\bar{v}co_2[R] - Caco_2[R]) = \dot{V}co_2[R] \qquad \text{Equation } 3$$

$$\dot{Q} = \frac{(\dot{V}co_2[NR] - \dot{V}co_2[R])}{(Caco_2[R] - Caco_2[NR] - (C\bar{v}co_2[R] - C\bar{v}co_2[NR]))} \qquad \text{Equation } 4$$

$$\dot{Q}_{reb} = \dot{Q} = \frac{(\dot{V}co_2[NR] - \dot{V}co_2[R])}{(Caco_2[R] - Caco_2[NR])} \qquad \text{Equation } 5$$

$$\dot{V}co_2 = \frac{1}{T} \times \int_0^T \dot{V} \times Fco_2 \times dt \qquad \text{Equation } 6$$

$$Caco_2(R) - Caco_2(NR) = 11.02 \times (Petco_2[R]^{0.396} - Petco_2[NR]^{0.396}) - 0.015 \times (15 - Hb) \times (Petco_2[R] - Petco_2[NR]) - 0.064 \times (95 - Sao_2) \qquad \text{Equation } 7$$

$$V_D/V_T = \frac{Paco_2}{(Paco_2 - P_Eco_2)} \qquad \text{Equation } 8$$

$$P\bar{v}co_2[R] = \frac{(4 \times Pco_2[15\ secs - 30\ secs] - V_{cat} \times P\bar{v}co_2[NR])}{(4 - V_{cat})} \qquad \text{Equation } 9$$

$$\dot{Q}sp/\dot{Q}t = \frac{(C\dot{c}o_2 - Cao_2)}{(C\dot{c}o_2 - C\bar{v}o_2)} \qquad \text{Equation } 10$$

$$C\dot{c}o_2 = (Hb \times 1.38) - (P_{AO_2} \times 0.0031) \qquad \text{Equation } 11$$

$$P_{AO_2} = Fio_2 \times (PB - P_{H_2O}) - Paco_2/RQ \qquad \text{Equation } 12$$

$$Cao_2 = (Hb \times Sao_2 \times 1.38) + (Pao_2 \times 0.0031) \qquad \text{Equation } 13$$

$$C\bar{v}o_2 = (Hb \times S\bar{v}o_2 \times 1.38) + (P\bar{v}o_2 \times 0.0031) \qquad \text{Equation } 14$$

$$\dot{Q}_{c,TD} = \dot{Q}_{i,TD} \times (1 - \dot{Q}sp/\dot{Q}t) \qquad \text{Equation } 15$$

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Concepts in Emergency and Critical Care

Permissive Hypercapnia in Acute Respiratory Failure

Akhil Bidani, MD, PhD; Alexander E. Tzouanakis, MD; Victor J. Cardenas, Jr, MD; Joseph B. Zwischenberger, MD

Objective.—To evaluate the potential efficacy of pressure limitation with permissive hypercapnia in the treatment of acute respiratory failure/adult respiratory distress syndrome on the basis of current theories of ventilator-induced lung injury, potential complications of systemic hypercarbia, and available human outcome studies.

Data Sources.—Articles were identified through MEDLINE, reference citations of published data, and consultation with authorities in their respective fields.

Study Selection.—Animal model experimentation and human clinical trials were selected on the basis of whether they addressed the questions of pressure limitation with or without hypercapnia, the pathophysiologic effects of hypercapnia, or the concept of ventilator-induced parenchymal lung injury. Frequently cited references were preferentially included.

Data Extraction.—Data were analyzed with particular emphasis on obtaining the following variables from the clinical studies: peak inspiratory pressures, tidal volumes, minute ventilation, and P_{CO_2}. Quantitative aspects of respiratory physiology were used to analyze the theoretical effects of permissive hypercapnia on ventilatory requirements in normal and injured lungs.

Data Synthesis.—Extensive animal model data support the hypothesis that ventilator-driven alveolar overdistention can induce significant parenchymal lung injury. The heterogeneous nature of lung injury in adult respiratory distress syndrome, with its small physiologic lung volume, may render the lung susceptible to this type of injury through the use of conventional tidal volumes (10 to 15 mL/kg). Permissive hypercapnia is an approach whereby alveolar overdistention is minimized through either pressure or volume limitation, and the potential deleterious consequences of respiratory acidosis are accepted. Uncontrolled human trials of explicit or implicit permissive hypercapnia have demonstrated improved survival in comparison with models of predictive mortality.

Conclusions.—Avoidance of alveolar overdistention through pressure or volume limitation has significant support based on animal models and computer simulation. Deleterious effects of the associated hypercarbia in severe lung injury do not appear to be a significant limiting factor in preliminary human clinical trials. Although current uncontrolled studies suggest benefit, controlled trials are urgently needed to confirm these findings before adoption of the treatment can be endorsed.

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CONVENTIONAL medical management of acute respiratory failure with mechanical ventilation is geared to achieve a "normal" P_{CO_2} of 40 mm Hg and an arterial blood pH of 7.40. Such a strategy led to the widespread use of tidal volumes (V_T) of 10 to 15 mL/kg, regardless of the inspiratory pressures required, in ventilator support of acute respiratory failure. During the past decade, the paradigm of maintaining normocapnia in mechanically ventilated patients has been reevaluated. Considerable data from animals and humans suggest that conventional V_Ts of 10 to 15 mL/kg may be associated with alveolar overdistention leading to "volutrauma"[1] that might exacerbate acute lung injury. Permissive hypercapnia represents an alternate approach in which a lower V_T of 5 to 8 mL/kg is used to prevent excessive alveolar distention.[2] Arterial P_{CO_2} is allowed to rise above 40 mm Hg, and no attempts are made to correct subsequent changes in blood pH. In this article, we examine the current thoughts regarding alveolar overdistention associated with "conventional" normocapnic mechanical ventilation in acute lung injury and provide a theoretical basis for the use of permissive hypercapnia. Studies of hypercapnia to date were reviewed, and potential problems associated with its application and resultant respiratory acidosis are discussed.[2]

VENTILATOR-INDUCED LUNG INJURY (VOLUTRAUMA)

Traditional respiratory support for adult respiratory distress syndrome (ARDS) has used volume-controlled mechanical ventilation with supraphysiologic V_T (10 to 15 mL/kg) because of the observation that high lung volumes minimized atelectasis and prevented deterioration of oxygenation in patients undergoing anesthesia.[3] This strategy often required high airway pressures to deliver these volumes and maintain normocapnia in patients with severe lung injury. In fact, the original description of ARDS included high inspiratory ventilator pressures as part of the definition.[4] In 1974, Webb and Tierney[5] recognized the possibility of ventilator-induced parenchymal lung injury as separate from the previously recognized forms of barotrauma. Rats ventilated at

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high airway pressures (45 cm H_2O) developed alveolar edema, hypoxemia, and decreased lung compliance, with death occurring within 1 hour. Webb and Tierney theorized that the interstitial edema may be caused by pulmonary interdependence and that the alveolar edema may be from depletion or inactivation of surfactant. Dreyfuss et al[6] likewise showed that application of high-inflation-pressure ventilation in rats resulted in a high-permeability edema of the lung after only 20 minutes, with histologic findings similar to those seen in ARDS in humans. To discern whether high alveolar pressure or alveolar overdistention was the likely causative factor in the observed pulmonary edema, rats were subjected to five ventilatory modes: (1) control group (low-pressure, low-volume positive-pressure ventilation), (2) high-pressure, high-volume group, (3) high-pressure, low-volume group, achieved by thoracoabdominal strapping, (4) low-pressure, high-volume group, achieved by iron lung ventilation, and (5) high-pressure, high-volume group with 10 cm H_2O positive end-expiratory pressure added.[7] No significant difference between the control and the high-pressure, low-volume group was seen; however, the lungs from the groups ventilated with high volumes developed severe high-permeability edema regardless of whether positive or negative pressure was the generating force. Hernandez et al[8] similarly found that chest wall restriction limits high airway pressure–induced lung injury in immature rabbits, with capillary filtration coefficient used as the marker of lung injury.[8] These studies suggested that alveolar overdistention was more important than high alveolar pressure in the generation of ventilator-induced lung injury in these acute (<1 hour) experimental models.

To evaluate a model with a time course more reflective of clinical experience, Tsuno et al[9] analyzed the histopathologic changes in baby pig lungs after mechanical ventilation at high peak airway pressures.[9] After ventilation at a peak inspiratory pressure of 40 cm H_2O for 22±11 hours, one group of pigs was killed and the lungs were examined. Alveolar hemorrhage, alveolar neutrophil infiltration, alveolar macrophage and type II pneumocyte proliferation, interstitial congestion and thickening, interstitial lymphocyte infiltration, emphysematous change, and hyaline membrane formation were all noted. Similar histopathologic changes appear in the early stages of ARDS. Another group of pigs continued to receive mechanical ventilation for an additional 3 to 6 days by means of conventional ventilatory measures (V_T, 15 mL/kg; $PaCO_2$, 40 mm Hg) and then killed. Histologic examination demonstrated the findings noted above coupled with prominent organized alveolar exudate, resembling the changes seen in the late stages of ARDS. A control group ventilated at a peak inspiratory pressure of 18 cm H_2O showed no histopathologic change in the lung.

These, as well as other studies by various investigators,[10,11] suggest a clear association between alveolar overdistention and lung injury similar to that seen in ARDS. However, the exact mechanism of the injury remains unclear. A study that addressed this issue was performed by Kawano et al,[12] in which a saline lung lavage was followed by controlled mechanical ventilation with a V_T of 12 mL/kg in three groups of rabbits: a normal group, a group rendered neutropenic by pretreatment with mechlorethamine hydrochloride, and a mechlorethamine-treated group that was retransfused with granulocytes before the study. The first and third groups developed a high-permeability pulmonary edema with hyaline membrane formation, while the neutropenic group showed none of these changes. These experimental findings suggest a prominent role for inflammatory cells in the development of the lung injury and argue against an injury that is entirely mechanical.

In regard to the applicability of these animal models to clinical experience, patients with normal lung compliance are not ventilated with high airway pressures (pressure-cycled ventilation), nor do they develop high inspiratory pressures with the use of traditional V_Ts (volume-cycled ventilation). Patients with ARDS, however, almost invariably require high inspiratory pressures to maintain adequate minute ventilation and normocapnia. Recent work by Gattinoni and colleagues[13] has provided compelling evidence that ARDS is a heterogeneous, not diffuse, lung injury, with areas of relatively normal lung interspersed with areas of alveolar and interstitial edema. The result is a smaller physiologic lung volume. Exposure of relatively normal alveoli with near normal compliance characteristics to high distending pressures would result in a larger delivered volume per lung unit, marked overdistention, and the possible increased risk of further lung injury. This scenario could conceivably occur regardless of which mode of ventilation generates the high inspiratory pressures.

The degree to which conclusions can be extrapolated from animal studies to humans is unknown, but the evidence for ventilator-induced lung injury is suggestive in its reproducibility among investigators and across species. In light of these data, coupled with the persistent high mortality associated with ARDS strategies to minimize potentia[illegible] including permissive hypercapn[illegible] subsequently developed.

THEORETICAL BASIS OF PERMISSIVE HYPERCAPNIA

The ventilatory requirements in patients with respiratory failure are determined by the "targeted" arterial P_{CO_2} and the rate of metabolic carbon dioxide production. In an elegant analysis, Rahn[14] discussed the teleologic rationale for the setpoints of a $PaCO_2$ of 40 mm Hg and an arterial pH of 7.40. On the basis of the α-stat hypothesis of pH regulation, which postulates that the need to maintain the relative ionization of imidazole histidine groups on cellular proteins determines intracellular pH, Rahn and colleagues[15] estimated that the "optimal" arterial blood pH at 37°C should be 7.4. If one accepts this value for blood pH, the next question is related to the "optimal" P_{CO_2} necessary to regulate blood pH at 7.4. As pointed out by Rahn,[14] blood pH could be maintained at 7.4 over a wide range of P_{CO_2} values, ranging from 2 mm Hg, which is typical for fish, to 60 mm Hg, found in a turtle at its maximum body temperature. Tenney and Bartlett[16] demonstrated that if one divides the basal metabolic rate by the minute ventilation and [illegible]s for weight-dependent changes [illegible] space and breathing frequencies, one arrives at a relatively constant P_{CO_2} for all mammals in the range between 30 and 40 mm Hg. Teleologically, the optimal P_{CO_2} for humans must balance the need for maintaining adequate arterial oxygenation and the energy expenditure for ventilation. From the alveolar gas equation at 37°C:

(1) $P_{AO_2}=F_{IO_2}(P_B-47)-P_{aCO_2}/R$,

where P_{AO_2} is the alveolar oxygen pressure, P_B is the barometric pressure, F_{IO_2} is the fractional concentration of oxygen in inspired air, 47 is the water vapor pressure in millimeters of mercury at 37°C, and R is the respiratory quotient. Additionally, alveolar P_{CO_2} (P_{ACO_2}) is related to the alveolar ventilation ($\dot{V}_A$) and the rate of metabolic CO_2 production ($\dot{V}_{CO_2}$):

(2) $P_{ACO_2}=(\dot{V}_{CO_2}/\dot{V}_A)(P_B)$.

Combining equations 1 and 2, the following is obtained:

(3) $P_{AO_2}=F_{IO_2}(P_B-47)-(\dot{V}_{CO_2}/\dot{V}_A)(P_B/R)$.

The dependence of P_{AO_2} and $PaCO_2$ on $\dot{V}_A$, calculated from equations 2 and 3 for a $\dot{V}_{CO_2}$ of 200 mL/min is shown in Figure 1. At an F_{IO_2} of 21%, an alveolar ventilation of approximately 3.7 L/min is necessary to maintain P_{AO_2} at [illegible] mately 100 mm Hg and $PaCO_2$ at [illegible] Hg. Further increase in $\dot{V}_A$ is associated with minimal increase in P_{AO_2}. However, when F_{IO_2} is increased to 30% P_{AO_2} can be maintained at approximately

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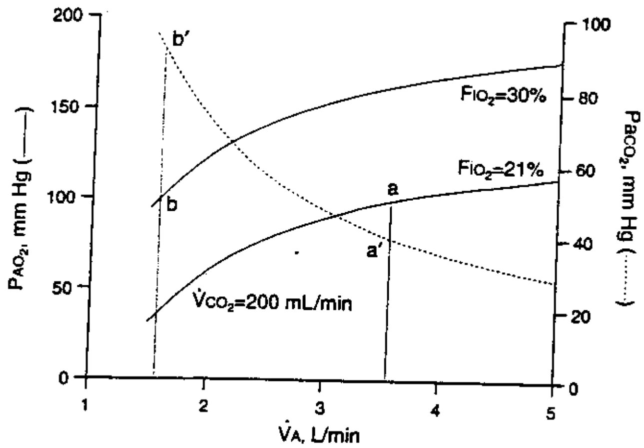

Figure 1.—Calculated alveolar PO_2 (PAO_2) (solid lines) and arterial blood PCO_2 ($PaCO_2$) (dashed lines) as a function of alveolar ventilation, $\dot{V}A$ (equation 3). Computed PAO_2 is shown for two levels of inspired oxygen concentration. For fractional concentration of oxygen in inspired air (FIO_2) of 0.21 and $\dot{V}A$ of 3.6 L/min, the predicted PAO_2 is 100 mm Hg (point a) and the $PaCO_2$ is 40 mm Hg (point a'). When FIO_2 is 0.30, $\dot{V}A$ can be reduced to 1.6 L/min while maintaining PAO_2 at 100 mm Hg (point b). The corresponding $PaCO_2$ at this level is 92 mm Hg (point b'). The rate of carbon dioxide excretion ($\dot{V}CO_2$) is set at 200 mL/min for all calculations. Vertical line indicates normal values.

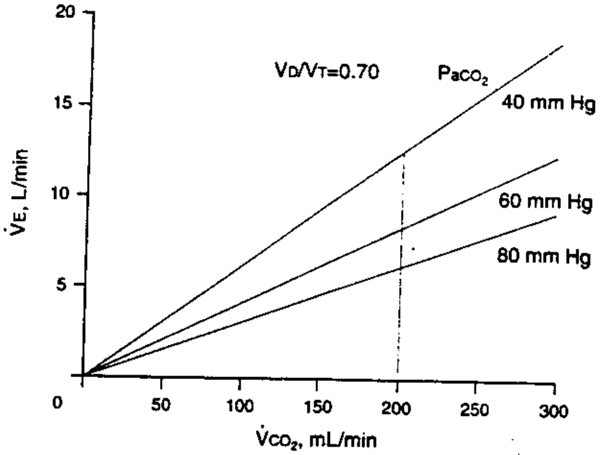

Figure 2.—Estimated minute ventilation requirement ($\dot{V}E$) as a function of the rate of carbon dioxide excretion ($\dot{V}CO_2$) for three levels of PCO_2. Calculations were performed (equation 2) assuming dead space fraction of 0.7. At an arterial PCO_2 ($PaCO_2$) of 40 mm Hg and $\dot{V}CO_2$ of 200 mL/min, required minute ventilation $\dot{V}E$ is 12.7 L/min. At PCO_2 of 60 mm Hg, the $\dot{V}E$ is 8.4 L/min, and at PCO_2 of 80 mm Hg, the $\dot{V}E$ is 6.3 L/min. VD/VT represents dead space volume/tidal volume. Vertical line indicates normal values.

100 mm Hg with a $\dot{V}A$ of only approximately 1.7 L/min and an associated $PaCO_2$ of approximately 85 mm Hg. Thus, in the presence of supplemental oxygen therapy with normal $\dot{V}$/blood flow relationships in the lung, minute ventilation can be substantially reduced without jeopardizing arterial oxygenation. The potential benefit of decreased ventilatory requirements during hypercapnia is even greater in patients receiving mechanical ventilation, since high dead-space fractions (dead space volume [VD]/VT >60%) are commonly associated with positive airway pressures, ventilator circuits, and acute lung injury. For a VD/VT of 0.7, the minute ventilation requirement in a patient with a $\dot{V}CO_2$ of 200 mL/min is approximately 12.7 L/min at a $PaCO_2$ of 40 mm Hg and approximately 6.3 L/min at a $PaCO_2$ of 80 mm Hg (Figure 2). Because of the hyperbolic relationship of $\dot{V}A$ and $PaCO_2$, 66% of this reduction occurs at the level of 60 mm Hg. Thus, even moderate increments in PCO_2 can result in significant reductions in minute ventilation.

Patients with ARDS demonstrate abnormal pulmonary gas exchange, with regions of low $\dot{V}$/blood flow and intraparenchymal shunting of blood past atelectatic alveoli and alveoli flooded with proteinaceous and inflammatory fluid. Judicious institution of positive end-expiratory pressure and supplemental oxygen can improve hypoxemia without the need for high levels of ventilation. Thus, even in the diseased lung, arterial oxygenation can be improved, independent of the reduced level of ventilation required to excrete CO_2 during hypercapnia. Therefore, CO_2 homeostasis can be maintained in patients with ARDS by using lower VTs (5 to 7 mL/kg) while minimizing alveolar overdistention and preserving adequate arterial oxygenation.

POTENTIAL PATHOPHYSIOLOGIC ABNORMALITIES ASSOCIATED WITH PERMISSIVE HYPERCAPNIA

The possible benefits of pressure limitation and the resultant hypercapnia in acute respiratory failure must be balanced against any potential physiologic costs that may come from alterations of CO_2 homeostasis. Carbon dioxide impacts cellular function through various mechanisms, including direct molecular CO_2 effects and "indirect" effects mediated via neurologic or humoral control pathways, and by its role in the maintenance of tissue pH. Difficulties may therefore arise in the interpretation of the observed results of hypercapnia.

Tissue Acidosis

Accumulation of CO_2 in arterial and mixed venous blood leads to an increase in the formation of intraerythrocytic carbonic acid. Buffering by hemoglobin results in the generation of bicarbonate ions, which leave the red blood cell in exchange for chloride. Because equilibration of bicarbonate ion across the capillary membrane occurs at a slower rate than the equilibration of molecular CO_2, an increased H^+ load to the interstitial and intracellular fluid results. At least three mechanisms normally regulate intracellular pH in hypercapnia: (1) physicochemical buffering, (2) consumption of organic acids, and (3) transmembrane fluxes of H^+ and HCO_3^-.[17,18] It has been estimated that cellular pH regulation is about 90% complete in the first 3 hours after the onset of hypercapnia,[19] but it may take significantly longer during conditions of poor organ perfusion and/or severe hypoxemia.[17] A reduction in intracellular pH may be associated with multiple abnormalities, including alterations of membrane electrolyte transport, disturbances of substrate delivery, impaired glucose utilization, and intracellular amino acid depletion,[17] the clinical significance of which has yet to be determined. Changes in blood flow and nutrient delivery also occur during hypercapnia and may affect cell function and viability.

Autonomic Effects of Hypercapnia

The response of the body to acute hypercapnia is extensively mediated by the sympathetic nervous system. In moderate hypercapnia ($PaCO_2$, <100 mm Hg), proportionate, linear increases in plasma levels of epinephrine and norepinephrine occur. At levels above 200 mm Hg, however, epinephrine release accelerates while norepinephrine levels maintain their previous rate of increment.[20] Direct measurements of sympathetic efferent nerve activity have shown significant augmentation during hypercapnia with or without hypoxia, and the elevation in catecholamine levels can be prevented by splanchnicectomy except at high PCO_2 levels, when direct stimu-

lation of the adrenal medulla ensues.[21] Moderate hypercapnia has also been observed to inhibit autonomic parasympathetic reflexes[22] and may be related to decreased acetylcholine hydrolysis under low pH conditions.

Effects on the Central Nervous System

Hypercapnia has multiple and often profound influences on brain function. The observed effects usually result from the summation of several discrete factors governed by carbon dioxide, including (1) control of cerebral blood flow, (2) intracranial pressure mediated by changes in cerebral blood flow, (3) intracellular pH of neurons, and (4) excitability of the neurons, including the reticular activating system.[23]

Carbon dioxide was the first gas to be used in the early search for a surgical anesthetic. However, hypercapnic narcosis was associated with significant ventilatory stimulation, circulatory alterations, increased muscle tone, and seizure activity. These characteristics prevented its use as a general anesthetic agent. Brain excitability, as tested by measuring the seizure threshold to chemical and electrical stimuli in rats, exhibits a triphasic response: (1) decreases with inspired CO_2 concentrations up to 15%, (2) increases accompanied by seizure activity at concentrations of 15% to 30%, and (3) induction of anesthesia at concentrations of 40%. This depressant effect probably results from a combination of inert gas narcotic effect, direct inhibition of synaptic transmission, and the depression of cellular function mediated by the reduction in intracellular pH.[18] Significant increases in cerebral blood flow, with resultant increases in intracranial pressures, can be seen with acute hypercapnia. Considerable experimental evidence suggests that arterial CO_2 is one of the primary determinants of cerebral vascular reactivity, but the exact mechanism remains unclear. In humans, acute changes in blood pH induced by infusions of sodium bicarbonate or ammonium chloride do not affect cerebral blood flow if the $PaCO_2$ of the blood is kept constant.[24] Similarly, in patients undergoing mechanical ventilation who have chronic CO_2 retention, acute reductions of $PaCO_2$ result in decreased cerebral blood flow.[25] However, other investigations have suggested that reactivity is not caused by direct action of molecular CO_2 on the vascular smooth muscle but results from the effect of $PaCO_2$ on extracellular fluid pH.[26,27] In addition, some experimental observations strongly suggest that extracellular H^+ concentration is not the only factor controlling cerebral vascular resistance, but that intracellular pH of the vascular smooth muscle[28] and extracellular K^+ or Ca^{++} concentrations[29] may also play significant roles.

Circulatory Responses to Hypercapnia

The influence of hypercapnia on the cardiovascular system is the result of the interplay between direct target organ effect and autonomic control. The effect of CO_2 on the isolated heart muscle is one of temporary depression of function,[30] probably as a result of change in intracellular pH. Carbon dioxide also has a depressant effect on the peripheral vascular smooth muscle of the precapillary resistance vessels.[31] However, in the intact subject, elevation in circulating catecholamine levels secondary to the sympathetic stimulatory effects of hypercapnia overcome the direct depressant effect, and the result is an increase in cardiac output, a slight decrease in peripheral resistance, and a resultant tendency toward increased blood pressure. The stimulatory effect can be abolished by β-adrenergic blockade.[32] Arrhythmias have also been been reported during acute hypercapnia at $PaCO_2$ levels above 80 mm Hg in the presence of anesthetic agents.

Regional blood flows appear to be affected by acute hypercapnia in an organ-specific fashion. Furthermore, CO_2 and pH are not the only factors governing regional blood flows. Anesthesia, surgical preparation, and positive-pressure ventilation can significantly alter observed flows; therefore, it is difficult to draw firm conclusions from the experimental evidence. Acute hypercapnia has been observed to cause reversible anuria in dogs during diffusion oxygenation.[33] This effect is presumably caused by sympathetic mediated constriction of the afferent glomerular arterioles, as the effect is abolished in the denervated kidney. Decreases in renal vascular resistance during exogenous administration of CO_2 without hypoxia[34] as well as increased renal blood flow during permissive hypercapnia[35] have been reported in other animal models. Blood flow to the splanchnic vascular bed has been demonstrated to increase[22,35-37] or decrease[38] as a result of acute hypercapnia. Mild hypercapnia has been shown to depress hepatic function in the dog.[37]

CLINICAL EXPERIENCE WITH PERMISSIVE HYPERCAPNIA

Clinical experience with permissive hypercapnia is limited, and only uncontrolled human studies exist at this time. Hickling et al[2] published retrospective data on 50 patients with severe ARDS treated with permissive hypercapnia. Peak inspiratory pressure was limited to less than 40 cm H_2O at all times and to less than 30 cm H_2O when [illegible] with the use of volume-cycled ventilation, V_Ts as low as 5 mL/kg, and synchronized intermittent mandatory ventilators mode to allow spontaneous respirations, while the PCO_2 was "permitted" to increase. Interestingly, the respiratory rate was frequently rapid and sometimes resulted in normocapnia or hypocapnia in those patients with lower lung injury scores. All patients had a lung injury score[39] of 2.5 or more and a mean PaO_2/FIO_2 ratio of 94. The mean maximum $PaCO_2$ was 62 mm Hg, and the highest was 129 mm Hg. No specific treatment was used to treat the respiratory acidosis, and the pH was allowed to fall as low as 7.02. The mean time from initiation of ventilation to the maximum $PaCO_2$ was 5.2 days, and the mean duration of ventilation was 8.1 days for survivors and 9.0 days for nonsurvivors. Mortality was significantly lower than that predicted by the Acute Physiology and Chronic Health Evaluation II (16% vs 39.6%). Lung injury scores and PaO_2/FIO_2 ratios were not significantly different between survivors and nonsurvivors. Subsequently, a similar uncontrolled prospective study by [illegible]ling[40] that used permissive hyper[illegible] in ARDS was reported to show [illegible]vival of 73.6% in a subgroup of pati[illegible] with lung injury scores of 2.5 or more.

The use of permissive hypercapnia has not been limited to ARDS. Darioli and Perret[41] published one of the first studies that purposefully used the strategy of limiting pressure and allowing hypercapnia. They studied its use in the management of 34 cases of status asthmaticus that required mechanical ventilation, maintaining peak airway pressures less than 50 cm H_2O; however, they also used neuromuscular blockade on occasion to achieve their end point. The mean time of hypoventilation was 2.5 days, although only six patients were hypoventilated for longer than 24 hours. All the patients survived, representing a marked decrease in mortality from that reported in previous studies. Complications were all reversible and included transient hypotension, nosocomial pneumonia, supraventricular tachyrhythmia, and a prolonged coma in one patient that was attributed to cerebral edema.

Attempts at pressure-volume limitation can also be found in the treatment of ARDS with extracorporeal lung [illegible]port and high-frequency ventila[illegible] In the mid 1970s, the US National E[illegible]tracorporeal Membrane Oxygenatio[illegible] (ECMO) Study[42] compared ECMO with conventional ventilation by means of a

prospective randomized design and found no significant difference between these groups, with an overall survival rate of 10%. Using patient entry criteria similar to those of the ECMO study, Gattinoni et al[43] demonstrated a marked decrease in mortality in patients treated with extracorporeal CO_2 removal ($ECCO_2R$) and low-frequency, pressure-limited ventilation with the use of ECMO survival as the historical control. One major difference in ventilatory management between the two trials was the limitation of peak inspiratory pressures in the $ECCO_2R$ study to 35 to 40 cm H_2O vs 50 cm H_2O in the ECMO treatment group. This improvement in survival has been duplicated at various centers with the use of ECMO criteria as historical controls, with an overall rate of 46%. These studies suggested that ventilator strategies designed to limit peak pressures and alveolar overdistention may favorably affect outcome compared with that of historical controls or Acute Physiology and Chronic Health Evaluation II predictions of mortality. Unfortunately, none of these trials included concurrent control groups. Recently, a protocol-driven, randomized controlled trial by Morris and colleagues[44] compared conventional ventilation ("old therapy") with pressure-controlled inverse ratio ventilation with or without $ECCO_2R$ ("new therapy") in 40 patients with ARDS. No significant difference in survival was found between the two groups, with rates of 42% and 33%, respectively, and an overall rate of 38%. Although they demonstrated significant improvement in survival compared with the ECMO study patients, both groups were not statistically different from those in previous $ECCO_2R$ studies. Of note, the majority of patients were hypercapnic at randomization, and although mean peak airway pressures were significantly lower in the new therapy group, they remained elevated (57.8 vs 49.5 cm H_2O).

Lewandowski et al[45] reported on the treatment of 38 patients with severe ARDS (lung injury score, >2.5) with the use of an integrated approach that included permissive hypercapnia, pressure-controlled ventilation, frequent body position changes, and inhalation of nitric oxide (seven patients). Eighteen patients were treated with $ECCO_2R$, with bypass being used initially if they fulfilled fast ECMO criteria[42] or subsequently if they worsened with the standard therapy. The overall survival rate was 84% (100% in the patients who did not require $ECCO_2R$ and 66% in the $ECCO_2R$ group).

Limitation of high airway pressures was also purported to be a potential benefit of high-frequency ventilation in acute respiratory failure in adults. However, randomized controlled studies have failed to demonstrate significant improvement in outcome over conventional ventilation.[46,47] High-frequency ventilation was usually associated with significantly lower peak airway pressures, and this casts some doubt on whether pressure limitation can effect a significant change in mortality. It must be noted that controls often demonstrated peak airway pressures less than 40 cm H_2O as well.[46] Also, although significantly lower than that of control groups, the peak inspiratory pressures of the high-frequency ventilation groups often remained greater than 40 cm H_2O.[47]

No controlled, prospective, randomized study convincingly links newer ventilator management strategies with reduced mortality. Epidemiologic data suggest that most patients with ARDS die of uncontrolled infection, not respiratory failure, and effecting a change in mortality through ventilator management may seem somewhat unlikely. However, if conventional ventilatory practices do exacerbate acute lung injury, approaches that ameliorate this iatrogenic insult could conceivably result in less severe total lung injury, decreased length of ventilation, reduced infectious complications, and potentially improved survival.

INITIATION OF PERMISSIVE HYPERCAPNIA

Two additional problems arise in a patient in whom a protocol of pressure-volume limitation with permissive hypercapnia is being initiated. The first one is the frequent need for neuromuscular paralysis to block the increased respiratory drive associated with acute elevations in P_{CO_2}. The second problem is that of the associated respiratory acidosis that develops in hypercapnic patients.

Neuromuscular Blockade

Significant degrees of hypercapnia are difficult to achieve in subjects with intact respiratory drives, even in conjunction with sedation by means of narcotics and/or benzodiazepines. Neuromuscular blocking agents have thus been widely used in permissive hypercapnia. Unfortunately, significant concerns regarding their use for this purpose have arisen recently. Segredo et al[48] recently reported on a series of 16 patients who received vecuronium bromide to facilitate mechanical ventilation. After cessation of the drug, seven of the 16 patients had prolonged neuromuscular blockade lasting from 6 hours to more than 7 days. They found no significant relationship between prolonged paralysis and the total dose of vecuronium or duration of therapy.

Also worrisome are reports of myopathies developing after the use of neuromuscular blocking agents. Shapiro et al[49] summarized the cases of 35 patients described in the literature since 1977 who developed a variant of classic steroid-induced myopathy after receiving systemic corticosteroids and neuromuscular blockade during mechanical ventilation for status asthmaticus. Patients tended to improve during the course of weeks to months, but some were left with persistent weakness. Douglass et al[50] studied 25 consecutive patients with status asthmaticus treated with mechanical ventilation, steroids, and vecuronium and found muscle weakness in nine patients. Patients who developed myopathy received significantly larger total doses of vecuronium. Neuropathies have also been reported in similar patient populations.[51] Although it is difficult to make firm conclusions on the basis of uncontrolled data, this remains an area of concern. Other agents (eg, propofol) to facilitate ventilation are under investigation.

Respiratory Acidosis

No definite data are available on the limits of tolerance to respiratory acidosis. A recent report[52] described a patient undergoing cosmetic facial surgery under general anesthesia via face mask for 4 to 6 hours. Despite adequate arterial oxygenation throughout the procedure, the patient remained in a deep coma after termination of anesthesia. Initial arterial blood gas analysis disclosed a profound respiratory acidosis, with arterial pH of 6.6 and $PaCO_2$ of 375 mm Hg. Graded increments in minute ventilation, after intubation, allowed for complete recovery and no sequela from the profound respiratory acidosis. Thus, significant hypercapnia and respiratory acidosis may be tolerated if tissue anoxia and ischemia are prevented. Moderate degrees of chronic respiratory acidosis are well tolerated in patients with chronic obstructive pulmonary disease and have not been shown to be associated with demonstrable abnormalities in central nervous system, renal, or cardiovascular function. In the Hickling et al trial,[2] no effort was made to correct the acute respiratory acidosis associated with the deliberate alveolar hypoventilation despite arterial pH values as low as 7.03. The issue of bicarbonate administration in systemic acidoses has been confined largely to metabolic acidosis, where it has not been shown to improve hemodynamics or patient outcome.[53-55] No study has specifically examined the use of bicarbonate administra-

tion in acute respiratory acidosis, except in asthma, where some benefit has been inferred,[56] and the degree of correction necessary during acute respiratory acidosis remains unknown. Maintaining arterial pH greater than 7.20 might theoretically minimize any adverse circulatory changes associated with respiratory acidosis, but this remains speculative at this point. Graded decrements in minute ventilation over several hours allow time for pH compensatory mechanisms (cellular buffers, renal compensation) to adjust to the progressive hypercapnic state. Alternatively, bicarbonate could be administered either intravenously or orally to ameliorate the respiratory acidosis, much as one would treat a severe metabolic acidosis. Some patients with [illegible] controlled metabolic acidoses, such as [illegible] sepsis or renal failure, might be poor candidates for permissive hypercapnia, because the combined metabolic and respiratory acidosis may be poorly tolerated.

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EDITORIAL

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Permissive hypercapnia in ARDS: just do it?

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'Nature does nothing without purpose or uselessly' (Aristotle, Politics). Why interfere with nature's principle to regulate the arterial carbon dioxide tension ($PaCO_2$) at a level of close to 40 mmHg in most mammals? A $PaCO_2$ of 40 mmHg guarantees the best balance between respiratory work and adequate arterial oxygenation. Apart from that, the most important inorganic buffering system in pH regulation is CO_2. It is hard to conceive that this principle no longer holds true in patients with ARDS and that the tolerance of elevated $PaCO_2$ values provides any benefit for the patient.

In patients with acute respiratory distress syndrome (ARDS) an increased dead-space-to-tidal volume ratio (V_D/V_T), an important determinant of minute ventilation ($\dot{V}_E$), is a common feature. Also most of the underlying diseases anteceding ARDS are characterized by a hypermetabolic state with enhanced CO_2 production ($\dot{V}_{CO_2}$). Recently, Kiiski and Takala [1] found that increased $\dot{V}_{CO_2}$ accounted for 56% of the excess $\dot{V}_E$ demand in ARDS. In practice, an extremely high $\dot{V}_{CO_2}$ has to be eliminated in patients with ARDS to keep the $PaCO_2$ normal. Even though the body is seldom able to regulate the underlying dynamics during the acute stage of the syndrome, the link between a high CO_2 load and poor CO_2 elimination by the failing lung appears solid. Attempts to unload the CO_2 by means of mechanical ventilation usually ends up in the application of large tidal volumes (V_T) and/or high airway pressures, modalities long since known to be extremely harmful to the injured lung by causing baro- and volutrauma.

According to current safety guidelines, a lung-protective ventilatory strategy for patients with ARDS should apply only moderate peak airway pressures (<3.4 kPa = 35 cm H_2O) [2] and small V_Ts (<8 ml/kg body wt.). PEEP levels should be sufficient to prevent alveolar collapse and airway closure. Precision adjustment of peak inspiratory pressure (PIP), V_T, and PEEP in a given patient should be accomplished by control of individually recorded pressure-volume curves of the respiratory system [3]. In this way frequently small V_Ts of 4–8 ml/kg body wt. are the result, accompanied by a marked rise in $PaCO_2$. Acceptance of hypercapnia resulting from this lung-protective ventilatory approach is termed "permissive hypercapnia" (PHC).

The credit for introducing PHC into ventilatory care for patients with ARDS goes to Hickling and colleagues [4]. Since 1984, they have gradually been adopting the policy of limiting PIP in patients with severe ARDS by reducing V_T, allowing spontaneous breathing with synchronized intermittent mandatory ventilation (SIMV) and disregarding hypercapnia. A retrospective analysis of 50 patients with severe ARDS revealed a hospital mortality significantly lower than that predicted by APACHE II scores (16% vs 39.6%). The authors confirmed these favorable results in a prospective trial investigating another 53 patients [5]. The initial reports were soon followed by clinical studies suggesting a positive impact of PHC on survival rates of patients with ARDS [6, 7]. Recently, Amato et al. [8] demonstrated in a small randomized controlled study of PHC that in the PHC treated group a better oxygenation was achieved with lower airway pressures than in the control group.

PHC has sneaked into clinical intensive care of patients with ARDS without having undergone a classic randomized controlled trial against standard treatment. This is not astonishing, given the problems clinicians have

in coping with maintenance of sufficient gas exchange in patients with ARDS. Even using aggressive mechanical ventilation with large V_Ts of 12–15 ml/kg body wt. and high PIP, normocapnia cannot be restored in such patients. Here, the caring physician is forced to accept hypercapnia. Theoretically, PHC offers the logical solution to the problems of baro- and volutrauma: it is a simple and easy-to-apply means of taking pressure and volume off the mechanically ventilated lung. The fact that PHC seems to be devoid of harmful side effects is surely another important reason why this option has gained ground in the therapy of patients with ARDS.

What principle objectives for further studies on PHC are desirable? The basic questions should be focused on reduction of ventilator-induced lung injury (i.e., baro- and volutrauma), undesirable side effects, and interactions with concurrently applied therapeutic measures. It is also indispensible to investigate the short- and long-term effects of PHC on pathophysiologic features and hemodynamics in ARDS. A subsidiary, yet secondary objective is the question of whether or not PHC has an impact on mortality in patients with ARDS. Until the basic questions are anwered it will continue to be inappropriate to demand a randomized controlled trial to check PHC's ability to reduce mortality in patients with ARDS.

The Thorens et al. investigation [9] published in this issue elucidates the short-term effects of PHC on hemodynamics, gas exchange, oxygen transport and oxygen consumption during mechanical ventilation in patients with ARDS. The astonishing result of this study is a lesson in pathophysiology: PHC is none other than hypercapnia – and hypercapnia does not evoke any unanticipated physiological effects in patients with ARDS. It does what it always does: it vasodilates and shifts the oxygen dissociation curve rightward with concomitant changes in the dependent physiological parameters. The results mainly confirm what clinicians also have observed in practice while applying PHC to patients with ARDS. Nevertheless, the importance of the Thorens et al. study must not be underestimated. This investigation provides essential data on the magnitude of changes occurring in hemodynamics, gas exchange and oxygenation, which are urgently needed for safe application of PHC to patients with ARDS. What has been long known is that in patients with ARDS there exists a linear positive relationship between the cardiac index (CI) and venous admixture ($\dot{Q}_{VA}/\dot{Q}_T$) [10]. This relationship still seems to be valid in hypercapnic patients with ARDS. The Thorens et al. data [9] show that PHC results in a mean rise in $\dot{Q}_{VA}/\dot{Q}_T$ of 6% (absolute value) combined with a mean rise in the CI of 0.7 l/min. These changes may, from a clinical point of view, appear acceptable but in 4 of the 11 investigated patients $\dot{Q}_{VA}/\dot{Q}_T$ increased by approximately 15% (absolute value), without a distinct increase in CI in 3 of them. Keeping in mind '*medicus nil noceat*', in the individual patient the clinician has to decide whether the worsening in $\dot{Q}_{VA}/\dot{Q}_T$ is outweighed by improvements in oxygen transport or other oxygenation or hemodynamic parameters. PHC may influence pulmonary vascular resistance (PVR) by single or combined effects of acidosis, hypercapnia, hypoxia, or changes in mean pulmonary artery pressure, pulmonary capillary wedge pressure and CI. In accordance with McIntyre et al. [11], but in contrast to others [12, 13], Thorens et al. [9] did not observe an increase in PVR. Should rises in PVR worsen the pulmonary hypertension in an individual patient with ARDS, it is comforting to know that small doses of inhaled nitric oxide are able to attenuate this effect [12].

Up to now, only vague recommendations but no clear-cut safety guidelines on the application of PHC exist, which is mainly due to the lack of studies investigating the effects of PHC on pathophysiologic features in patients with ARDS. The Thorens et al. study [9] is an important contribution to forming a basis for further definition of safety guidelines for PHC. The study, however, offers more. Together with recent knowledge about PHC, it tells us: PHC in ARDS – just do it! But monitor PHC adequately, consider the contraindications well, and carefully weigh advantages against disadvantages in the individual patient. The Thorens et al. results [9] should not make the clinician who applies PHC to patients with ARDS less vigilant, but they may surely make him feel safer.

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WHITE PAPER

RESPIRONICS
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Parameter Calculations in the CO_2SMO Plus!® Respiratory Profile Monitor and NICO® Cardiopulmonary Monitor

TECHNICAL CONSIDERATIONS

Technical Staff
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INTRODUCTION

The purpose of this document is to list, define and describe in detail the calculations required to compute the parameters reported by both the CO_2SMO Plus! Respiratory Profile Monitor and NICO Cardiopulmonary Monitor. Both monitors consist of a microprocessor-based data acquisition system that measures flow, pressure, CO_2 and oxygen saturation data.

Principles of Operation – Flow is measured with a fixed orifice differential flow sensor. Airway and barometric pressure are measured with absolute pressure transducers. Airway pressure is measured relative to the barometric pressure. CO_2 is measured by a mainstream infrared absorption (IR) technique with a solid state sensor. Oxygen saturation is measured with ratiometric technique based using red and infrared absorbance of oxy- and deoxy- hemoglobin.

DEFINITIONS

Averaging – Unless otherwise noted, all parameters are computed on a breath-by-breath basis with a moving average over the last eight breaths or one minute of complete breaths, whichever is less. Note that if a rate corresponding to less than eight breaths per minute of either a spontaneous or mechanical breath type occurs, only breaths in the last minute are used for that average.

Neonatal vs Pediatric vs Adult – The software distinguishes between neonatal, pediatric and adult airway sensors. If the neonatal sensor is detected, the neonatal parameter set applies. The parameter RSBI applies only to pediatric and adult subjects and C20/C only applies to neonates. Additionally, the software applies different correction factors to the flow measurement based upon which sensor is connected. These correction factors adjust the measured values in order to correct for differences in geometry and flow velocity profiles of each of the flow sensors.

BTPS – All volume parameters are considered to be in body temperature pressure saturated (BTPS) units unless otherwise noted.

Spontaneous vs. Mechanical Breath Discrimination – The pressure recognition threshold for differentiating "spontaneous" from ventilator-delivered breaths is applied on a breath-to-breath basis and can be adjusted by the user. To differentiate, the software compares the peak inspiratory pressure (PIP) to this threshold level which is the baseline pressure level (PEEP) plus a user-defined offset. If the PIP is greater than this threshold level it will be categorized as a mechanical breath. If the peak inspiratory pressure is less than or equal to this threshold level, the breath is considered to be a "spontaneous" breath. The default value for the user-defined offset is 6 cm H2O for adults and neonates.

Breath Detection – Detection of start of inspiration and expiration is performed with a robust threshold method, which requires that minimum flows and volumes be attained. Different thresholds are used for neonatal, pediatric and adult flow sensors. Once flow crosses an initial level, a breath is suspected. If the measured volume for a suspect breath meets the minimum volume requirements for inspiration and expiration the breath has been officially detected. Minimum detectable volume thresholds are 1, 5 and 20 ml for the neonatal, pediatric and pediatric/adult sensors, respectively.

Deadbands – To minimize the effect of drift, flow measurement systems employ deadbands about the zero level. For the Series 3 Flow Sensors the flow deadband thresholds are 0.2, 0.5 and 2 L/min for the neonatal, pediatric and pediatric/adult sensors, respectively.

Parameter Abbreviations – For each displayed parameter, the abbreviation used is shown with each parameter definition.

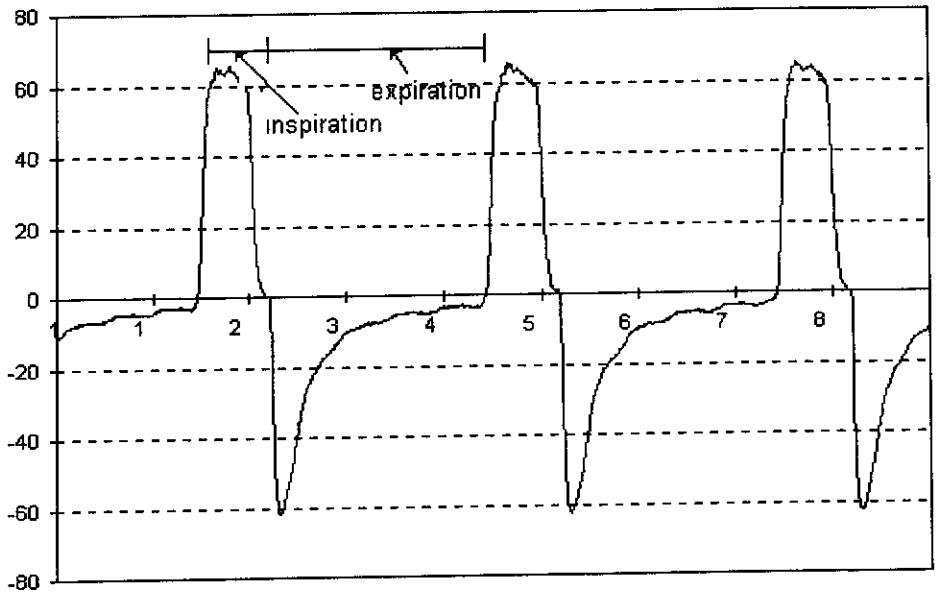

Figure 1. Breath interval delineation, flow waveform (flow in LPM vs. time in seconds)

TIMING

The breathing cycle can be divided into three intervals:

- Inspiration
- Expiration
- Pause

The automatic determination of these reference points can be hindered by zero-point drift, coughing, swallowing and cardiogenic oscillations (2). A robust flow detection algorithm is used to minimize the sensitivity to these effects. The volume is computed from the flow samples using trapezoidal integration.

Ventilatory Period (T_{tot}) *(sec)* – The time from the beginning of inspiratory flow of one breath to the beginning of inspiratory flow for the next breath (total cycle time); the sum of inspiratory time and expiratory time; the reciprocal of ventilatory frequency.

Inspiratory Phase (inspiration) – The portion of the ventilatory cycle from the beginning of inspiratory flow to the beginning of expiratory flow. Any inspiratory pause is included in the inspiratory phase.

Inspiratory or Inspired Time (Ti) *(in sec)* – The duration of the inspiratory phase (the time from start of inspiration to end of inspiration).

Expiratory Phase (expiration) – The portion of the ventilatory cycle from the beginning of expiratory flow to the beginning of inspiratory flow.

Expiratory or Expired Time (Te) *(in sec)* – The duration of the expiratory phase (the time from start of expiration to end of expiration).

Frequency or Respiratory Rate *(in breaths/min)* – Measured from start of inspiration of $breath_N$ to start of inspiration of $breath_{N+1}$ (T_{tot}) and computed as an eight breath moving average of $60/T_{tot}$ and updated breath-by-breath. Composite (all breaths), mechanical and spontaneous frequencies are all separately computed as an eight breath moving average.

Inspiratory-Expiratory Ratio (I:E) – Calculated as the ratio of the inspiratory time (time between start and end of inspiration) and expiratory time (time between end inspiration/start expiration and start of next inspiration) using all breaths and updated on a breath by breath basis. The output of this ratio is displayed in the form of:

(a) 1:x if the computed ratio is less than 1:1

(b) x:1 if the computed ratio is greater than 1:1 and shown to one decimal place.

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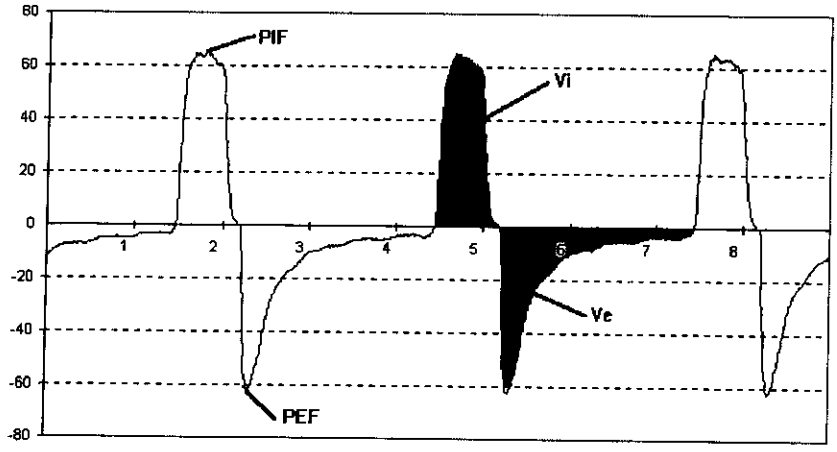

Figure 2. Flow waveform with peak inspiratory flow (PIF), peak expiratory flow (PEF), inspiratory volume (Vi) and expiratory volume (Ve) shown.

FLOW AND VOLUMES

Peak Expiratory Flow (PEF) *(in L/min)* – The largest value flow sampled during expiration.

Peak Inspiratory Flow (PIF) *(in L/min)* – The largest value flow sampled during inspiration.

Minute Ventilation (MV) *(in L/min)* – The quantity of gas exhaled expressed as volume per minute, and is calculated by expressing the eight-breath moving average of expiratory volume in terms of volume per minute and updated every breath. Total minute ventilation is calculated using all breaths. Mechanical and spontaneous minute ventilations are separately calculated using only mechanical and spontaneous breaths, respectively and may not sum to the value shown for the total minute ventilation due to averaging over different time intervals.

Expiratory Volume (Vt e) *(in mL)* – The largest volume value recorded during the expiratory interval.

Inspiratory Volume (Vt i) *(in mL)* – The largest volume value recorded during the inspiratory interval.

Corrected Tidal Volume (Vt mech) *(ml/kg) (averaged) (in mL/kg)* – Calculated as the eight-breath average total expired mechanical tidal volume divided by the user-specified patient weight.

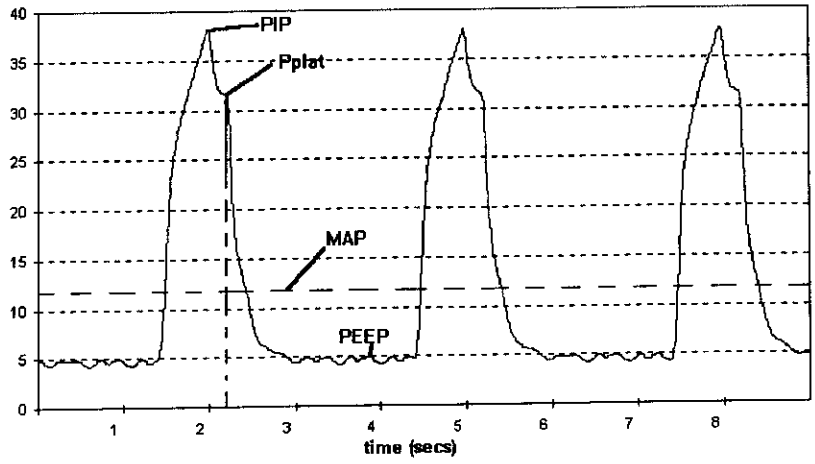

Figure 3. Pressure Waveform with peak inspiratory pressure (PIP), plateau pressure (Pplat), mean airway pressure (MAP) and PEEP shown.

PRESSURES

Mean Airway Pressure (MAP) *(in cm H_2O)* – Calculated by averaging all of the pressure samples over the last ventilatory cycle (12,13). This includes any pause intervals that may be present.

Peak Inspiratory Pressure (PIP) *(in cm H_2O)* – The largest absolute pressure value acquired during the inspiratory period.

Negative Inspiratory Pressure (NIP) *(in cm H_2O)* – Calculated as the difference between the PEEP level and minimum pressure during inspiration.

Positive End-Expiratory Pressure (PEEP) *(in cm H_2O)* – The average value of the pressure values in a window of the pressure waveform within the last 40% of the expired volume. The averaging window width varies between 70 to 150 ms as a function of the respiratory rate. The software searches from the end of breath point backwards in time and saves the average pressure value in the window if all of the pressure values in that window fall within a predetermined tolerance of 0.3 cm H_2O. If the PEEP window cannot be used due to high frequency of breathing or 'unstable' pressures, the last value of the airway pressure during expiration is then used as the PEEP value.

Auto-PEEP – Usually considered to exist when inspiration occurs and the expired flow has not reached zero (no Pause apparent) because insufficient time has elapsed to allow the lung to passively deflate (11,21). This determination is made using both the pressure level measured at the flow reversal between expiration and inspiration and the width of the expiratory pause interval. This pressure level is compared to the PEEP level and if it exceeds the PEEP level by greater than 1 cm H_2O or the expiratory pause interval is minimal (<= 20 ms) in duration) then the existence of auto-PEEP is indicated to the user.

Plateau (Peak Static) Pressure (Pplat) *(in cm H_2O)* – The sum of end-expiratory central airway pressure (PEEP) and the pressure required to distend the thorax by the tidal volume (21). Pplat is measured at the end of inspiration under stop flow conditions by a transient occlusion or by a machine-imposed end-inspiratory pause. It decays to a plateau value over 0.3 to 2.0 seconds. The values for Pplat are generally 1 to 5 cm H_2O less than the pressure recorded at flow cessation. The plateau pressure is only reported if a sufficient period of no flow exists. *Note: This parameter is not calculated for neonates.*

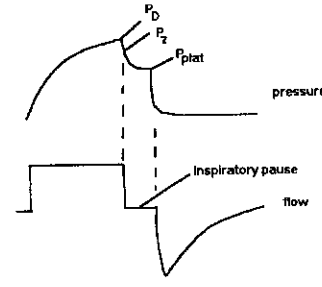

Figure 4. *Plateau Pressure Determination where P_D is the pressure just before the start of the inspiratory pause, P_z is the pressure at the start of the inspiratory pause, P_{plat} is the pressure at the end of the inspiratory pause.*

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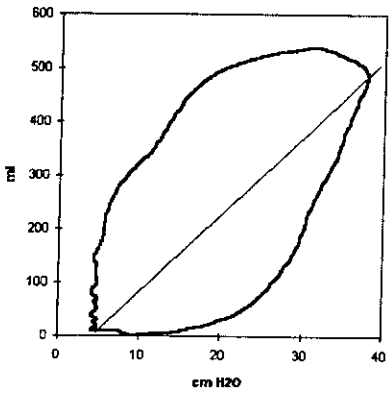

Figure 5. Dynamic Compliance – The slope of the line connecting the zero flow crossing points.

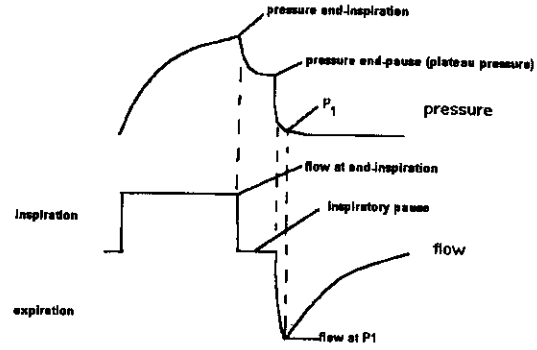

Figure 6. Resistance – Points traditionally used for calculations.

Dynamic Compliance (C_{dyn}) (mechanical) *(in mL/cm H_2O)* – The ratio of the change in volume to the change in pressure over inspiration (16). Traditionally, dynamic compliance has been calculated, per this definition, as the ratio of the maximum inspiratory volume over the difference between P_{exp} and P_{insp} (see Figure 1). At present, a more robust estimator of dynamic compliance is computed by least squares fitting of the flow, volume and pressure raw waveform data to a simple model (see following page details).

Static Compliance (C_{st}) (mechanical) *(in mL/cm H_2O)* – Calculated for mechanical breaths that have an inspiratory pause (i.e. value for plateau pressure can be determined). It is calculated as the ratio of the tidal volume at the beginning of the inspiratory hold (assumed to be at maximum inspiratory tidal volume) divided by the difference between the plateau pressure and PEEP.

Compliance Over the Last 20% of Breath/Cdyn (C_{20}/C) (mechanical) of a Mechanical Breath Inspiration (used for neonates only) – The $\Delta V/\Delta P$ during the last 20% of inspiratory pressure (5) divided by Cdyn. C_{20} is calculated as the ratio of the volume change (V_{insp}-$V_{P0.8max}$) over the last 20% of inspiratory pressure change (PIP-$P_{0.8max}$), where V_{insp} is the inspiratory volume, PIP is the peak inspiratory pressure, $P_{0.8max}$ is 80% of that PIP, and $V_{P0.8max}$ is the volume at 80% of PIP.

Airway Resistance–Inspired (R_{awi}) (mechanical) *(in cm H_2O/L/sec)* – The ratio of driving pressure during expiration to the end inspiratory flow. The driving pressure is the difference between the end inspiratory pressure and the plateau pressure. This resistance represents the dynamic resistance to inspiratory airflow created by the breathing circuit, ET tube, and major airways of the lung (see note 1).

Airway Resistance–Expired (Rawe) (mechanical) *(in cm H_2O/L/sec)* – The ratio of driving pressure during expiration to the maximum expiratory flow. The driving pressure is the difference between the plateau pressure and pressure at the maximum expiratory flow (see note 1).

[1] Airway resistance, per the above definitions, cannot be measured during sine and decelerating flow patterns or during spontaneous breathing. Traditionally, if they are calculated as defined above they may only be calculated during breaths that contain an inspiratory hold. At present, more robust estimators of inspiratory and expiratory airway resistance are computed by least squares fitting of the flow, volume and pressure raw waveform data to a simple model.

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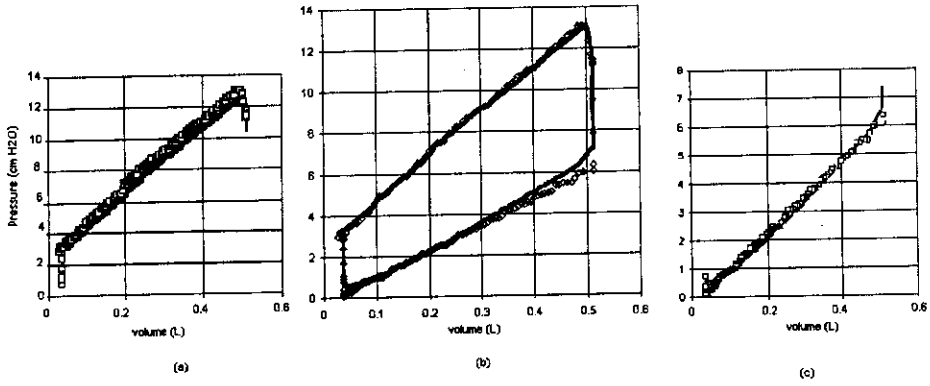

Figure 7. Pressure-Volume Curves – Data sample and least squares curve fit; (a) Inspiration, (b) Whole Breath, (c) Expiration

LEAST SQUARES RESISTANCE AND COMPLIANCE

The least squares fitting methods for calculating resistance and compliance were first described in the late 1960's (24). Resistance and compliance values were computed based upon the measurement of patient airflow, volume and intraesophageal pressure. Some investigators have applied this methodology with airway pressure instead of intraesophageal pressure. Other investigators have applied this approach to more complicated models of the respiratory system that included higher order terms and terms for inertance. Use of this modeling approach is common in the neonatal respiratory mechanics literature (19).

The least squares fitting method assumes a specific model for the respiratory system and fits the waveform data to that model. It is applied during inspiration, expiration and over the whole breath cycle. It uses all of the data points in the breath cycle and tends to be a more robust method than methods that rely on the difference between two points in the breathing cycle such as the Jonson (8) or Suter (20) methods for resistance. The lung is assumed to be a single compartment, linear model consisting of a compliance in series with a resistance that can be mathematically expressed as:

$$\Delta P_i = R\dot{V}_i + \frac{1}{C}V_i$$

where R is a resistive term, C a compliance term, _Pi – the i^{th} pressure difference, Vi – the i^{th} volume sample, and Vi i^{th} flow sample. The pressure difference is the pressure relative to a baseline level. The PEEP of the prior breath is used as the baseline level. Pulmonary inertance is not included in the equation above because of its small contribution to the total pressure change even during exercise (25). The least squares method minimizes the sum of squares between the observed 'pressure', $P_{observed}$ and the best fit curve, $P_{bestfit}$.

$$S = \Sigma(P_{BestFit} - P_{Observed})^2$$

To 'minimize' the error between the best fit and observed pressures, the partial derivatives of S with respective to R and C are computed, set to zero and solved for R and C. This results in expressions for R and C consisting of cross-products of volume and flow, pressure and volume and flow themselves.

$$R = \frac{\sum V^2 \sum P\dot{V} - \sum \dot{P}V \sum \dot{V}V}{\sum V^2 \sum \dot{V}^2 - (\sum V\dot{V})^2}$$

$$C = \frac{\sum V^2}{\sum PV - R\sum V\dot{V}}$$

The summations of these cross-products are accumulated throughout the inspiratory and expiratory portions of the breath from which dynamic compliance and resistance values are calculated.

The determination of the dynamic compliance value is based upon the data samples for a complete breath from the beginning of inspiration to the end of expiration. The inspiratory and expiratory resistance values are based upon the data samples for the inspiratory and expiratory portions of the cycle, respectively. The adequacy of the "model" can be visually assessed by substituting the values determined and plotting the data samples and best fit curve on the same axis. Figure 7 illustrates the fit for inspiration, expiration and the whole breath. Higher order terms can be added to correct to the small difference between the model and the actual curve for the whole breath plot.

Total Inspiratory Work of Breathing-Ventilator (mechanical) (WOBvent) *(in J/L)* is the work done by the ventilator on the respiratory system, and is the sum of the work required to ventilate the lung and work to move the chest wall of the relaxed or paralyzed patient (14,15). WOBvent is calculated by summing over inspiration the product of the driving pressure (airway pressure) and volume change in the sample interval. This work is then normalized to the inspiratory tidal volume. All of the work calculations involve the computation of areas using forms of work = integral over the specified time interval of P ΔV, where P is the driving pressure and ΔV is change in volume (or similarly PV dt, where PV is the product of the driving pressure and volume). The driving pressure P is the difference between the airway pressure and the baseline pressure (Paw-PEEP) for 'passive inflation.' Note that this WOB does not include PEEP work, since PEEP is used as the baseline pressure rather than atmospheric pressure.

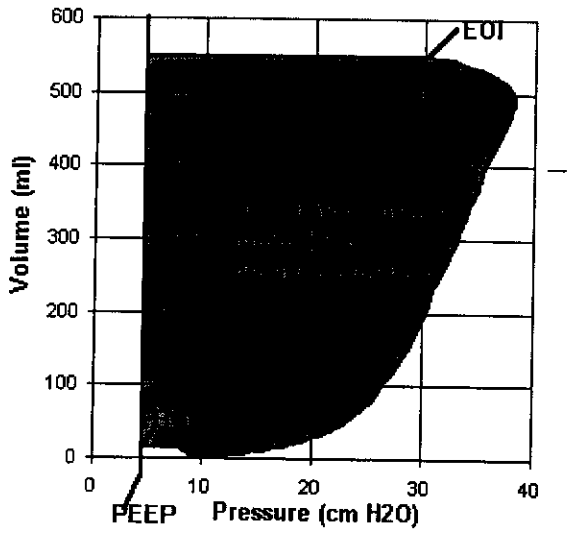

Figure 8. Inspiratory work of breathing. BOI = beginning of inspiration, EOI = end of inspiration

Rapid Shallow Breathing Index (RSBI) *(in breaths/min/liter)* is the respiratory rate divided by the average spontaneous tidal volume (26). It is calculated only if spontaneous breaths are detected and the respiratory rate of those breaths is less than 57 breaths/minute.

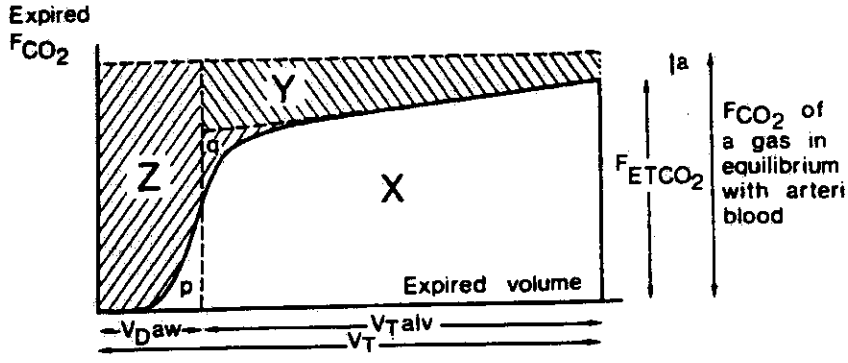

Figure 9. Airway dead space as illustrated by a CO_2 / Volume Plot. Triangles p and q are of equal area. "a" equals the end tidal-arterial FCO_2 difference. Area X is the volume of CO_2 in the breath, while areas Z and Y are defects in CO_2 elimination which represent wasted ventilation due to airway deadspace (Vdaw) and alveolar deadspace (Vd_{alv}), respectively (from Fletcher).

CO_2 VS. VOLUME

The CO_2 versus volume plot (Figure 9) is a graphical presentation of measurements such as CO_2 production, and airway and physiologic dead space.

Volume of CO_2/Minute (VCO_2-STPD) *(in mL/min)* – Calculated as an average of the CO_2 volume/breath. The CO_2 volume per breath is calculated by summing the product of % CO_2 and volume samples over the whole breath from inspiration to the end of expiration. The inspired/rebreathed CO_2 volume is subtracted from the expired CO_2 volume. VCO_2 requires different averaging intervals for different applications, as such a range of averaging intervals including 1 breath, 8 breaths, 1 minute, 3 minute and 10 minutes. The 1, 3 and 10 minute averaging intervals use 15 second updates. Although commonly referred to as CO_2 production, this value represents the volume of CO_2 exhaled per minute rather than the volume of CO_2 produced by metabolism.

Volume of CO_2/Minute/kg (VCO_2 /kg- STPD) – Averaged VCO_2 (using the selected averaging interval) normalized by the user-specified patient weight in kg.

Airway (Anatomic) Dead Space (Ineffective Tidal Volume) (Vd aw) *(mL)* – The volume of the conducting airways at the 'midpoint' of the transition from dead space to alveolar gas. This dead space, also known as Fowlers dead space(7), was originally implemented for nitrogen. The extrapolated phase III slope is used and the value at which volumes of CO_2 represented by areas p and q are equal is determined. The slope of phase III is computed by linear regression of the points bounded by 30 to 70% of expired CO_2 volume (1,2,10,23).

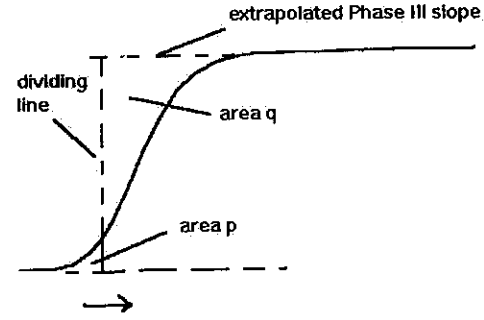

Figure 10 Airway Dead Space Determination – dividing line is moved until areas p and q are equal.

Alveolar Tidal Volume (Effective Tidal Volume) (Vt_{alv}), *(in mL)* – Calculated as the difference between the expired tidal volume and total airway dead space.

Alveolar (Effective) Minute Ventilaton (MV_{alv}) *(in L/min)* – Computed using the alveolar (effective) tidal volume to calculate minute volume and total airway dead space.

Mixed Expired CO_2 ($PeCO_2$ or $FeCO_2$) *(in mmHg, % or kPa – user selectable)* – The volume weighted 1 or 3** minute average CO_2 updated every 15 seconds. It is calculated by dividing the volume of CO_2 for a minute interval by the total expired volume for the same interval.

** NICO Software 5.0 or later.

Vd/Vt (Physiologic) (Vd/Vt phys) – Calculated as ($PaCO_2$ - $PeCO_2$) / $PaCO_2$ where $PaCO_2$ and $PeCO_2$ are the arterial and mixed expired PCO_2, respectively. The original Bohr equation is ($PACO_2$ -$PeCO_2$) / $PACO_2$ where $PACO_2$ is alveolar CO_2. Enghoff altered the this equation by substituting $PaCO_2$, the partial pressure of CO_2 in arterial blood, for $PACO_2$ (4). The $PaCO_2$ value is user entered.

Physiologic Dead Space (Vd phys) *(in mL)* – Considered the total dead space of the patient and as calculated includes alveolar, anatomic/airway and apparatus dead spaces.

Alveolar Dead Space (Vd_{alv}) *(in mL)* – Considered the dead space that is not airway dead space volume and is calculated by subtracting the airway dead space volume from the 'physiologic' dead space.

End Tidal CO_2 ($PetCO_2$) *(in mmHg, % or kPa – user selectable)* – Calculated by performing an 80 ms moving average of the expiratory CO_2 samples and reporting the largest average value over the expiratory interval as the end-tidal value. Breath to breath, 10 and 20 second interval averages are user selectable.

Inspired CO_2 *(in mmHg, % or kPa – user selectable)* – Calculated as the minimum value of the moving average of the CO_2 sample over the last 20 seconds. This value is reported only when greater than 3 mmHg of CO_2 is present for the last 20 seconds.

PULSE OXIMETRY

Functional Saturation (SpO_2) *(in %)* – Defined as 100*(HbO2/100-(COHb+METHb)) where HbO_2 , COHb and METHb are the fractional hemoglobin, carboxyhemoglobin and methemoglobin, respectively. Functional saturation represents the amount of oxyhemoglobin as a percentage of the hemoglobin that can be oxygenated. Dysfunctional hemoglobin (COHb and METHb) are not included in the measurement of functional saturation.

Pulse Rate (PR) (beats/min) – Calculated by measuring the time interval between the peaks of the infrared light waveform.

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Selecting the Right Flow Sensor

with Respironics Novametrix Series 3 Combined CO_2/Flow Sensors

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ABSTRACT

Respironics Novametrix Series 3 Combined CO_2/Flow Sensors–Selecting the Right Sensor–Respironics Novametrix Technical Report 9901. The Respironics Novametrix Series 3 Combined CO_2/Flow Sensors are reviewed and the selection criteria of ETT, flow, volume, patient age, deadspace and resistance is discussed.

INTRODUCTION

Mainstream capnography and spirometry in a single compact sensor has only become available with the recent introduction of the Series 3 combined CO_2/Flow sensors from Respironics Novametrix. Additionally, these sensors are relatively inexpensive, have minimal dead space and resistance, work well over relatively wide flow ranges and require no calibration. However no single sensor will work over the range spanning from a neonate to an adult. To span this wide range, Respironics Novametrix has designed three CO_2/Flow sensors that are for use with the neonate/infant, infant/pediatric and pediatric/adult patient (Figure 1). Since this is a combined CO_2/flow sensor and the patient flows are not known ahead of time, it may not be clear in some patients which sensor is best. For example, the neonatal combined sensor is appropriate for most neonates; however, a larger full-term infant may require the pediatric combined sensor. The pediatric ICU, on the other hand, would require all three of the Series 3 combined sensors since the patients range from infants to young adults. Likewise, the adult combined sensor is appropriate for most adults; however, one may require the pediatric sensor for the smaller adult. The purpose of this technical report is to provide guidelines to allow the user to better select the proper sensor for monitoring.

The criteria for selecting which sensor to use includes ETT size, patient age, flow/volume values, and the acceptable levels of deadspace and resistance. Each will be discussed.

For a thorough description of issues associated with flow measurement, see Technical Report 9705–Flow Measurement with Respironics Novametrix Series 3 Flow Sensors–Technical Issues.

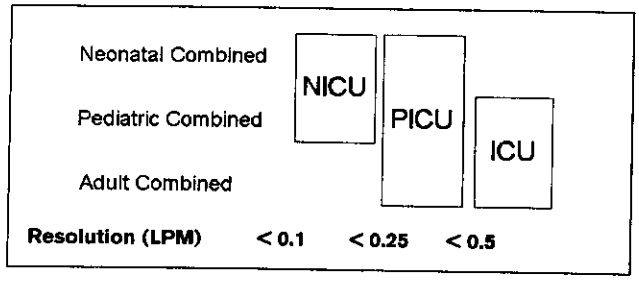

Figure 1. Sensors for NICU, PICU and adult ICU.

ETT

The recommended endotracheal tube (ETT) size ranges are printed on the sensor package (Table 1). In many cases the recommended ETT size would be sufficient. However, other factors need to be considered and these ranges overlap so additional criteria must be applied.

Flow/Volume

Since this is a flow sensor, the most obvious criteria would be to use the expected or actual flow range or peak flow expected in a particular patient. Table 1 provides the total operating ranges for each of the Series 3 Combined CO_2 Flow Sensors. However, the flow range depends upon ventilation mode and the patient's status, which may not be known prior to placement in the breathing circuit with enough precision to choose the best sensor. Additionally, the ventilators' "measured volume" is often displayed, but can be significantly higher than the actual delivered volume due to compression loss in the breathing circuit. Also note that a patient on a mode such as SIMV may span a large range in volume because the patient receives mechanical breaths and may have respiratory efforts with small spontaneous breaths. If these 'efforts' or small breaths are to be reported then the minimum detectable volume must be considered. The Respironics Novametrix breath detection algorithm uses as one of its screening criteria minimum detectable volumes of 1, 5 and 20 ml for the neonatal, pediatric and pediatric/adult sensors, respectively. Thus, if these efforts are to be detected then the appropriate sensor should be chosen.

Table 1. Nominal Ranges and Values of Selection Criteria for the Combined CO_2/Flow Sensors

	Primary Criteria			*Secondary Criteria*			
	ETT Range (mm)	Min. Volume (ml)	Max. Volume (ml)	Min. Flow* (LPM/ml/sec)	Max. Flow** (LPM/ml/sec)	Dead Space (ml)	ID*** (mm)
Neonatal Combined	2.5-4.0	1	100	0.2 3	25 417	< 1	5
Pediatric Combined	3.5-6.0	30	400	0.5 8	120 2000	< 4	10
Adult Combined	≥ 5.5	200	3000	2.0 33	180 3000	8	15

* **Min. Flow**–nominal minimum flow of sensor; ** **Max. Flow**–nominal maximum flow of sensor; *** **ID**–nominal inner bore diameter of sensor
Note: Min. Volume and Max. Volume values represent the recommended operating range in volume for each flow sensor and not necessarily the absolute minimum and maximum volume values.

Patient Age

The patient age range for each sensor depends upon the flow range, which is affected by ventilatory mode and patient status. As such, the patient's resistance, compliance and deadspace should also be considered. For example, a 2-year-old child receiving mechanical ventilation would most likely use the pediatric combined sensor. However, if the child is breathing spontaneously the deadspace may be higher than desired so a neonatal combined sensor might be the correct choice. Table 2 provides nominal age ranges for each of the combined sensors.

Table 2. Nominal Age Ranges for the Combined CO_2/Flow Sensors

	Age Range	
	Low	High
Neonatal Combined	–	2 – 4 yrs
Pediatric Combined	2 – 4 yrs	12 – 18 yrs
Adult Combined	12 – 18 yrs	–

Dead Space and Resistance

The design goals of the Respironics Novametrix CO_2/flow sensors were two-fold:

- Minimize the resistance as measured by the pressure loss across the sensor while maintaining the maximum possible recoverable differential pressure drop between the ports. For a fixed orifice flowmeter, due to the parabolic nature of resistance the device is typically much less resistive at low and moderate flows than devices with a linear flow-pressure relationship. When reading resistance specifications it is important to consider both the flow rate at which the pressure drop is reported and the nature of the flow-pressure relationship (Figure 2).
- Minimize the deadspace so that the volume of rebreathed gas is kept small while maximizing entrance length and insensitivity to changes in inlet conditions.

The design of the Series 3 flow sensors have sought to achieve these balances without compromising the performance in patients.[1]

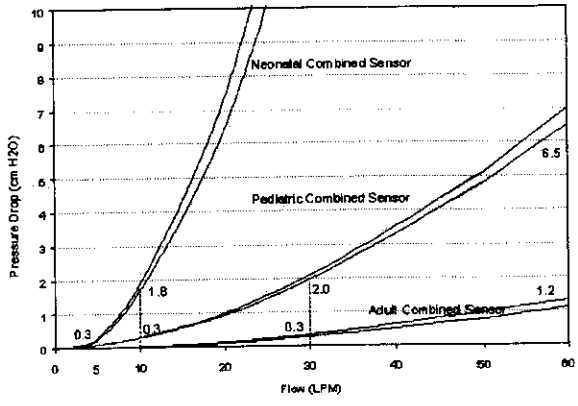

Figure 2. Inspiratory and expiratory resistance as a function of flow for the neonatal, pediatric and pediatric/adult combined sensors. Two curves are shown for each sensor. The higher of the two curves is the inspiratory curve. Representative values are shown at 5, 10, 30 and 60 LPM.

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Flow Measurement

with Respironics Novametrix Series 3 Flow Sensors

TECHNICAL ISSUES

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ABSTRACT

Flow measurement issues with mechanically ventilated patients are reviewed with particular emphasis on the Respironics Novametrix Series 3 flow sensors. Flow sensor technology in the critical care setting is reviewed.

INTRODUCTION

The measurement of flow on mechanically ventilated patients requires attention to:

- sensor(s) location
- gas composition
- gas temperature
- inlet conditions
- humidity
- dead space
- effective resistance of breathing circuit
- operating range of flow sensor

When comparing flow measured by two different devices all of these considerations must be taken into account. In addition, the degree of inter-unit and inter-sensor variability must be included in any evaluation.

FLOW SENSOR OVERVIEW

Introduction–Airway Flow Measurement Techniques

Various technologies have been used to measure airway flow. Many of these techniques were developed strictly for precise short term laboratory measurements. These applications require meticulous attention to detail including calibration and operator attendance at all times.

For the relatively dry gas, laboratory quality airflow measurements, great attention is placed upon accuracy, calibration, repeatability, and precision. Flowmeters that perform suitably in these environments include Fleisch and Lilly style pneumotachometers, hot wire anemometers, rotating vane spirometers and ultrasonic vortex shedding flowmeters. Hot wire anemometers (also known as thermal dissipation devices), based upon the convective cooling by the flowing gas, often use heated (>300°C) platinum or a platinum alloy. As such these devices are inappropriate when flammable gases are present (Yoshiya). Rotating vane spirometers tend to underestimate at low flows and overestimate at high flows due to friction and inertia of the turbine (Hsley,Yeh). Overall, in respiratory research the most widely used flow measurement device is the Fleisch type differential pressure with a heated screen orifice.

A continuous, bi-directional airway flow measurement device that can be placed proximal to the patient and used in critical care environments has been of great interest. The continuous monitoring environment demands simplicity, reliability, ease of use and ability to continue working in wet, often mucous filled circuits for long periods of time without operator intervention. These devices should be relatively inexpensive, have minimal dead space, work over wide flow ranges and require minimal or no calibration. Devices typically designed for the pulmonary function environment will generally not work well in continuous monitoring applications.

Due to the requirements in the critical care environment, a different type of flow device is required. These devices fall under the general description of fixed or variable orifice (aperture) differential pressure pneumotachometers. These flow measurement devices are usually simpler in construction, are typically lightweight plastic and thus can be disposable and designed to operate in wet, mucus filled patient airway circuits. Flow devices that offer the most promise in continuous proximal, bi-directional monitoring are those that utilize differential pressure pneumotachography.

Differential Pressure Flow Sensors–Theory of Operation

Differential pressure flow sensors incorporate some type of restriction (point orifice, variable flap, vena constriction, annular obstruction, target or linear flow restrictor) that generates a

pressure difference across the sensor. Flexible tubing, attached to either side of the flow obstruction, transmits the differential pressure signal to a sensitive pressure sensor located inside a monitor at the bedside. Factors that influence the measurement of flow for this type of sensor include the gas molecular weight, temperature and airway pressure.

Fleisch Type

The popular Fleisch pneumotach uses small capillary tubes to ensure laminar flow through the sensor body thereby producing a nearly linear relationship between flow and differential pressure. While it is an excellent device for short term monitoring, it is easily contaminated by sputum and water condensate. Also due to its relatively large surface area (dead space) it is often not suited for continuous respiratory monitoring. In addition, it is heavy, costly and difficult to clean.

Lilly Type

The Lilly type flowhead uses a metal mesh for the flow restrictor. Hans Rudolph Company manufactures a version of this flowmeter that utilizes three screens to create a linear flow/differential pressure relationship. The Lilly suffers from the same problems as the Fleisch in monitoring continuous proximal airway flows.

Variable Orifice Type

The variable orifice type flow sensors have become popular in the long-term critical care monitoring environment due to their improved immunity to artifactual flow signals caused by moisture and secretions in the breathing circuit (Osborn). These flow sensors use a flexible sheet material (plastic or stainless steel) to create an opening that is small when flow is low and wider as flow increases. This dynamically changing orifice results in a more linear relationship between differential pressure and flow, allowing a larger range of flows to be measured accurately than is traditionally allowed by a fixed orifice type of device. The variable orifice flowmeter works quite well under conditions of moisture and mucous.

The variable orifice type flowmeter's accuracy depends, however, upon the consistent stress-strain characteristics of the variable orifice flap which can be degraded by inter-device variations created during manufacturing or intra-device changes due to fatigue during long-term use. In order to solve this problem, some manufacturers offer sensors with device specific factory pre-calibration parameters stored within a memory chip attached within the flowmeter connector. Variable flap flowmeters can be very susceptible to changes in flow patterns generated by different breathing circuit adapters (inlet configurations) placed immediately prior to the flowmeter. Bicore, Bird and Carlsbad manufacture variable orifice type flowmeters such as the VarFlex™ flow transducer, Partner™ IIi Volume monitor flow sensor, and the H7400 AccuTach™ flow sensor, respectively.

Fixed Orifice type

The pressure drop across a fixed orifice flow sensor is, in general, proportional to the square of the flow (see Figure 1). Microprocessors can be programmed to store the parameters of these flow sensors and to compensate for this non-linear pressure-flow relationship. In addition, recent advances in differential pressure sensor technology have made it possible to measure the very low flows reliably. The Respironics Novametrix Series 3 Flow Sensors are considered to be fixed orifice, target flowmeters. Although the Datex D-Lite® sensor (Merlainen) and MedGraphics preVent™ Pneumotach (Porszasz) are also fixed orifice designs, as Pitot tubes they measure the velocity of gas flow and as such are based upon different measurement principles than target flowmeters such as the Respironics Novametrix Series 3 sensors.

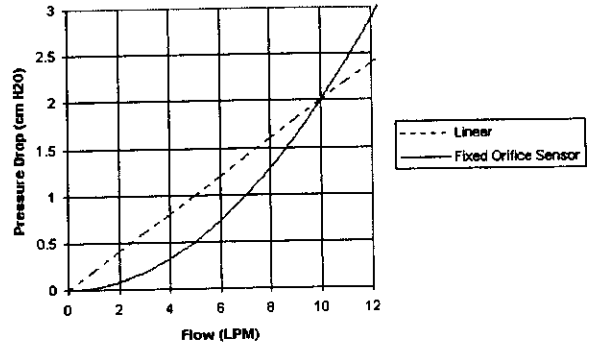

Figure 1. Flow versus Pressure Drop for a "Linear" device (i.e. Fleisch pneumotachograph) and "Non-Linear" device (fixed orifice flow sensor) over the neonatal flow range

Respironics Novametrix Flow Sensor(s)

The adult flow and combined CO_2/flow sensors feature a target geometry composed of a center strut and side-mounted flow restrictions (having a notch in the strut) that are designed to

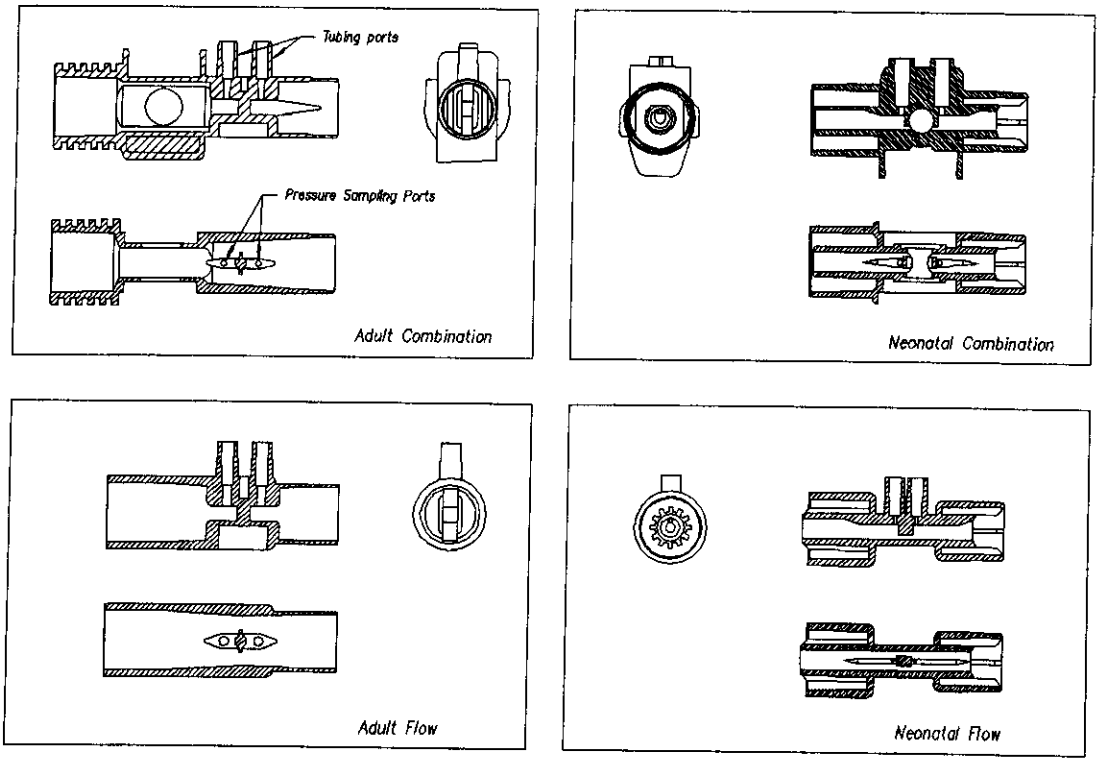

Figure 2. Adult, neonatal, combination adult and combination neonatal CO_2/flow sensors–side, top and end sections (US Patents 4,859,858; 4,859,859; 4,914,720; 4,958,075; 5,146,092; 5,379,650; 5,535,633; 5,616,923; 5,693,944; 5,793,044; 5,789,660; 6,126,610; 6,312,389). (Other Patents Pending). Combination pediatric CO_2/flow sensor not shown.

minimize localized streamline effects about the pressure sensor aperture. This significantly improves its performance compared to variable orifice flowmeters with changes in upstream geometry (adapter configurations). The design allows for immunity to unpredictable flow velocity profiles, without the need to add excessive length to the flow sensor adapter (minimal dead space). On the other hand, the neonatal flow sensors feature a target geometry composed of a center strut without the side-mounted flow restrictions to maintain an acceptable level of flow resistance. In order to reduce mechanical deadspace, the combination pediatric/adult and neonatal CO_2/flow sensors are single piece designs.

As they have no moving parts, these flow sensors are simpler to construct and do not require user pre-calibration. Each configuration is characterized once at the factory, and with manufacturing control, individual sensor calibration is not required.

As previously noted, with a fixed orifice device, the differential pressure varies as the square of the flow. The measured flow should be corrected by use of empirically determined coefficients due to variations from this relationship and the assumptions made in developing the flow equations.

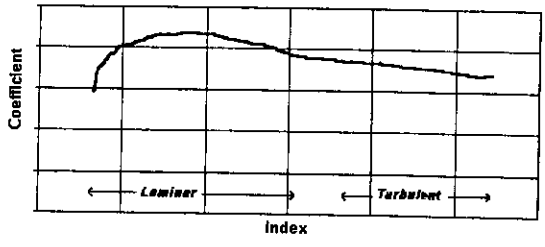

Figure 3. Representative Correction Coefficient Curve

The relationship between the measured differential pressure to flow (L/min) can be described by the equation,

$$\frac{P_m T_{std}}{P_{std} T_m} K \sqrt{\Delta P}$$

where P_m P_{std} T_m and T_{std} are the measured and standard pressures (in mmHg) and temperatures (in °K), respectively; K is a correction factor that includes gas composition and other factors and ΔP is the differential pressure (in mmHg). The $P_m T_{std}/P_{std} T_m$ is the ideal gas law correction of calculated flow

to standard conditions. Inspiratory and expiratory phases are treated separately with regards to temperature and gas composition. For example in an unheated breathing circuit supplied with 'room' air, inspiratory air may be considered to be at near room temperature and consisting of nominally 21% oxygen and balance nitrogen and expiratory air at body temperature (or near body temperature less 2-4°C for temperature drop from 'lungs' to sensor) and consisting of nominally 16% oxygen, 5% carbon dioxide and balance nitrogen. While in a heated circuit with elevated oxygen (such as 60% FiO_2), the values used for both temperature and gas composition would be quite different.

FACTORS AFFECTING FLOW READINGS

Sensor Location

Proximal flow measured at the patient's airway can be substantially different from flow measured inside or at the ventilator. Many ventilators measure flow, not at the proximal airway, but close to the ventilator (see Table 1). This can result in a substantial difference between what is delivered to the patient and what the ventilator reports as delivered due to the wasted compression volume. This wasted portion of the tidal volume does not ventilate the patient, remains within the breathing circuit and tends to elongate and distend the breathing circuit tubing and compress the gas. A correction for this effect which is proportional to the inspiratory peak pressure is applied by some ventilators given that the breathing circuit compliance is known. Even with this correction applied precise estimation of the compression volume is difficult due to variations between individual breathing circuits, use of humidifiers, HMEs and other circuit components. Thus for monitoring patients the sensor should be placed between the breathing circuit wye and the endotracheal tube.

Table 1. Flow Sensor Location (adapted from Tobin).

Ventilator	Flow Sensor	Site
Bear 5	Vortex shedding	Distal to exhalation valve
Bird 6500ST	Variable Orifice	At exhalation valve outlet
Hamilton Veolar	Variable Orifice	Proximal airway
Puritan-Bennett 7200a	Hot wire	Distal to exhalation valve

Gas Composition

Accurate flow measurement requires that the nominal values for inspiratory and expiratory gas composition be provided. The user can choose typical ambient values for oxygen, carbon dioxide, and nitrogen if one is testing with a calibration syringe or typical patient values. Compensations for additional gases such nitrous oxide, helium, or an anesthetic agent are available. The effect of not properly compensating for the gas concentrations may result in a significant change in the reported flow value (see Table 2). Gas composition correction assumes the viscosity can be computed as the linear combination of the product of each individual viscosity and its gas fraction.

Table 2. Changes in Reported Flow and Percentage Difference with Different Gas Compositions (at 35°C).

N2 %	O2 %	CO_2 %	He %	N_2O %	Agent %	Flow l/min	% Diff
79	21	0	–	–	–	100.0	–
79	16	5	–	–	–	99.0	1
Elevated Oxygen							
70	30	–	–	–	–	99.4	1
60	40	–	–	–	–	98.7	1
40	60	–	–	–	–	97.4	3
20	80	–	–	–	–	96.1	4
0	100	–	–	–	–	94.9	5
Anesthesia							
0	60	0	–	40	0	87.6	12
0	55	5	–	40	0	86.8	13
0	40	0	–	60	0	84.0	16
59	40	0	–	0	1	96.1	4
35	60	0	–	0	5	86.4	14
25	60	0	–	0	15	72.1	28
Heliox							
–	40	–	60	–	–	143.5	44
–	30	–	70	–	–	159.2	59
–	20	–	80	–	–	180.5	81

Gas Temperature

Accurate flow measurement also requires that the nominal values for inspiratory and expiratory gas temperature values be considered. The software provides defaults for typical patient values. If the inspired air is heated in the ventilator circuit, greater accuracy can be achieved by entering the set temperature of the heater as the inspiratory temperature.

Inlet Conditions

The adult and neonatal flow sensors have been designed to be insensitive to changes in inlet conditions. For example, changing the proximal connections from a direct endotracheal tube (ET) connection to a connection via an elbow has a dramatic change on the cross-sectional profile of the flow entering the flow sensor but a robust design should have little effect on the flow measured (see Figure 4).

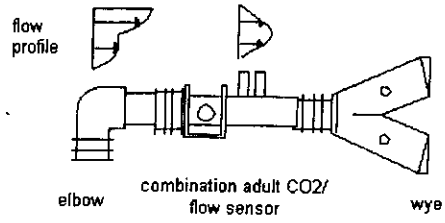

Figure 4. Combination adult CO_2/flow sensor in-circuit with example expiratory flow velocity profiles.

Even small changes in the geometry of the breathing circuit tubing relative to the flow sensor can have significant effect on the measured flow. The Series 3 adult and neonatal flow sensor are only slightly affected (typically <5%) by such changes, whereas, other devices can be significantly affected. For example, it has been demonstrated that Fleisch pneumotachographs connected between the wye and endotracheal tubes exhibit a flow rate dependent error in measured flow up to 10% (Kreit).

To quantify this effect in the Series 3 flow sensors, commonly used adapters were attached individually to the inlet of the flowmeter and the resulting changes in flow recorded. To test the Series 3 flow sensors, flows of 20 and 60 L/min, and 5 and 20 L/min were used for the adult and neonatal flow sensors, respectively. Various elbows, endotracheal tubes CO_2 airway adapters, Heat Moisture Exchanger (HME) and straight 22 to 15 mm adapters were used to test expiratory flows and different wyes were used to test inspiratory flows.

If sufficient entrance length is provided in the flow sensor then laminar flow and a consistent flow velocity profile can be achieved. However, this is usually not practical so entrance length to a flow sensor must be traded off against the design requirement of minimal deadspace. Thus, a balance has been sought between low deadspace and insensitivity to changes in inlet conditions. The design of the Series 3 flow sensors has sought to achieve this balance.

Humidity

The Series 3 flow sensors have been designed to be insensitive to moisture accumulation on the flow sensor. The measurement and generation of the pressure drop can be affected by moisture. The user's manual and product package labeling indicate the pressure ports should be directed upwards to prevent fluid from draining into them. The shape and placement of the target are such to minimize accumulations on the sensor. However, proper breathing circuit maintenance and avoiding gravity dependent positions within the breathing circuit is still required to avoid pooling of water and sputum in the flow sensor. Bench and clinical testing in fully saturated breathing circuits have demonstrated that the effect of moisture is typically negligible in the adult sensors and small in the neonatal sensors.

When the Series 3 flow sensors are used in a heated breathing circuit, the body temperature (i.e. 37°C) for the nominal expired gas temperature should be entered and the reported volumes will be in Body Temperature Pressure Saturated (BTPS). If the Series 3 flow sensors are used for testing in a dry room temperature circuit, the room temperature should be entered and the reported volumes will be in Ambient Temperature Pressure (ATPx).

Dead Space – Equipment

The term "Wasted Ventilation" or respiratory dead space is considered to be the volume of each breath that is inhaled but does not participate in gas exchange. However, in clinical settings the term is used inconsistently and, depending on how it is measured, may describe different volumes (see Figure 5). The explanation for this confusion is that the volume of dead space that is measured is dependent on the method of measurement, and whether or not the patient is intubated, breathing spontaneously or ventilated, tidal volume, body position at the time of the measurement, and a number of other variables.

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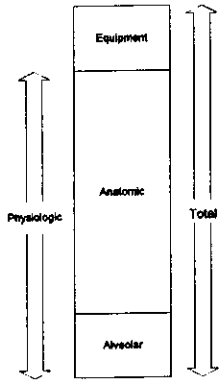

Figure 5. Breakdown of Different Deadspace Volumes

The equipment (i.e. apparatus) dead space in the ventilator circuit (See Figure 6) can be substantial relative to the total tidal volume, especially when large HME filters are used. One of the design goals for each of the flow sensors was to keep the added deadspace to a minimum (<10 ml for the adult flow sensors and < 1 ml for the neonatal sensors).

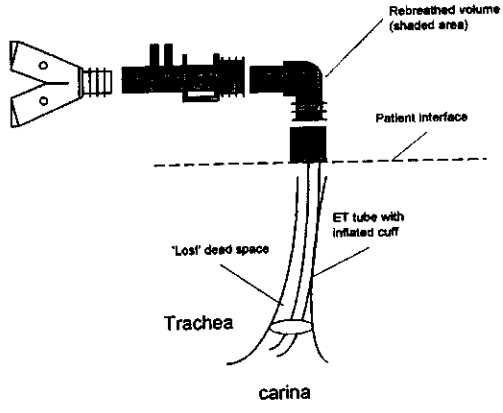

Figure 6. Anatomic and apparatus dead space in intubated patient

Effective Resistance of Breathing Circuit

The addition of a flow sensor to a breathing circuit should have minimal impact on the measured quantity - flow. One of the design goals was to minimize the resistance as measured by the pressure loss across the sensor while maintaining as large as possible recoverable differential pressure drop between the ports. Typically, resistance of a flow meter in product specifications and standards for pulmonary function testing is stated in terms of a pressure drop or resistance at a particular flow rate. For a fixed orifice flowmeter, due to the parabolic nature of resistance the device is typically much less resistive at low and moderate flows than devices that have a linear flow-pressure relationship. Conversely at higher flows it is more resistive than the linear flow devices. For example, let's consider the two devices with identical pressure drop at 10 LPM and the flow-pressure characteristics as in Figure 1. With a typical inspiratory square waveform or sinusoidal waveform with PIFs of 6 and 10 LPM, respectively, the added work for the Series 3 neonatal sensor would be less in both conditions. When reading resistance specifications it is important to consider both the flow rate at which the pressure drop is reported and the nature of the flow-pressure relationship. In addition, for devices that do not have a linear relationship a more relevant measure would be a flow-pressure plot or a better figure of merit that reports the added work of breathing due to the device under specified conditions rather than the pressure drop at a particular flow rate.

Operating Range of Flow Sensor

While the operating range for flow is constrained by the range of the pressure sensors and electronics, the operating range of derived parameters such as volume must be considered in light of the flow sensor range and physiological limits. For example, the specification for the adult tidal volume range is from 100 ml to 3000 ml. However, the system cannot measure these volumes to the stated accuracy at all possible I:E ratio and frequency settings because of the high limit of 180 LPM or low limit of 2 LPM. Consider the frequency range from 2 to 120 breaths per minute and the volume range with a typical I:E ratio. The drawing of a rectangle below with the range limits might imply that all combinations within that area are possible. However, flow and physiological limitations must be considered and instead the hatched area is the region which can be measured given the 1:2 I:E ratio and flow range of 2 to 180 LPM. As a reference point, competitive flowmeters do not have such a wide operating range.

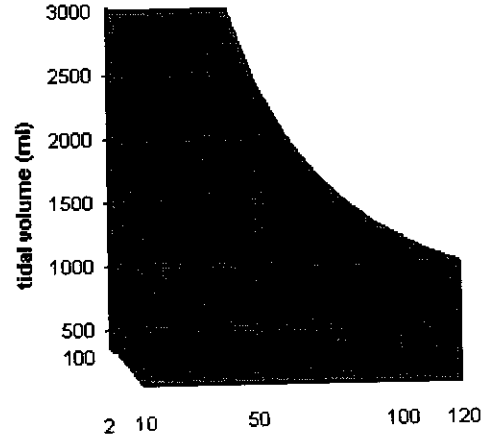

Figure 7. Example Operating Range of Adult Flow Sensor (Upper range of neonatal flow sensor shown as dashed line)

Inter-Sensor Variability

The Series 3 flowmeters use a fixed orifice type design which allows for a single piece injection molded part. This means that there should be no need for individual device calibration of the flow/pressure characteristics. To compare the variability between 20 adult flow sensors, volume tests were performed at a nominal flow rate of 60 LPM. Similarly, to compare the variability between 20 neonatal flow sensors, volume tests were performed at nominal flow rates of 10 and 20 LPM. The same module was used to remove the effect of inter-unit differences. The average inspiratory and expiratory percent error of the 20 different devices tested for each flow was computed. The error, the standard deviation of the average volumes for the 20 devices, a measure of the sensor to sensor variability, was also computed. The standard deviations for all of the sensors (< 1%) are well within the ability to accurately repeat the volume test which shows that interchangeability is excellent and that individual characterization (thus calibration) of each flow adapter is not required.

Inter-Unit Variability

Due to tolerances in the manufacturing process there is a small amount of variability in the data acquisition electronics from unit to unit. To determine the variation at different flow rates between different units, 4 modules were tested with the same neonatal flow sensor and inter-device differences computed. Inter-unit differences were determined to be less than 1% overall which is considered excellent inter-unit variability. The coefficient of variation was typically less than 0.5% except at the lowest flow setting which are the most difficult to measure with high accuracy and repeatability.

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Mainstream or Sidestream Capnography?

TECHNICAL CONSIDERATIONS

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ABSTRACT

Technical aspects of mainstream and sidestream capnography are described and contrasted. Issues such as leaks, contamination and artifacts are reviewed. The clinical implications of these different approaches are discussed and the benefits of mainstream capnography highlighted.

TABLE OF CONTENTS

INTRODUCTION

Infrared measurement of carbon dioxide monitoring (capnography) dates back to the 1940's [1,2]. In the 1950's these bulky and fragile instruments were adapted for medical use. Consistent with other gas measurement modalities such as mass spectrometry, these early devices were sidestream (i.e., diverting) sampling systems. Representative systems include rack mountable systems such as the Beckman LB-1 and LB-2 analyzers that were considered the gold standard for carbon dioxide measurement in the 1970's. Similarly, early mainstream devices [3] were physically large, cumbersome and impractical for clinical use. Advancements in both mainstream and sidestream technology decreased the size of these devices to allow their inclusion in clinical monitors. However, it was not until the introduction of the HP 47210A (Fig. 1) in the early 1980s that mainstream devices began to be used in the clinical environment [4,5].

While both mainstream and sidestream devices continued to improve in performance, the primary criticisms of mainstream technology have been largely overcome with the introduction of solid state sources, improved optics and miniaturization while sidestream technology still suffers from its fundamental limitations. This paper contrasts the two approaches to capnography.

Overview of Differences between Mainstream and Sidestream Capnography

A capnometer, by definition is either diverting (i.e., sidestream) or non-diverting (i.e., mainstream). A diverting capnometer transports a portion of a patient's respired gases from the sampling site, through a sampling tube, to the sensor whereas a non-diverting capnometer does not transport gas away from the sampling site [6,7]. In other words, one can view the difference between mainstream (non-diverting) capnography and sidestream (diverting) capnography as clinically measuring carbon dioxide at the sample site versus measuring carbon dioxide in the monitor distant from the sample site.

The measurement of the partial pressure of a gas significantly distant from the sampling site raises a number of "laws of physics" issues including (1) water removal, (2) different conditions at the sampling site and sample cell in terms of temperature and humidity, (3) mixing of the sample gas as it is drawn through the cell, (4) variable pressure drop across the tubing and the possible misrepresentation of the partial pressure values due to the above and other effects and (5) dynamic distortions to the waveform. While some of these effects can be compensated for or corrected by other measurements or by the assumption of nominal values, other effects cannot.

With mainstream devices, the sensor consisting of the sample cell and infrared bench is placed at the airway. This location results in a "crisp" graphical representation of the time varying CO_2 value (capnogram) that reflects in real-time the partial pressure of carbon dioxide within the airway. On the other hand, sidestream devices aspirate a sample of gas from the breathing circuit through a six to eight foot long small bore tube at a flow rate that may vary as much as ±20% (Table 2). This sample is then often passed through a water trap and drying tubing prior to being analyzed in a sample cell. Using a remote location results in a delay time of up to several seconds and a rise time

distortion of perhaps greater than 200 ms (Table 2). This delay in total response time can be significant due to the need to provide to the clinician an earliest warning as possible [8].

Comparisons of devices from different manufacturers are often complicated by the use of different terminology and definitions[1] for delay and rise time, resulting in confusion for the user. Tables 1 and 2 compare mainstream and sidestream in general terms and specific systems, respectively.

Mainstream Capnography Overview

Mainstream capnography can be viewed as illustrated in Figure 7(a). The sample cell, referred to as the cuvette, serves as the airway adapter and is located in line with the respiratory gas stream obviating the need for gas sampling and scavenging. It interfaces directly to the infrared (IR) bench. A source emits infrared radiation that includes the absorption band for carbon dioxide.

Carbon dioxide within the sample gas preferentially absorbs this radiation at some wavelengths and passes other wavelengths (Figure 9). Photodetectors, typically located on the other side of the airway adapter, measure the transmitted radiation as it passes through the IR transmitting windows of the cuvette. A multi-conductor, lightweight, flexible cable transmits the amplified detected signals to the monitor from which the partial pressure of carbon dioxide is calculated and displayed graphically in the form of a capnogram. The monitor contains only electronics associated with control and measurement functions of the infrared bench.

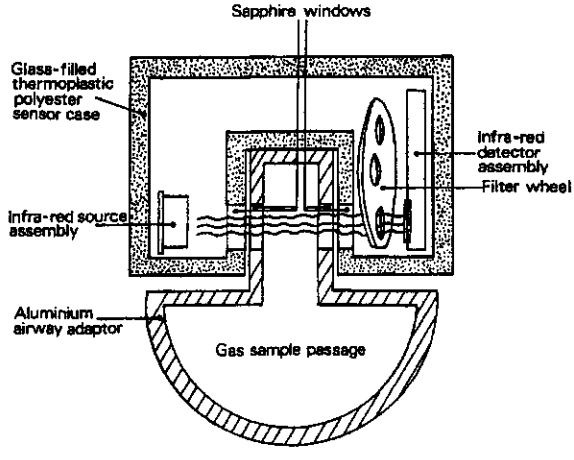

Figure 1. Cross-sectional view of a mechanical mainstream sensor (HP 47210A) (from Kinsella [4], © The Board of Management and Trustees of the British Journal of Anaesthesia. Reproduced by permission of Oxford University Press/British Journal of Anaesthesia.)

The disadvantages of mainstream sensors presented by some authors and manufacturers of side-stream systems are primarily technological in nature and often relate to prior generations of that technology. These disadvantages are often listed in older reviews [9,10] of the technology while more recent reviews note otherwise [11]. This includes possible damage during handling, increased mechanical deadspace, issues of additional weight on airway, and use limited to only intubated patients. For example, the mainstream IR benches have been in the past termed "vulnerable to costly damage." While earlier IR benches were vulnerable primarily due to the use of moving parts such as chopper or filter wheels (Figure 1), newer mainstream IR benches often utilize all solid state designs (Figure 2) that have been shown to be robust enough to survive repeated 6 foot drops onto hard floors and have been in use in high impact areas such as the emergency room, ambulances and transport for over 10 years.

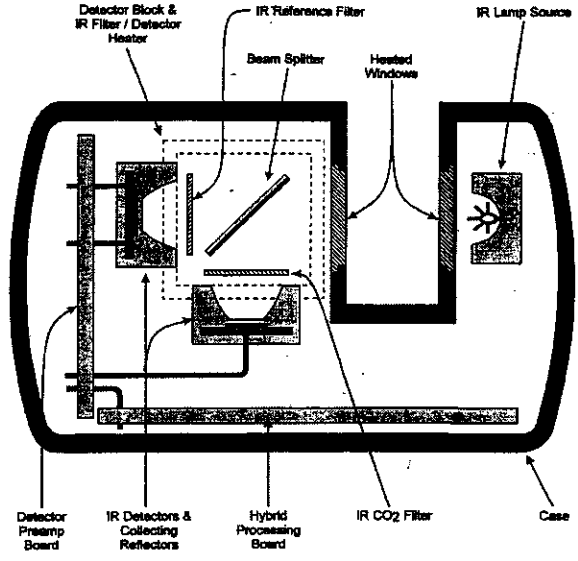

Figure 2. Cross-section of representative solid-state mainstream design (CAPNOSTAT®).

Additionally, claims of accidental extubation by mainstream devices have not been seen in practice. In fact, a recent search of the FDA's Center for Devices and Radiological Health online MAUDE[2] database found only one report relating to extubation and capnography which happened to be with a sidestream system [12].

[1] *The definitions as defined by the international standard "ISO 9918–Capnometers for Use with Humans-Requirements" shall be used.*

[2] *October 2001 search represents reports of adverse events involving medical devices and consists of voluntary reports since June, 1993, user facility reports since 1991, distributor reports since 1993, and manufacturer reports since August, 1996.*

Current generation mainstream devices, besides being relatively light, and low in deadspace have generally demonstrated better performance than sidestream system in terms of signal fidelity and end-tidal measurements particularly at higher respiratory rates in small children [13]. Careful airway adapter design and advances in technology have minimized the concerns for deadspace and weight for almost all patient populations and environments of use. Heated cuvette windows minimize effects from airway moisture. As with any airway adapter used for gas monitoring (either mainstream or sidestream), improper connection to other breathing circuit elements can cause artifacts in the capnogram. For example, a partial disconnection of a mainstream adapter may mimic a "curare-cleft" capnograph [14] but is easily recognizable.

For accurate end-tidal CO_2 monitoring, particularly with non-intubated patients receiving supplemental oxygen, sidestream sampling systems may not accurately reflect the capnogram because of the dilution effects of the supplemental flow of gases. Also, sidestream units do not adequately monitor both nasal and oral airflow. While mainstream devices may also be used on non-intubated patients, either as a sidestream sensor using an appropriate adapter or as a mainstream sensor with a facemask (Figure 3), the use of a low deadspace good sealing facemask combined with a mainstream airway adapter allows for superior CO_2 monitoring and volumetric capnography [15]. This is especially useful for field use (EMS) applications and during non-intubated conscious sedation.

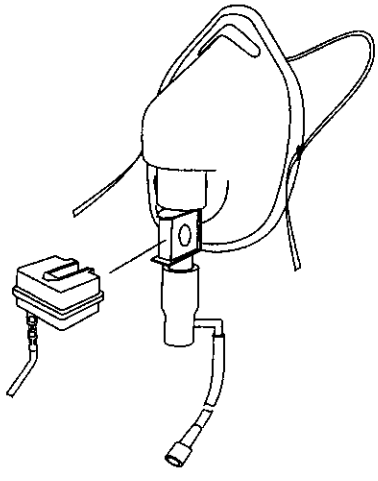

Figure 3. Face mask that allows mainstream capnography for use on non-intubated patients receiving supplemental oxygen (Respironics $CapnO_2$mask™)

Sidestream Capnography Overview

Sidestream gas analyzers utilize a long sampling plastic tube connected to an adapter in the breathing circuit (such as a T-piece at the endotracheal tube or mask connector) or a nasal catheter. The sample gas is continuously aspirated from the breathing circuit through the sampling tube and into the sample cell within the monitor (Figure 7(b)) at sample flow rates ranging from 50 to 250 ml/min (Table 2).

The location of the sampling port varies and may range anywhere from an elbow connected to an endotracheal tube to the wye connector. For example, it may be placed on the ventilator side of an in-line filter or HME. This results in a drier sampling tube with the inherent risk of significant distortion of the capnographic waveform and lower end-tidal values [16,17]. It may be also placed on the patient side of the filter resulting in possible accumulation of condensate and patient secretions in the sampling system. The sampling tube typically hangs free between the breathing circuit and monitor where it is vulnerable to being crushed, kinked and may be damaged during machine movement.

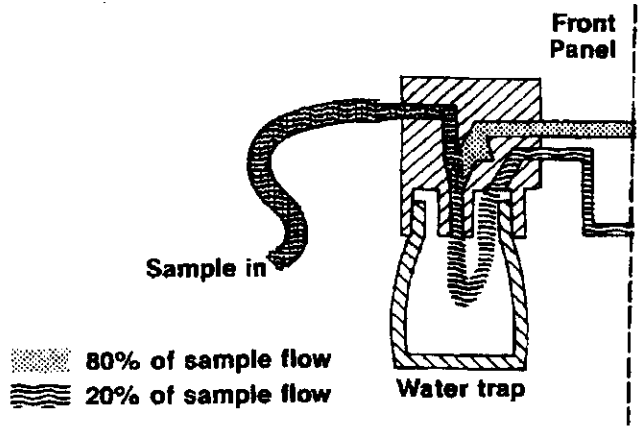

Figure 4. Illustrative Water trap of a capnometer. Sample gas is separated into two parts. The lighter portion (approx. 80%), which contains no particulate water, is drawn into the measuring chamber. Because the heavier portion (approx. 20%) takes longer to make the 180-degree turn, the particulate matter falls out (owing to inertia) into the water trap jar. (Adapted from Mogue LR et al. J Clin Monit. 1988; 4(2): 115-21. © Lippincott Williams & Wilkins, with permission)

The sampled gas that is withdrawn from the patient may contain anesthetic gases and as such should be routed back to a gas scavenging system or returned to the patient breathing system to avoid "pollution" of the operating room environment [18], costs associated with greater usage of anesthetic gases [19], and possible exposure risks in underventilated areas [20,21].

Condensation from humidified sample gas in combination with patient secretions can block and contaminate the sampling line requiring frequent replacement. To protect the sample cell from condensate, the distal end of the sampling tube is often connected to a water trap and water vapor permeable tubing such as Nafion® tubing. Water trap and filter design effectiveness vary between manufacturers but no water trap or filter is immune to eventual clogging and distortion of the capnogram particularly if preventive maintenance is inadequate. In one monitor, transposed sampling tube connections to water trap resulted in mixing of inspired and expired gases and a dramatic damping of the capnographic waveform [22]. To make matters worse, the distortion by some water traps may only be apparent under specific conditions, appear in either the inspiratory or expiratory phase and change as a function of respiratory rate [23] (Figure 5).

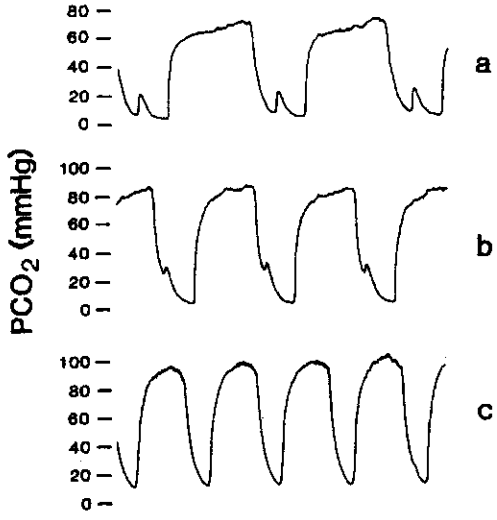

Figure 5. Distortion as a function of respiratory rate. Capnograms recorded experimentally with the endotracheal tube partially obstructed (A) 6 breaths/min, the CO_2 artifact appears during the inspiratory phase, (B) 8 breaths/min the artifact appears in the expiratory phase (C) 12/min, the artifact is disguised by the expiratory phase. (Adapted from Van Genderingen HR, et al. Capnogram artifact during high airway pressures caused by a water trap. Anesthesia & Analgesia. 1987; 66(2): 185-7. © Lippincott Williams & Wilkins, with permission)

Additionally, sources of leaks external to the monitor such as loose fittings [25], cracked or slit sampling tubes [26,27], cracked sample filters [28] and cracked airway adapters [29] along with sources of leaks internal to the monitor such as partial disconnection [30] (Figure 6) have been reported as causes of significant artifact in the capnogram. Leaks as well as obstructions can occur at any of the numerous connection points and tubes within the sidestream sampling system. The resulting distorted waveforms and the end-tidal values can be significantly different from actual, may not be detectable by normal calibration procedures [30] and pose a potential hazard to the patient. However, sidestream systems with an external removable sample cell are less susceptible to errors of this type. While more recent designs of airway adapters for sidestream systems reduce the likelihood of aspirating secretions by the use of sampling ports that are located in the center of the adapter rather than at the wall, they are still susceptible to the problems outlined above.

Figure 6 – Patient capnogram resulting from an internal gas analyzer leak, consisting of a long plateau phase followed by a brief peak. Plateau PCO_2 values correlated well with $PaCO_2$, whereas peak PCO_2 values were over 30 mmHg higher than $PaCO_2$. (From Healzer JM et al. Internal gas analyzer leak resulting in an abnormal capnogram and incorrect calibration. Anesthesia & Analgesia. 1995;81(1):202-3 © Lippincott Williams & Wilkins, with permission)

Even with no leaks or obstructions in the sampling system, significant distortion of the capnogram may still occur. At the sample tubing-airway interface, expired gas may be diluted with entrained ambient air whenever the gas flow rate falls below the "constant" sample flow rate [31]. The design of the sampling tube and its positioning within the breathing circuit or nares (if a nasal catheter is used) can affect the quantity of surrounding air that is entrained along with the expired gas. Within the sample tube itself dispersion may occur due to the effects of velocity profile and diffusion. [31] Additionally, the sample flow rate may vary significantly as a function of a number of factors including the sample tube length [32], airway pressure, and the presence of an exhaust line occlusion [33].

The use of sidestream monitoring requires that careful attention be paid both to the physical setup external and internal to the monitor, as well as careful interpretation of the capnographic waveform.

TECHNICAL ISSUES

Infrared Spectroscopy

Infrared absorption methods of gas measurement can be sensitive and selective as well as provide a continuous, accurate, precise, and rapid response that is not saturated nor damaged by high concentrations of the "target" gases. One target gas is carbon dioxide which has a very strong absorption band at 4.26 mm. Various approaches for infrared absorption measurement of CO_2 have been implemented (Table 2). The source of infrared radiation may be broadband or narrow band. It may be pulsed or constant (with a mechanical chopper). For narrow band emission, some sidestream monitors use an electric discharge source consisting of a hermetically sealed glass tube containing a gas. The gas is excited by the application of a high voltage, radio frequency electromagnetic field. This results in the emission of a narrow IR spectrum.

The detection of the infrared radiation typically uses a detector sensitive in the IR band such as lead selenide detector. Benches with broadband sources also utilize reliable and stable narrow band filters in front of the detectors to measure in band signal for CO_2 and separately out of band signal as a reference channel. Thus one can select only a portion of the CO_2 band effectively eliminating any interference from water vapor or even closer bands of N_2O. The absorption of the IR radiation by CO_2 is non-linear, affected by the presence of other gases and proportional to gas concentration, path length and absorption coefficient of the particular gas. The non-linearities, path length and specifics of the bench design are compensated for by an empirical lookup table that translates the measured signals to a value in CO_2 which is then corrected by most manufacturers for the effects of gases such as oxygen and nitrous oxide.

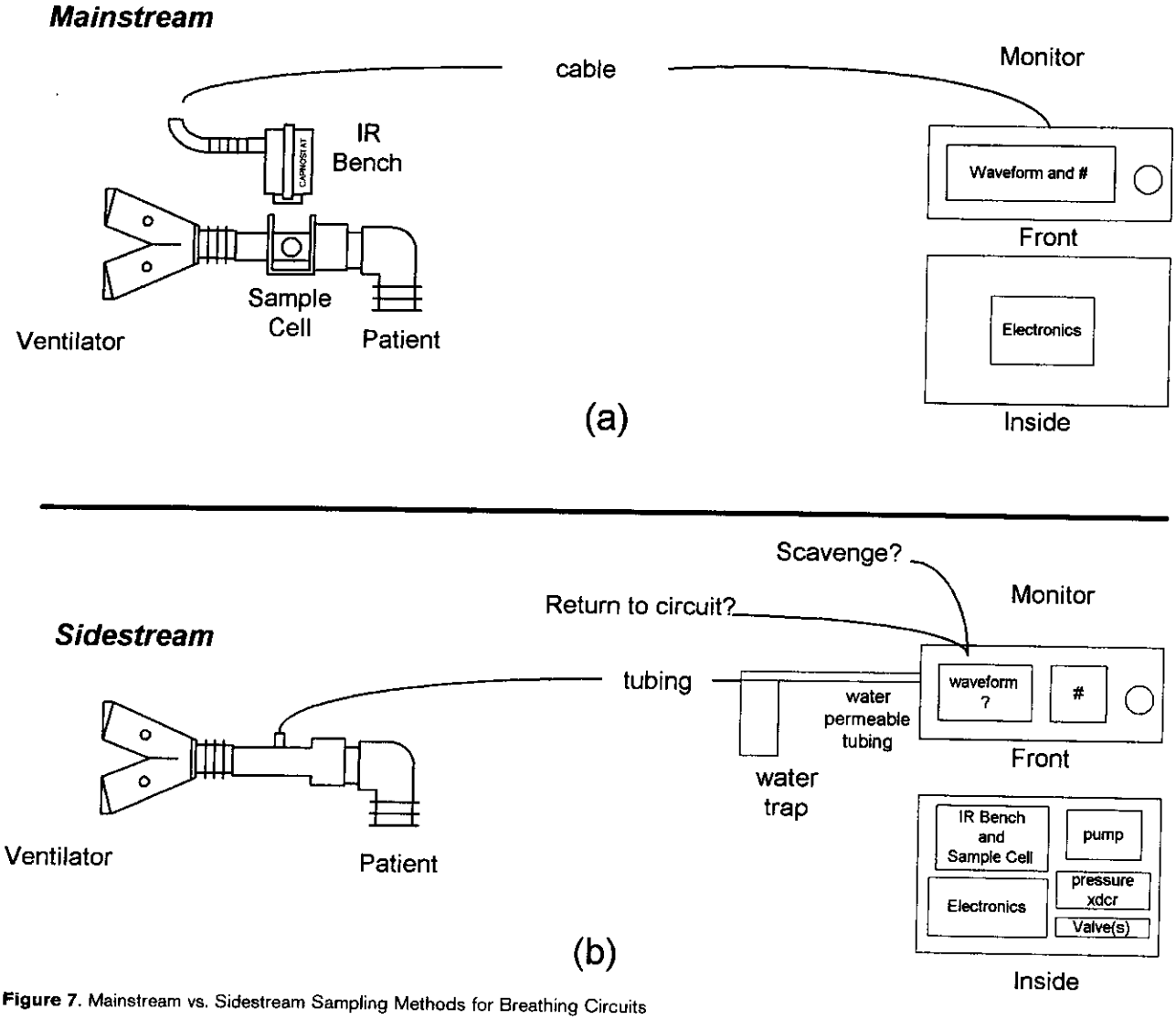

Figure 7. Mainstream vs. Sidestream Sampling Methods for Breathing Circuits

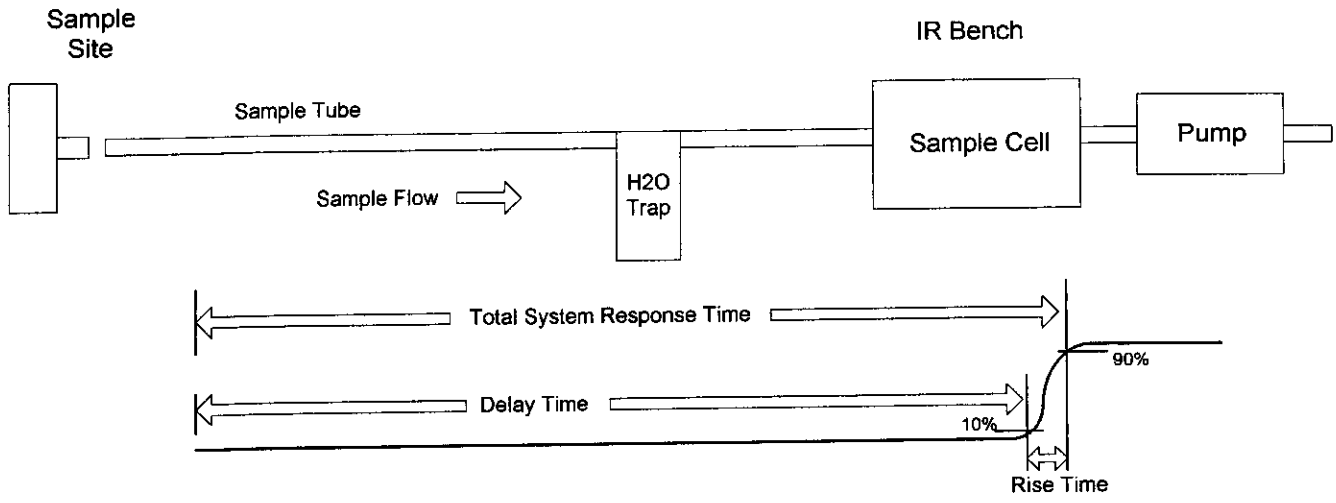

Figure 8 – Physical Components of a gas sampling system with total system response time, delay time and rise time illustrated. Mainstream systems do not suffer from the depicted delay time.

Interference Effects

The measured absorption of CO_2 can be altered by cross-interference and collision broadening due to the presence of gases such as nitrogen, nitrous oxide and oxygen. Cross-interference, the overlapping of absorption bands of other gases, can occur from nitrous oxide due to the presence of strong absorption bands that slightly overlap both edges of the carbon dioxide band (Figure 9). The impact of this effect can vary significantly between devices [34]. However, the use of narrow band sources or narrow band filters in front of the detector with sufficiently small half power bandwidths can effectively eliminate the effect of cross-interference.

On the other hand, collision broadening tends to be less device-specific [34] and is a complex function of the total pressure and the presence of other gases. Carbon dioxide displayed as a partial pressure constituent in a gas mixture and changes in atmospheric pressure and circuit pressure will alter this relationship. Pressure influences the width of the IR absorption band. As pressure decreases (either due to changes in total pressure or the partial pressure of CO_2), less intermolecular collisions occur and the bandwidth narrows. Similarly, as the pressure increases, more collisions occur and the bandwidth increases. [36] In effect, the absorption band is spread out and the use of narrow band sources or filters fail to correct for this effect. This effect is typically compensated for in the system's software using nominal values.

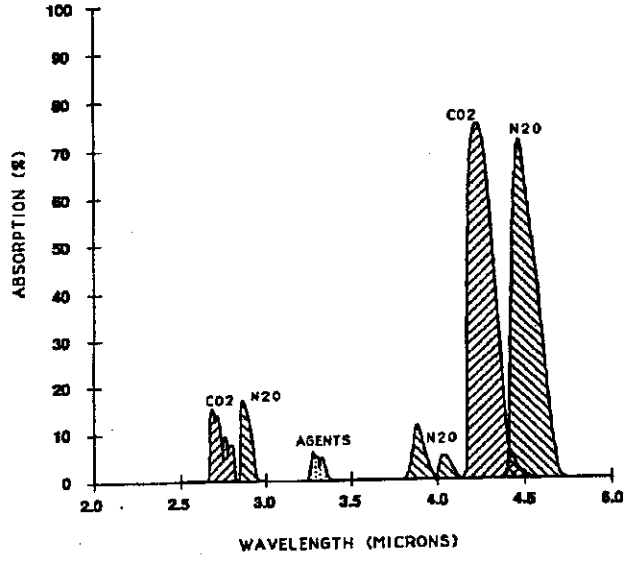

Figure 9. The infrared absorption spectrum for the gases carbon dioxide (CO_2) and nitrous oxide (N_2O) and the volatile anesthetic agents. (From Raemer DB. Accuracy of end-tidal carbon dioxide tension analyzers. J Clin Monit. 1991; 7(2): 195-208. © Lippincott Williams & Wilkins, with permission)

Water Vapor

Mainstream infrared analyzers, when located near the patient connection, measure gas near Body Temperature and Pressure, Saturated conditions (BTPS). Water vapor effects can cause cross-interference (absorption band overlap) and collision broadening but the band at 4.26 microns is relatively free from

any water vapor absorption effects and shows minimal collision broadening effects. Partial pressure dilution effects, on the other hand, are of concern. This has been effectively minimized in mainstream systems by heating the airway adapter and its windows above body temperature or by using coatings. How close the exact water vapor pressure is to BTPS conditions depends on factors including the presence and type of humidification, fresh gas flow, length of time in use and ambient temperature [35]. Normally, exhaled gas is fully saturated at or slightly less than 37°C. This results in a water vapor pressure of 47 mmHg.

In side-stream systems the temperature of the sampled gases decreases toward room temperature during its transit from the patient connection to the monitor. [37] This results in condensate forming on the walls of the tubing and a resulting decrease in the partial pressure of water vapor from the BTPS value of 47 mm Hg to much lower values. With the inclusion of water permeable tubing, such as Nafion® brand tubing, the water vapor pressure in the tubing will tend to equilibrate with the water vapor pressure in the room.[3] This decrease in water vapor pressure can cause an apparent increase in CO_2 concentration [38]. Sidestream devices compensate with software for water vapor removed and as a result may introduce errors since assumed conditions may be very different from actual, and physical conditions may change over time. Mainstream capnometers will correctly read the partial pressure of CO_2 at the conditions in the breathing circuit typically at or near BTPS and do not require software compensation for water vapor.

Contamination Issues

Condensed water or water-like mixtures have other very serious effects such as obstruction of the sampling line or airway adapter. If droplets appear within the cuvette optical path, severe scattering and absorption can occur. However, true single beam ratiometric optical systems (i.e., the CAPNOSTAT) can successfully compensate for the contamination if scattering/absorption effects are not spectrum dependent. Dust particles and optically opaque particles do not appreciably affect system precision.

Contaminants may partially obstruct the sampling tubes of side-stream capnometers and increase resistance to flow in these tubes thus affecting the response time and accuracy of the CO_2 measurement. In more severe cases, the sampling tube may be occluded. Some monitors compensate by either increasing the sampling flow or attempting to purge the sample tubes when an increased pressure drop is sensed across a flow restriction. In spite of the presence of water traps and water permeable tubing, liquids may be aspirated into the monitor's internal components. This can result in degradation of the monitor's performance as seen by distorted waveforms and deterioration over-time of these internal components. This degradation of performance would require monitor checks to be performed. This may not be possible in an "expeditious" manner due to the responsibilities of the anesthesiologist during a surgical procedure or the critical care physician in the intensive care unit and may lead to the discounting or disregarding of the capnograhic values.

Clinical Implications

Mainstream and sidestream capnography has been reviewed and contrasted. The limitations of the technologies and design choices and their performance in the different clinical environments and patient populations that they may be used on must be considered. Their value as a "front-line" monitor is well established [39]. A detailed study of adverse events found that capnography was critical for the detection of general anesthesia incidents. The study also reported failures of capnography to detect problems when it should have and it was noted that about a third of these failures were due to problems with sidestream gas sampling and a third due to the improper setting of alarms. Also, the importance of capnography during clinical events such as cardiac or respiratory arrest cannot be underestimated. In fact "of all monitors currently in use during cardiac arrest, capnography furnishes the best real-time, continuous information regarding the effectiveness of resuscitative efforts." [8,40] Therefore, it is of critical importance that the capnography technology used be robust, artifact free and accurately reflect what is being monitored.

Use in Neonatal Patients – Generally, sidestream capnographs may not be accurate in neonatal and pediatric patients because they aspirate a significant portion of the patient's total ventilation [41]. For example, a neonate with a ventilation of 250 ml/min (tidal volume of 5 and rate of 50 b/min) and a sidestream sampling rate of 50 ml/min is losing 20% of his ventilation to the sidestream sampling system. With a ventilation of 50 ml/min (1 ml and 50 b/min) the consequences can be

[3] *Note that the driving force here is the water vapor pressure gradient, not the total pressure. Thus, the only issue is whether it is wetter inside or outside. (From Perma Pure® website).*

quite severe. Older sidestream designs used sample rates as high as 250 ml/min but newer designs have reduced the flow rate, the diameter of the sampling tube and sample cell. This tradeoff decreases the ventilation levels that can be monitored while at the same time potentially increasing the possibility of occlusion.

Use of Water Traps – The use of water traps, particularly in intensive care, can easily lead in some designs to partial failure or blockage of the trap causing dramatic changes in waveforms and end-tidal values. This is particularly significant in systems that do not show the capnogram.

End-tidal CO_2 – The specifics of each manufacturer's algorithm for end-tidal measurements such as averaging windows, breath-to-breath averaging and its definition of end-tidal values must be considered when interpreting data. This is particularly important if no waveform is displayed. Unfortunately, whether the reported end-tidal value is the partial pressure of CO_2 at the end of expiration or the largest value during the "expiratory" period defined by the capnogram (which can be elongated by rebreathing) or something entirely different depends upon the manufacturer, and often is not disclosed.

Extubation – Historically, the primary concerns of mainstream based systems are related to size and weight. However, the reduction in both size and weight have alleviated these concerns to the point that with proper attention to the breathing circuit, the risks of extubation are minimal. In fact there are no reports of an extubation attributable to the use of a mainstream sensor [12]. Endotracheal tube position is commonly verified by observing expired CO_2 during a series of manual short breaths. It has been noted that the long transport delays often associated with side-stream sampling may result in an excessive delay in observing the presence of expired CO_2 and possible false diagnosis of esophageal intubation [42].

Burns – Since the windows of the mainstream sample cell are heated to slightly above body temperature, burn issues have been raised by some authors. The temperature during normal operation of a heated mainstream sensor will not reach a temperature high enough to cause even redness of the skin. Proper attention to fail-safe design that limits the amount of power delivered have all but eliminated this concern.

Nonintubated subjects – Issues relating to nonintubated subjects have also been raised. The dual use of some mainstream devices and their interfacing to facemasks allow their use in an even broader array of patients and clinical conditions than sidestream systems.

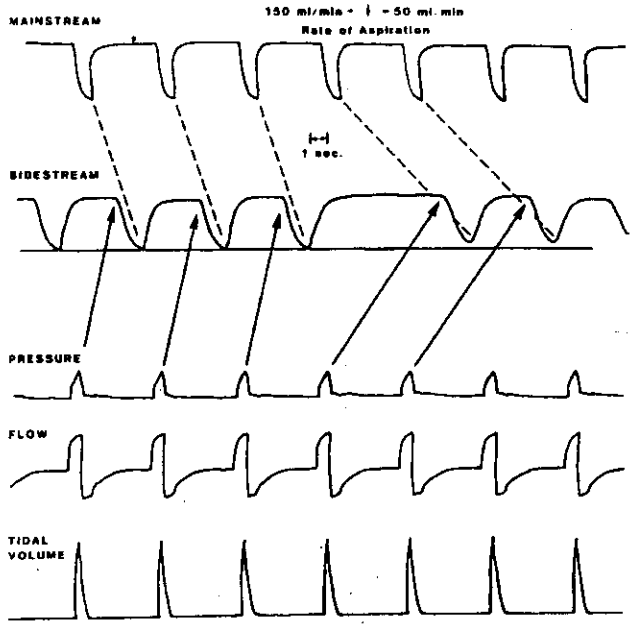

Figure 10. Relationship between capnogram (both mainstream and sidestream) and other "pneumatic" parameters of pressure and flow. Note the time delay and dampening effects from reducing the sample flow rate in the sidestream system (from [43])

Artifacts – Artifacts in sidestream CO_2 waveforms can take on many forms. For example, excessive dampening of the response (Figure 10) can occur. In some circumstances the artifact may resemble physiologic changes which may be characteristic of diseases such as some forms of restrictive or obstructive lung disease. [13] For example, a falsely low value for end-tidal CO_2 may lead the clinician to believe that alveolar ventilation is adequate when, in fact, it is not. [13] It is also noted that "the inability of the capnogram to return to zero baseline on inspiration, a common artifact of sidestream recordings, may suggest rebreathing of CO_2 and prompt unnecessary changes in fresh gas flow or modifications to the patient circuit." [13]

Volumetric Capnography and Beyond

Coupling mainstream capnography with mainstream flow and pressure measurement provides the capability of measuring anatomic and physiologic deadspace ratios, CO_2 elimination, pulmonary capillary blood flow and a whole range of physiologic indices that allow insight into many cardiopulmonary disorders including adult (acute) respiratory distress syndrome, chronic obstructive pulmonary disease, asthma, and pulmonary embolism.

Conclusions

The shape and trends of the CO_2 waveforms contain valuable information that is not available from any other source. Omitting the CO_2 waveform is like omitting the ECG and arterial waveforms or worse. Subtle changes in waveforms can reflect actual or impending problems with endotracheal tubes, ventilators, circuit valve, soda lime absorbers, airway mechanics, respiratory drive, cardiovascular systems, level of neuromuscular blockade, and other important conditions. It is important that the waveform faithfully reflect what's occurring at the airway. [44]

Mainstream capnography reliably reflects what is occurring at the airway and has proven itself as a robust and widely applicable monitoring method for the present and future.

Table 1. Comparison of Mainstream and Sidestream Carbon Dioxide Analyzers

Features	*Mainstream*	*Sidestream*
Airway Connections		
Location of infrared analysis unit ("bench"/sensor)	At the airway connector	In the monitor
Size of airway connector	Small	Small
Weight of airway connection	Airway adapter light; additional weight associated with sensor	Airway adapter light; additional weight associated with tubing
Location of airway connector	End of endotracheal tube (typically)	End of endotracheal tube (may replace "angle" connector)
Use on extubated patients	Yes with a facemask or mouthpiece. Some monitors use a special airway adapter and contain a pump to convert to sidestream mode	Yes with nasal adapter or oxygen prongs
Connecting tube or cable	Thin, medium weight flexible cable No sample tube	Small bore sample tube
Required components to "sample" gas	Airway adapter and sensor	Airway adapter, sample tube, filters, water trap (optional), water permeable tubing
Airway connector disposable or reusable	Sensor reusable; airway adapters are reusable or disposable	Airway adapters are reusable or disposable
Durability of airway connector	Durable	Varies
Cost of replacing airway connector	Sensor expensive to replace; Airway adapter inexpensive	Airway adapter inexpensive but on very wet patients may require hourly change, contamination of analyzer and pneumatic system may be costly to replace unless using system with removable sample cell
Can be used in collaboration with simultaneous oxygen administration	Yes with facemask. Accurately captures both oral and nasal gases. Mouthpiece or where available Sidestream mode with nasal cannula	Yes with nasal prong. Probable dilution of sample with supplemental O_2 present
Easy to use when patient is in unusual positions such as in prone position	Yes	Yes
Sample volume drawn	None	Less than 250 ml/min (sampled gas may be returned to circuit)
Deadspace added to airway connector	Low (< 1 ml in neonates)	Low

Table 1 continued. Comparison of Mainstream and Sidestream Carbon Dioxide Analyzers

Features	*Mainstream*	*Sidestream*
Warm-up		
Warm-up time	Varies	Varies
User tasks during warm-up	Zero and calibration may be required by some devices	Zero and calibration may be required by some devices
Zeroing and Calibration		
Zeroing	Manual–user can mount sensor on zero cell or adapter and wait for stabilization (< 20 sec)	Automatic–requires internal valving and sometimes external gas tanks
Accuracy of zeroing	Accurate–may use separate ref cell or airway adapter	Accurate–uses sample tubing and adapter that will be used during monitoring
Zeroing during use	Manual only, user must mount sensor on zero cell or adapter and wait for stabilization (< 20 sec)	Automatic at preset intervals or manual
Calibration (span)	Routinely not required.	Routinely not required
Calibration to reference gas cylinder	Not frequently required. User attaches sensor to reference cell	Calibration is normally required once every 1–6 months
Response and Signal Fidelity		
Delay between sampling and waveform display	None	Less than 3 seconds
Sensor 10-90% rise time	Typically < 70 millisecs	Typically > 200 millisecs
Waveform display	Crisp. No deformity of capnogram due to non-dispersion of gases	Smooth appearance because it is filtered by the sample line artifact and slower response time
Accuracy of waveform shape	Excellent No affect due to variable pressure drop	Variable–depends upon factors including sample rate, mixing, and sample cell design
Numeric display	Breath to breath or averaged end-tidal and breathing frequency.	Breath to breath or averaged end-tidal and breathing frequency.
Moisture and Contaminations		
Changes in water vapor pressure	Not affected	Affected due to condensation and drying of sample

Table 1 continued. Comparison of Mainstream and Sidestream Carbon Dioxide Analyzers

Features	*Mainstream*	*Sidestream*
Moisture and Contaminations, contined		
Moisture handling	Sensor at airway adapter contains a heater or other means to prevent condensation, water droplets may condense on window but usually clear rapidly	Water trap–modern water traps can be extremely efficient but may clog (some use Nafion® tubing which equilibrates with ambient humidity)
Potential of cross-contamination between patients	None–Disposable or reusable airway adapter can be sterilized and then reused at no risk of contamination.	Varies–airway adapter and sample tubes can be disposed at low cost or sterilized and reused at no risk of contamination provided no purging or return of gas to patient breathing circuit
Zeroing and Calibration		
Gas scavenging	Not required	Gas outlet on monitor can be scavenged or permanently installed to return sampled gas to a connector at expiratory valve on circle system; potential "pollution" risk with anesthetic agents
Use in true closed circuit anesthesia	Yes	Yes, provided sampled gas returned to circuit
Compensation		
Compensation for nitrous oxide concentration	Manual or automatic	Manual or automatic
Compensation for oxygen concentrations	Manual or automatic	Manual or automatic
Barometric pressure compensation	Yes.	Yes.
Airway pressure compensation	Not required.	Pressure fluctuations due to sampling system (i.e, pump variations) may be compensated with measurement of pressure
Numeric display	Breath to breath or averaged end-tidal and breathing frequency	Breath to breath or averaged end-tidal and breathing frequency
Neonatal Use		
Suitable for Neonatal use	Yes. Low deadspace neonatal airway adapters available	Varies
Monitor		
Size and weight of monitor	Medium to small. Bedside and handheld	Medium. Bedside and handheld
Battery-operated monitor available	Yes	Yes

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Table 2. Specifications of Selected Mainstrean and Sidestream IR Capnometers

	Mainstream		***Sidestream***		
	Agilent	**Respironics**	**Datex-Ohmeda**	**Oridion**	**SIMS BCI**
Model	M1016A	CO_2SMO Plus!®	Capnomac Ultima™	VitalCap™	CapnoCheck® Plus
Source	Steady state source with chopper wheel	Pulsed source solid state	–	Pulsed source electric discharge	Pulsed source with narrow band filter at source
Sampling Flow ml/min ±%	n/a**	n/a**	200 ± 20 ±10%	50 ±7.5 ±15%	120±20 ±17%
Sample Rate (Hz)	–	87	–	40	–
Interference Comp.					
N_2O	Yes****	Yes ***	Yes	Included in CO_2 accuracy specs	Yes with nominal value
O_2	Yes****	Yes***	Yes	–	–
Calibration method	Reference Cells	Zero Cell or use adapter (< 20 sec)	Every 6 months	Self Cal, Check 1x yr	Manual 2 point
Response time (ms)	< 125	< 60	–	2450 typ; 2900 max	–
Delay time (ms)	Negligible	Negligible	–	Approx 2000 190 neo	–
Rise time (ms) (10%–90%) *	< 125	< 60	< 360	250 adult	375 0 to 90%
Purging mode	n/a	n/a	Pulls water and mucous to trap	Monitor clears if circuit blocked	–
Liquid trap/filter	n/a	n/a	Gas-permeable and liquid impermeable filter	Water vapor-permeable tubing, water trap and hydro-phobic filters	Water trap/filter

(Data excerpted from Product Comparison Table–Outpatient Care Technology August/September 2001, product literature and manuals from the individual manufacturers or its OEMs and other publications)

Notes:

n/a = not applicable

Dash shown if data was not available to author.

* Unless otherwise noted rise time is the time required to achieve a rise from 10% to 90% of the final CO_2 value in the capnometer when a step function change in CO_2 concentration or partial pressure occurs at the sample site. (ISO 9919)

** Mainstream devices listed can operate in sidestream mode using mainstream sensor with sidestream adapter/module.

*** User selectable values

**** Nominal value assumed unless actual values available.

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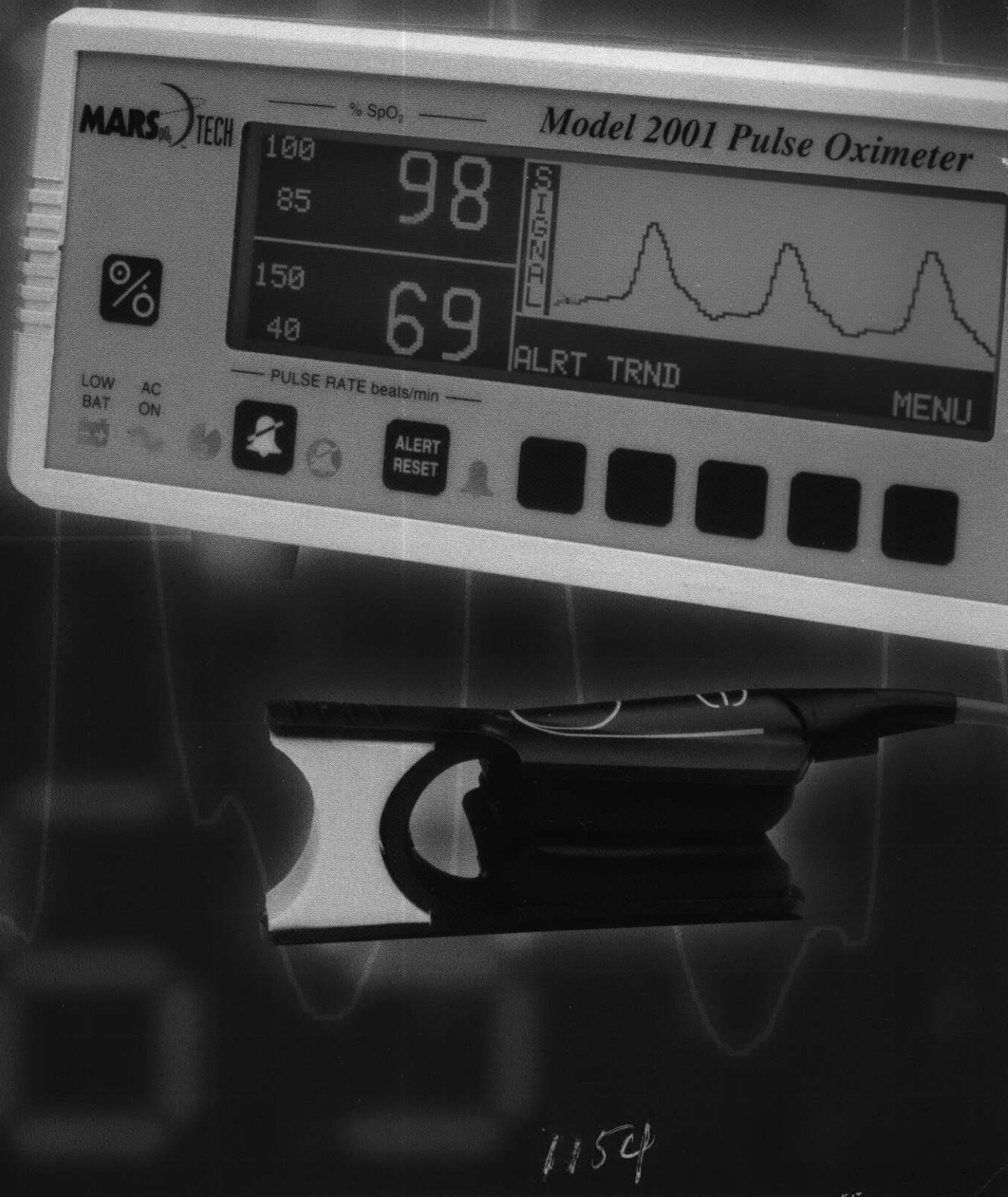
MONITOR TECHNOLOGY

Pulse oximeter technology:
an evolution to the most reliable system on the market today.



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NOVAMETRIX
MEDICAL SYSTEMS INC.

Novametrix recognizes the importance of providing full-featured pulse oximetry to accommodate the wide variety of clinical requirements of hospitals. To best serve clinicians, Novametrix has designed its pulse oximetry products according to its four-point philosophy since its entry into the pulse oximeter marketplace in 1985. This philosophy holds that every pulse oximeter monitor should: (1) never give an incorrect SpO_2 reading; (2) function continuously even in the presence of motion or poor quality signals; (3) alert the clinician with meaningful messages; and (4) allow staff to configure the monitor to the appropriate clinical environment.

Meeting the challenge to provide reliable clinical data

Patient care is partially dependent upon information from many sources, including monitoring systems, such as a pulse oximeter. Signal disrupting artifacts such as motion, low perfusion and arrhythmias have been a technical obstacle in the development of accurate, reliable patient monitoring technology.

First generation pulse oximetry technology relied on analog circuitry and slow microprocessors. These monitors had extremely low-resolution front ends and could not "view" the entire signal thus isolated segments were separated and analyzed. This technique was prone to errors and resulted in less than adequate pulse oximeter performance.

Novametrix Pulse Oximetry Milestones	
1985	Entered pulse oximetry market.
1987	Super-Bright™ Sensor Technology.
1990	World's first digital pulse oximeter.
1992	2nd generation, Improved signal range, IABP.
1993	Venus U.S. Patent (digital oximeter) #5,190,038.
1995	Venus U.S. Patent (digital oximeter) #5,398,680.
1998	Venus U.S. Patent (digital oximeter) #5,820,550.
1999	$MARSpO_2$™ (Motion Artifact Rejection System)*

* Patent Pending

The New World of "digital" oximetry

In 1990, as a response to the limitations of first generation oximetry technology, Novametrix introduced a new signal processing technique known as "Digital" oximetry. This sweeping innovation improved pulse oximetry by using a high-resolution "digital" front end enabling the monitor to continually process the entire signal, instead of isolated segments. When signal artifacts are detected, they are compared to "stored data" which allows the system to determine the confidence level of the data. In essence, digital oximetry improved the overall performance of pulse oximeters. However, in certain clinical environments, particularly where motion or low perfusion was present and due to limitations in processing power, challenges to the system to clearly identify a signal still occurred.

Making the best even better

With the advent of more powerful Digital Signal Processors (DSP), pulse oximetry technology is now capable of removing a wide variety of signal artifacts, allowing the correct calculation of saturation and pulse rate, even in the presence of high levels of motion or low perfusion. Novametrix' remarkable new Motion Artifact Rejection System (MARS) represents the evolution of this reliable digital technology foundation. By combining Novametrix' existing high-resolution front end with a more powerful microprocessor, MARS achieves a higher level of performance in those challenging clinical environments such as the NICU and PICU.

$MARSpO_2$ Technology - the next generation in pulse oximetry

Recently introduced motion artifact rejection monitors have featured several different methods to reduce the effect of artifacts, which may be related to patient motion or low perfusion. These methods include:

1. filter based modeling which adapt filter coefficients based upon the estimated noise levels
2. adaptive noise cancellation which is a technique for removing noise from a signal IF the "noise" signal or a signal closely related to it can be independently sampled or generated.

MARS reduces the effect of artifact by combining our existing high-resolution digital signal processing platform with the new five step MARS algorithm. This algorithm includes frequency and spectral peak analysis to select peak frequency candidates, time domain filtering to

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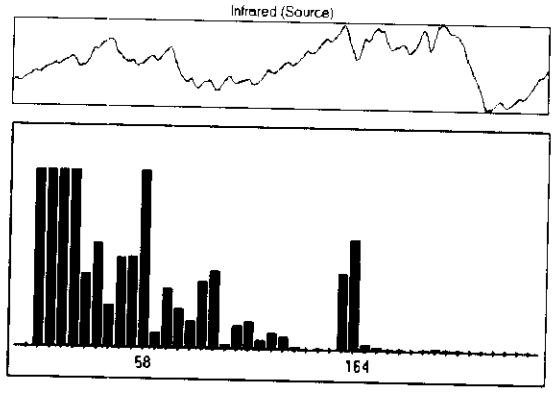

Figure 3 -Power spectrum of IR signal with several interfering frequency components.

As transient or periodic artifacts such as motion are increasingly introduced into the signal the characteristics of the power spectrum become more complicated (Figure 3). In fact, the interfering peaks may be significantly larger in amplitude than the pulse rate associated peaks. The spectral peak analysis identifies spectral peaks that may or may not be the pulse rate (i.e. candidate peaks) using search methods and shape analysis. Additional descriptive criteria are then applied to choose the most likely candidates.

Step 3 - Time Domain Filtering

Once the candidate peaks have been selected, narrow band filters centered on the pulse rate of the candidate peak are applied to the raw time domain signal to accentuate the frequency components at or near the pulse rate. This process of filtering improves the signal-to-noise ratio, and allows the calculation of saturation using a 'cleaner' signal.

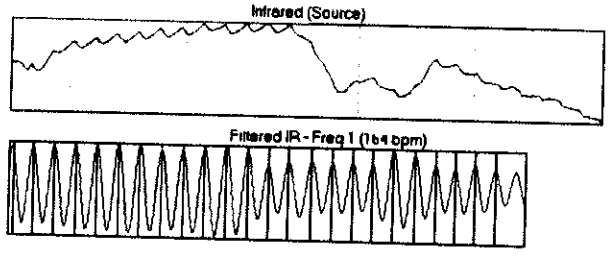

Figure 4 - Raw Infrared Signal from a infant with significant low frequency artifact and resulting filtered infrared signal with delineation of pulse peaks.

Step 4 - Pulse Window Analysis

For each filtered time window the peaks and other time points are determined which allows for the calculation of parameters such as pulse rate, SpO_2, pulse width and amplitude for each pulse. Additional parameters representing the confidence for each of the power spectrum peak candidates are then calculated using this data and from the filtered time window data. These measures relate to a number of factors including the variability of descriptive parameters such as pulse width, pulse rate, amplitude, and SpO_2. Additionally, a pulse window may be rejected as a possible valid pulse window if it meets any of the global rejection criteria. For example, if the number of peaks in the pulse window is two or less, then the given pulse window cannot be selected as a pulse candidate.

Step 5 - Arbitration

These pulse window measures, in conjunction with a decision tree, are used to determine which filtered 'window' (i.e. candidate peak) should be accepted as the most appropriate for calculation of pulse rate and SpO_2.

Summary

In summary, the MARS technology incorporated into Novametrix pulse oximeters provides the next evolutionary step in pulse oximetry signal processing. At Novametrix, our mission is to assist hospitals in providing the ultimate standard of clinical care. Don't your patients deserve the best?

Novametrix
Medical Systems Inc.
5 Technology Drive,
Wallingford, CT 06492
(800) 243-3444
(203) 265-7701
www.novametrix.com

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remove noise from the candidates, pulse window analysis to analyze selected filtered candidates and finally an arbitration method used to determine which candidate is selected.

How it Works

The "front-end" of all Novametrix pulse oximeters consist of signal conditioning and data acquisition of the raw non-scaled 20-bit red and IR signals at a sampling rate of 100 Hz. The MARSpO_2 algorithm uses a moving window of approximately 10 seconds of raw data (Figure 1) which is analyzed every 1/2 second to calculate a value for SpO_2 and pulse rate.

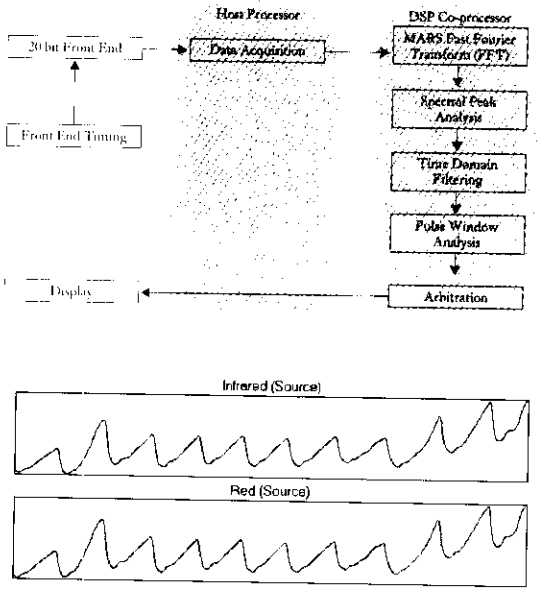


Figure 1 - Raw red and IR input signals

Frequency analysis determines a set of possible pulse rates which coupled with selective filtering of the raw signals reduces the effects of artifact. A set of saturation values based upon the processed red and IR segment of data can then be computed. The results of this processing is input to an arbitrator which selects the correct pulse rate and saturation value to display.

The MARSpO_2 algorithm, which is the implementation of this approach, can be outlined as consisting of five basic steps. The steps are:

1. Frequency domain transformation
2. Spectral Peak Analysis
3. Time Domain Filtering
4. Pulse Window Analysis
5. Arbitration

Step 1 - Frequency Domain Transformation

To transform the IR signal from the time to the frequency domain, computationally efficient algorithms such as the Fast Fourier Transform (FFT) are utilized. However, prior to transformation into the frequency domain, standard pre-processing of the signals is required such as windowing to minimize frequency artifacts due to spectral leakage. Figure 2 illustrates the power spectra of a windowed infrared signal with a low level of artifact.

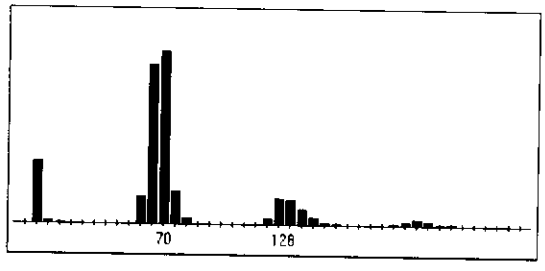


Figure 2 -Power Spectrum of IR signal with primary frequency peak at 70 bpm and a secondary frequency peak at 128 bpm.

Step 2 - Spectral Peak Analysis

Upon transformation to the frequency domain, the power at each frequency component is analyzed relative to the other components as well as to the absolute frequencies. For example, components greater or less than physiological maximum or minimum pulse rates can be attributed to artifact and are not analyzed.

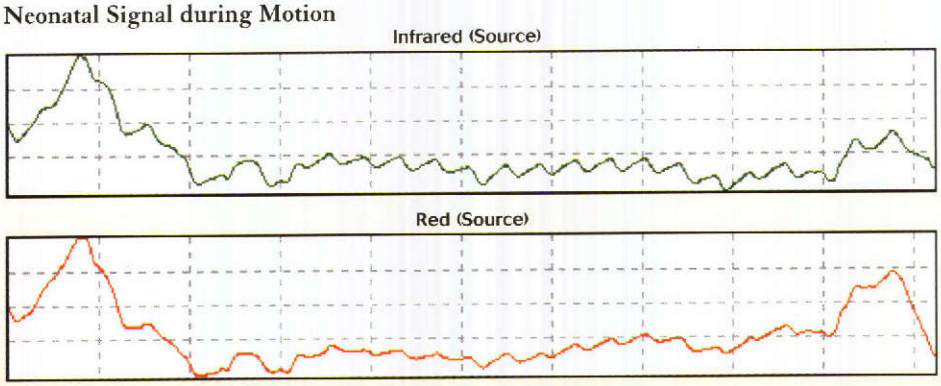
MARSpO_2 TECH

The MARSpO_2 algorithm takes advantage of the tendency of the pulse rate to be a rhythmic signal whereas imposed artifacts are usually not correlated with the patient's pulse rate. Given this tendency, the power spectrum of an epoch of data will often contain a power spectral peak at the pulse frequency and additional power spectral peaks representing artifacts. If the pulse rate is relatively constant over the ten second analysis window, the power spectral peak representing the pulse rate will dominate, and the peak relating to the artifacts will be less since its spectrum tends to fluctuate more over time.

Putting it All Together

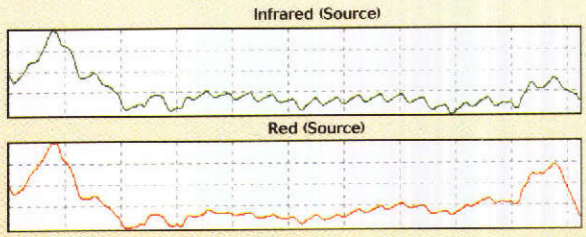
The following is an example which illustrates the steps of the MARSSpO_2 algorithm using a signal obtained from a moving neonatal patient.

Neonatal Signal during Motion

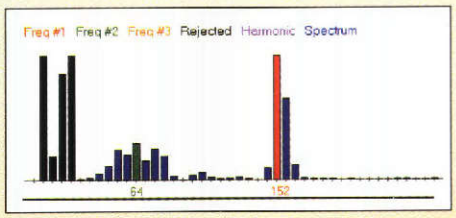


Step 1 - Frequency Domain Transformation

The most likely pulse rate candidate are identified from a 10 second window of data. The MARS algorithm will plot the frequencies of the infrared signal in a graph called Fast Fourier Transform.



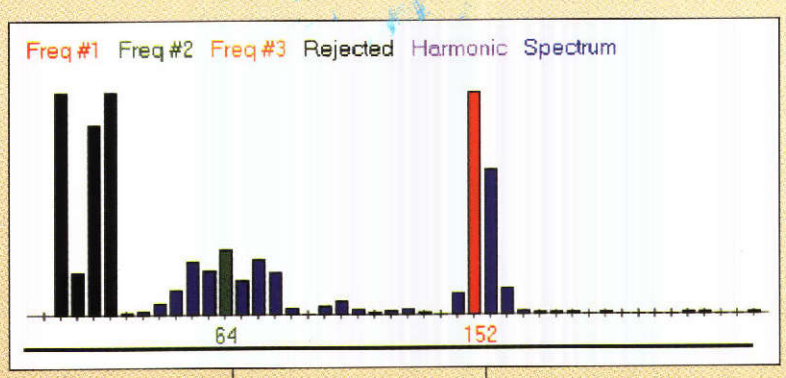
10 seconds of data is acquired by the monitor.



The frequencies of the IR signal are plotted to select real pulse rate "candidates."

Step 2 - Spectral Peak Analysis

After the frequencies are plotted, MARS uses spectral peak and shape analysis to determine the optimal pulse rate "candidates." Normal pulse signals (unaffected by motion) will have only one narrow frequency peak. However, during periods of motion, MARS may select up to three likely candidates to analyze.



Candidate A
Pulse Rate Frequency=64

Candidate B
Pulse Rate Frequency=152

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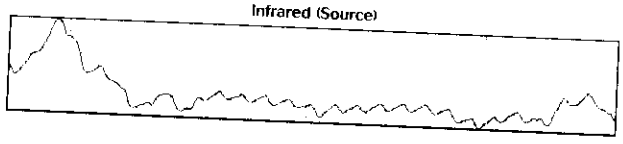
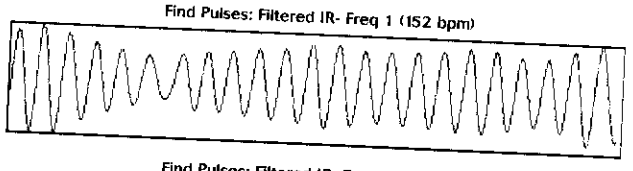
Step 3 - Time Domain Filtering

The selected "candidate" infrared signals are then filtered at a rate equivalent to each of their respective frequencies. By filtering the raw signal at its frequency the noise is removed from the signal leaving the actual pulse signals.

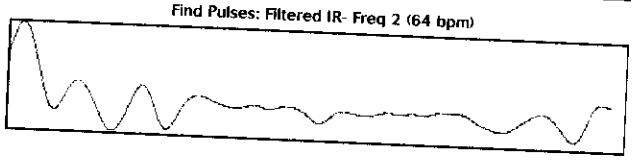
Original Raw Infrared Signal



Selected pulse candidates after filtering is applied



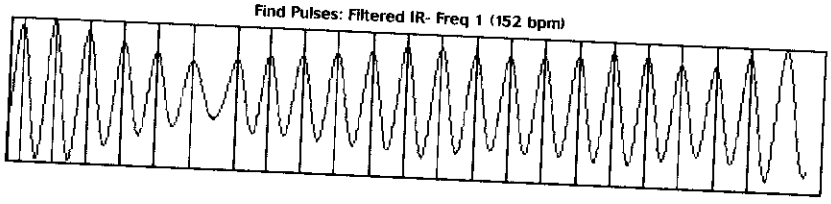
Candidate B
Pulse Rate Frequency=152



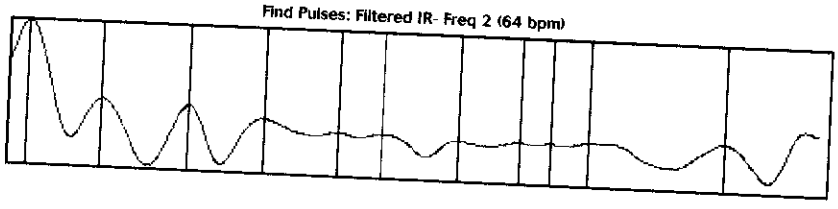
Candidate A
Pulse Rate Frequency=64

Step 4 - Pulse Window Analysis

The peaks are detected and SpO_2, pulse rate, pulse width and amplitude values for each filtered candidates are then calculated and analyzed. The vertical lines represent the peaks of possible pulses.



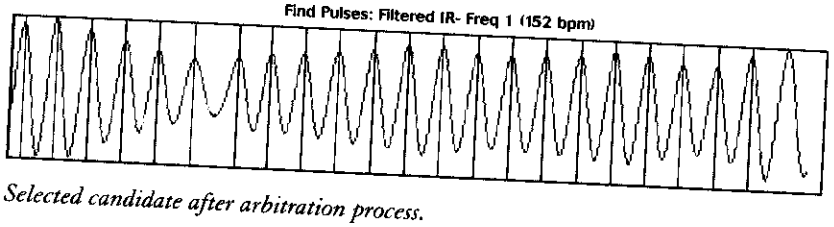
Candidate B
Pulse Rate Frequency=152
SpO_2=98%



Candidate A
Pulse Rate Frequency=64
SpO_2=90%

Step 5 - Arbitration

The parameters calculated during the pulse window analysis are then passed on to an arbitrator which determines a confidence factor for each candidate. The data from the selected candidate is then displayed on the monitor.



Candidate B
Pulse Rate Frequency=152
SpO_2=98%

Selected candidate after arbitration process.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Memorandum

From: Reviewer(s) - Name(s) Lisa Harris

Subject: 510(k) Number K030886/S1

To: The Record - It is my recommendation that the subject 510(k) Notification:

☐ Refused to accept.
☐ Requires additional information (other than refuse to accept).
☑ Is substantially equivalent to marketed devices.
☐ NOT substantially equivalent to marketed devices.
☐ Other (e.g., exempt by regulation, not a device, duplicate, etc.)

Is this device subject to Section 522 Postmarket Surveillance?	☐ YES	☑ NO
Is this device subject to the Tracking Regulation?	☐ YES	☑ NO
Was clinical data necessary to support the review of this 510(k)?	☐ YES	☑ NO
Is this a prescription device?	☑ YES	☐ NO
Was this 510(k) reviewed by a Third Party?	☐ YES	☑ NO
Special 510(k)?	☐ YES	☑ NO
Abbreviated 510(k)? Please fill out form on H Drive 510k/boilers	☐ YES	☑ NO

Truthful and Accurate Statement ☐ Requested ☑ Enclosed
☑ A 510(k) summary OR ☐ A 510(k) statement
☐ The required certification and summary for class III devices N/A
☑ The indication for use form

Combination Product Category (Please see algorithm on H drive 510k/Boilers) N

Animal Tissue Source ☐ YES ☑ NO Material of Biological Origin ☐ YES ☑

The submitter requests under 21 CFR 807.95 (doesn't apply for SEs):
☐ No Confidentiality ☐ Confidentiality for 90 days ☐ Continued Confidentiality exceeding 90

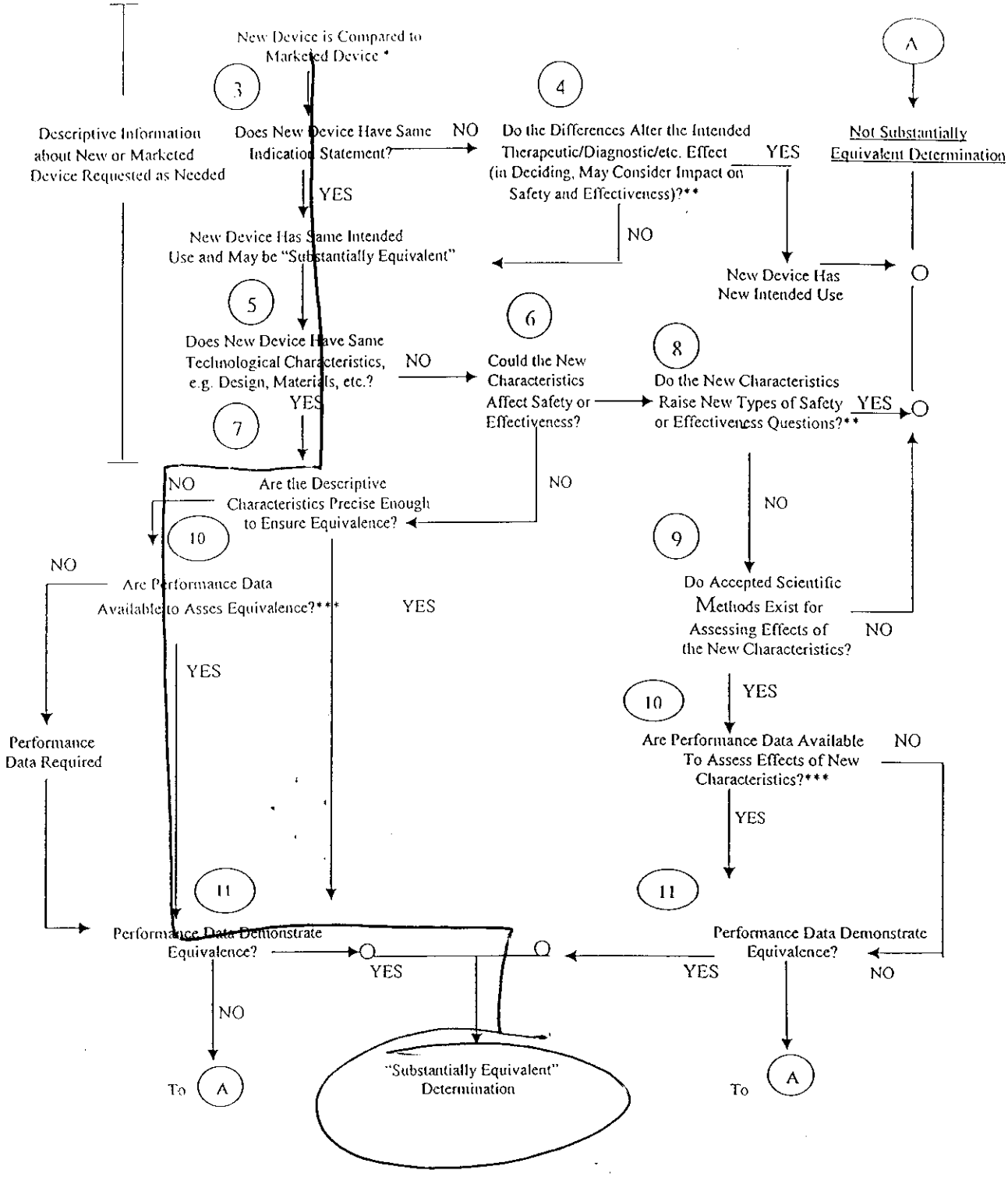
Predicate Product Code with class: ~~Additional Product Code(s) with panel (optional):~~

73 CCK, 73BZF, 74DQA → Class II (2nd)

Review: (Branch Chief) G Tritchler for JXH (Branch Code) 10/7/03 (Date)

Final Review: (Division Director) [signature] 10/7/03 (Date)

510(k) "SUBSTANTIAL EQUIVALENCE" DECISION-MAKING PROCESS



- ✣ 510(k) Submissions compare new devices to marketed devices. FDA requests additional information if the relationship between marketed and "predicate" (pre-Amendments or reclassified post-Amendments) devices is unclear.
- ✣✣ This decision is normally based on descriptive information alone, but limited testing information is sometimes required.
- ✣✣✣ Data maybe in the 510(k), other 510(k)s, the Center's classification files, or the literature.

REVISED:3/14/95

THE 510(K) DOCUMENTATION FORMS ARE AVAILABLE ON THE LAN UNDER 510(K) BOILERPLATES TITLED "DOCUMENTATION" AND MUST BE FILLED OUT WITH EVERY FINAL DECISION (SE, NSE, NOT A DEVICE, ETC.).

"SUBSTANTIAL EQUIVALENCE" (SE) DECISION MAKING DOCUMENTATION

K 030886/S1

Reviewer: Lisa Harris

Division/Branch: DAGID/ARDB

Device Name: NICO with MARS

Product To Which Compared (510(K) Number If Known): K982979

	YES	NO	
1. Is Product A Device	✓		If **NO** = Stop
2. Is Device Subject To 510(k)?	✓		If **NO** = Stop
3. Same Indication Statement?	✓		If **YES** = Go To 5
4. Do Differences Alter The Effect Or Raise New Issues of Safety Or Effectiveness?	—		If **YES** = Stop **NE**
5. Same Technological Characteristics?	✓		If **YES** = Go To 7
6. Could The New Characteristics Affect Safety Or Effectiveness?	—		If **YES** = Go To 8
7. Descriptive Characteristics Precise Enough?		✓	If **NO** = Go To 10 If **YES** = Stop **SE**
8. New Types Of Safety Or Effectiveness Questions?	—		If **YES** = Stop **NE**
9. Accepted Scientific Methods Exist?	—		If **NO** = Stop **NE**
10. Performance Data Available?	✓		If **NO** = Request Data
11. Data Demonstrate Equivalence?	✓		Final Decision: SE

Note: In addition to completing the form on the LAN, "yes" responses to questions 4, 6, 8, and 11, and every "no" response requires an explanation.

1. Intended Use: See Review Memo

2. Device Description: Provide a statement of how the device is either similar to and/or different from other marketed devices, plus data (if necessary) to support the statement. Is the device life-supporting or life sustaining? Is the device implanted (short-term or long-term)? Does the device design use software? Is the device sterile? Is the device for single use? Is the device over-the-counter or prescription use? Does the device contain drug or biological product as a component? Is this device a kit? Provide a summary about the devices design, materials, physical properties and toxicology profile if important.

EXPLANATIONS TO "YES" AND "NO" ANSWERS TO QUESTIONS ON PAGE 1 AS NEEDED

1. Explain why not a device:

2. Explain why not subject to 510(k):

3. How does the new indication differ from the predicate device's indication:

4. Explain why there is or is not a new effect or safety or effectiveness issue:

5. Describe the new technological characteristics:

6. Explain how new characteristics could or could not affect safety or effectiveness:

7. Explain how descriptive characteristics are not precise enough:

8. Explain new types of safety or effectiveness questions raised or why the questions are not new:

9. Explain why existing scientific methods can not be used:

10. Explain what performance data is needed:

11. Explain how the performance data demonstrates that the device is or is not substantially equivalent:

ATTACH ADDITIONAL SUPPORTING INFORMATION

4

DEPARTMENT OF HEALTH AND HUMAN SERVICES **MEMORANDUM**

Food and Drug Administration
Office of Device Evaluation
9200 Corporate Boulevard
Rockville, MD 20850

Premarket Notification [510(k)] Review
K030886/S001

10/7/03

Date: October 7, 2003
To: The Record
From: Lisa E. Harris, Biomedical Engineer

Office: HFZ-480
Division: DAGID/ARDB

Company Name: Respironics Novametrix, Inc.
Device Name: NICO with MARS, Model 7300
Contact: Michael J. Malis
Phone: (203) 697-6442

Fax: (203) 284-0753

I. Purpose

The sponsor wishes to introduce a new multiparameter monitor into the US market.

II. Device Description

A. Intended Use/Indications for Use

The device is intended to provide (1) cardiac output monitoring via the method of partial rebreathing in adult patients receiving mechanical ventilation during general anesthesia and in the intensive care unit (ICU), (2) spirometric and carbon dioxide monitoring in neonatal, pediatric, and adult patients during general anesthesia and in the ICU and emergency department (ED). Separate combination CO2/flow sensors are provided for adult, pediatric, and neonatal use, and (3) continuous, non-invasive monitoring of functional arterial oxygen saturation and pulse rate in neonatal, pediatric, and adult patients during both no motion and motion conditions and for patients who are well or poorly perfused during general anesthesia and in the ICU and ED.

B. Summary

Life-supporting or life-sustaining?	☐Yes	☑No
Implant?	☐Yes	☑No
Sterile?	☐Yes	☑No
Single use?	☐Yes	☑No
Prescription use?	☑Yes	☐No
Home use?	☐Yes	☑No
Transportable?	☐Yes	☑No

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Drug or biological combination product?	☐Yes	☑No
Kit?	☐Yes	☑No
Software driven?	☑Yes	☐No
Electrically Operated?	☑Yes	☐No

C. Materials/Biocompatibility

A list of general materials of the device is provided at page 19 of the submission. Some biocompatibility test information is provided in Appendix 4D.

D. Design/Specifications

The NICO with MARS is a combination of the CO2SMO Plus! with NICO monitor (K982499) and MARSPO2 monitor (K993979, K000794). It has been designed to use neonatal, pediatric, and adult combined CO2/flow sensors and single patient use or reusable pulse oximetry sensors. It noninvasively calculates cardiac output using established physiological principles by the application and removal of a rebreathed volume in a patient's breathing circuit and the analysis of that response. The flow sensors connect to a patient airway circuit and provide physiological information to the NICO with MARS. The monitor integrates the data and provides a graphical display for respiratory mechanics, CO2, pulse oximetry and cardiac output monitoring. The parameters directly measured and computed by the monitor include airway flow and pressure, volume, CO2, and oxygen saturation. The monitor calculates flow by measuring the pressure drop across a known resistance placed in the circuit.

E. Sterilization/Reuse

The device is not provided sterile. The device allows for mainstream sampling where the sensor is placed at the patient's airway allowing the inspired and expired gas to pass directly across the sensor. It is unclear if the CapnoStat CO2 sensor that the CO2/Flow sensor mates with contacts the gas path. The CapnoStat can be cleaned and disinfected with 70% isopropyl alcohol, 2% gluteraldehyde, or 10% bleach solution (BUT MAY NEED HLD). The NICO sensor (incorporating a rebreathing valve, an adjustable rebreathing volume, and an adult CO2/Flow sensor is disposable and single patient use only. In summary, all material components which contact the exhaled gas path are single patient, disposable. Therefore, high level disinfection is not necessary.

F. Labeling

The device labels and User's Manual are provided in Appendix 1 of the submission. The device is labeled as prescription use only.

G. Performance Testing

Some performance test information is provided in Appendices 4A and 4B.

H. Clinical Testing

A summary of clinical testing is provided. Clinical reports for a study performed for the device in a clinical setting, de-saturation testing, application of Y-sensor tape strips and butterfly tape, and for cardiac output estimation performance is provided.

I. Software

Version: 5.0
Level of Concern: moderate
Software description: The software acquires data, processes data, displays, and controls the device alarms.
Device Hazard Analysis: Section VII
Software Requirements Specifications: Appendix 5, B
Architecture Design Chart: Appendix 5, C
Design Specifications: Appendix 5, B
Traceability Analysis/Matrix: Appendix 5, B
Development: Appendix 5, A
V&VT: Appendix 5, E
Revision level history: Appendix 5, p.43
Unresolved anomalies: none known

J. Environmental Testing

Electrical Safety:

Battery power	yes
Electrical power indicators	yes
Overcurrent protection	yes
Dielectric Withstand	yes
AC power grounding and polarity	yes
Leakage current	yes

Electromagnetic Compatibility:

Emissions:

Radiated (30, 37 db/uV at 10/30 m)	yes
Conducted	yes
Magnetic fields	

Immunity

ESD (± 2,4,6 kV contact, ±2,4,6,8 kV air)	yes
Radiated electromagnetic fields (3 V/m)	yes
Steady-State voltage	yes
Dropout	yes
Slow sags and surges	yes
Fast transient bursts	yes
Fast surges	yes
Conducted electromagnetic energy	yes
Magnetic fields	yes

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Mechanical:

Shock	yes
Sinusoidal vibration	yes
Random vibration, wide band	yes
High and low temp and humidity	yes
Surface temperature	yes
Drop test	yes

K. Certifications/Statements/Standards Met

510(k) Summary	-	Section VIII
Truthful and Accurate Statement	-	Section IX
Indications for Use	-	request revision

L. Predicate Devices

CO_2SMO Plus! with NICO, Model 8200	K982499
MARSPO$_2$, Model 2001	K993979, K000794

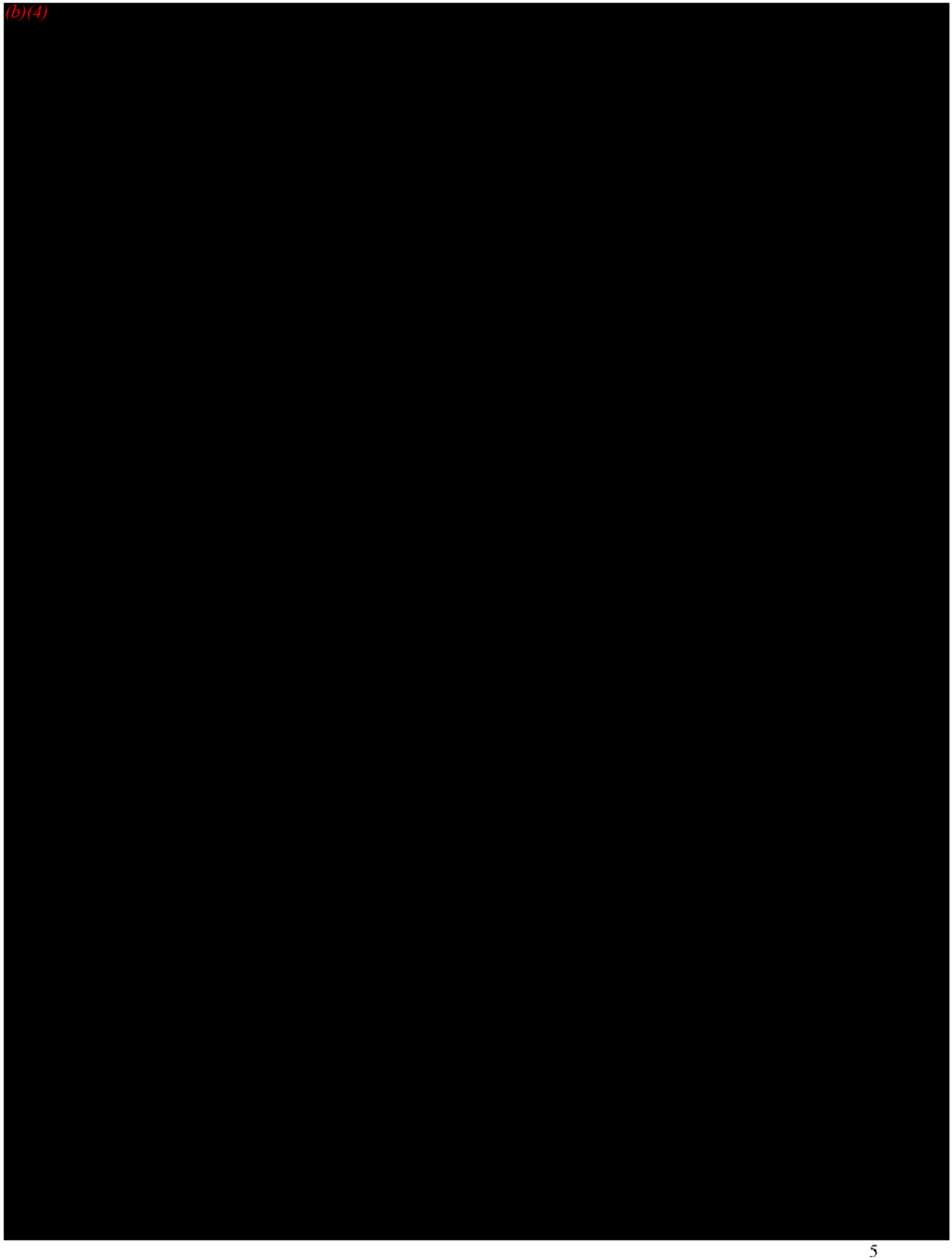
III. Correspondence

(b)(4)

[redacted]

11

(b)(4)



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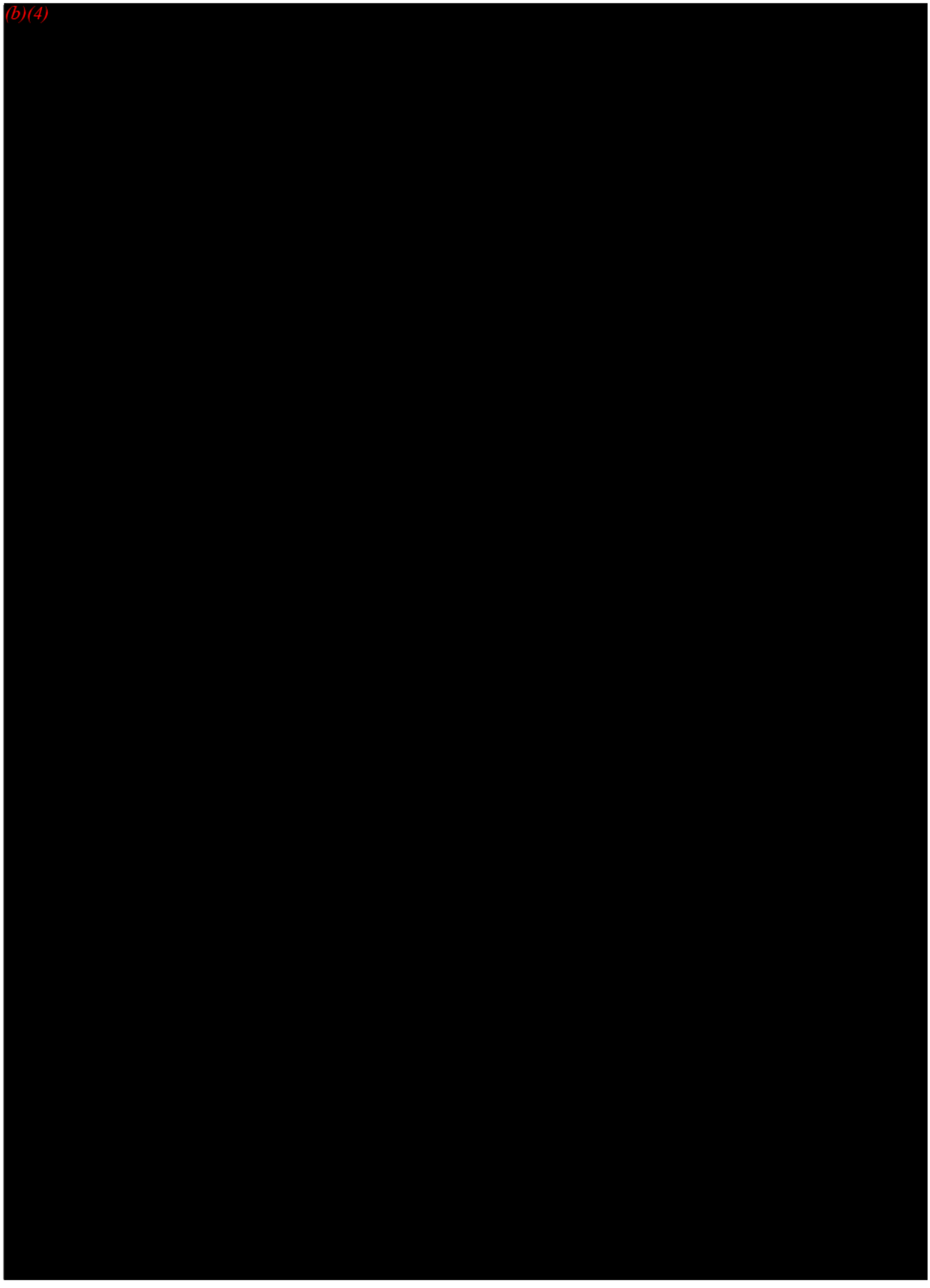

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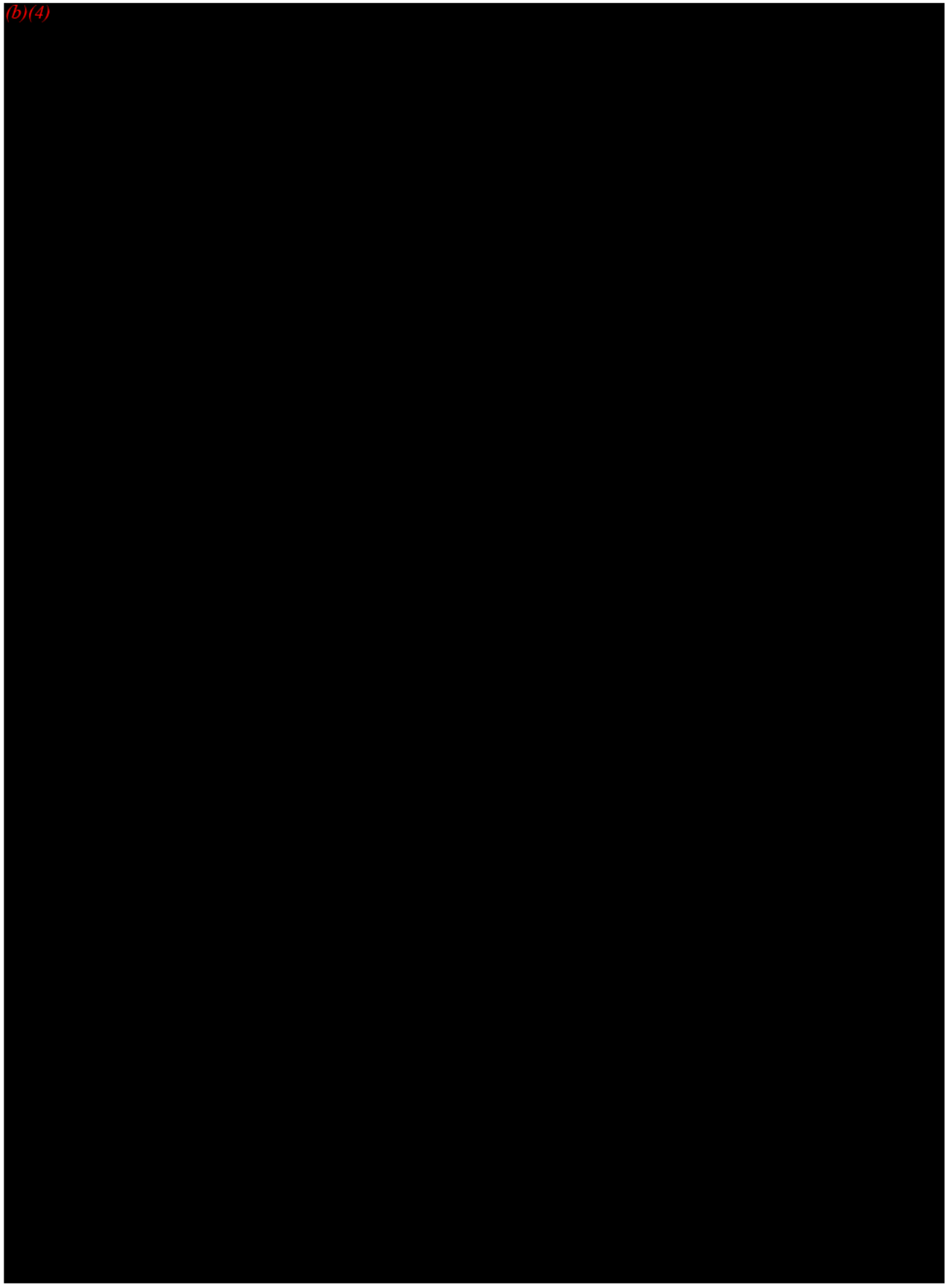
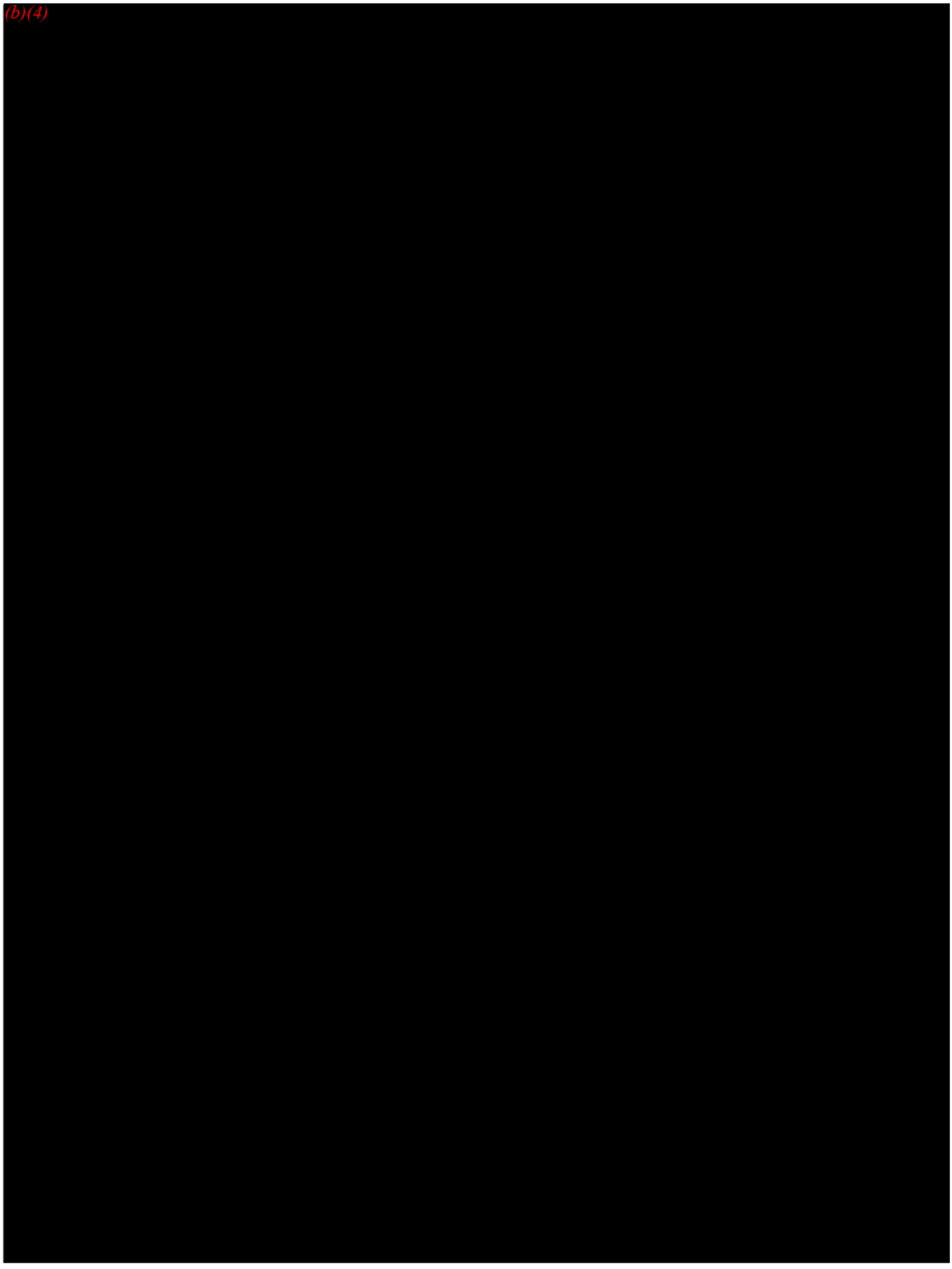


(b)(4)

[redacted]

15



October 6, 2003
I called Michael Malis of Respironics to request additional clarification for Items 2f, 3e, 4, and 6. He is going to gather this information for me by the end of the day and provide it either by email or fax. The requested information was sent via email on October 7, 2003. I have no further concerns with the device.

IV. Substantial Equivalence

There are no new types of safety and effectiveness issues with this device.

V. Recommendation

I recommend that the device be found substantially equivalent to:
73 CCK, 73 BZK, 74 DQA

Classification should be based on:
868.1400 Class II (two)

Lisa E. Harris 10/7/2003

Harris, Lisa E

From: Malis, Michael [Michael.Malis@respironics.com]
Sent: Tuesday, October 07, 2003 11:40 AM
To: LEH@CDRH.FDA.GOV
Subject: Re: K030886 - NICO with MARS

Specs.pdf (12 KB) 8920-03.pdf (43 KB) 3108-02.pdf (70 KB) 8932-00.pdf (19 KB) On_Off_accuracy.pdf (27 KB)

Dear Ms. Harris,

Here are the attached files that address the questions you presented yesterday.

(b)(4)

[redacted]

Kind regards,

Mike Malis

==========

CONFIDENTIALITY NOTICE

This message, together with any attachments, may be legally privileged and is confidential information intended only for the use of the individual or entity to which it is addressed. It is exempt from disclosure under applicable law including court orders. If you are not the intended recipient, you are hereby notified that any use, dissemination, distribution or copy of this message, or any attachment, is strictly prohibited. If you have received this message in error, please notify the original sender and delete this message, along with any attachments, from your computer.

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- Neonatal: 1-100
- Airway Pressure Range (cmH_2O): ± 120
  - Accuracy: greater of 0.5 cmH_2O or ± 2% reading
- Gas composition effects: O_2, anaesthetic agent, CO_2, N_2O, N_2, He (operator selectable)

SpO_2

- Oxygen Saturation
  - Range: 0-100%
  - Accuracy: ± 2% for 70 -100%, ± 3% during motion conditions, for 1 standard deviation, unspecified for 0-69%. Applies to Finger Sensor, Y-Sensor®, and Single Patient Use (SPU) sensors. Use of the earclip can add an additional 1%.
  - Averaging Time: 2 seconds, or selectable, none, 2, 4, or 8 seconds (MARS Mode only).
  - Display Resolution: 1%
  - Settling Time: Display settles to within 1% of the final reading less than 15 seconds after the sensor is properly applied.
- Pulse Rate:
  - Range: 30-250 beats per minute
  - Accuracy: ± 1% of full scale (for 1 standard deviation or approximately 68% of readings)
  - Averaging Time: 8 seconds, or selectable 0, 2, 4, or 8 seconds, based on SpO_2 setting (MARS Mode only).
  - Display Resolution: 1 bpm
  - Settling Time: Display settles to within 1% of the final reading less than 15 seconds after the sensor is properly applied.

Monitor Specifications

- Classification (IEC601-1): Class I/internal power source, type BF, continuous operating mode, enclosure protection rating IPX0.
- Operating Environment: 50-104° F (10-40° C), 10-90% relative humidity (non-condensing)
- Size: Height 6.5 in., Width 10.75 in., Depth 9.5 in.
- Weight: 9 lbs, 6 oz.
- Power: 100-240 VAC, 50-60 Hz, 70VA
- Fuse Rating: 100-120 VAC, 1.0 A/250 V Slo-Blo (x2); 200-240 VAC, T 500 mA/250 V (x2)
- Battery: Internal, Sealed lead-acid gel-cell, 45 minute life on full charge (on-screen life indicator), 12 hours recharge time.
- Display: 4.625 x 3.5 inch EL, 320 x 240 pixels
- Electromagnetic Emissions: Conforms to EMC Directive 93/42/EEC, CISPR Class A. Tested to EN55011 (1998) and CISPR11 (1999).
- Electromagnetic Immunity: Conforms to EMC Directive 93/42/EEC. Tested to IEC60601-1-2 (2001), IEC61000-4-2 (2001) ESD, IEC61000-4-3 (2002) RF, IEC61000-4-4 (1995) EFT, IEC61000-4-5 (2001) Surge, IEC61000-4-6 (2001) Conducted RF, IEC61000-4-8 (2001) Magnetic Fields, IEC61000-4-11 (2001) Voltage Dips, Interruptions and Variations, IEC61000-3-2 (2001) Harmonic Distortion, IEC61000-3-3 (2002) Voltage Fluctuations and Flicker.

RS232 Communications

- RS232 Communications Ports:

Pin #	RS232-1	RS232-2	RS232-3
2	Rx	Rx	Rx
3	Tx	Tx	Tx
5	Ground	Ground	Ground
7	n/a	RTSB	n/a
8	n/a	CTSB	n/a
9	n/a	Power	n/a

Analog Specifications

- Analog Input/Output Port (selectable, 0 to 1 volt range):
  - C.O. - Cardiac Output, 0-20 L/m, 50mV/L/m
  - CI - Cardiac Index, 0-20 L/m, 50mV/L/m
  - SV - Stroke Volume, 0-20 L/m, 50mV/L/m
  - PCBF - 0-20 L/m, 50 mV/L/m
  - $ETCO_2$ - 0-150 mmHg, 0-20 kPa or %, 6.67mV/mmHg
  - SpO_2 - 0-100%, 10mV/%

Rebreathing Paused

- The NICO monitor automatically pauses the rebreathing cycle and generates a display message under any of these conditions:
  - $ETCO_2$ is less than or equal to 15 mmHg (2.0 kPa or %), or greater than or equal to 85 mmHg (11.5 kPa or %)
  - Respiration rate is less than or equal to 3 or greater than or equal to 60 br/min.
  - VCO_2 is less than or equal to 20 mL/min.
- The rebreathing cycle automatically restarts when the condition is corrected.

Entering Patient Data

NICO monitoring can be enhanced by the entry of key patient specific data including respired gas composition (anesthetic agent, balance gas, and inspired O_2), patient height and weight, and arterial blood gas data ($PaCO_2$, PaO_2, Hb or Hct). Inclusion of ABG data is especially important when gas exchange impairment is expected (i.e., high shunt or deadspace). **ABG samples should not be obtained during the rebreathing phase of the 3-minute NICO cycle.**

Patient data should be updated in the **DATA ENTRY** screen whenever possible. The screen may be accessed at any time by pressing the **DATA ENTRY** key.

DATA ENTRY settings The following table lists the parameters and ranges accessible in the **DATA ENTRY** screens.

Label	Parameter	Default	Range/Units	Description
INSP O_2	Inspired Oxygen	40%	21-100 %	Percent of oxygen in the inspired gas. Must be entered in order for NICO to accurately calculate parameters. (See "Gas Compensation Effects on CO_2" on page 62).
INSP AGENT	Inspired Anesthetic Agent	0%	0-20 %	Percent of anesthetic agent in the inspired gas. Must enter percent delivered in order to accurately calculate parameters.
BALANCE	Gas Balance	N_2	N_2, He, or N_2O	N_2, He or N_2O. Must select the correct balance in the inspired gas in order to accurately calculate parameters.
HEIGHT	Patient Height	--	35-91 in 90-230 cm	Enter patient height for CI calculations.
WEIGHT	Patient Weight	--	55-551 lb 25-250 kg	Enter patient weight for CI calculations.
ABG DATA ENTRY Screen				
$PaCO_2$	Arterial Carbon Dioxide	40 mmHg (5.4 kPa or %) ("--" displayed until an initial value is entered)	0-250 mmHg 0.0-20.0 kPa 0.0-20.0 %	Partial pressure of carbon dioxide in arterial blood. Enter this value for calculation of Vd alv (alveolar deadspace), Vd/Vt (deadspace to tidal volume ratio). Must enter correct ABG time in order to accurately calculate parameters. Entering this value can also enhance the accuracy of cardiac output parameters (C.O., SV, and CI).

DATA ENTRY settings The following table lists the parameters and ranges accessible in the **DATA ENTRY** screens.

Label	Parameter	Default	Range/Units	Description
INSP O_2	Inspired Oxygen	40%	21-100 %	Percent of oxygen in the inspired gas. Must be entered in order for NICO to accurately calculate parameters. (See "Gas Compensation Effects on CO_2" on page 62).
INSP AGENT	Inspired Anesthetic Agent	0%	0-20 %	Percent of anesthetic agent in the inspired gas. Must enter percent delivered in order to accurately calculate parameters.
BALANCE	Gas Balance	N_2	N_2, He, or N_2O	N_2, He, or N_2O. Must select the correct balance in the inspired gas in order to accurately calculate parameters.
HEIGHT	Patient Height	--	35-91 in 90-230 cm	Enter patient height (unavailable for neonatal patients in Respiratory Mechanics mode).
WEIGHT	Patient Weight	--	Neonatal: 0.22 - 44.09 lb 0.10 - 20.00 kg Pediatric: 0.2 - 220.2 lb 0.1 - 99.9 kg Adult: 55-551 lb 25-250 kg	Enter patient weight for respiratory mechanics calculations.
ABG DATA ENTRY Screen				
$PaCO_2$	Arterial Carbon Dioxide	40 mmHg (5.4 kPa or %) ("--" displayed until an initial value is entered)	0-250 mmHg 0.0-20.0 kPa 0.0-20.0 %	Partial pressure of carbon dioxide in arterial blood. Enter this value for calculation of Vd alv (alveolar deadspace), Vd/Vt (deadspace to tidal volume ratio). Must enter correct ABG time in order to accurately calculate parameters.
PaO_2	Arterial Oxygen	FiO_2*(Pb-47 mmHg) ("--" displayed until an initial value is entered)	0-750 mmHg 0.0-99.5 kPa 0.0-99.5 %	Partial pressure of oxygen in arterial blood. Enter a value for this parameter if desired; does not affect CO_2/flow calculations.
Hb	Hemoglobin Concentration or Hematocrit	11.0 gm/dL 6.8 mmol/L 33 % ("--" displayed until an initial value is entered)	Hb: 5.0-20.0 gm/dL Hb: 3.1-12.4 mmol/L Hct: 0-60 %	Concentration of hemoglobin or hematocrit in the blood. Enter a value for this parameter if desired; does not affect CO_2/flow calculations.
MARK ABG TIME	Time when ABG blood sample is drawn	Current Time	hh:mm (hours:minutes)	Enter time ABG is drawn. Only accepts time since $ETCO_2$ was first detected.

Gas Compensation Effects on CO_2

Accuracy of the displayed CO_2 value is dependent on correct gas compensation settings. The table below demonstrates the effect on CO_2 of improper gas compensation settings.

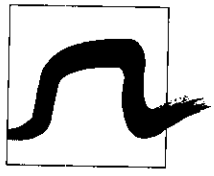
Compensation Settings		INSP Gas Used				
O_2 % Setting	N_2O (ON/OFF)	21% O_2 (bal N_2)	40% O_2 (bal N_2)	40% O_2 (bal N_2O)	60% O_2 (bal N_2)	100% O_2
21	OFF	0.0%	-1.6%	8.1%	-3.2%	-6.3%
40*	OFF	1.6%	0.0%	9.8%	-1.6%	-4.8%
60	OFF	3.3%	1.7%	11.7%	0.0%	-3.2%
100	OFF	6.7%	5.0%	15.3%	3.3%	0.0%
100	ON	7.2%	5.5%	15.9%	3.8%	0.5%
60	ON	-2.6%	-4.1%	5.3%	-5.7%	-8.7%
40	ON	-7.5%	-9.0%	0.0%	-10.5%	-13.3%
21	ON	-12.1%	-13.5%	-5.0%	-15.0%	-17.7%

*Monitor default setting

Negative values reflect an underestimation of displayed CO_2 (display reads low).
Positive values reflect an overestimation of displayed CO_2 (display reads high).

Reference Handbooks

For a discussion on waveform interpretations, refer to the Respironics Novametrix Reference Handbooks on capnography, respiratory mechanics, and pulse oximetry. Contact Respironics Novametrix Customer Service or your local sales representative for more information.



Single Patient Use

Pediatric/Adult Airway Adapter

(Catalog No. 6063)

For use with Novametrix CAPNOSTAT® mainstream CO_2 sensors (Catalog No. 7067 or 7167)

⚠ Refer to User's Manual prior to use

LOT:

QTY:

Novametrix PN: 8920-02-03
Artwork, Label, carton top

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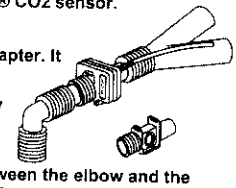
Pediatric/Adult Airway Adapter
REF 6063

◀TEAR TO OPEN

Single Patient Use Only

For monitoring Pediatric/Adult patients with endotracheal tube size greater than 4.0mm with the Novametrix CAPNOSTAT® CO2 sensor.

Verify the adapter is intact. Press the CAPNOSTAT® CO2 sensor onto the airway adapter. It will "click" into place when properly seated.



Perform an Airway Zero only if prompted by the monitor (see User's Manual for further details).

Install at the proximal end of the circuit between the elbow and the ventilator wye. If using an HME, place adapter between HME and wye. The cord of the CAPNOSTAT® CO2 sensor should be facing away from the patient. For optimal results, DO NOT place the adapter between the ET tube and the elbow.

Ensure the integrity of the patient breathing circuit after insertion of the airway adapter.

⚠ Refer to user's manual prior to use

Sterilization will likely compromise system performance.

CAUTION: USA law restricts this device to sale by or on the order of a licensed medical practitioner.

LOT

novametrix™

Wallingford, CT U.S.A. 06492
(800) 243-3444 or (203) 265-7701 www.novametrix.com

US PATENTS 4,859,858 4,859,859 4,914,720 5,146,092 5,153,436 5,793,044 5,616,923 5,693,944; other foreign and US patents pending.

CE 0086

3108-02-02

Novametrix PN: 3108-02-02

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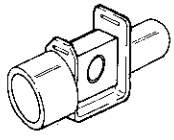
Pediatric/Adult

Airway Adapter



Novametrix PN: 8932-02-00
Artwork, Label, Carton side

25

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration

Memorandum

From: Reviewer(s) - Name(s) Lisa Harris

Subject: 510(k) Number K030886

To: The Record - It is my recommendation that the subject 510(k) Notification:

- ☐ Refused to accept.
- ☑ Requires additional information (other than refuse to accept). AI
- ☐ Is substantially equivalent to marketed devices.
- ☐ NOT substantially equivalent to marketed devices.

De Novo Classification Candidate? ☐ YES ☐ NO

- ☐ Other (e.g., exempt by regulation, not a device, duplicate, etc.)

Is this device subject to Postmarket Surveillance?	☐ YES	☐ NO
Is this device subject to the Tracking Regulation?	☐ YES	☐ NO
Was clinical data necessary to support the review of this 510(k)?	☐ YES	☐ NO
Is this a prescription device?	☐ YES	☐ NO
Was this 510(k) reviewed by a Third Party?	☐ YES	☐ NO
Special 510(k)?	☐ YES	☐ NO
Abbreviated 510(k)? Please fill out form on H Drive 510k/boilers	☐ YES	☐ NO

This 510(k) contains:

Truthful and Accurate Statement ☐ Requested ☐ Enclosed
(required for originals received 3-14-95 and after)

- ☐ A 510(k) summary OR ☐ A 510(k) statement
- ☐ The required certification and summary for class III devices
- ☐ The indication for use form (required for originals received 1-1-96 and after)

Animal Tissue Source ☐ YES ☐ NO

The submitter requests under 21 CFR 807.95 (doesn't apply for SEs):

☐ No Confidentiality ☐ Confidentiality for 90 days ☐ Continued Confidentiality exceeding 90 day

Predicate Product Code with class: Additional Product Code(s) with panel (optional):

Review: JAW (Branch Chief) ARDS (Branch Code) 6/7/03 (Date)

Final Review: _____ (Division Director) _____ (Date)

Revised:8/17//99

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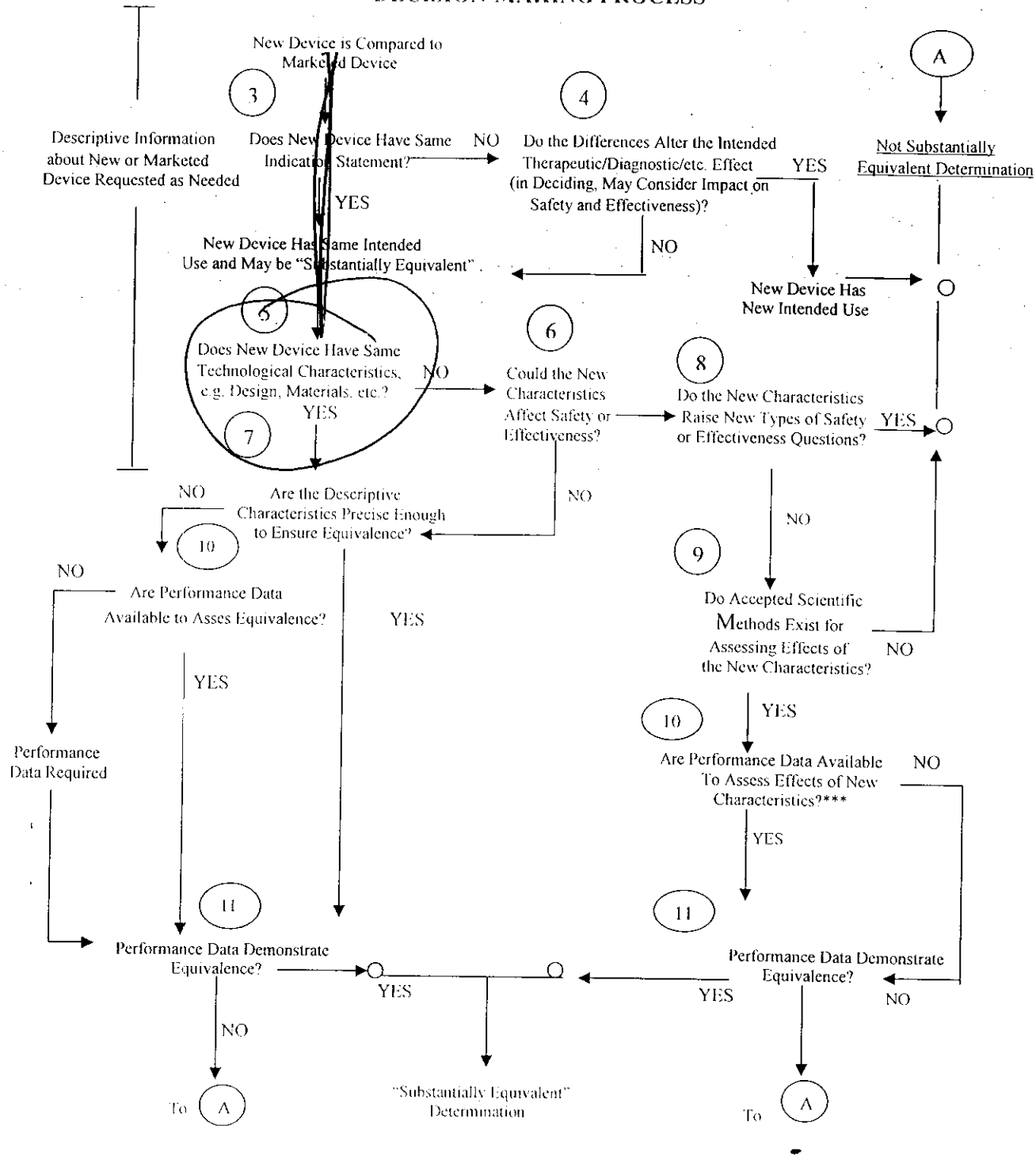
510(k) "SUBSTANTIAL EQUIVALENCE" DECISION-MAKING PROCESS



❖ 510(k) Submissions compare new devices to marketed devices. FDA requests additional information if the relationship between marketed and "predicate" (pre-Amendments or reclassified post-Amendments) devices is unclear.

❖❖ This decision is normally based on descriptive information alone, but limited testing information is sometimes required.

❖❖❖ Data maybe in the 510(k), other 510(k)s, the Center's classification files, or the literature.

DEPARTMENT OF HEALTH AND HUMAN SERVICES **MEMORANDUM**

Food and Drug Administration
Office of Device Evaluation
9200 Corporate Boulevard
Rockville, MD 20850

Premarket Notification [510(k)] Review
K030886

Date: June 12, 2003
To: The Record
From: Lisa E. Harris, Biomedical Engineer

Office: HFZ-480
Division: DAGID/ARDB

Company Name: Respironics Novametrix, Inc.
Device Name: NICO with MARS, Model 7300
Contact: Michael J. Malis
Phone: (203) 697-6442

Fax: (203) 284-0753

I. Purpose

The sponsor wishes to introduce a new multiparameter monitor into the US market.

II. Device Description

A. Intended Use/Indications for Use

The device is intended to provide (1) cardiac output monitoring via the method of partial rebreathing in adult patients receiving mechanical ventilation during general anesthesia and in the intensive care unit (ICU), (2) spirometric and carbon dioxide monitoring in neonatal, pediatric, and adult patients during general anesthesia and in the ICU and emergency department (ED). Separate combination CO2/flow sensors are provided for adult, pediatric, and neonatal use, and (3) continuous, non-invasive monitoring of functional arterial oxygen saturation and pulse rate in neonatal, pediatric, and adult patients during both no motion and motion conditions and for patients who are well or poorly perfused during general anesthesia and in the ICU and ED.

B. Summary

Life-supporting or life-sustaining?	☐Yes	☑No
Implant?	☐Yes	☑No
Sterile?	☐Yes	☑No
Single use?	☐Yes	☑No
Prescription use?	☑Yes	☐No
Home use?	☐Yes	☑No
Transportable?	☐Yes	☑No

Drug or biological combination product?	☐Yes	☑No
Kit?	☐Yes	☑No
Software driven?	☑Yes	☐No
Electrically Operated?	☑Yes	☐No

C. Materials/Biocompatibility

A list of general materials of the device is provided at page 19 of the submission. Some biocompatibility test information is provided in Appendix 4D.

D. Design/Specifications

The NICO with MARS is a combination of the CO2SMO Plus! with NICO monitor (K982499) and MARSPO2 monitor (K993979, K000794). It has been designed to use neonatal, pediatric, and adult combined CO2/flow sensors and single patient use or reusable pulse oximetry sensors. It non0invasively calculates cardiac output using established physiological principles by the application and removal of a rebreathed volume in a patient's breathing circuit and the analysis of that response. The flow sensors connect to a patient airway circuit and provide physiological information to the NICO with MARS. The monitor integrates the data and provides a graphical display for respiratory mechanics, CO2, pulse oximetry and cardiac output monitoring. The parameters directly measured and computed by the monitor include airway flow and pressure, volume, CO2, and oxygen saturation. The monitor calculates flow by measuring the pressure drop across a known resistance placed in the circuit.

E. Sterilization/Reuse

The device is not provided sterile. The device allows for mainstream sampling where the sensor is placed at the patient's airway allowing the inspired and expired gas to pass directly across the sensor. It is unclear if the CapnoStat CO2 sensor that the CO2/Flow sensor mates with contacts the gas path. The CapnoStat can be cleaned and disinfected with 70% isopropyl alcohol, 2% gluteraldehyde, or 10% bleach solution (BUT MAY NEED HLD). The NICO sensor (incorporating a rebreathing valve, an adjustable rebreathing volume, and an adult CO2/Flow sensor is disposable and single patient use only.

F. Labeling

The device labels and User's Manual are provided in Appendix 1 of the submission. The device is labeled as prescription use only.

G. Performance Testing

Some performance test information is provided in Appendices 4A and 4B.

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H. Clinical Testing

A summary of clinical testing is provided. Clinical reports for a study performed for the device in a clinical setting, de-saturation testing, application of Y-sensor tape strips and butterfly tape, and for cardiac output estimation performance is provided.

I. Software

Version: 5.0

Level of Concern: moderate

Software description: The software acquires data, processes data, displays, and controls the device alarms.

Device Hazard Analysis: Section VII

Software Requirements Specifications: Appendix 5, B

Architecture Design Chart: Appendix 5, C

Design Specifications: Appendix 5, B

Traceability Analysis/Matrix: Appendix 5, B

Development: Appendix 5, A

V&VT: Appendix 5, E

Revision level history: Appendix 5, p.43

Unresolved anomalies: none known

J. Environmental Testing

Electrical Safety:

Battery power	yes
Electrical power indicators	yes
Overcurrent protection	yes
Dielectric Withstand	yes
AC power grounding and polarity	yes
Leakage current	yes

Electromagnetic Compatibility:

Emissions:	
Radiated (30, 37 db/uV at 10/30 m)	yes
Conducted	yes
Magnetic fields	
Immunity	
ESD (± 2,4,6 kV contact, ±2,4,6,8 kV air)	yes
Radiated electromagnetic fields (3 V/m)	yes
Steady-State voltage	yes
Dropout	yes
Slow sags and surges	yes
Fast transient bursts	yes
Fast surges	yes
Conducted electromagnetic energy	yes
Magnetic fields	yes

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Mechanical:

Shock	yes
Sinusoidal vibration	yes
Random vibration, wide band	yes
High and low temp and humidity	yes
Surface temperature	yes
Drop test	yes

K. Certifications/Statements/Standards Met

510(k) Summary	-	Section VIII
Truthful and Accurate Statement	-	Section IX
Indications for Use	-	request revision

L. Predicate Devices

CO_2SMO Plus! with NICO, Model 8200	K982499
MARSPO$_2$, Model 2001	K993979, K000794

III. Correspondence

(b)(4)

[redacted]

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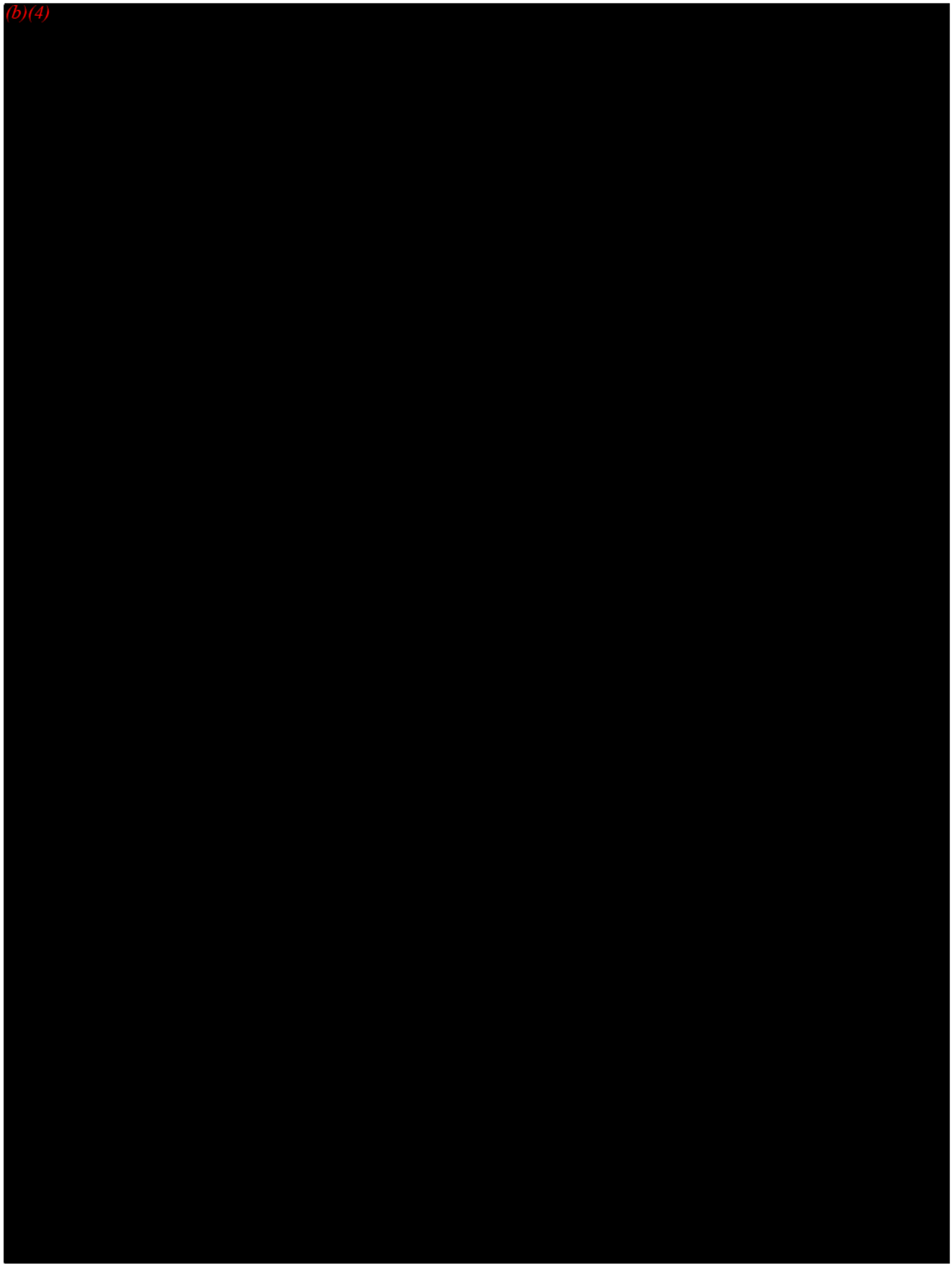
(b)(4)



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(b)(4)

[redacted]

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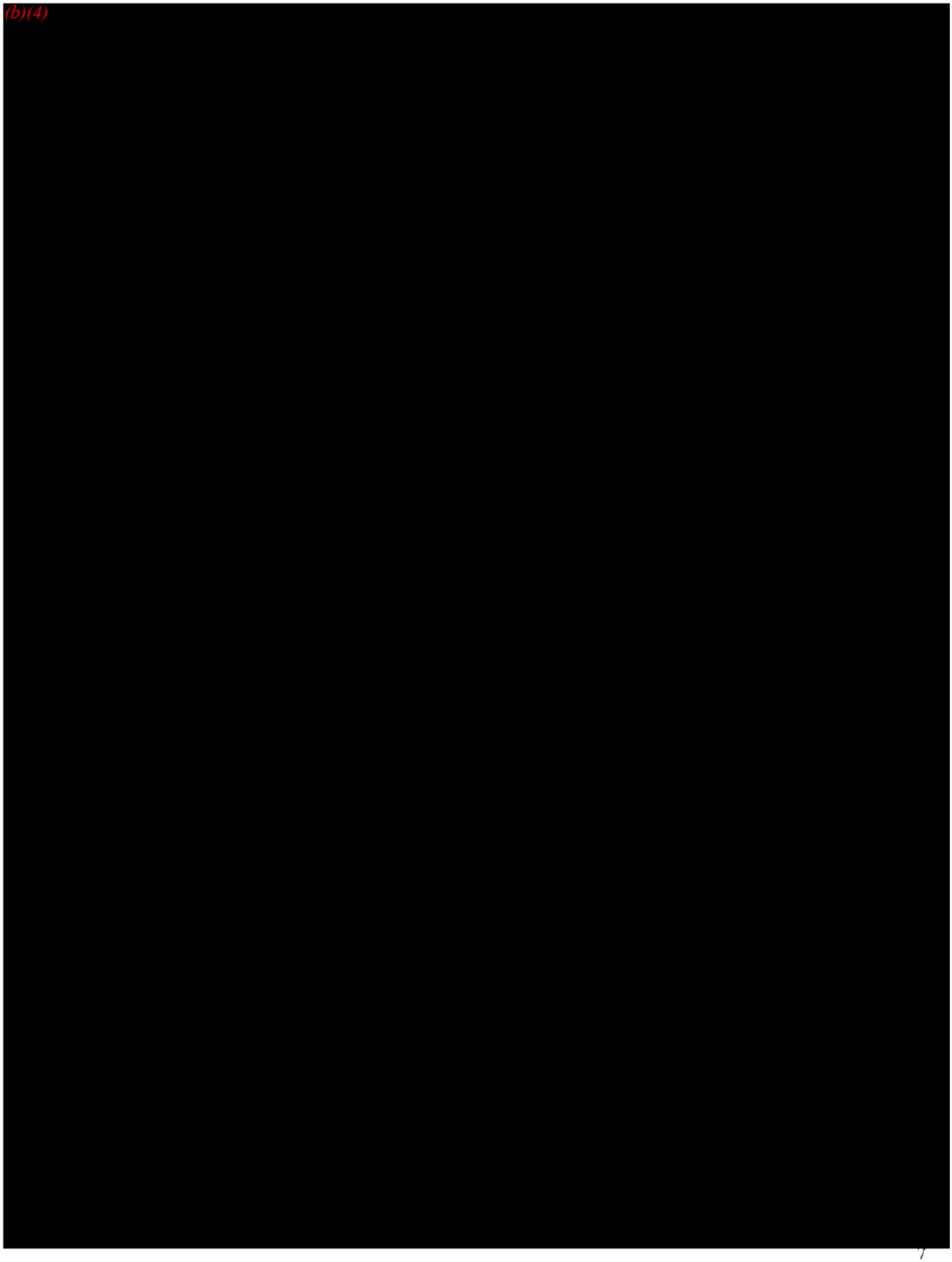

(b)(4)

IV. Substantial Equivalence

Additional information is necessary in order to determine substantial equivalence.

V. Recommendation

I recommend that the file be placed on hold pending the above information.

6/17/2003

Lisa E. Harris

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SCREENING CHECKLIST
FOR ALL PREMARKET NOTIFICATION [510(k)] SUBMISSIONS

510(k) Number: K09 0886

The cover letter clearly identifies the type of 510(k) submission as (Check the appropriate box):

☐ Special 510(k) - Do Sections 1 and 2

☐ Abbreviated 510(k) - Do Sections 1, 3 and 4

☒ Traditional 510(k) or no identification provided - Do Sections 1 and 4

Section 1: Required Elements for All Types of 510(k) submissions:

	Present or Adequate	Missing or Inadequate
Cover letter, containing the elements listed on page 3-2 of the Premarket Notification [510)] Manual.	✓	
Table of Contents.	✓	
Truthful and Accurate Statement.	✓	
Device's Trade Name, Device's Classification Name and Establishment Registration Number.	✓	
Device Classification Regulation Number and Regulatory Status (Class I, Class II, Class III or Unclassified).	✓	
Proposed Labeling including the material listed on page 3-4 of the Premarket Notification [510)] Manual.	✓	
Statement of Indications for Use that is on a separate page in the premarket submission.	✓	
Substantial Equivalence Comparison, including comparisons of the new device with the predicate in areas that are listed on page 3-4 of the Premarket Notification [510)] Manual.	✓	
510(k) Summary or 510(k) Statement.	✓	
Description of the device (or modification of the device) including diagrams, engineering drawings, photographs or service manuals.	✓	
Identification of legally marketed predicate device. *		
Compliance with performance standards. * [See Section 514 of the Act and 21 CFR 807.87 (d).]		
Class III Certification and Summary. **		
Financial Certification or Disclosure Statement for 510(k) notifications with a clinical study. * [See 21 CFR 807.87 (i)]		
510(k) Kit Certification ***		

* - May not be applicable for Special 510(k)s.

** - Required for Class III devices, only.

*** - See pages 3-12 and 3-13 in the Premarket Notification [510)] Manual and the Convenience Kits Interim Regulatory Guidance.

Section 2: Required Elements for a SPECIAL 510(k) submission:

	Present	Inadequate or Missing
Name and 510(k) number of the submitter's own, unmodified predicate device.		
A description of the modified device and a comparison to the sponsor's predicate device.		
A statement that the intended use(s) and indications of the modified device, as described in its labeling are the same as the intended uses and indications for the submitter's unmodified predicate device.		
Reviewer's confirmation that the modification has not altered the fundamental scientific technology of the submitter's predicate device.		
A Design Control Activities Summary that includes the following elements (a-c):		
a. Identification of Risk Analysis method(s) used to assess the impact of the modification on the device and its components, and the results of the analysis.		
b. Based on the Risk Analysis, an identification of the required verification and validation activities, including the methods or tests used and the acceptance criteria to be applied.		
c. A Declaration of Conformity with design controls that includes the following statements:		
A statement that, as required by the risk analysis, all verification and validation activities were performed by the designated individual(s) and the results of the activities demonstrated that the predetermined acceptance criteria were met. This statement is signed by the individual responsible for those particular activities.		
A statement that the manufacturing facility is in conformance with the design control procedure requirements as specified in 21 CFR 820.30 and the records are available for review. This statement is signed by the individual responsible for those particular activities.		

Section 3: Required Elements for an ABBREVIATED 510(k)* submission:

	Present	Inadequate or Missing
For a submission, which relies on a guidance document and/or special control(s), a summary report that describes how the guidance and/or special control(s) was used to address the risks associated with the particular device type. (If a manufacturer elects to use an alternate approach to address a particular risk, sufficient detail should be provided to justify that approach.)		
For a submission, which relies on a recognized standard, a declaration of conformity [For a listing of the required elements of a declaration of conformity, SEE **Required Elements for a Declaration of Conformity to a Recognized Standard,** which		

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is posted with the 510(k) boilers on the H drive.]		
For a submission, which relies on a recognized standard without a declaration of conformity, a statement that the manufacturer intends to conform to a recognized standard and that supporting data will be available before marketing the device.		
For a submission, which relies on a non-recognized standard that has been historically accepted by FDA, a statement that the manufacturer intends to conform to a recognized standard and that supporting data will be available before marketing the device.		
For a submission, which relies on a non-recognized standard that has not been historically accepted by FDA, a statement that the manufacturer intends to conform to a recognized standard and that supporting data will be available before marketing the device and any additional information requested by the reviewer in order to determine substantial equivalence.		
Any additional information, which is not covered by the guidance document, special control, recognized standard and/or non-recognized standard, in order to determine substantial equivalence.		

* - When completing the review of an abbreviated 510(k), please fill out an Abbreviated Standards Data Form (located on the H drive) and list all the guidance documents, special controls, recognized standards and/or non-recognized standards, which were noted by the sponsor.

Section 4: Additional Requirements for ABBREVIATED and TRADITIONAL 510(k) submissions (If Applicable):

	Present	Inadequate or Missing
a) Biocompatibility data for all patient-contacting materials, OR certification of identical material/formulation:		
b) Sterilization and expiration dating information:		
i) sterilization process		
ii) validation method of sterilization process		
iii) SAL		
iv) packaging		
v) specify pyrogen free		
vi) ETO residues		
vii) radiation dose		
viii) Traditional Method or Non-Traditional Method		
c) Software Documentation:		

Items with checks in the "Present or Adequate" column do not require e additional information from the sponsor. Items with checks in the " Missing or Inadequate" column must be submitted before substantive review of the document.

Passed Screening ✓ Yes ___ No

Reviewer: _____

Concurrence by Review Branch: _____

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Date: MAR 21 2003

The deficiencies identified above represent the issues that we believe need to be resolved before our review of your 510(k) submission can be successfully completed. In developing the deficiencies, we carefully considered the statutory criteria as defined in Section 513(i) of the Federal Food, Drug, and Cosmetic Act for determining substantial equivalence of your device. We also considered the burden that may be incurred in your attempt to respond to the deficiencies. We believe that we have considered the least burdensome approach to resolving these issues. If, however, you believe that information is being requested that is not relevant to the regulatory decision or that there is a less burdensome way to resolve the issues, you should follow the procedures outlined in the "A Suggested Approach to Resolving Least Burdensome Issues" document. It is available on our Center web page at: http://www.fda.gov/cdrh/modact/leastburdensome.html

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REVISED:3/14/95

THE 510(K) DOCUMENTATION FORMS ARE AVAILABLE ON THE LAN UNDER 510(K) BOILERPLATES TITLED "DOCUMENTATION" AND MUST BE FILLED OUT WITH EVERY FINAL DECISION (SE, NSE, NOT A DEVICE, ETC.).

"SUBSTANTIAL EQUIVALENCE" (SE) DECISION MAKING DOCUMENTATION

K_____

Reviewer:_____

Division/Branch:_____

Device Name:_____

Product To Which Compared (510(K) Number If Known):_____

	YES	NO	
1. Is Product A Device			If NO = Stop
2. Is Device Subject To 510(k)?			If NO = Stop
3. Same Indication Statement?			If YES = Go To 5
4. Do Differences Alter The Effect Or Raise New Issues of Safety Or Effectiveness?			If YES = Stop NE
5. Same Technological Characteristics?			If YES = Go To 7
6. Could The New Characteristics Affect Safety Or Effectiveness?			If YES = Go To 8
7. Descriptive Characteristics Precise Enough?			If NO = Go To 10 If YES = Stop SE
8. New Types Of Safety Or Effectiveness Questions?			If YES = Stop NE
9. Accepted Scientific Methods Exist?			If NO = Stop NE
10. Performance Data Available?			If NO = Request Data
11. Data Demonstrate Equivalence?			Final Decision:

Note: In addition to completing the form on the LAN, "yes" responses to questions 4, 6, 8, and 11, and every "no" response requires an explanation.

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1. Intended Use:

2. Device Description: Provide a statement of how the device is either similar to and/or different from other marketed devices, plus data (if necessary) to support the statement. Is the device life-supporting or life sustaining? Is the device implanted (short-term or long-term)? Does the device design use software? Is the device sterile? Is the device for single use? Is the device over-the-counter or prescription use? Does the device contain drug or biological product as a component? Is this device a kit? Provide a summary about the devices design, materials, physical properties and toxicology profile if important.

EXPLANATIONS TO "YES" AND "NO" ANSWERS TO QUESTIONS ON PAGE 1 AS NEEDED

1. Explain why not a device:

2. Explain why not subject to 510(k):

3. How does the new indication differ from the predicate device's indication:

4. Explain why there is or is not a new effect or safety or effectiveness issue:

5. Describe the new technological characteristics:

6. Explain how new characteristics could or could not affect safety or effectiveness:

7. Explain how descriptive characteristics are not precise enough:

8. Explain new types of safety or effectiveness questions raised or why the questions are not new:

9. Explain why existing scientific methods can not be used:

10. Explain what performance data is needed:

11. Explain how the performance data demonstrates that the device is or is not substantially equivalent:

ATTACH ADDITIONAL SUPPORTING INFORMATION

Internal Administrative Form

	YES	NO
1. Did the firm request expedited review?		✓
2. Did we grant expedited review?		✓
3. Have you verified that the Document is labeled Class III for GMP purposes?		✓
4. If, not, has POS been notified?		✓
5. Is the product a device?	✓	
6. Is the device exempt from 510(k) by regulation or policy?		✓
7. Is the device subject to review by CDRH?	✓	
8. Are you aware that this device has been the subject of a previous NSE decision?		✓
9. If yes, does this new 510(k) address the NSE issue(s), (e.g., performance data)?		✓
10. Are you aware of the submitter being the subject of an integrity investigation?		✓
11. If, yes, consult the ODE Integrity Officer.		✓
12. Has the ODE Integrity Officer given permission to proceed with the review? (Blue Book Memo #I91-2 and Federal Register 90N0332, September 10, 1991.		✓

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DEPARTMENT OF HEALTH AND HUMAN SERVICES Public Health Service

Food and Drug Administration
Center for Devices and
Radiological Health
Office of Device Evaluation
Document Mail Center (HFZ-401)
9200 Corporate Blvd.
Rockville, Maryland 20850

July 14, 2003

RESPIRONICS NOVAMETRIX, INC.
5 TECHNOLOGY DR.
WALLINGFORD, CT 06492
ATTN: MICHAEL MALIS

510(k) Number: K030886
Product: NICO WITH MARS, MODEL 7300

The additional information you have submitted has been received.

We will notify you when the processing of this submission has been completed or if any additional information is required. Please remember that all correspondence concerning your submission MUST be sent to the Document Mail Center (HFZ-401) at the above letterhead address. Correspondence sent to any address other than the one above will not be considered as part of your official premarket notification submission. Also, please note the new Blue Book Memorandum regarding Fax and E-mail Policy entitled, "Fax and E-Mail Communication with Industry about Premarket Files Under Review. Please refer to this guidance for information on current fax and e-mail practices at www.fda.gov/cdrh/ode/a02-01.html.

The Safe Medical Devices Act of 1990, signed on November 28, states that you may not place this device into commercial distribution until you receive a letter from FDA allowing you to do so. As in the past, we intend to complete our review as quickly as possible. Generally we do so 90 days. However, the complexity of a submission or a requirement for additional information may occasionally cause the review to extend beyond 90 days. Thus, if you have not received a written decision or been contacted within 90 days of our receipt date you may want to check with FDA to determine the status of your submission.

If you have procedural or policy questions, please contact the Division of Small Manufacturers International and Consumer Assistance (DSMICA) at (301) 443-6597 or at their toll-free number (800) 638-2041, or contact me at (301) 594-1190.

Sincerely yours,

Marjorie Shulman
Supervisory Consumer Safety Officer
Premarket Notification Section
Office of Device Evaluation
Center for Devices and
Radiological Health

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K030886/S1

HOSPITAL DIVISION
5 Technology Drive
Wallingford, Connecticut 06492-1950
Phone: 203-265-7701
Fax: 203-284-0753

RESPIRONICS
www.respironics.com

July 11, 2003

Food and Drug Administration
Center for Devices and Radiological Health
Document Mail Center (HFZ-401)
9200 Corporate Boulevard
Rockville, MD 20850

Attention: Division of Anesthesiology, General Hospital,
Infection Control, and Dental Devices

Re: K030886
NICO with MARS, Model 7300

Dear Sir or Madam:

In reference to your letter dated June 17, 2003, attached please find our response to your questions for NICO with MARS (ref. K030886). We believe that we have addressed all of the issues raised in your letter and if you have any questions please do not hesitate to contact me at 203-697-6442.

Sincerely,

Michael Malis

Michael J. Malis
Regulatory & QA Manager
(203) 697-6442
(203) 284-0753 (facsimile)

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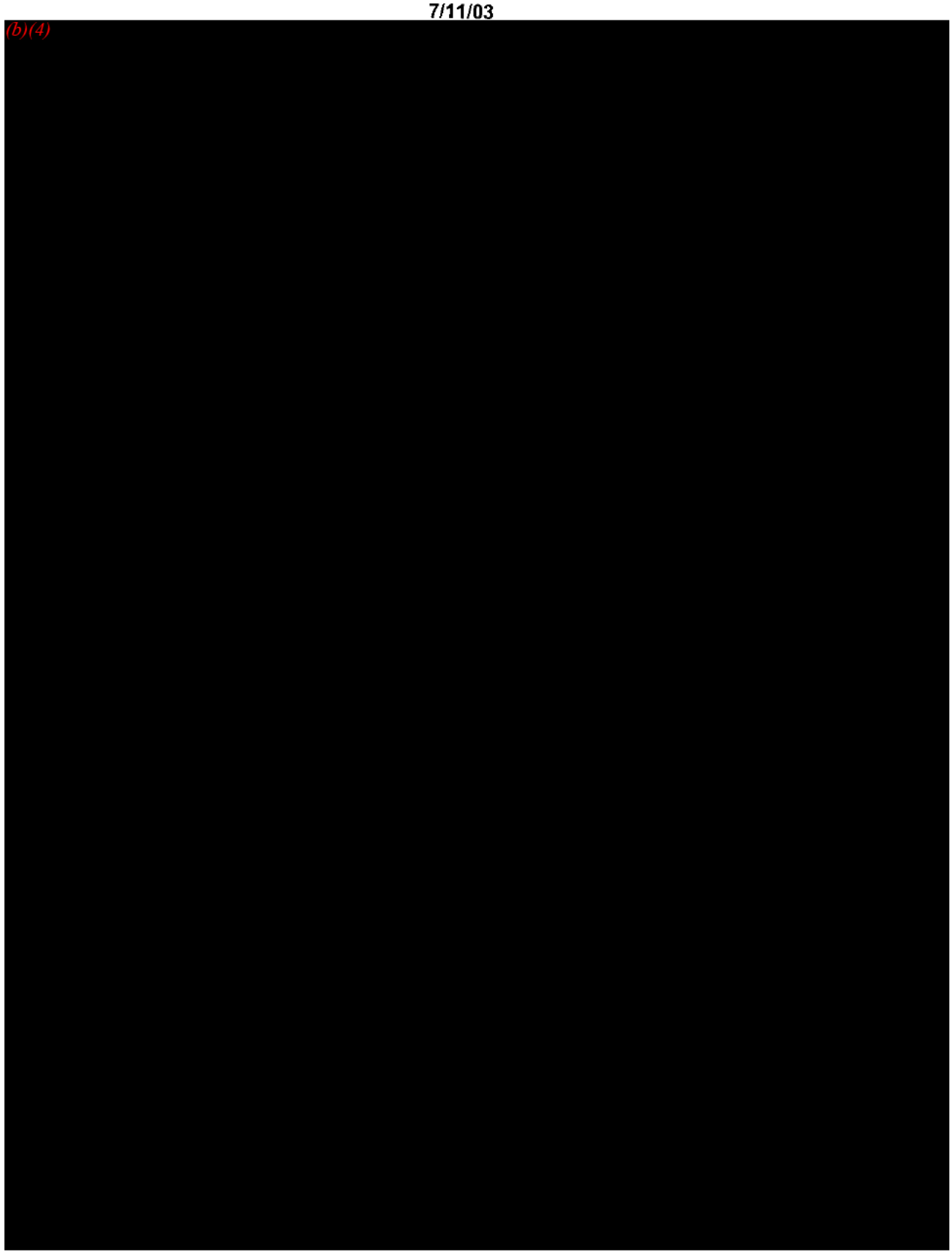
5K11

Responses to Reviewer Comments
7/11/03

(b)(4)



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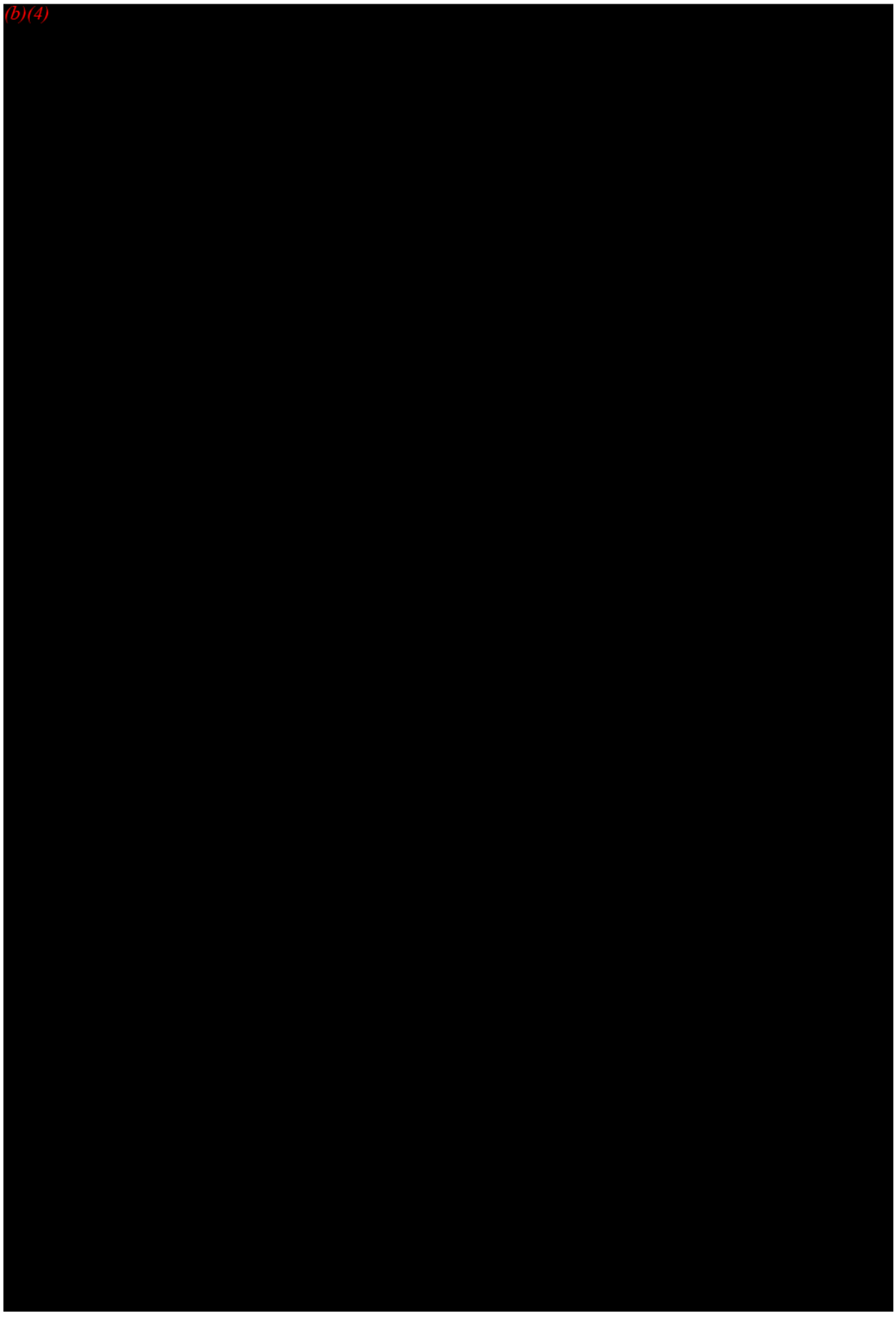

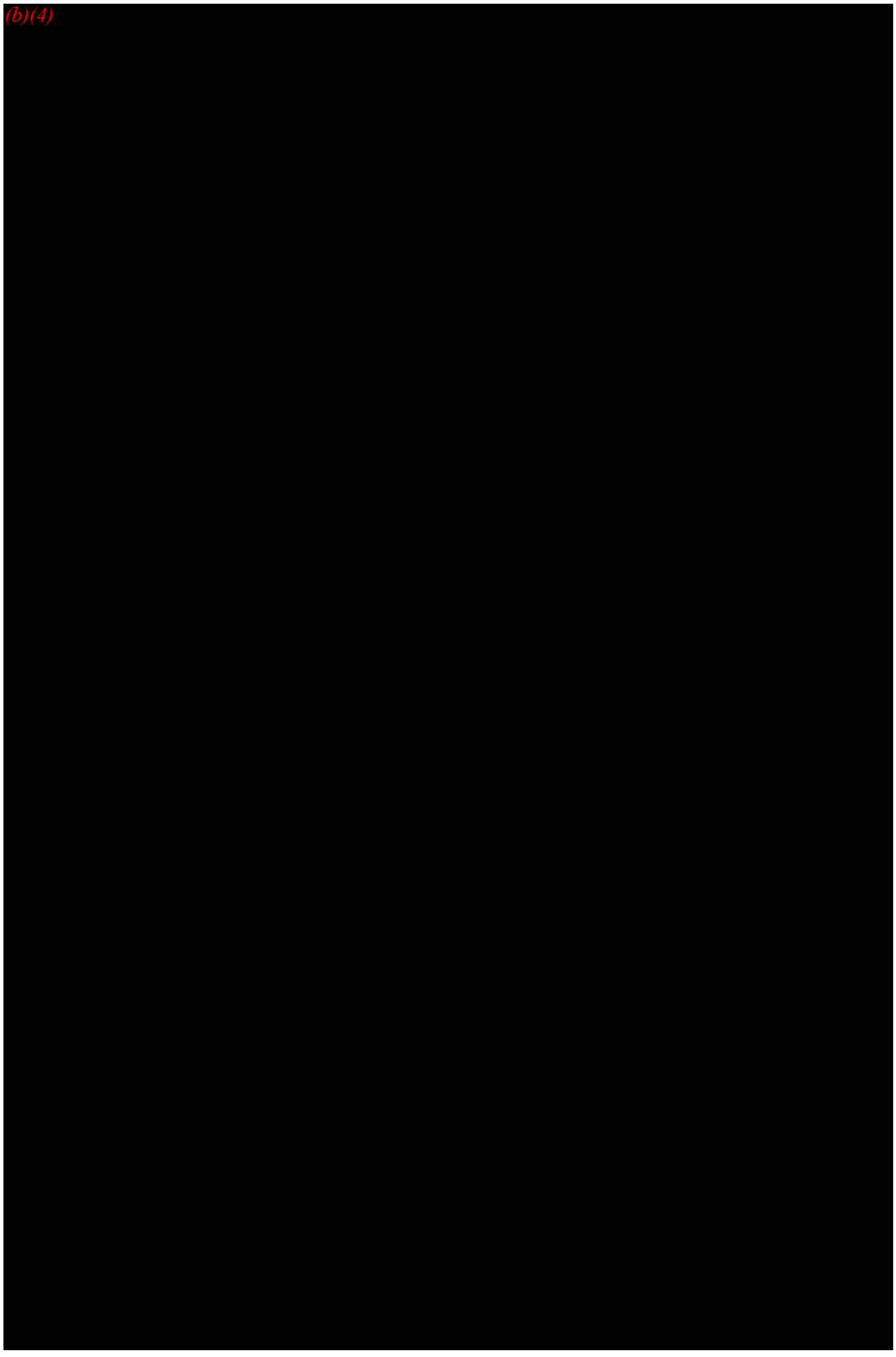

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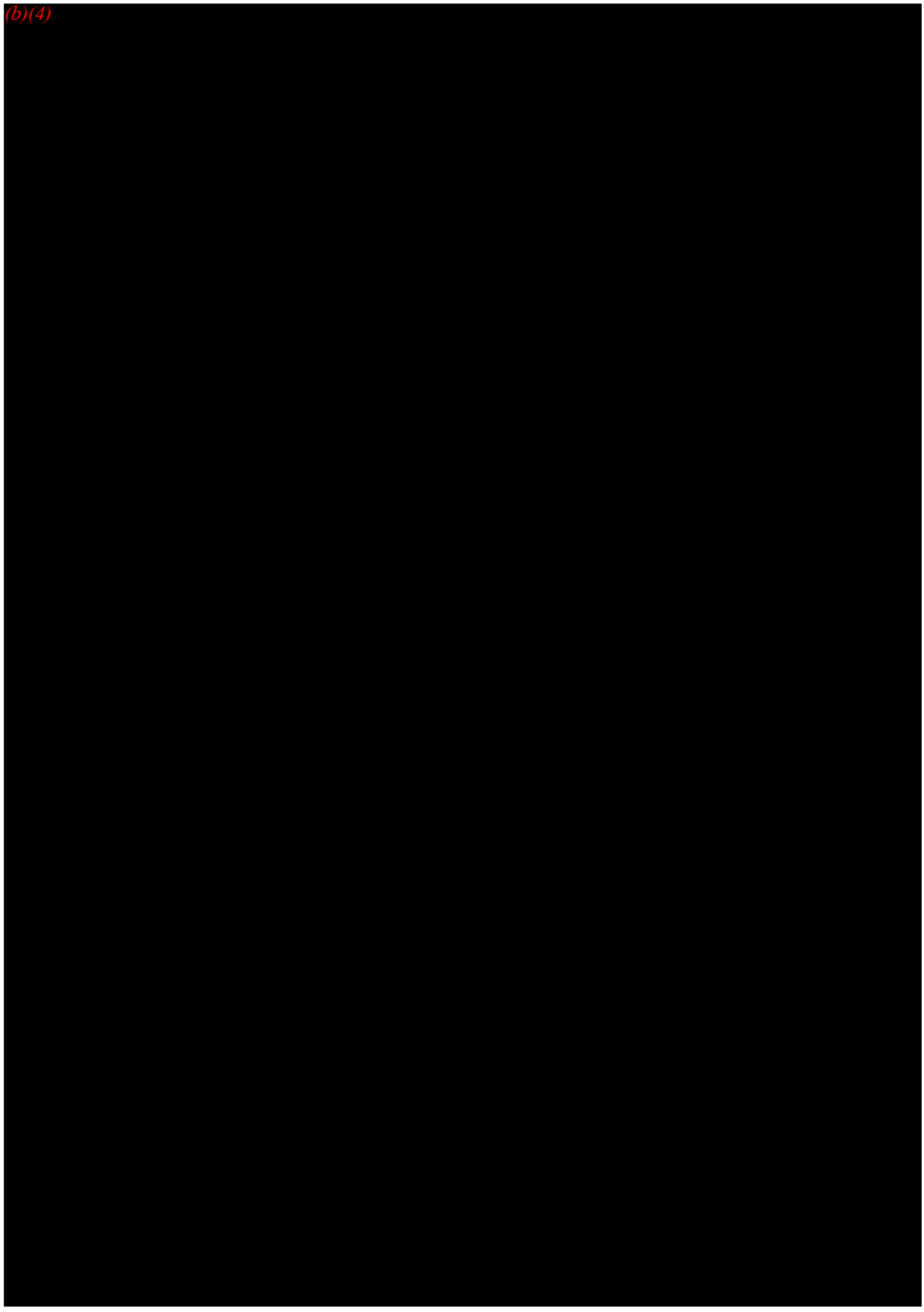

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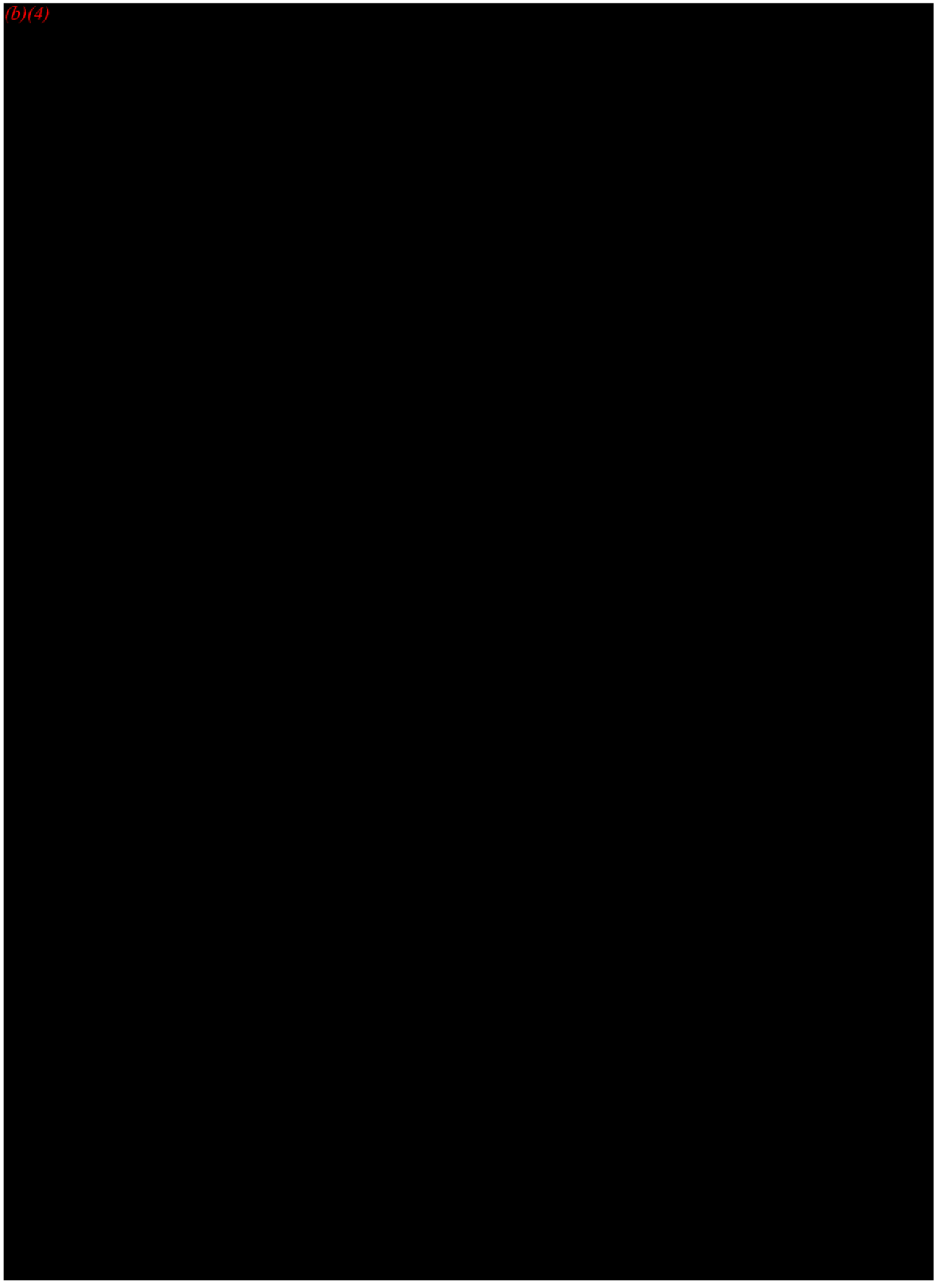


(b)(4)

Attachments

1. Revised pages from the Users Manual. Includes pulse oximetry specification listing sensor types; text regarding O2 and N2O compensation, Revised instructions for use for SPO2 sensor cleaning, and Revised labeling attached. (Front Panel).
2. Test cases for each interface
3. Test cases for alarms
4. Biocompatibility certification statements
5. Magnetic field emissions per MIL-STD
6. Revised intended use statements, and 510(k) summary section.

NICO®

Welcome

General Description

NICO®, a Cardiopulmonary Management System from Respironics Novametrix, LLC., non-invasively measures and displays cardiac output (C.O.). The NICO monitor, Model 7300, also displays cardiac index, stroke volume and pulmonary capillary blood flow, as well as various respiratory monitoring parameters including CO_2 elimination (VCO_2) and alveolar minute ventilation. In Respiratory Mechanics mode, the NICO system can be used as a respiratory profile monitor, without cardiac output displayed. In either mode, the monitor provides the clinician with important information to aid in precise and efficient patient management.

Indications

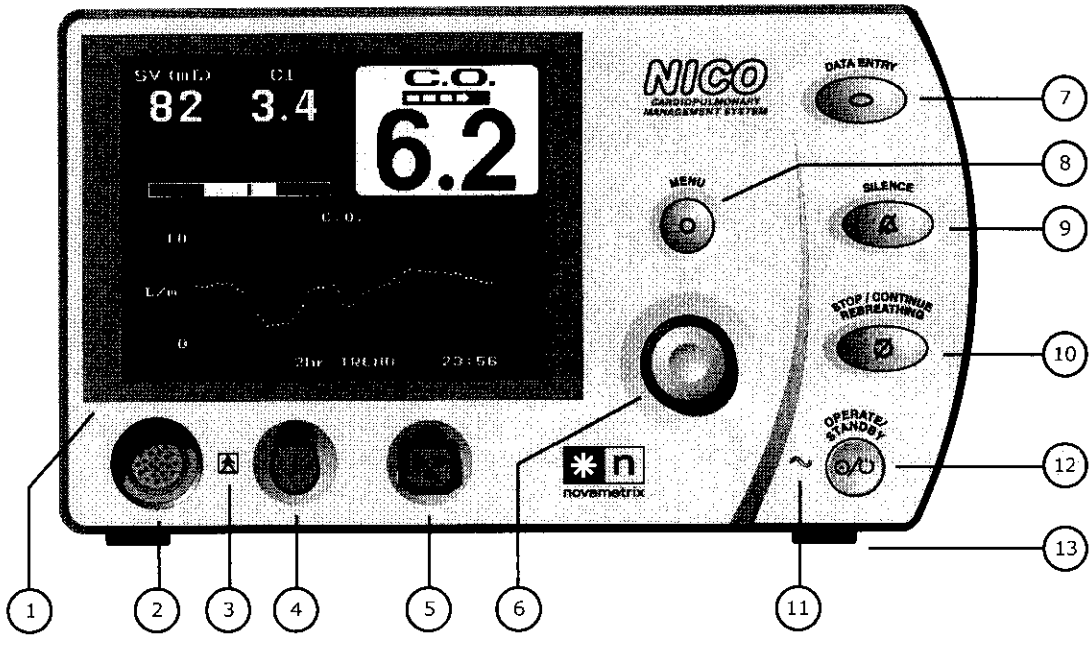
The NICO monitor is indicated for use by technically skilled clinical personnel. In Cardiac Output mode, the monitor is used for the monitoring of cardiac output and various respiratory parameters of adult patients receiving mechanical ventilation. In Respiratory Mechanics mode, the NICO monitor is used for monitoring the respiratory parameters of adult, pediatric and neonatal patients. The pulse oximeter in the NICO monitor is intended to be used for monitoring oxygen saturation and pulse rate in all critical monitoring environments including ventilatory support and anesthesia. It is designed to monitor all patient areas including adult, pediatric and neonatal. The NICO monitor is not intended for any other purpose.

Contraindications

In Cardiac Output mode, use of the NICO monitor is contraindicated in patients in whom a small rise (3-5 mmHg, 0.4-0.67 kPa) in their $PaCO_2$ level cannot be tolerated.

Front Panel

The NICO monitor's front panel includes a display screen, sensor input connectors, a control knob, and operational push button keys and indicators that are explained below.



Rebreathing Paused

- The NICO monitor automatically pauses the rebreathing cycle and generates a display message under any of these conditions:
  - $ETCO_2$ is less than or equal to 15 mmHg (2.0 kPa or %), or greater than or equal to 85 mmHg (11.5 kPa or %)
  - Respiration rate is less than or equal to 3 or greater than or equal to 60 br/min.
  - VCO_2 is less than or equal to 20 mL/min.
- The rebreathing cycle automatically restarts when the condition is corrected.

Entering Patient Data

NICO monitoring can be enhanced by the entry of key patient specific data including respired gas composition (anesthetic agent, balance gas, and inspired O_2), patient height and weight, and arterial blood gas data ($PaCO_2$, PaO_2, Hb or Hct). Inclusion of ABG data is especially important when gas exchange impairment is expected (i.e., high shunt or deadspace). **ABG samples should not be obtained during the rebreathing phase of the 3-minute NICO cycle.**

Patient data should be updated in the **DATA ENTRY** screen whenever possible. The screen may be accessed at any time by pressing the **DATA ENTRY** key.

DATA ENTRY settings The following table lists the parameters and ranges accessible in the **DATA ENTRY** screens.

Label	Parameter	Default	Range/Units	Description
INSP O_2	Inspired Oxygen	40%	21-100 %	Percent of oxygen in the inspired gas. Must be entered in order for NICO to accurately calculate parameters. If FiO_2 is less than 60% and N_2O is selected as the balance gas, an incorrect INSP O_2 setting may cause the reported CO_2 value to be overestimated (too high) by up to 11.7% of its reading. If FiO_2 is greater than 60% and N_2 is selected as the balance gas, an incorrect INSP O_2 setting may cause the reported CO_2 value to be underestimated (too low) by up to 6.4% of its reading.
INSP AGENT	Inspired Anesthetic Agent	0%	0-20 %	Percent of anesthetic agent in the inspired gas. Must enter percent delivered in order to accurately calculate parameters.
BALANCE	Gas Balance	N_2	N_2, He, or N_2O	N_2, He or N_2O. Must select the correct balance in the inspired gas in order to accurately calculate parameters.
HEIGHT	Patient Height	--	35-91 in 90-230 cm	Enter patient height for CI calculations.
WEIGHT	Patient Weight	--	55-551 lb 25-250 kg	Enter patient weight for CI calculations.
ABG DATA ENTRY Screen				

DATA ENTRY settings The following table lists the parameters and ranges accessible in the **DATA ENTRY** screens.

Label	Parameter	Default	Range/Units	Description
INSP O_2	Inspired Oxygen	40%	21-100 %	Percent of oxygen in the inspired gas. Must be entered in order to accurately calculate parameters. If FiO_2 is less than 60% and N_2O is selected as the balance gas, an incorrect INSP O_2 setting may cause the reported CO_2 value to be overestimated (too high) by up to 11.7% of its reading. If FiO_2 is greater than 60% and N_2 is selected as the balance gas, an incorrect INSP O_2 setting may cause the reported CO_2 value to be underestimated (too low) by up to 6.4% of its reading.
INSP AGENT	Inspired Anesthetic Agent	0%	0-20 %	Percent of anesthetic agent in the inspired gas. Must enter percent delivered in order to accurately calculate parameters.
BALANCE	Gas Balance	N_2	N_2, He, or N_2O	N_2, He, or N_2O. Must select the correct balance in the inspired gas in order to accurately calculate parameters.
HEIGHT	Patient Height	--	35-91 in 90-230 cm	Enter patient height (unavailable for neonatal patients in Respiratory Mechanics mode).
WEIGHT	Patient Weight	--	Neonatal: 0.22 - 44.09 lb 0.10 - 20.00 kg Pediatric: 0.2 - 220.2 lb 0.1 - 99.9 kg Adult: 55-551 lb 25-250 kg	Enter patient weight for respiratory mechanics calculations.
ABG DATA ENTRY Screen				
$PaCO_2$	Arterial Carbon Dioxide	40 mmHg (5.4 kPa or %) ("--" displayed until an initial value is entered)	0-250 mmHg 0.0-20.0 kPa 0.0-20.0 %	Partial pressure of carbon dioxide in arterial blood. Enter this value for calculation of Vd alv (alveolar deadspace), Vd/Vt (deadspace to tidal volume ratio). Must enter correct ABG time in order to accurately calculate parameters.
PaO_2	Arterial Oxygen	FiO_2*(Pb-47 mmHg) ("--" displayed until an initial value is entered)	0-750 mmHg 0.0-99.5 kPa 0.0-99.5 %	Partial pressure of oxygen in arterial blood. Enter a value for this parameter if desired; does not affect CO_2/flow calculations.
Hb	Hemoglobin Concentration or Hematocrit	11.0 gm/dL 6.8 mmol/L 33 % ("--" displayed until an initial value is entered)	Hb: 5.0-20.0 gm/dL Hb: 3.1-12.4 mmol/L Hct: 0-60 %	Concentration of hemoglobin or hematocrit in the blood. Enter a value for this parameter if desired; does not affect CO_2/flow calculations.

NICO®

Maintenance

This section details routine maintenance procedures for the NICO® monitor, its sensors and accessories.

Cleaning and Disinfection

To clean and/or disinfect the monitor and its accessories:

Single Patient Use NICO Sensor

- Treat the NICO Sensor in accordance with hospital protocol for single-patient use items.

CO_2/Flow Sensors

- Treat CO_2/Flow sensors in accordance with hospital protocol for single-patient use items.

CAPNOSTAT® CO_2 Sensor

- Do not immerse the sensor. Do not disinfect the sensor.
- The sensor can be cleaned and disinfected by wiping with solutions such as a 70% isopropyl alcohol, 2% gluteraldehyde, or 10% bleach solution. Then wipe down with a water dampened clean cloth to rinse. Dry before use.
- Make certain that the sensor windows are clean and dry before reuse.

NICO Monitor

- Do not immerse the monitor. Do not disinfect the monitor.
- Turn the monitor off and unplug from the AC power source before cleaning.
- The monitor can be cleaned and disinfected by wiping with solutions such as a 70% isopropyl alcohol, 2% gluteraldehyde, or 10% bleach solution. Then wipe down with a water dampened clean cloth to rinse. Dry before use.

SpO_2 Finger Sensor

- Do not immerse the finger sensor. Do not disinfect the finger sensor.
- The sensor can be cleaned and disinfected by wiping with solutions such as a 70% isopropyl alcohol, 2% gluteraldehyde, or 10% bleach solution. Then wipe down with a water dampened clean cloth to rinse. Dry before use.
- Make certain that the finger sensor windows are clean and dry before reuse.
- After cleaning the finger sensor, perform a Quick Check to verify the sensor is functional (See "Sensor Quick Check" on page 75).

SpO_2 Y-Sensor

- The Y-Sensor may be immersed up to—but not including—the connector, in solutions such as a 70% isopropyl alcohol, 2% gluteraldehyde, or 10% bleach solution. Rinse thoroughly with water and dry before use. (Do not rinse the connector).
- After cleaning or disinfecting the Y-Sensor, perform a Quick Check to verify the sensor is functional (See "Sensor Quick Check" on page 75).

SpO_2 Tapes and Foam Wraps

- Treat tapes and foam wraps in accordance with hospital protocol for single-patient use items.

Ear Clip

- Clean with a cloth dampened with 70% isopropyl alcohol. After cleaning, thoroughly wipe the ear clip with a clean, water dampened cloth.

- Neonatal: 1-100
- Airway Pressure Range (cmH_2O): ± 120
  - Accuracy: greater of 0.5 cmH_2O or ± 2% reading
- Gas composition effects: O_2, anaesthetic agent, CO_2, N_2O, N_2, He (operator selectable)

SpO_2

- Oxygen Saturation
  - Range: 0-100%
  - Accuracy: ± 2% for 70 -100%, ± 3% during motion conditions, for 1 standard deviation, unspecified for 0-69%. Applies to Finger Sensor, Y-Sensor®, and Single Patient Use (SPU) sensors.
  - Averaging Time: 2 seconds, or selectable, none, 2, 4, or 8 seconds (MARS Mode only).
  - Display Resolution: 1%
  - Settling Time: Display settles to within 1% of the final reading less than 15 seconds after the sensor is properly applied.
- Pulse Rate:
  - Range: 30-250 beats per minute
  - Accuracy: ± 1% of full scale (for 1 standard deviation or approximately 68% of readings)
  - Averaging Time: 8 seconds, or selectable 0, 2, 4, or 8 seconds, based on SpO_2 setting (MARS Mode only).
  - Display Resolution: 1 bpm
  - Settling Time: Display settles to within 1% of the final reading less than 15 seconds after the sensor is properly applied.

Monitor Specifications

- Classification (IEC601-1): Class I/internal power source, type BF, continuous operating mode, enclosure protection rating IPX0.
- Operating Environment: 50-104° F (10-40° C), 10-90% relative humidity (non-condensing)
- Size: Height 6.5 in., Width 10.75 in., Depth 9.5 in.
- Weight: 9 lbs, 6 oz.
- Power: 100-240 VAC, 50-60 Hz, 70VA
- Fuse Rating: 100-120 VAC, 1.0 A/250 V Slo-Blo (x2); 200-240 VAC, T 500 mA/250 V (x2)
- Battery: Internal, Sealed lead-acid gel-cell, 45 minute life on full charge (on-screen life indicator), 12 hours recharge time.
- Display: 4.625 x 3.5 inch EL, 320 x 240 pixels
- Electromagnetic Emissions: Conforms to EMC Directive 93/42/EEC, CISPR Class A. Tested to EN55011 (1998) and CISPR11 (1999).
- Electromagnetic Immunity: Conforms to EMC Directive 93/42/EEC. Tested to IEC60601-1-2 (2001), IEC61000-4-2 (2001) ESD, IEC61000-4-3 (2002) RF, IEC61000-4-4 (1995) EFT, IEC61000-4-5 (2001) Surge, IEC61000-4-6 (2001) Conducted RF, IEC61000-4-8 (2001) Magnetic Fields, IEC61000-4-11 (2001) Voltage Dips, Interruptions and Variations, IEC61000-3-2 (2001) Harmonic Distortion, IEC61000-3-3 (2002) Voltage Fluctuations and Flicker.

RS232 Communications

- RS232 Communications Ports:

Pin #	RS232-1	RS232-2	RS232-3
2	Rx	Rx	Rx
3	Tx	Tx	Tx
5	Ground	Ground	Ground
7	n/a	RTSB	n/a
8	n/a	CTSB	n/a
9	n/a	Power	n/a

Analog Specifications

- Analog Input/Output Port (selectable, 0 to 1 volt range):
  - C.O. - Cardiac Output, 0-20 L/m, 50mV/L/m
  - CI - Cardiac Index, 0-20 L/m, 50mV/L/m
  - SV - Stroke Volume, 0-20 L/m, 50mV/L/m
  - PCBF - 0-20 L/m, 50 mV/L/m
  - $ETCO_2$ - 0-150 mmHg, 0-20 kPa or %, 6.67mV/mmHg
  - SpO_2 - 0-100%, 10mV/%

Respironics Novametrix

CONFIDENTIAL

EPD98145-008
Host Communications - Command Set Test

(b) (6) [redacted]

Author: [redacted]

Editor: [redacted]

Approvals:

(b) (6) [redacted]

Engineering:

Peer Review ____ Date 19 Feb 2003

Software Coordinator ____ Date 19 Feb 2003

Project Manager ____ Date 18 Feb 03

Revision Record

Revision	Date	Prepared By	Changes
(b) (6), (b) (4) [redacted]			

Referenced Documents

(b)(4) [redacted]

Test

(b)(4) [redacted]

Step	Operator Actions	Expected Result	Response
(b)(4)			

Step	Operator Actions	Expected Result	Reference

(b)(4)

[redacted]

Step	Operator Actions	Expected Result	Response
(b)(4)			

Step	Operator Actions	Expected Result	Response
(b)(4)			

45

Step	Operator Actions	Expected Result	Response
(b)(4)	[redacted]		

Step	Operator Actions	Expected Result	Response
(b)(4)			

Respironics Novametrix

CONFIDENTIAL

EPD98145-009
Host Communications: Waveform Mode Test

Editors: (b) (6) [redacted]

Approvals:

Engineering: (b) (6) [redacted]

Peer Review — Date 18 Feb 03

Project Manager — Date 18 Feb 03

Software Coordinator — Date 18 Feb 2003

Revision Record

Revision	Date	Prepared By
(b) (6), (b) (4) [redacted]		

48

Referenced Documents

(b)(4) [redacted]

Test

(b)(4) [redacted]

Step	Operator Actions	Expected Result	Response
(b)(4)	[redacted]		

50

EPD98145-92
HP VueLink Interface: Data Validation

Editor: (b) (6) [redacted]

Approvals:

Engineering: (b) (6) [redacted]

Peer Review Date 6Dec 2000

Software Coordinato Date 7Dec 2000

Project Manager Date 6Dec 2000

Revision Record

Revision	Date	Prepared By
(b) (4), (b) (6) [redacted]		

Referenced Documents

(b)(4)

[redacted]

Test

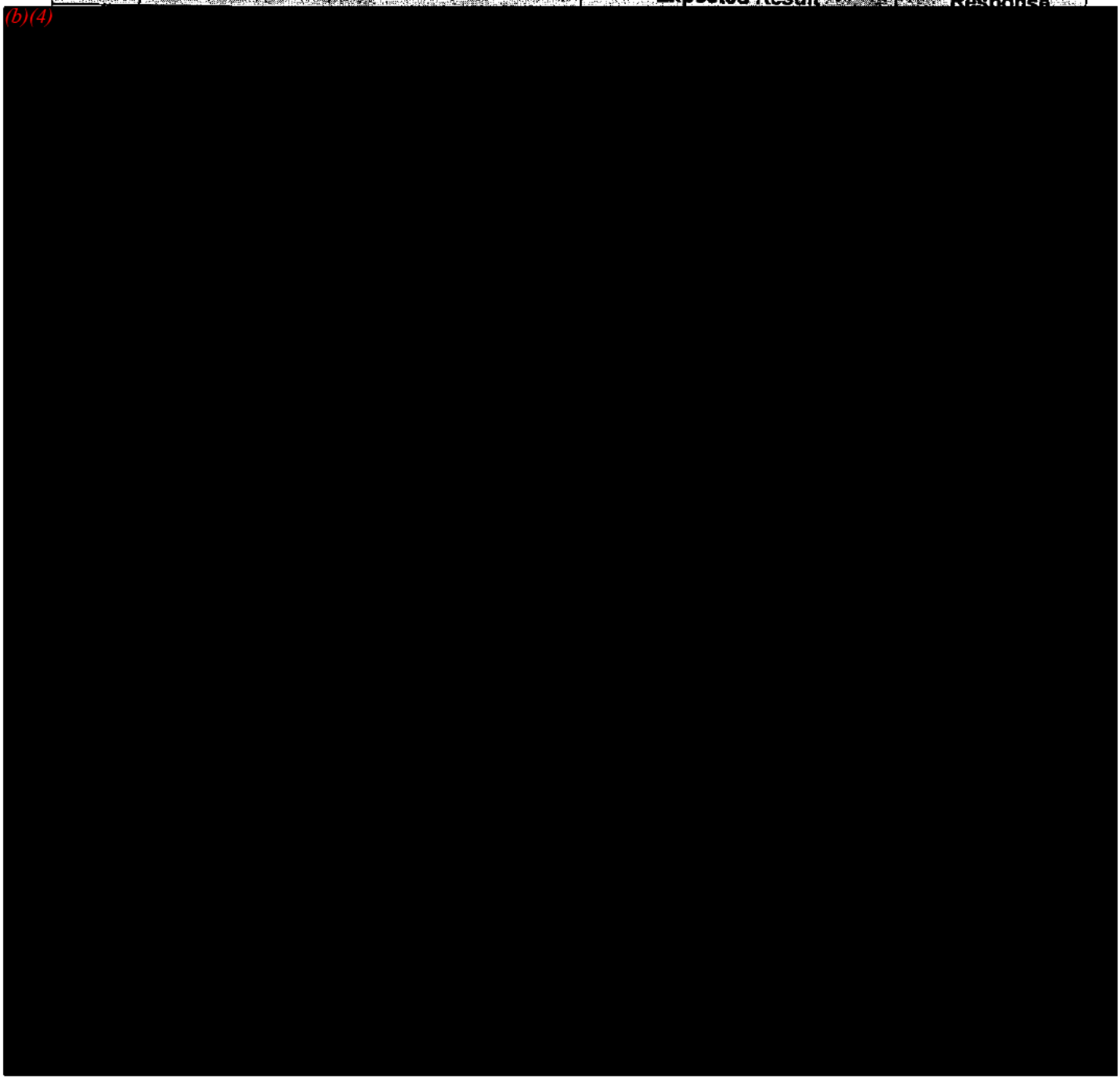
(b)(4)

[redacted]

Step	Operator Actions	Expected Result	Response
(b)(4)	[redacted]		

Step	Operator Actions	Expected Result	Response

(b)(4)



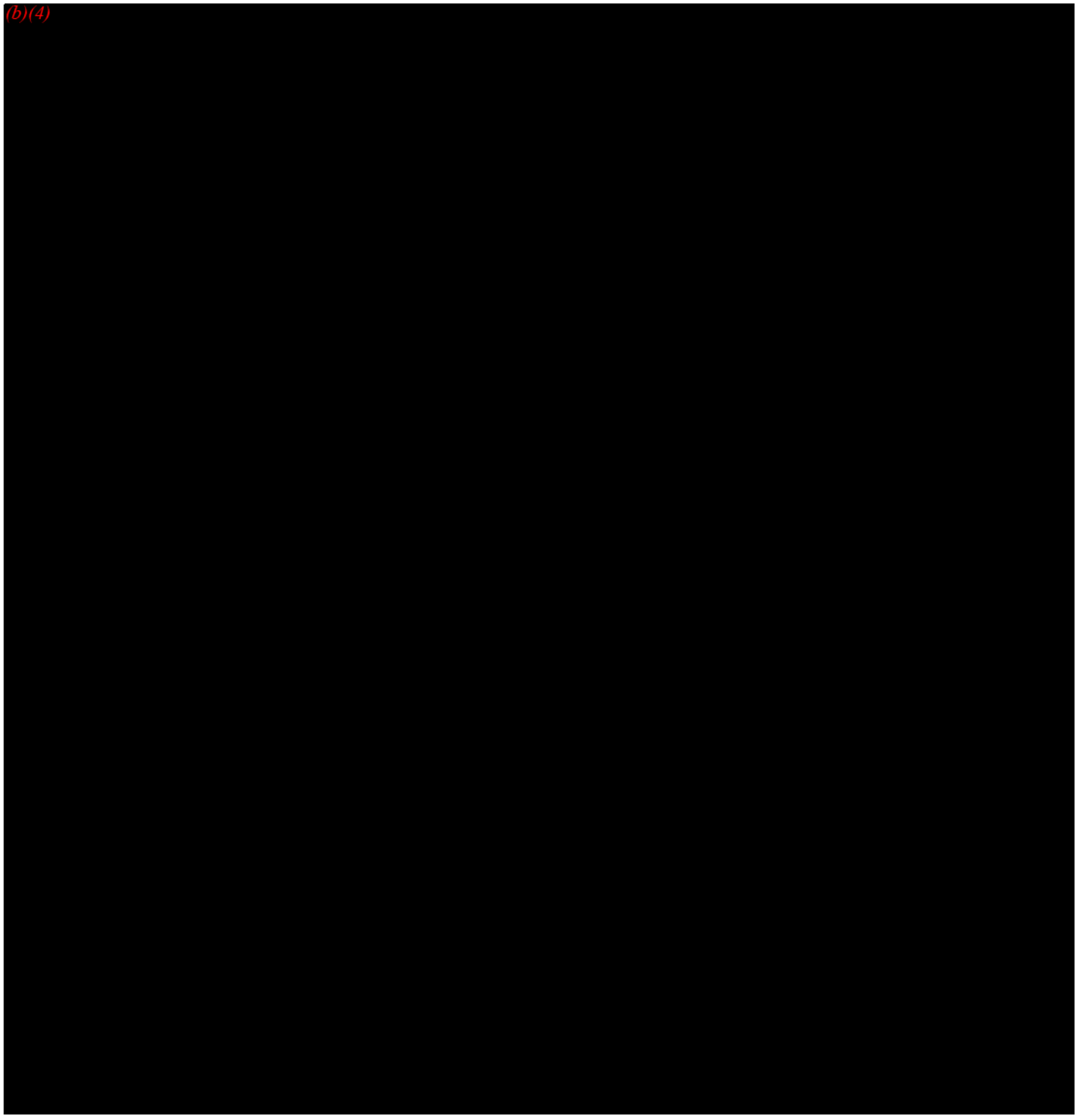
Step	Operator Actions	Expected Result	Response
(b)(4)	[redacted]		

Step	Operator Actions	Expected Result	Response
(b)(4)	[redacted]		

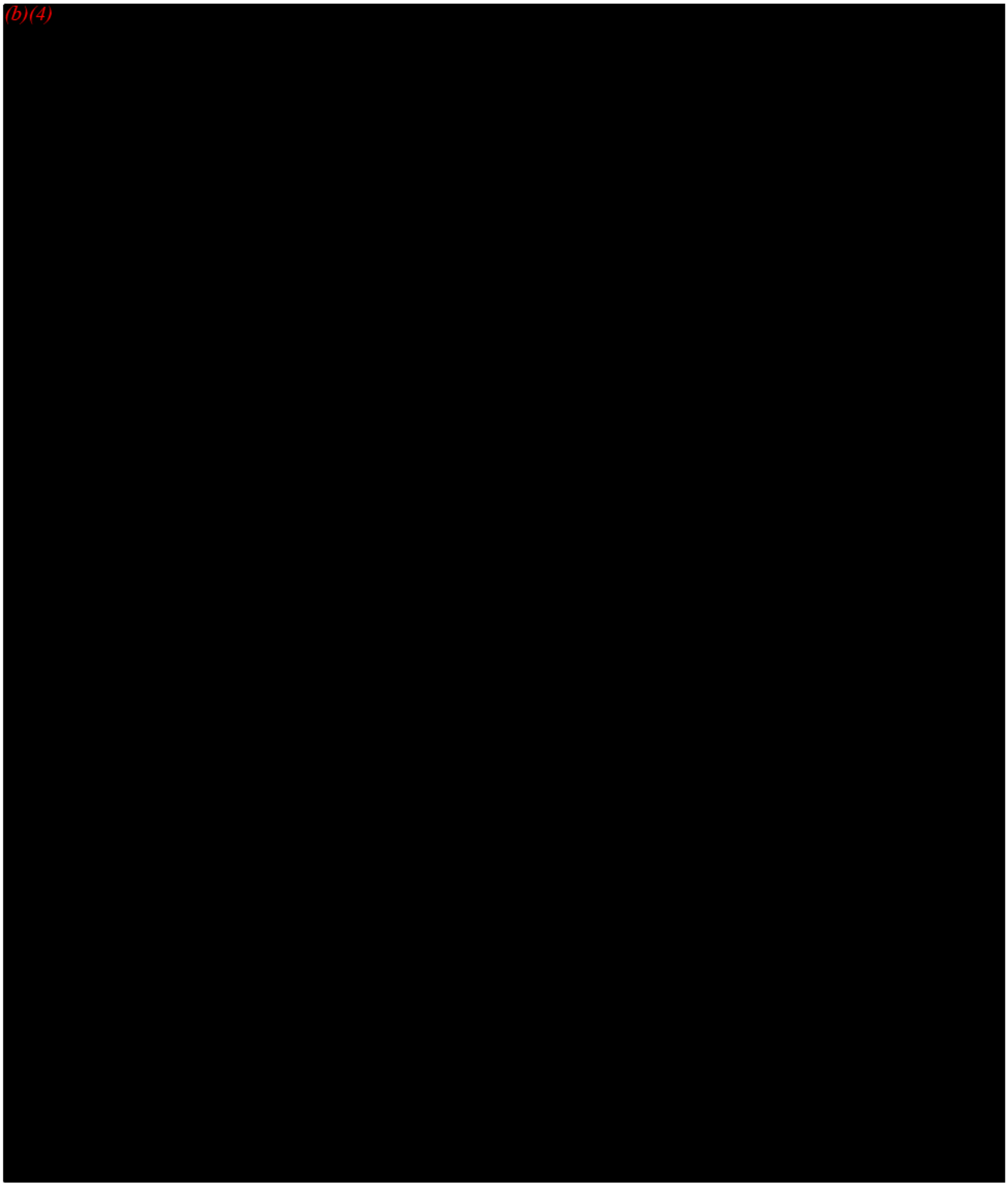
Step	Operator Actions	Expected Result	Response
(b)(4)	[redacted]		

57

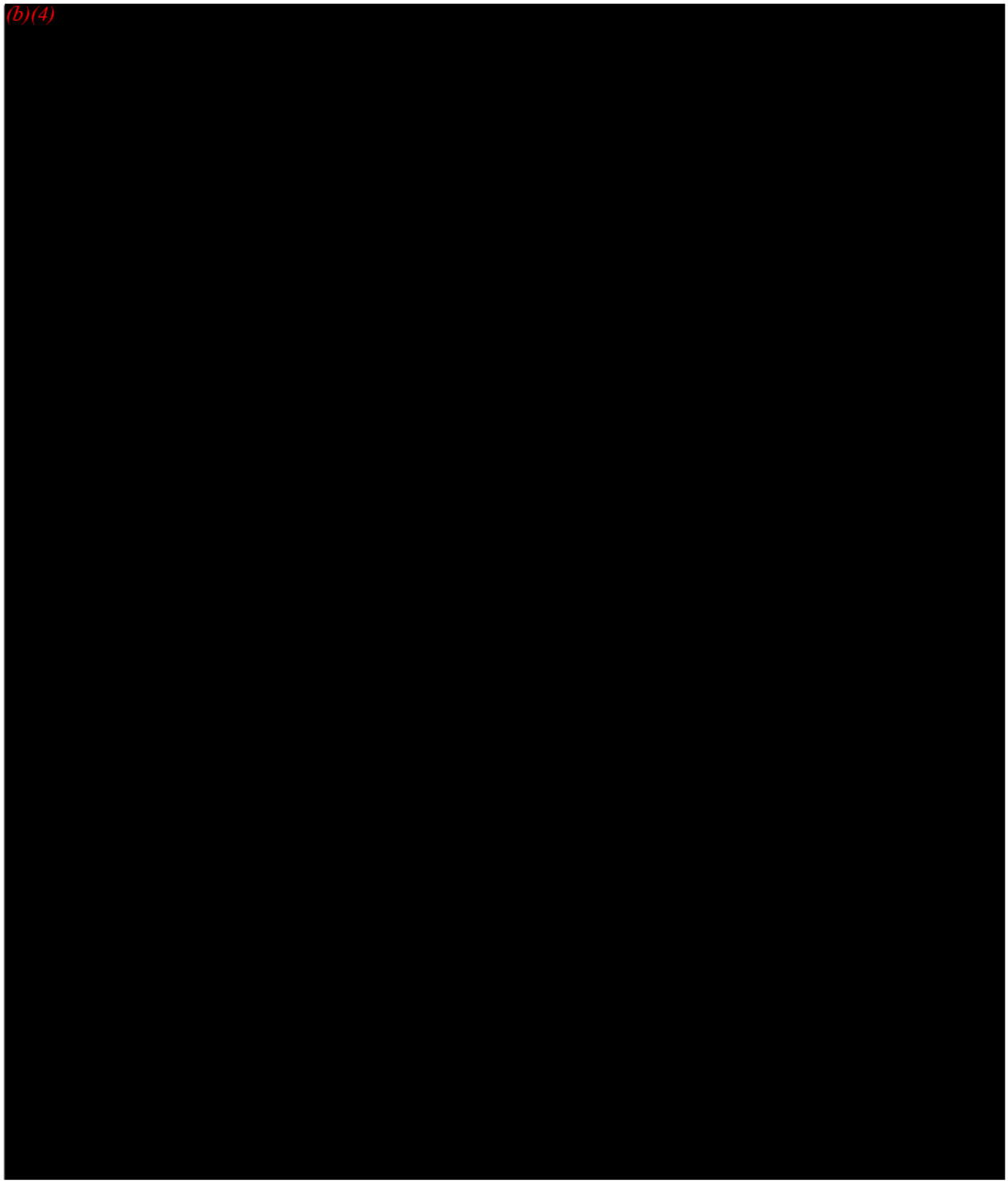
(b)(4)



(b)(4)



(b)(4)



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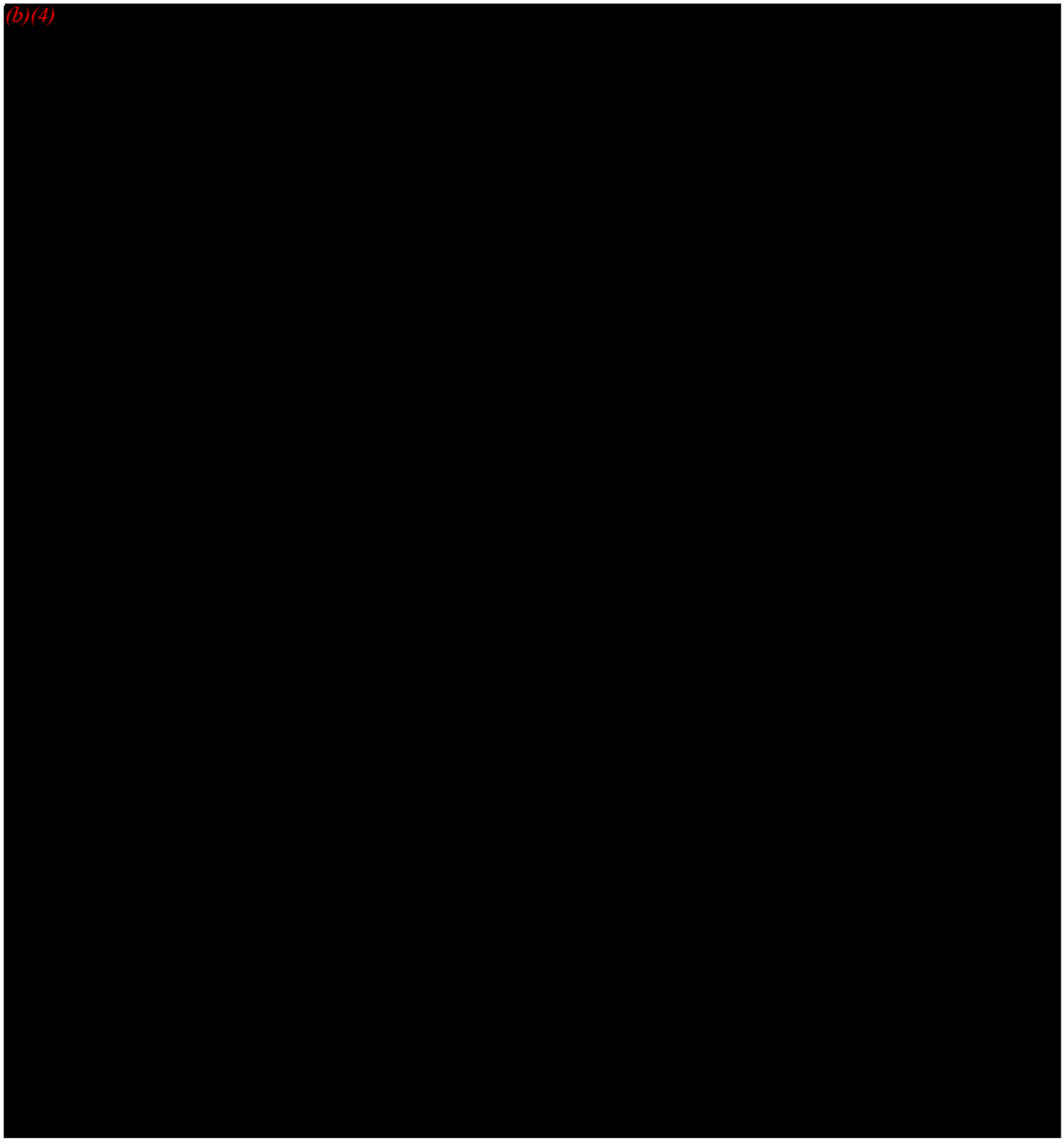


Novametrix Medical Systems 1 hr CONFIDENTIAL

EPD98145-93
HP VueLink Interface: Specification File Validation

Author: (b) (6) [redacted]

Approvals:

Engineering: (b) (6) [redacted]

Peer Review _____ Date 6 Dec 2000

Software Coordinator _____ Date 7 Dec 2000

Project Manager _____ Date 6 Dec 2000

Revision Record

Revision	Date	Prepared By
(b)(4) [redacted]		

62

Referenced Documents

Test

(b)(4)

[redacted]

Step	Operator Actions	Expected Result	Response

(b)(4)

[redacted]

Step	Operator Actions	Expected Result	Response
(b)(4)	[redacted]		

Step	Operator Actions	Expected Result	P
(b)(4)			

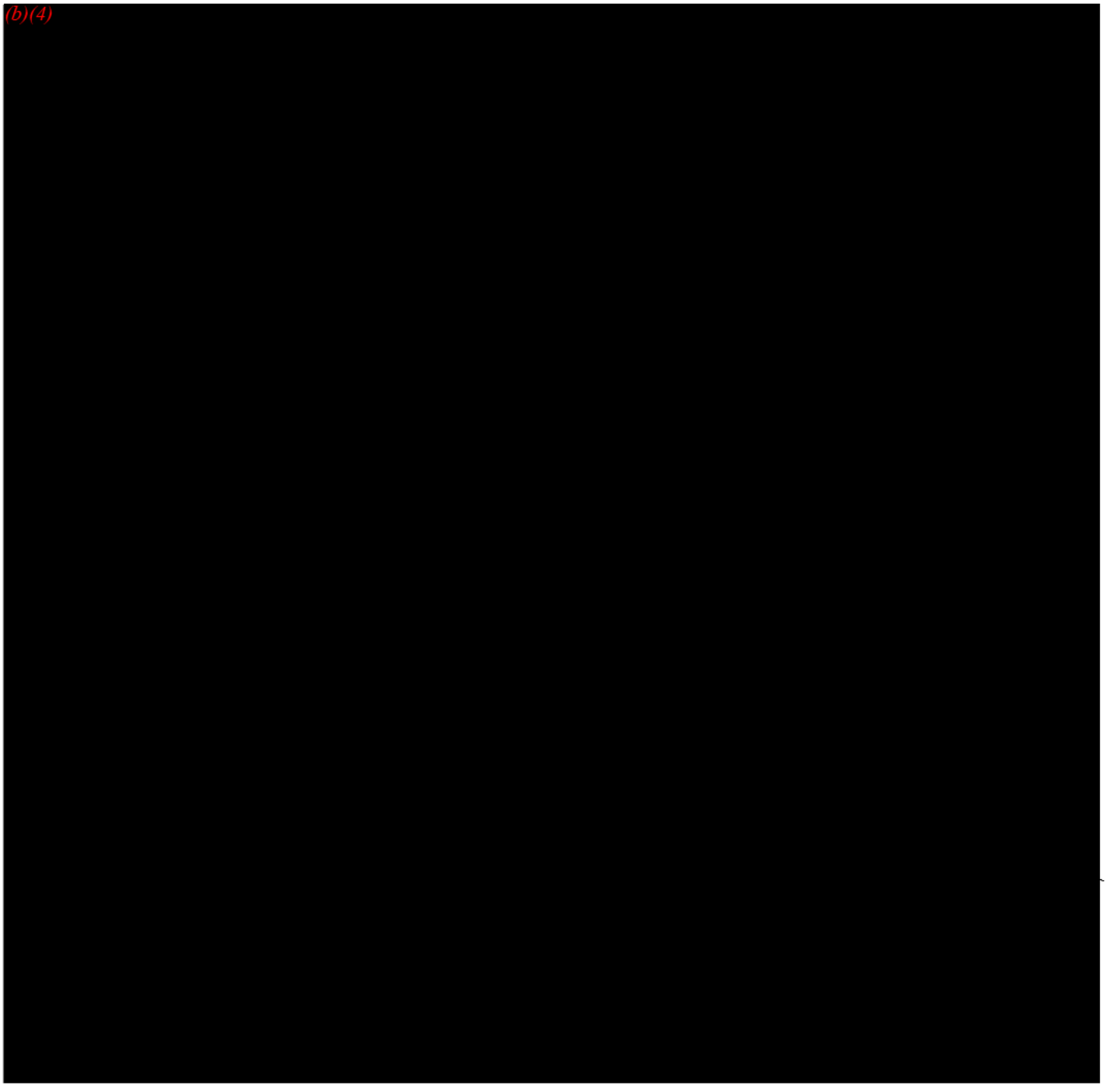
Step	Operator Actions	Expected Result	Response
(b)(4)	[redacted]		

Step	Operator Actions	Expected Result	Response
(b)(4)			

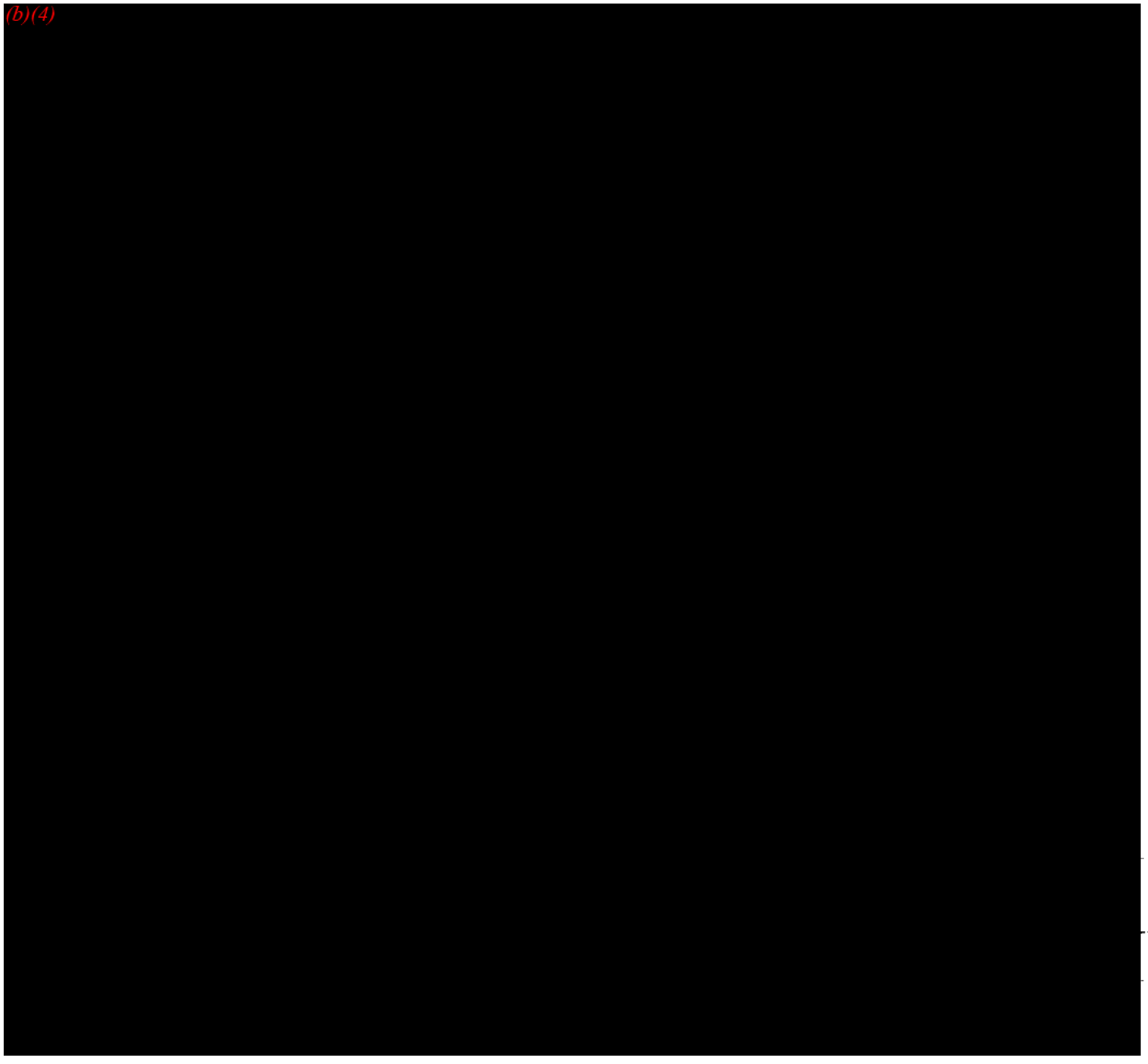
(b)(4)

68

(b)(4)



(b)(4)



70

EPD98145-94
HP VueLink Interface: Communication Faults

Author (b) (6) [redacted]

Approvals:

Engineering: (b) (6) [redacted]

Peer Review Date 6Dec2000

Software Coordinator Date 4Dec2000

Project Manager Date 6Dec2000

Revision Record

Revision	Date	Prepared By
(b)(4) [redacted]		

71

Referenced Documents

Test

(b)(4)

[redacted]

Step	Operator Actions	Expected Result	Response

(b)(4)

[redacted]

Step	Operator Actions	Expected Result	Response
(b)(4)	[redacted]		

Step	Operator Actions	Expected Result	
(b)(4)	[redacted]		

EPD98145-115
Serial Communications: N-395 Interface

Author: (b) (6) [redacted]

Approvals:

(b) (6) [redacted]

Engineering:

Peer Review — Date 19 Feb 2003

Project Manager — Date 11 Feb 03

Software Coordinator — Date 19 Feb 2003

Revision Record

Revision	Date	Prepared By	Changes
(b)(4) [redacted]			

75

Referenced Documents

(b)(4) [redacted]

Test

(b)(4) [redacted]

Step	Operator Actions	Expected Result	Report
1.0	Initialization		

(b)(4) [redacted]

Step	Operator Actions	Expected Result	Response if not as expected

(b)(4)

[redacted]

Step	Operator Actions	Expected Results	System Response
(b)(4)			

Step	Operator Actions	Expected Result	Responsible Person
(b)(4)			

Step	Operator Actions	Expected Results	Pass/Fail
(b)(4)			

Step	Action/Activity	Expected Result	Response
(b)(4)			

EPD98145-119
Serial Communications: Flexport Interface

Author: (b) (6) [redacted]

Approvals:

(b) (6) [redacted]

Engineering:

Peer Review Date 19 Sept 01

Project Manager Date 19 Sept 01

Software Coordinat Date 19 Sept 2001

Revision Record

Revision	Date	Prepared By	Changes
(b) (6), (b) (4) [redacted]			

Referenced Documents

(b)(4) [redacted]

Test

(b)(4) [redacted]

Step	Operator Actions	Expected Result	Response
(b)(4) [redacted]			

Step	Operator Actions	Expected Result	Response
(b)(4)	[redacted]		
	the menu.		

Step	Operator Actions	Expected Result	Response
(b)(4)			

Step	Operator Actions	Expected Result	Response
(b)(4)	[redacted]		

Step	Operator Actions	Expected Result	Response
(b)(4)			

Step	Operator Actions	Expected Result	Response
(b)(4)	[redacted]		

Step	Operator Actions	Expected Result	Response
(b)(4)	[redacted]		

Step	Operator Actions	Expected Result	Response
(b)(4)	[redacted]		

Step	Operator Actions	Expected Result	Response
(b)(4)	[redacted]		

Step	Operator Actions	Expected Result	Response
(b)(4)	[redacted]		

Step	Operator Actions	Expected Result	Response
(b)(4)	[redacted]		

Step	Operator Actions	Expected Result	Response Done
(b)(4)	[redacted]		

Step	Operator Actions	Expected Result	

(b)(4)

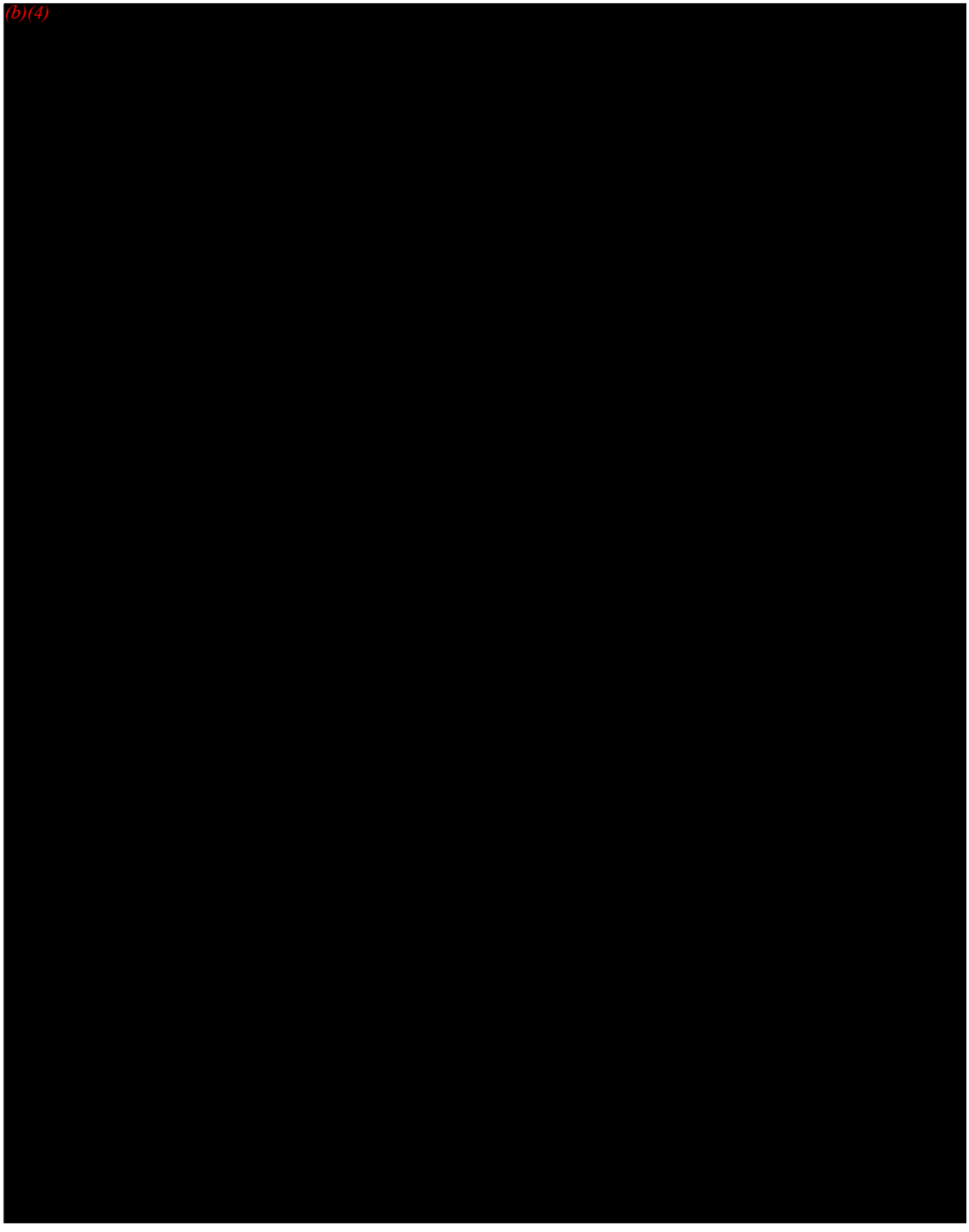
[redacted]

(b)(4)

[redacted]

96

(b)(4)



(b)(4)

98

EPD98145-074
User Interface: Set Alerts Screen - Adjustments

Editor: (b) (6) [redacted]

Approvals:

(b) (6) [redacted]

Engineering:

Peer Review — Date 10 Feb 2003

Project Manager — Date 10 Feb 03

Software Coordinator — Date 10 Feb 2003

Revision Record

Revision	Date	Prepared By	Changes
(b) (6), (b) (4) [redacted]			

Referenced Documents

(b)(4) [redacted]

Test

(b)(4) [redacted]

Step	Operator Action	Expected Result	P/F
(b)(4) [redacted]			

100

Step	Operator Actions	Expected Results	Pass/Fail
(b)(4)			

101

Step	Operator Actions	Expected Result	Response
(b)(4)			

102

Step	Operator Action	Expected Result	Pass/Fail
(b)(4)			
	the set values in Table 3.		

Step	Operator Actions	Expected Results	Pass/Fail
(b)(4)			

Step	Operator Actions	Expected Result	Response

(b)(4)

[redacted]

Connec
Adult
Sensor
MP 3-3

105

(b)(4)

[redacted]

106

(b)(4)

[redacted]

107

EPD98145-128
User Interface - Invalid Limits Settings Test

Author (b) (6) [redacted]

Approvals:

Engineering: (b) (6) [redacted]

Peer Review — Date 10 Feb 2003

Project Manager — Date 10 Feb 03

Software Coordinator — Date 10 Feb 2003

Revision Record

Revision	Date	Prepared B
(b) (6), (b) (4) [redacted]		

108

Referenced Documents

(b)(4) [redacted]

Test

(b)(4) [redacted]

(b)(4) [redacted]

Step	Operator Actions	Expected Results	Responses
(b)(4)			

110

Step	Operator Actions	Expected Result	Response
(b)(4)	[redacted]		

111

EPD98145-123
User Interface: Set Alerts Screen - Auto Limits

Edito [redacted]

Approvals:

Engineering:

Peer Review [redacted] Date 10 Feb 2003

Project Manager Date 10 Feb 03

Software Coordinat Date 10 Feb 2003

Revision Record

Revision	Date	Prepared By	Changes
[redacted]			

Referenced Documents

(b)(4) [redacted]

Test

(b)(4) [redacted]

Step	Operator Actions	Expected Results
(b)(4) [redacted]		

Step	Operator Actions	Expected Result	Response
(b)(4)			

Step	Operator Actions	Expected Result	
(b)(4)	[redacted]		

115

(b)(4)

116

EPD98145-122
User Interface: Set Alerts Screen
Limit Violations - Mechanics Mode

(b) (6) [redacted]

Edito

Approvals:

Engineering:

Peer Review (b) (6) [redacted] Date 10 Feb 2003

Project Manager Date 10 Feb 03

Software Coordinator Date 10 Feb 2003

Revision Record

Revision	Date	Prepared By	Chan
(b) (6), (b) (4) [redacted]			

117

Referenced Documents

(b)(4) [redacted]

Test

(b)(4) [redacted]

Step	Operator Actions	Expected Result
(b)(4) [redacted]		

118

Step	Operator Actions	Expected Result	Response
(b)(4)	[redacted]		

119

Step	Operator Actions	Expected Result	Response
(b)(4)	[redacted]		

Step	Operator Actions	Expected Result	Response
(b)(4)	[redacted]		

121

(b)(4)

122

EPD98145-121
User Interface: Set Alerts Screen - No Resp Timeout

Editor (b) (6) [redacted]

Approvals:

Engineering: (b) (6) [redacted]

Peer Review — Date 10 Feb 2003

Project Manager — Date 10 Feb 03

Software Coordinator — Date 10 Feb 2003

Revision Record

Revision	Date	Prepared By
(b) (6), (b) (4) [redacted]		

Referenced Documents

(b)(4) [redacted]

Test

(b)(4) [redacted]

Step	Operator Actions	Expected Result	Pass
(b)(4) [redacted]			

Step	Operator Actions	Expected Result	Response
(b)(4)	[redacted]		

EPD98145-120
User Interface: Set Alerts Screen
Limit Violations - NICO Mode

Editor: (b) (6) [redacted]

Approvals:

(b) (6) [redacted]

Engineering:

Peer Review — Date 10 Feb 2003

Project Manager — Date 10 Feb 03

Software Coordinato — Date 10 Feb 2003

Revision Record

Revision Date

(b) (6), (b) (4) [redacted]

126

Referenced Documents

(b)(4) [redacted]

Test

(b)(4) [redacted]

Step	Operator Actions	Expected Result	Pass/Fail
(b)(4) [redacted]			

Step	Operator Actions	Expected Result	Response
(b)(4)	[redacted]		

Step	Operator Actions	Expected Result	Reference
(b)(4)			

Step	Operator Actions	Expected Result	Response
(b)(4)	[redacted]		

130

Step	Operator Actions	Expected Results	Pass/Fail
(b)(4)			

Step	Operator Actions	Expected Results	Response
(b)(4)			

Step	Operator Actions	Expected Results
(b)(4)	[redacted]	

Step	Operator Actions	Expected Result	Response
(b)(4)	[redacted]		

134

Step	Operator Actions	Expected Results	R
(b)(4)	[redacted]		

Biocompatibility

Biocompatibility Certification for Components in Gas Path– Combined CO2/flow sensors and NICO sensors

The Medical Grade PVC tubing of the pediatric/adult CO2/flow sensor, NICO CO2/flow sensor, neonatal CO2/flow sensor and pediatric CO2/flow sensor of the NICO with MARS is identical to the pediatric/adult CO2/flow sensor, NICO CO2/flow sensor, and neonatal CO2/flow sensor, respectively of the CO2SMO Plus! with NICO Model 8200 as it was approved in K982499 in formulation, processing, and sterilization, and no other chemicals have been added (e.g., plasticizers, fillers, color additives, cleaning agents, mold release agents, etc.).

The Polycarbonate body of the pediatric/adult CO2/flow sensor, and neonatal CO2/flow sensor of the NICO with MARS is identical to the pediatric/adult CO2/flow sensor, and neonatal CO2/flow sensor, respectively of the CO2SMO Plus! with NICO Model 8200 as it was approved in K982499 in formulation, processing, and sterilization, and no other chemicals have been added (e.g., plasticizers, fillers, color additives, cleaning agents, mold release agents, etc.).

The Polycarbonate body of the pediatric CO2/flow sensor of the NICO with MARS is identical to the pediatric/adult CO2/flow sensor of the CO2SMO Plus! with NICO Model 8200 as it was approved in K982499 in formulation, processing, and sterilization. A color additive was added and the Tripartite tests were repeated for the this sensor and is attached.

The window film of the pediatric/adult CO2/flow sensor, NICO CO2/flow sensor, neonatal CO2/flow sensor and pediatric CO2/flow sensor of the NICO with MARS is identical to the pediatric/adult CO2/flow sensor, NICO CO2/flow sensor, neonatal CO2/flow sensor and pediatric CO2/flow sensor, respectively of the CO2SMO Plus! with NICO Model 8200 as it was approved in K982499 in formulation, processing, and sterilization, and no other chemicals have been added (e.g., plasticizers, fillers, color additives, cleaning agents, mold release agents, etc.).

The Propylene/Ethylene/Copolymer Combined CO2/Flow Sensor expandable tubing portion of the valve of the standard NICO sensor of the NICO with MARS is identical to the standard NICO sensor of the CO2SMO Plus! with NICO Model 8200 as it was approved in K982499 in formulation, processing, and sterilization, and no other chemicals have been added (e.g., plasticizers, fillers, color additives, cleaning agents, mold release agents, etc.).

The Propylene/Ethylene/Copolymer Combined CO2/Flow Sensor expandable tubing portion of the valve of the small and large NICO sensor of the NICO with MARS is identical to the standard NICO sensor of the CO2SMO Plus! with NICO Model 8200 as it was approved in K982499 in formulation, processing, and sterilization. A color additive was added and the Tripartite tests were repeated for the these loops and was provided with the submission.

The silicone rubber used for the NICO valve diaphragm of the NICO with MARS is similar to the NICO valve diaphragm of the CO2SMO Plus! with NICO Model 8200 as it was approved in K982499 in formulation, processing, and sterilization. Certification of biocompatability testing per ISO 10993-1 is attached.

The Modified Acrylic used for the NICO combined CO2/Flow Sensor body, NICO valve body, connecting rod in the valve body and the male connector of the NICO combined CO2/Flow Sensor of the NICO with MARS is identical to the NICO combined CO2/Flow Sensor body, NICO valve body, connecting rod in the valve body and the male connector of the NICO combined CO2/Flow Sensor, respectively of the CO2SMO Plus! with NICO Model 8200 as it was approved in K982499 in formulation, processing, and sterilization, and no other chemicals have been added (e.g., plasticizers, fillers, color additives, cleaning agents, mold release agents, etc.).

M. Malis 7/11/03

Michael J Malis
RA/QA Manager
Respironics Novametrix, LLC

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BIOSERVICE
SCIENTIFIC LABORATORIES GMBH

BIOCOMPATIBILITY
CERTIFICATE

Testmaterial: Elastosil® LR3003/20 A,B Control No: 1823SL

Manufacturer: WACKER Chemie GmbH, Germany
WACKER Silicones Corporation, USA
WACKER Chemicals East Asia Ltd., Japan

Studies performed: The following studies were performed in order to determine the biocompatiblity of the test item according to ISO 10993-1:

CYTOTOXICITY
HEMOLYSIS
PYROGENICITY
SENSITISATION
DERMAL IRRITATION
IMPLANTATION (90 days)

Results: **The test item showed no relevant biological effects in the studies performed.**

Suitable for use in manufacturing of medical devices for short term (no longer than 30 days) implant applications in accordance with the Wacker Health Care Letter and Guidelines.

BSL BIOSERVICE Scientific Laboratories GmbH Munich
Behringstraße 6
D-82152 Planegg

BIOSERVICE Scientific Laboratories GmbH GLP EN 45001

Dr. Albrecht Poth
Manager Biological Safety Testing

Date: December 28, 1998

(b)(4) Third Party Test Data

(b)(4) Third Party Test Data

(b)(4) Third Party Test Data

(b)(4) Third Party Test Data

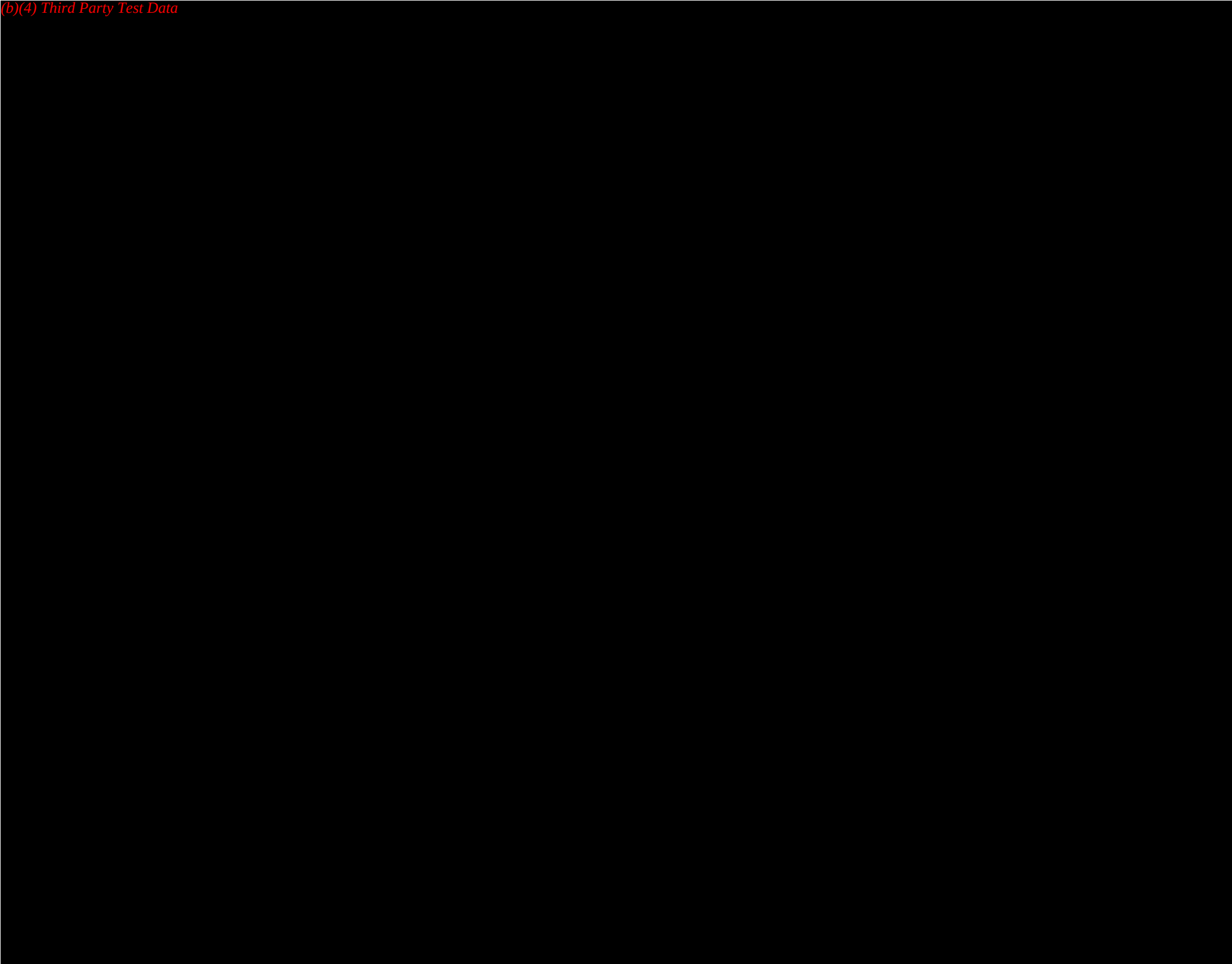
(b)(4) Third Party Test Data

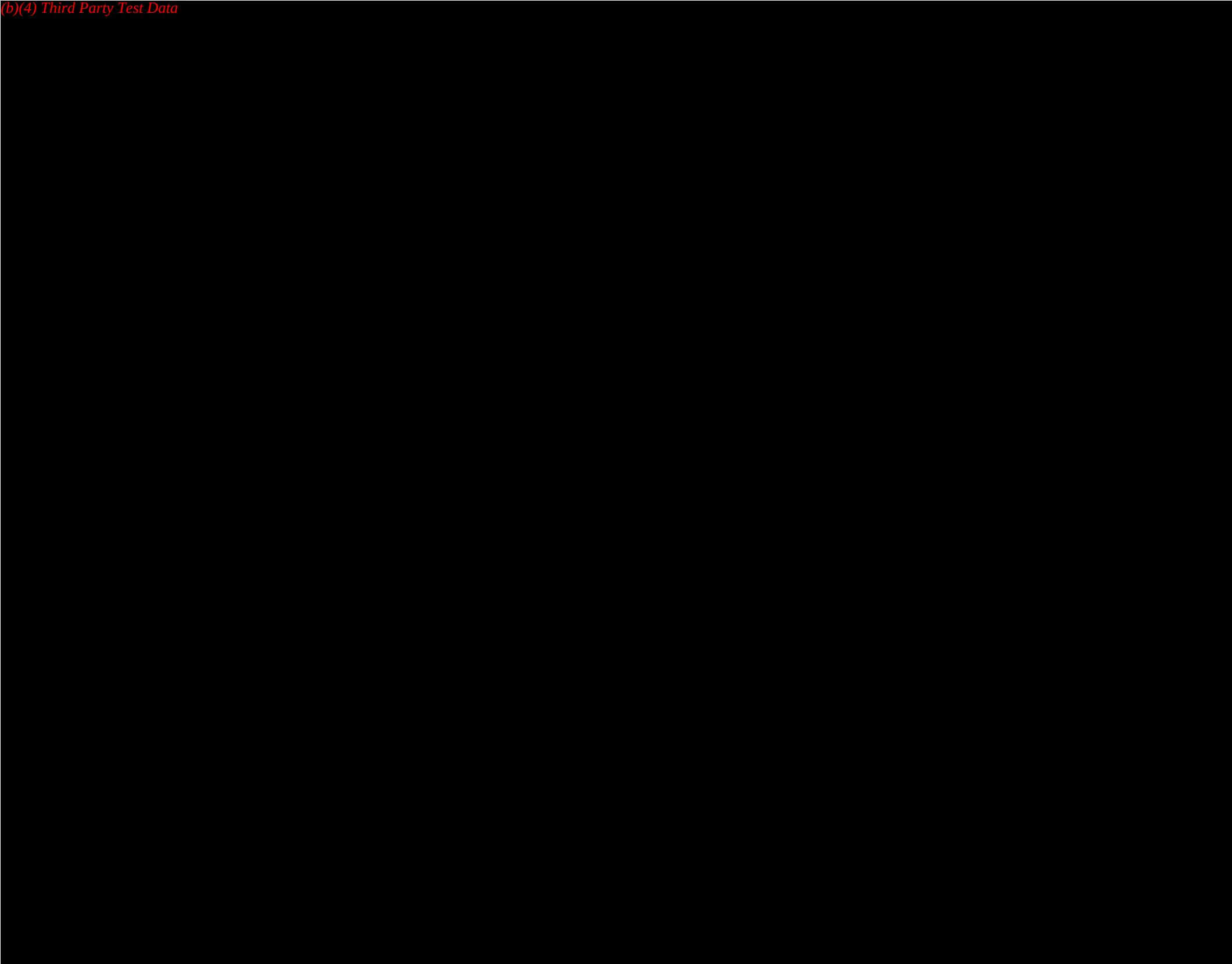
(b)(4) Third Party Test Data

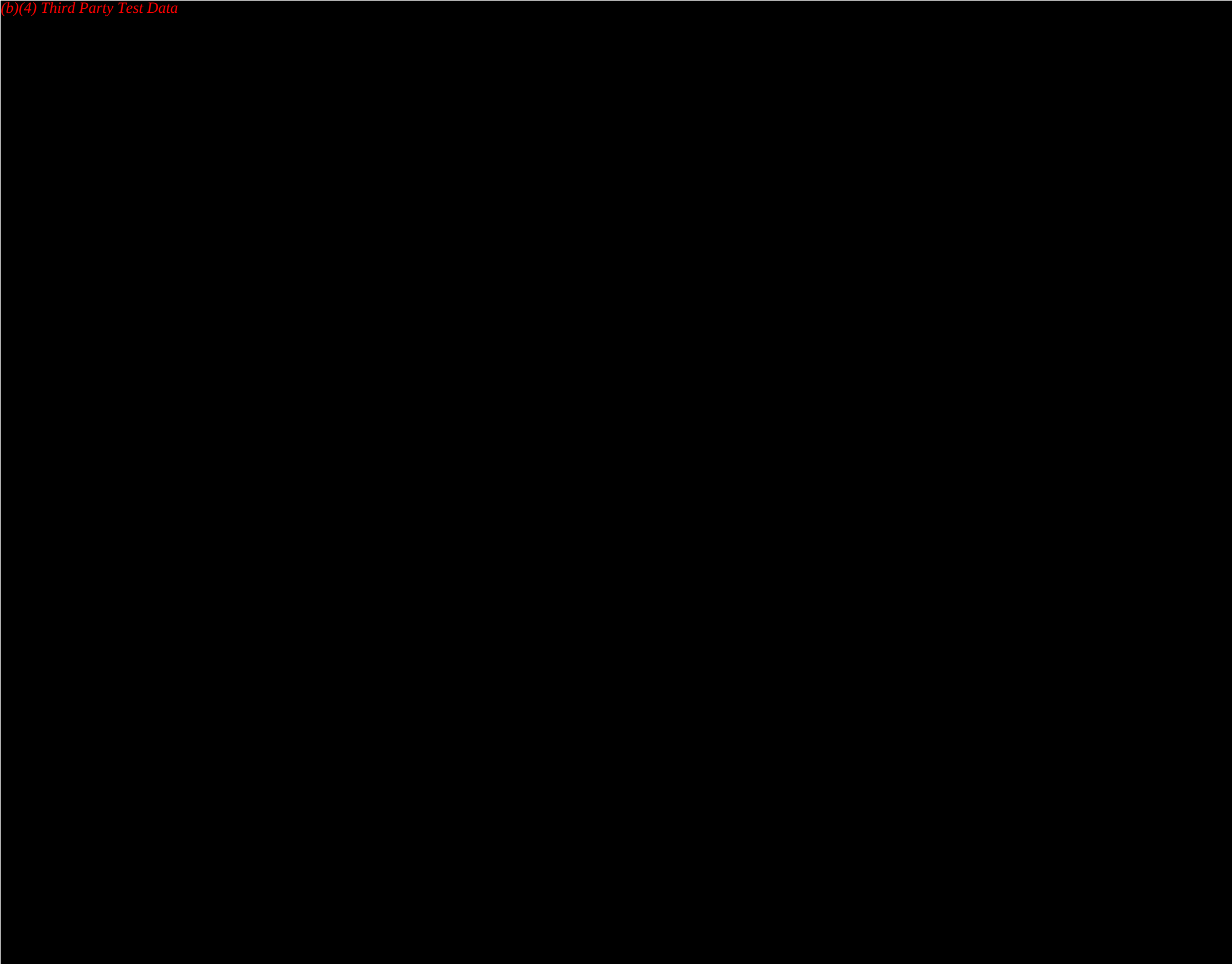
(b)(4) Third Party Test Data

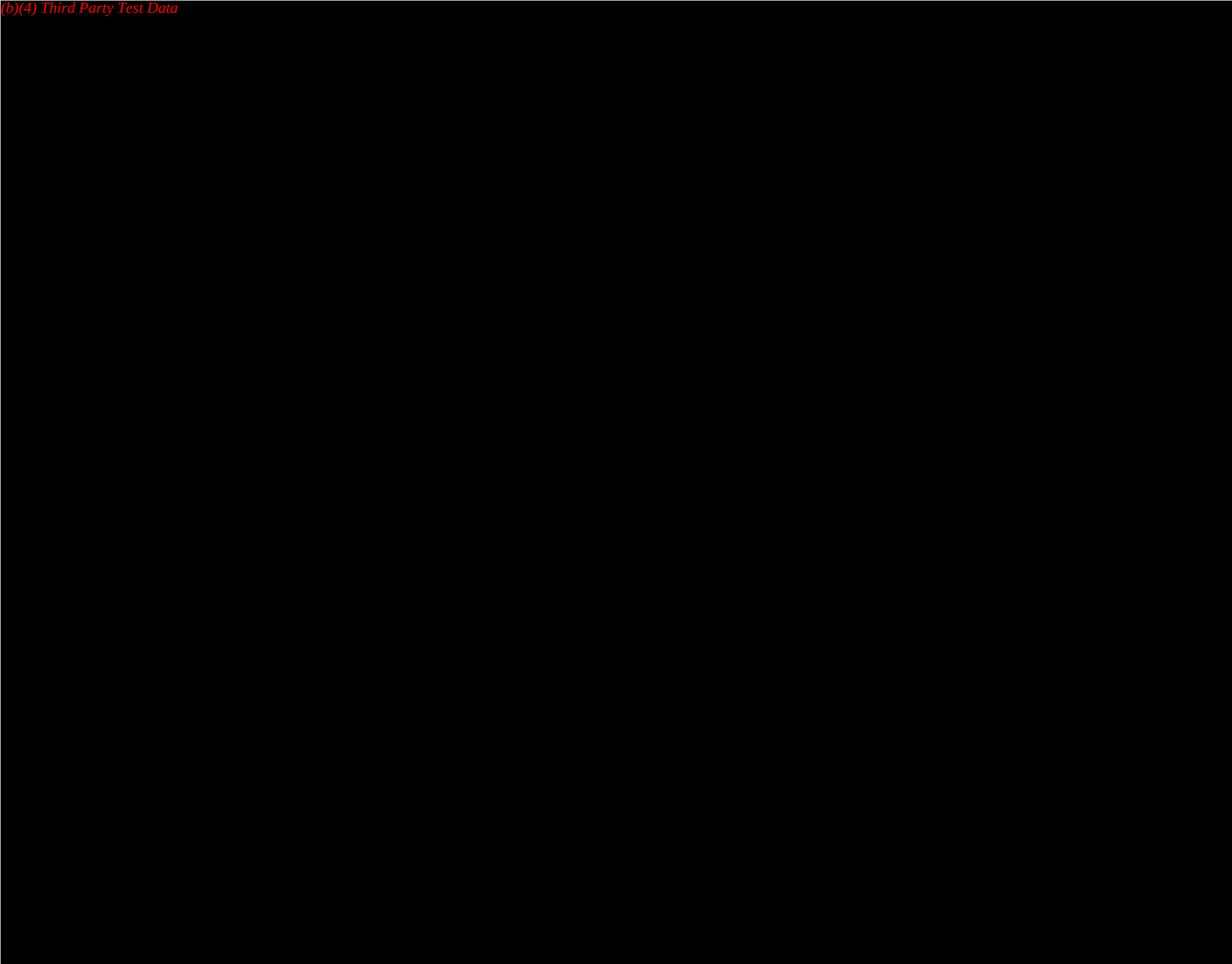
(b)(4) Third Party Test Data

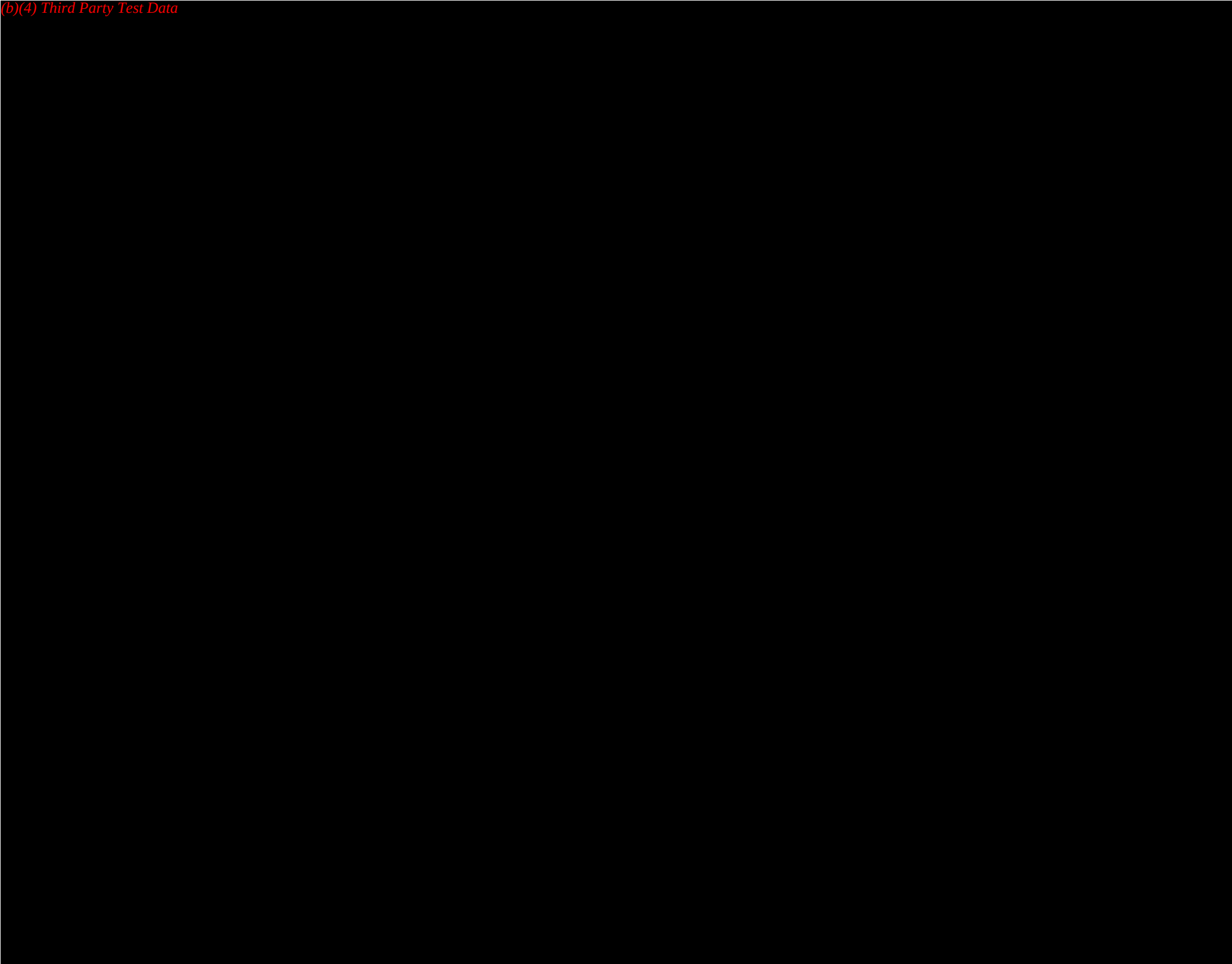
(b)(4) Third Party Test Data


(b)(4) Third Party Test Data


(b)(4) Third Party Test Data


(b)(4) Third Party Test Data


(b)(4) Third Party Test Data


(b)(4) Third Party Test Data

INTENDED USE

Intended Use

The intended use of the NICO monitor, Model 7300 is to provide:

- cardiac output monitoring via the method of partial rebreathing in adult patients receiving mechanical ventilation during general anesthesia and in the intensive care unit (ICU).

- spirometric, and carbon dioxide monitoring in neonatal, pediatric and adult patients during general anesthesia and in the intensive care unit (ICU) and the emergency department (ED). Separate combination CO_2/flow sensors are provided for adult, pediatric and neonatal use.

- continuous, non-invasive monitoring of functional arterial oxygen saturation and pulse rate in neonatal, pediatric and adult patients during both no motion and motion conditions and for patients who are well or poorly perfused during general anesthesia and in the intensive care unit (ICU) and the emergency department (ED).

The use of the NICO monitor Model 7300 for cardiac output monitoring is contraindicated in patients in which a small rise (3-5 mmHg) in their arterial partial pressure of CO_2 level cannot be tolerated.

Proposed Labeling and Instructions for Use

The draft user's manual, product literature, pouch labeling and front, top and rear panel labeling may be found in Appendices 1A, 1B, 1C, and 1D, respectively.

510(k) Number (if known):_____

Device Name:_____ **NICO with MARS**_____

Indications For Use:

The intended use of the NICO monitor, Model 7300 is to provide:

- cardiac output monitoring via the method of partial rebreathing in adult patients receiving mechanical ventilation during general anesthesia and in the intensive care unit (ICU).

- spirometric, and carbon dioxide monitoring in neonatal, pediatric and adult patients during general anesthesia and in the intensive care unit (ICU) and the emergency department (ED). Separate combination CO_2/flow sensors are provided for adult, pediatric and neonatal use.

- continuous, non-invasive monitoring of functional arterial oxygen saturation and pulse rate in neonatal, pediatric and adult patients during both no motion and motion conditions and for patients who are well or poorly perfused during general anesthesia and in the intensive care unit (ICU) and the emergency department (ED).

The use of the NICO monitor Model 7300 for cardiac output monitoring is contraindicated in patients in which a small rise (3-5 mmHg) in their arterial partial pressure of CO_2 level cannot be tolerated.

(PLEASE DO NOT WRITE BELOW THIS LINE - CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use_____ **OR** **Over-The-Counter Use**_____
(Per 21 CFR 801.109)

(Optional Format 1-2-96)

510(K) SUMMARY

July 11, 2003

a. Applicant's Name and Address

Respironics Novametrix Inc.
5 Technology Drive
Wallingford, CT 06492

b. Contact Person

Michael J. Malis
Q.A. and Regulatory Manager
(203) 697-6442
(203) 284-0753 (facsimile)

c. Name of Device

Device Names (Proprietary/Trade Names):	NICO, Model 7300
Device Name (Common Name):	multiparameter monitor (monitoring spirometer, CO_2 monitor, pulse oximeter and cardiac output monitor with partial rebreathing valve).
Classification:	Class II, 21 C.F.R. 868.1850, 868.1400, 870.2700, 868.5675

d. Equivalent Devices

Substantial equivalence to the following legally marketed predicate devices with the same or similar indications for use has been demonstrated by a comparison of product features as described in the labeling and promotional literature for predicate devices and for the Model 7300, as well as testing to accepted industry standards. In addition, controlled hypoxia studies were conducted to establish the Model 7300 pulse oximetry accuracy and to ensure that the sensors meet their currently published accuracy specifications with the Model 7300. The predicate devices are as follows:

1. CO2SMO Plus! with NICO, Model 8200 (K982499)
2. MARSPO2, Model 2001 (K993979, K000794).

e. Device Description

The NICO monitor Model 7300 is intended for non-invasive monitoring of the inspired and expired airflow and airway pressure of intensive care unit (ICU), anesthesia and emergency room (ER) patients, as well as capnography and pulse oximetry in all of these clinical settings. As is its predicate device *CO_2SMO Plus! with NICO, NICO with MARS* is designed to use neonatal, pediatric, and adult combined CO_2/flow sensors and single patient use or reusable pulse oximetry sensors. It non-invasively calculates cardiac output using established physiological principles by the application and removal of a rebreathed volume in a patient's breathing circuit and the analysis of that response. The *NICO with MARS* is intended to provide cardiac output monitoring in mechanically ventilated patients in the operating room and intensive care units. It is intended to serve the same purposes as the CO_2SMO Plus! with NICO and MARSPO$_2$, Model 2001.

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Oxygen saturation is measured with ratiometric technique using red and infrared absorbance of oxy- and deoxyhemoglobin and pulse rate is measured using the time between successive pulses. The O_2 saturation sensors are already legally marketed as accessories to the Model 2001 monitor. As the Model 2001 monitor, the Model 7300 with MARS consists of a dual microprocessor based data acquisition system that measures oxygen saturation data. The firmware for the second microprocessor, a digital signal processor, performs the filtering, pulse rate and saturation calculations of the existing algorithms and additional calculations which analyze the incoming signals and perform noise reduction on that signal when the presence of noise is detected.

The Model 7300 can be powered by either an internal power supply operating on AC or by a sealed rechargeable lead-acid gel battery. Audible and visual alarms for high/low saturation and pulse rate are available. There is also a serial port that provides user configurable data output capable of communicating with printers and other devices.

f. Intended Use

The intended use of the NICO monitor, Model 7300 is to provide:

- cardiac output monitoring via the method of partial rebreathing in adult patients receiving mechanical ventilation during general anesthesia and in the intensive care unit (ICU).

- spirometric and carbon dioxide monitoring in neonatal, pediatric and adult patients during general anesthesia and in the intensive care unit (ICU) and the emergency department (ED). Separate combination CO_2/flow sensors are provided for adult, pediatric and neonatal use.

- continuous, non-invasive monitoring of functional arterial oxygen saturation and pulse rate in neonatal, pediatric and adult patients during both no motion and motion conditions and for patients who are well or poorly perfused during general anesthesia and in the intensive care unit (ICU) and the emergency department (ED).

The use of the NICO monitor Model 7300 for cardiac output monitoring is contraindicated in patients in which a small rise (3-5 mmHg) in their arterial partial pressure of CO_2 level cannot be tolerated. The intended use, patient population and environments of use are the same or similar to the predicate devices, CO_2SMO Plus! with NICO, Model 8200 and MARSPO_2, Model 2001

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g. Technological Characteristics

The *NICO with MARS* uses flow sensors that are considered to be a fixed orifice, target flowmeters and as such the pressure drop is proportional to the square of the flow. Combination CO_2/flow sensors are available in three flow ranges that are tailored for neonates, pediatric patients and adults.

The *NICO with MARS* uses an infrared absorption (IR) technique for monitoring CO_2. The principle is based on the fact that CO_2 molecules absorb infrared light energy of specific wavelengths, with the amount of energy absorbed being directly related to the CO_2 concentration Solid state CO_2 sensors (such as the Capnostat) use a beam splitter to simultaneously measure the IR light at two wavelengths: one which is absorbed by CO_2

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and one which is not. The wavelength which is not absorbed by CO_2 is related to the intensity of the IR light source. Also, the IR light source is electronically pulsed (rather than interrupting the IR beam with a chopper wheel) in order to eliminate effects of changes in electronic components.

The *NICO with MARS* measures oxygen saturation and pulse rate with sensors that contain red and infrared light sources. Since oxygen saturated blood absorbs different amounts of light at each wavelength (red and infrared) as compared with unsaturated blood, the amount of light absorbed at each wavelength by the blood in each pulse can be used to calculate oxygen saturation. The light energy from red (660 nm) and infrared (940 nm) LEDs is beamed through a sample cell- a pulsating vascular bed, the patient's finger or toe for example. The remaining light energy not absorbed by the sample cell reaches a photodiode, on the opposing side of the sensor. The signal received by the photodiode is split into its red and infrared components, sampled, software filtered and displayed as a numerical value for oxygen saturation and as a waveform, the plethysmogram.

Functional saturation represents the amount of oxyhemoglobin as a percentage of the hemoglobin that can be oxygenated. Dysfunctional hemoglobin (COHb and METHb) are not included in the measurement of functional saturation. Pulse rate is calculated by measuring the time interval between the peaks of the infrared light waveform. The *NICO with MARS* must be used in conjunction with the Novametrix SuperBright™ series of oxygen saturation sensors. MARS technology exploits the computational power of the digital signal processing to replace the pulse rate interval and rate-based decision tree algorithm of prior devices with a more robust frequency-based algorithm.

A variation on the traditional rebreathing methods, the non-invasive differential Fick partial re-breathing technique is used in the NICO with MARS monitor. The change in VCO_2 and the change in end-tidal CO_2 in response to a change in ventilation is used to determine pulmonary capillary blood flow. This value is then corrected for the effect of shunt to determine cardiac output.

h. Certification Statement

In accordance with the requirements of 21 CFR 807.87(j), the following certification is provided:

Respironics Novametrix, Inc. believes that all data and information submitted in this premarket notification are truthful and accurate and no material fact has been omitted.

M. Malis 7/10/03

Michael J Malis
Q.A. and Regulatory Manager

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