



**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY**

I Background Information:

A 510(k) Number

K191298

B Applicant

Abbott Point of Care Inc.

C Proprietary and Established Names

i-STAT CHEM8+ cartridge with the i-STAT 1 System

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
JFL	Class II	21 CFR 862.1160 - Bicarbonate/Carbon Dioxide Test System	CH - Clinical Chemistry

II Submission/Device Overview:

A Purpose for Submission:

Modification of a previously cleared device - modification to the i-STAT CHEM8+ (blue) cartridge on the i-STAT 1 Analyzer.

B Measurand:

Total carbon dioxide (TCO₂)

C Type of Test:

Quantitative, Ion Specific Electrode (Potentiometric method)

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

The i-STAT CHEM8+ cartridge with the i-STAT 1 System is intended for use in the in vitro quantification of total carbon dioxide in arterial or venous whole blood in point of care or clinical laboratory settings.

Carbon dioxide measurements are used in the diagnosis, monitoring, and treatment of numerous potentially serious disorders associated with changes in body acid-base balance.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

For Point-of-Care or clinical laboratory setting

D Special Instrument Requirements:

i-STAT 1 Analyzer

IV Device/System Characteristics:

A Device Description:

The i-STAT 1 System consists of the i-STAT 1 Analyzer, the i-STAT cartridges and accessories (i-STAT 1 Downloader/Recharger, electronic simulator and portable printer) and the i-STAT test cartridges. The system is designed for use by trained medical professionals at the patient point of care or in the clinical laboratory and is for prescription use only.

The i-STAT 1 Analyzer (previously cleared under k103195 as the i-STAT 1 Wireless Analyzer) is a handheld analytical device designed to run i-STAT test cartridges. The instrument interacts with the cartridge to move fluid across the sensors and generate a quantitative result.

The single-use, disposable i-STAT CHEM8+ (blue) cartridge contains test reagents to analyze whole blood at the point of care or in the clinical laboratory for total carbon dioxide and other analytes. The cartridge format allows all the tests in the cartridge to be performed simultaneously. The cartridges contain the required sensors, a fluid pouch, a sample entry well and closure, fluid channels, waste chamber, and the necessary mechanical features for controlled fluid movement within the cartridge. Cartridges require two to three drops of whole blood which are typically applied to the cartridge using a transfer device, by the trained user before the cartridge is placed within the analyzer.

B Principle of Operation:

TCO2 is a potentiometric test in the i-STAT CHEM8+ Cartridge. Potentiometry is the measurement of difference in potential that exists between an active working sensor and an independent reference sensor. Both these sensors need to be present within the same cartridge for a potentiometric test to give a result. The active working sensor responds to change in the activity (concentration) of the substance to be measured when the sample contacts that active working sensor. The potential of the reference electrode does not change because it is not in contact with patient sample. A potential (or voltage) corresponding to the analyte concentration is generated at the active working sensor and measured by the i-STAT analyzer. The test concentrations are calculated from the measured potential through the Nernst equation. The Nernst equation relates the measured potential to the activity of the ion being measured. The measured TCO2 test method is calibrated to the International Federation of Clinical Chemistry (IFCC) TCO2 reference method with an algorithm based on the Henderson-Hasselbalch equation, which uses pH, PCO2, and ionic strength (Na) measurements.

V Substantial Equivalence Information:**A Predicate Device Name(s):**

Synchron Systems TCO2 Reagent on Unicel DxC 600/800 SYNCHRON Clinical System

B Predicate 510(k) Number(s):

K042291

C Comparison with Predicate(s):

Device & Predicate Device(s):	<u>K191298</u>	<u>K042291</u>
Device Trade Name	i-STAT CHEM8+ Cartridge with the i-STAT 1 System (TCO2)	SYNCHRON Systems TCO2 Reagent on UniCel DxC 600/800 SYNCHRON Clinical System
General Device Characteristic Similarities	<u>K191298</u>	<u>K042291</u>
Intended Use/Indications For Use	Intended for use in the <i>in vitro</i> quantification of total carbon dioxide Carbon dioxide measurements are used in the diagnosis, monitoring, and treatment of numerous potentially serious disorders associated with changes in body acid-base balance.	Same

Reportable Range	5-50 mmol/L (mEq/L)	Same
General Device Characteristic Differences	<u>K191298</u>	<u>K042291</u>
Sample Type	Arterial or venous whole blood	Serum or plasma
Sample Volume	95 µL	0.5 mL (500 µL)
Reagent Format	Cartridge	Reagent handling system, stored within analyzer

VI Standards/Guidance Documents Referenced:

CLSI EP05-A3: Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline-Third Edition

CLSI EP06-A: Evaluation of the Linearity of Quantitative Measurement Procedures

CLSI EP07-A2: Interference Testing in Clinical Chemistry; Approved Guideline – Second Edition

CLSI EP 17-A2, Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

Precision studies were conducted following the recommendations in CLSI EP05-A3.

Internal site precision (aqueous control material)

A single site precision study using five concentration levels of commercially available calibration verification samples were tested using one lot of i-STAT CHEM8+ (blue) cartridges and twelve i-STAT 1 analyzers. Each sample was measured in duplicates per run, with two runs per day for 20-days resulting in a total of 80 test results per level. The results are summarized below.

TCO2 Level	Mean (mmol/L)	Within-run		Between Run		Between Day		Total	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV
L1	12.2	0.26	2.1	0.08	0.7	0.08	0.7	0.29	2.4
L2	18.2	0.30	1.6	0.07	0.4	0.07	0.4	0.31	1.7
L3	23.6	0.58	2.5	0.21	0.9	0.15	0.6	0.64	2.7
L4	31.8	1.26	4.0	0.20	0.6	0.49	1.5	1.36	4.3
L5	44.3	0.69	1.6	0.32	0.7	0.53	1.2	0.93	2.1

Internal site precision (whole blood)

A single site precision study was conducted using samples targeted to three levels within the test reportable range. Venous whole blood collected in lithium heparinized tubes from a healthy subject was altered via tonometry to prepare the different sample levels. The samples were tested using one lot of i-STAT CHEM8+ (blue) cartridges and 35 i-STAT 1 Analyzers. The results of the whole blood precision are shown below.

TCO2 Level (mmol/L)	N	Mean (mmol/L)	SD	%CV
5-15	35	8.8	0.92	10.5
20-29	29	24.9	0.77	3.1
>29-40	25	30.9	0.80	2.6

Point of Care precision (aqueous control material)

A three site precision study was performed using a panel of five aqueous control solutions containing different levels of TCO2. Each sample was assayed at each site once per day for five days across each of six analyzers for a total of 90 measurements. At each site, all testing was conducted by three operators with one per site using one lot of i-STAT CHEM8+ (blue) cartridges. The results were analyzed for within-day (between-analyzer), within-site, and overall (summation of between-site, between-day and between-analyzer) variance components and provided in the table below:

Sample	Mean (mmol/L)	Within-day		Within-site		Overall	
		SD	%CV	SD	%CV	SD	%CV
Level 1	12.0	0.18	1.5	0.18	1.5	0.18	1.5
Level 2	18.1	0.32	1.8	0.35	1.9	0.36	2.0
Level 3	23.9	0.45	1.9	0.52	2.2	0.52	2.2
Level 4	45.1	0.77	1.7	0.84	1.9	0.87	1.9
Level 5	33.2	0.73	2.2	0.73	2.2	0.77	2.3

Point of Care precision (whole blood)

A whole blood repeatability analysis was conducted using the data collected across three point of care sites. Two hundred and seventy-nine samples (178 venous and 101 arterial) were measured in duplicate using 3 lots of i-STAT CHEM8+ cartridges and 18 i-STAT 1 Analyzers by multiple POC operators at each site. The mean values for each sample were divided into four subintervals for each sample type taking into consideration the medical decision levels of 6, 20, and 33 mmol/L.

The results are provided in the tables below:

Venous whole blood:

Sample Range (mmol/L)	N	Mean (mmol/L)	SD	%CV
7 - 15	15	9.43	0.483	5.1
15 - 25	61	21.25	0.665	3.1
25 - 35	82	27.72	0.625	2.3
35 - 47	20	39.33	1.037	2.6

Arterial whole blood:

Sample Range (mmol/L)	N	Mean (mmol/L)	SD	%CV
14 - 15	3	14.33	0.577	4.0
15 - 25	46	22.29	0.521	2.3
25 - 35	48	28.10	0.520	1.9
35 - 50	4	39.50	0.866	2.2

2. Linearity:

The linearity of the TCO₂ assay on the i-STAT CHEM8+ (blue) cartridge was evaluated based on the recommendations in CLSI EP06-A. For this study, the sample preparation recommended in the CLSI EP06-A guidance was not followed. Due to the sample preparation process and in order to limit degassing, the intermediate levels were prepared individually rather than mixing high and low samples. Nine venous whole blood samples collected in lithium heparin tubes spanning the reportable range for the i-STAT TCO₂ were prepared through a process of tonometry and acid/base addition. Each sample was measured in replicates of 15 using five lots of i-STAT CHEM8+ (blue) cartridges on 39 i-STAT 1 Analyzers. Results of the linear regression analysis are presented in the table below.

Analyte (mmol/L)	Range Tested (mmol/L)	Slope	Intercept	R ²
TCO ₂	3.56 - 52.26	1.028	-0.126	0.9938

The linearity study data supports the claimed measuring range for the TCO₂ assay of 5 – 50 mmol/L.

3. Analytical Specificity/Interference:

The analytical specificity of the i-STAT TCO₂ assay on the i-STAT CHEM8+ (blue) cartridge was established following the recommendations in CLSI EP07-A2. Interference testing was conducted using lithium heparin venous whole blood samples prepared by tonometry to high and low levels of TCO₂. The effect of each substance at each TCO₂ level was evaluated by comparing the performance of a test sample spiked to a high concentration of the substance and a control sample spiked with an equal volume of solvent. A substance was identified as an interferent if the difference between the spiked test sample and the control was greater than the allowable error defined as the greater of 4 mmol/L or 10% of the mean TCO₂ result for the control sample.

The following table lists the concentrations of each substance at which no significant interference was found.

Substance	Highest concentration at which no interference was observed
Bilirubin	20 mg/dL
Hemoglobin	200 mg/dL
Intralipid	7092 mg/dL
Triglyceride	3233.8 mg/dL

Substance	Highest concentration at which no interference was observed
Thiopental	6.01 mg/dL

4. Assay Reportable Range:

See section A.2 Linearity

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

Traceability

The i-STAT test for TCO₂ is metrologically traceable to the IFCC TCO₂ reference method¹. Due to direct traceability to this TCO₂ reference method, the CHEM8+ is independent of the pH and PCO₂ traceability.

¹ IFCC Reference Measurement Procedure for Substance Concentration Determination of Total Carbon Dioxide in Blood, Plasma or Serum. Clin. Chem. Lab. Med. 2001; 39(3): 283-289.

6. Detection Limit:

The detection limits are supported by the linearity study (please see section 2 above). In addition, a limit of quantitation (LoQ) study TCO₂ on the i-STAT CHEM8+ Cartridge with the i-STAT 1 Analyzer was conducted following the recommendations in CLSI EP17-A2.

Limit of Quantitation (LoQ)

The LoQ for TCO₂ was evaluating using lithium heparin venous whole blood samples collected from a healthy subject each day. The samples were altered via tonometry and pH adjustment to levels below the lower limit of the reportable range and the TCO₂ concentration was value assigned using a reference method. Each sample was measure in 15 replicates per day for four days across each of two i-STAT CHEM8+ (blue) cartridge lots for a total of 120 cartridges. The LoQ was calculated for each of the two lots. The sponsor defined LoQ as the greater of the two lots at which the lowest concentration met the pre-defined total error goal of ≤ 4.00 mmol/L. The LoQ was determined to be 4 mmol/L, which is below the lower limit of the reportable range (5 – 50 mmol/L).

7. Assay Cut-Off:

Not applicable.

B Comparison Studies:

1. Method Comparison with Predicate Device:

The accuracy of the TCO₂ assay on the i-STAT CHEM8+ (blue) cartridge on the i-STAT 1 Analyzer was evaluated by a method comparison study for agreement with the predicate device. The study was conducted across three point of care sites. A total of 294 specimens, 183 lithium heparin venous whole blood specimens and 111 lithium heparin arterial whole blood specimens were tested. Twenty-one of 294 samples (7.14%) were contrived. The data

was analyzed separately for venous whole blood and arterial whole blood samples by Passing-Bablok regression analysis comparing the first replicate of the candidate device results to the singlicate result of lithium heparin plasma samples on the predicate device. Results are presented in the tables below.

Passing-Bablok Regression Summary of Venous Data

Site	N	Sample Range Tested (mmol/L)	Regression Equation	r
1	23	19 – 33	$y = 1.83 + 0.98x$	0.87
2	50	9 – 41	$y = 0.00 + 1.00x$	0.98
3	93	15 – 46	$y = 0.00 + 1.08x$	0.98
combined	183*	6 – 46	$y = -0.01 + 1.05x$	0.98

* Includes 17 contrived specimens.

Passing-Bablok Regression Summary of Arterial Data

Site	N	Sample Range Tested (mmol/L)	Regression Equation	r
1	53	14 – 39	$y = 3.58 + 0.97x$	0.96
2	48	15 – 50	$y = 1.00 + 1.00x$	0.96
3	6	23 – 29	N/A	
combined	111*	7 – 50	$y = 1.07 + 1.03x$	0.94

* Includes 4 contrived specimens.

2. Matrix Comparison:

Not applicable. Lithium heparin whole blood is the only acceptable sample type for this device.

C Clinical Studies:

1. Clinical Sensitivity:

Not Applicable.

2. Clinical Specificity:

Not Applicable.

3. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):

Not Applicable.

D Clinical Cut-Off:

Not Applicable.

E Expected Values/Reference Range:

Expected values for TCO₂ assay on the i-STAT CHEM8+ (blue) cartridge are cited from literature* .

Analyte	Unit	Reference Range	
		arterial	venous
Total Carbon Dioxide (TCO ₂)	mmol/L	23–27	24–29

*Calculated from Siggard-Andersen nomogram: E.L. Pruden, O. Siggard-Andersen, and N.W. Tietz, Blood Gases and pH, in Tietz Textbook of Clinical Chemistry, Second Edition, ed. C.A. Burtis and E.R. Ashwood. (Philadelphia: W.B. Saunders Company, 1994).

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

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