510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY AND INSTRUMENT COMBINATION TEMPLATE

A. 510(k) Number:

K073537

B. Purpose for Submission:

New Device

C. Measurand:

Neonatal Bilirubin

D. Type of Test:

Quantitative, CO-oximetry

E. Applicant:

Siemens Medical Care Solutions, Inc.

F. Proprietary and Established Names:

Neonatal Bilirubin (nBili) on Rapiblab models 1245 and 1265

G. Regulatory Information:

1. Regulation section:

   CFR 21 Section 862.1113 Bilirubin (total and unbound) in the neonate test system

2. Classification:

   Class I, reserved

3. Product code:

   MQM

4. Panel:

Clinical Chemistry (75)

H. Intended Use:

1. Intended use(s):

   See indications for use below

2. Indication(s) for use:

   The neonatal bilirubin test intended use on the Rapidlab 1245 and Rapidlab 1265 analyzers is an in vitro diagnostic test for the determination of total neonatal bilirubin (nBili) concentration in whole blood of newborn infants. Meaurement of nBili aids in assessing the risk of kernicterus.

3. Special conditions for use statement(s):

   For prescription use only. For neonatal use only.

4. Special instrument requirements:

   Siemens Rapidlab 1245 or 1265

I. Device Description:

Neonatal Bilirubin (nBili) is a new parameter enabled on models 1245 and 1265 of the Rapidlab® 1200 blood gas family of instruments. It is intended as an in vitro diagnostic test for the determination of total neonatal Bilirubin (nBili) concentration in the whole blood of newborn infants. Enabling the nBili measurement is accomplished through software design changes introduced in Rapidlab Software Version 2.1. No hardware /mechanical changes were needed.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Radiometer ABL800 FLEX

2. Predicate 510(k) number(s):

   k043218

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Specimen type	Whole blood	Whole blood
Technology	Automated co-oximetry using spectral analysis	Automated co-oximetry using spectral analysis
Measured parameter	Total bilirubin	Total bilirubin

Differences		
Item	Device	Predicate
Intended population	Neonates	Neonates and Adults
Measuring range	2.0-30.0	0.0 – 58.5 mg/dL
Calibration	2 point using automated on-board reagent	2 point using external calibration solution
Sample during measurement	Non-hemolyzed whole blood	Whole blood hemolyzed on-board

K. Standard/Guidance Document Referenced (if applicable):

Not applicable

L. Test Principle:

The Rapidlab 1200 System uses multiple wavelength spectrophotometry (CO oximetry) to measure the transmission of light through a sample of neonate whole blood to determine concentrations of hemoglobin derivatives and bilirubin.

The Rapidlab 1200 System aspirates the whole blood sample at the sample port and then transfers the sample to the CO-ox module. As the sample flows through an optical chamber, the CO-ox module optics head directs light through the sample and to a polychromator that measures the intensity of transmitted light at different wavelengths.

Iterative least squares analysis is used to determine raw bilirubin values. Raw values are then corrected for hematocrit to produce nBili results.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. *Precision/Reproducibility:*

      Freshly drawn (same day) whole blood samples were spiked to several bilirubin concentrations across the claimed measuring range. Samples were adjusted for tHb

from 2.5 to 24.5 g/dL and tonometered to approximately 98% O_2Hb and used to account for different hemoglobin levels in the analysis of each level. The samples were assayed in 3 replicates over several days on each instrument, for each level, mode, device, and tHb level. The within run %CV was calculated from the pooled within run standard deviation of these 3 replicates. The results are summarized below.

Rapidlab 1245 nBili Testing

Level	Mode	Device	n	WRSD	% Within Run CV	Mean (mg/dL)
5	CO-ox	Capillary	95	0.28	5.6	5.0
5	Full	Capillary	98	0.42	8.6	4.9
5	Full	Syringe	102	0.31	5.8	5.3
8	CO-ox	Capillary	27	0.39	5.1	7.7
8	Full	Capillary	31	0.34	4.4	7.7
8	Full	Syringe	36	0.29	3.5	8.3
12	CO-ox	Capillary	99	0.44	3.5	12.6
12	Full	Capillary	99	0.48	3.8	12.6
12	Full	Syringe	99	0.42	3.3	12.9
20	CO-ox	Capillary	97	0.73	3.3	22.0
20	Full	Capillary	96	0.76	3.5	21.8
20	Full	Syringe	99	0.52	2.3	22.5

Rapidlab 1265 nBili Testing

Level	Mode	Device	n	WRSD	% Within Run CV	Mean (mg/dL)
5	CO-ox	Capillary	91	0.44	9.6	4.6
5	Full	Capillary	98	0.43	9.6	4.5
5	Full	Syringe	104	0.42	8.8	4.8
8	CO-ox	Capillary	36	0.68	9.6	7.1
8	Full	Capillary	36	0.30	4.2	7.2
8	Full	Syringe	36	0.25	3.2	7.9
12	CO-ox	Capillary	105	0.53	4.4	12.0
12	Full	Capillary	106	0.60	5.0	12.1
12	Full	Syringe	105	0.36	2.9	12.5
20	CO-ox	Capillary	103	0.55	2.6	20.8
20	Full	Capillary	104	0.74	3.5	21.2
20	Full	Syringe	106	0.49	2.2	21.9

Quality control materials, including manual (QC) and automatic (AutomaticQC), were analyzed on the Rapidlab 1245 system and the Rapidlab 1265 system. Manual QC is performed by the operator while AutomaticQC is performed automatically by the system based on the QC frequency defined in the system software.

Precision of manual aqueous quality control materials was estimated using a minimum of 4 Rapidlab 1245 systems and a minimum of 4 Rapidlab 1265 systems. Controls were measured over a minimum of 10 days. AutomaticQC is automatically scheduled to run (single sample) independently 3 times per day The within run and total %CVs were calculated and results are summarized below.

Precision on Manual QC Rapidlab 1245 System

Level	n	Mean	WRSD	% WRCV	Total SD	% Total CV
1	133	20.0	0.24	1.2	0.48	2.4
2	135	12.4	0.25	2.0	0.45	3.6
3	136	5.1	0.23	4.5	0.27	5.3

Precision on AutomaticQC Rapidlab 1245 System

Level	n	Mean	WRSD	% WRCV	Total SD	% Total CV
1	194	19.9	0.28	1.4	0.51	2.6
2	197	11.8	0.30	2.5	0.34	2.9
3	196	4.9	0.12	2.4	0.13	2.7

Precision on Manual QC Rapidlab 1265 System

Level	n	Mean	WRSD	% WRCV	Total SD	% Total CV
1	159	20.2	0.25	1.2	0.66	3.3
2	159	12.4	0.38	3.1	0.62	5.0
3	159	5.2	0.19	3.7	0.27	5.2

Precision on AutomaticQC Rapidlab 1265 System

Level	n	Mean	WRSD	% WRCV	Total SD	% Total CV
1	218	20.2	0.26	1.3	0.40	2.0
2	214	12.1	0.26	2.1	0.27	2.2
3	226	5.0	0.16	3.2	0.19	3.8

b. Linearity/assay reportable range:

The reportable range is 2.0 to 30 mg/dl. A linearity study was performed be using a naturally occurring low sample with a measured bilirubin concentration of 0.2 mg/dL and a spiked high sample with a measured concentration of 77.1 mg/dL. Nine intermediate samples were made by combining proportions of the low and high samples volumetrically. The high, low, and intermediate samples were run in replicates of four in one day. The data was analysed in accordance with CLSI EP-6. There was no evidence of extreme nonlinearity or outliers with any of the results. First, second, and third order regressions were performed and indicated statistically non-linear regression coefficients. The cubic model was found to be the best mathematical fit and the differenced between the linear and cubic predicted values were assessed. The differences between the fits were found to be within the sponsor's acceptance criteria indicating a clinically insignificant difference between the linear and cubic predicted values. These results demonstrate the linearity of the device across the claimed measuring range.

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

There is no separate calibrator value assignment for nBili. The critical parameter that requires calibration for nBili is the path length which is accomplished with the total

hemoglobin, tHb, value assignment. The tHb calibrator was cleared under k031560.

d. Detection limit:

The limit of detection was determined in accordance with CLSI EP-17A. Eight unique whole blood specimens were exposed to a photolysing light source overnight to create the blank samples. These samples were each assessed in replicates of ten on two instruments over a minimum of five operating days. The limit of blank (LOB) was calculated from these results using the 95th percentile of the ascending rank ordered values for each instrument. The mean LOB calculated from the two instruments was 0.1 mg/dL.

In order to calculate the limit of detection (LOD), eight unique whole blood samples, with bilirubin concentrations in the range of 0.5 to 2.0 mg/dL were each assessed in replicates of ten on two instruments over a minimum of five operating days. The LOD was calculated as LOD = LOB + Cβ(Std Dev) and resulted in a mean LOD from the two instruments of 0.7 mg/dL.

e. Analytical specificity:

Interference testing was performed by spiking fresh whole blood samples to approximately 20 mg/dL bilirubin, then spiking these samples with interferents at the concentrations shown below. Control samples were made by spiking the same whole blood samples with the same volume of diluent as the interferent. All samples were tested and the interference spiked test samples were compared to the diluent spiked control samples. A two-tail t-test was conducted to assess the observed differences between the interference and control samples. With the exception of lipids, all substances tested showed a discernable statistical difference between the test and control samples. The table below was included in the labeling to show the interference testing results. Hemoglobin interference was deemed unnecessary due to the design of the instrument.

Potential Interferent	Level Tested	Effect of Interference
Lipid	5% volume Intralipid, in plasma (4980 mg/dL)	0.0%
CyanMethemoglobin	10%	92.6%
Beta-carotene	2.5 mg/dL, in plasma	10.0%
Evans Blue	5 mg/L	-5.4%
Indocyanine Green	5 mg/L	1.4%
Methylene Blue	50 mg/L	-66.3%
Sulfan Blue	10 mg/L	58.5%

f. Assay cut-off:

Not applicable

2. Comparison studies:

   a. Method comparison with predicate device:

   A method comparison study was performed comparing the Rapidlab to the predicate device. Ninety nine samples with concentrations ranging from 2 to 30 mg/dL were evaluated on both analyzers. These samples consisted of 77 natural patient samples and 22 spiked samples. A linear regression calculation was performed with the following results: $y = 0.95x - 0.149$, $r^2 = 0.983$.

   b. Matrix comparison:

   Not applicable

3. Clinical studies:

   a. Clinical Sensitivity:

   Not applicable

   b. Clinical specificity:

   Not applicable

   c. Other clinical supportive data (when a. and b. are not applicable):

   Not applicable

4. Clinical cut-off:

   Not applicable

1. Expected values/Reference range:

   Reference ranges for the assay are shown in the table below.

Expected Values*

Age	mg/dL
Premature Infants	
≤ 1 day	< 8.0
1–2 days	< 12.0
3–5 days	< 16.0
Full Term Infants	
≤ 1 day	< 6.0
1–2 days	< 8.0
3–5 days	< 12.0

* Tietz NW, Textbook of Clinical Chemistry (1986), pg 1815.

N. Instrument Name:

Rapidlab 1245 and Rapidlab 1265

O. System Descriptions:

1. Modes of Operation:

   Neonatal Bilirubin (nBili) is a new parameter enabled on models 1245 and 1265 of the Rapidlab® 1200 blood gas family of instruments. It is available with Rapidlab Software Version 2.1. Models 1245 and 1265 currently measure a number of parameters that have been previously cleared under K031560. With the planned release of software version 2.1 the ability to measure nBili parameter will be added.

2. Software:

   FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:

   Yes ___X____ or No _____

3. Specimen Identification:

   Samples are identified by barcode.

4. Specimen Sampling and Handling:

   Users follow the same sample handling process already in place for other measuring parameters on RL1200 blood gas instrument. Users can analyze samples using the sample collection devices and whole blood is collected in a heparanized syringe or capillary.

5. Calibration:

   The same calibration procedures are required as in k031560. The tHb calibration curve is used in nBili measurements. The targeted calibration points for tHb are:

   - Calibration Point: 0 g/dL
   - Slope Point: 15 g/dL

6. Quality Control:

   The same Quality Control (QC) procedures are recommended as in k031560. The nBili QC is dependent on tHb QC. As a result, if tHb or any of the four CO-ox fractions (FO2Hb, FCOHb, FMetHb, and FHHb) fail or miss QC, nBili is also marked QC Failed or QC Missed. On the other hand, if nBili fails or misses QC, tHb and the other CO-ox fractions will not be affected. The optional AutomaticQC module allows the system to automatically analyze QC materials at pre-programmed intervals. The manual QC mode allows the users to manually run QC as desired.

P. Other Supportive Instrument Performance Characteristics Data Not Covered In The "Performance Characteristics" Section above:

Not applicable

Q. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

R. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.