510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K183680

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
JPI	Class II	21 CFR 864.6400 - Hematocrit Measuring Device	HE - Hematology

II Submission/Device Overview:

A Purpose for Submission:
Modification of a previously cleared device — modification to the i-STAT CHEM8+ (blue) cartridge run on the i-STAT 1 Analyzer

B Measurand:
Hematocrit

C Type of Test:
Quantitative conductivity (electrical) measurement

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 hematocrit in arterial or venous whole blood in point of care or clinical laboratory settings.

Hematocrit measurements can aid in the determination and monitoring of normal or abnormal total red cell volume status that can be associated with conditions including anemia and erythrocytosis.

The i-STAT Hematocrit test has not been evaluated in neonates.

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 and the i-STAT CHEM8+ (blue) 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 hematocrit 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:

The Hematocrit test on the i-STAT CHEM8+ cartridge uses the conductivity method. The measured conductivity of the sample is inversely proportional to the number of red blood cells in the sample. In a whole blood sample, the plasma conducts electrical current and blood cells act as insulators. The hematocrit sensor, contained in the test cartridge, first measures the electrical conductivity of the calibrant solution, followed by the conductivity of the whole blood sample. The hematocrit result (expressed as % packed cell volume or %PCV) is calculated from the ratio of the sample conductivity to the calibrant conductivity. The conductivity of the sample is also a function of the plasma electrolyte concentration. The i-STAT Hematocrit test algorithm uses the measured electrolyte concentration in the sample (e.g. the sodium concentration) in the calculation of the test result. As a measured electrolyte concentration is required to calculate a hematocrit result, the Hematocrit test is always paired with the Sodium test in the i-STAT CHEM8+ cartridge.

V Substantial Equivalence Information:

A Predicate Device Name(s):
i-STAT Hematocrit test with i-STAT Alinity System

B Predicate 510(k) Number(s):
K163342

C Comparison with Predicate(s):

Device & Predicate Device(s):	K183680	K163342
Device Trade Name	i-STAT CHEM8+ Cartridge with the i-STAT 1 System (Hematocrit)	i-STAT Hematocrit Test on the i-STAT EC4+ Cartridge with the i-STAT Alinity System
General Device Characteristic Similarities		
Intended Use/Indications For Use	The i-STAT CHEM8+ cartridge with the i-STAT 1 System is intended for use in the in vitro quantification of hematocrit in arterial or venous whole blood in point of care or clinical laboratory settings. Hematocrit	The i-STAT Hematocrit test is intended for use in the in vitro quantification of packed red blood cell volume fraction in arterial or venous heparinized whole blood, or in arterial or venous non-anticoagulated whole blood.

	measurements can aid in the determination and monitoring of normal or abnormal total red cell volume status that can be associated with conditions including anemia and erythrocytosis. The i-STAT Hematocrit test has not been evaluated in neonates.	Hematocrit measurements can aid in the determination and monitoring of normal or abnormal total red cell volume status that can be associated with conditions including anemia and erythrocytosis. The i-STAT Hematocrit test with the i-STAT Alinity System has not been evaluated in neonates. The i-STAT Hematocrit test with the i-STAT Alinity System is not for use with capillary samples.
Principle of Measurement	Hematocrit is measured using the conductivity method.	Same
Reportable Range	15 – 75% packed cell volume (PCV)	Same
Analysis Time	~ 2 minutes	Same
Reagent Format	Cartridge	Same
General Device Characteristic Differences		
Sample Type	Lithium heparin anticoagulated arterial and venous whole blood	Lithium heparin anticoagulated and non-anticoagulated arterial and venous whole blood
Sample Volume	95 µL	65 µL

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: A Statistical Approach; Approved Guideline

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

CLSI EP17-A2: Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline – Second Edition

CLSI H7-A3: Procedure for Determining Packed Cell Volume by the Microhematocrit Method; Approved Standard – Third Edition

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

The study designs and analyses for precision studies were based on recommendations from CLSI EP05-A3: *Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline – Third Edition*.

Internal site precision (aqueous control material)
A single site precision study using four concentration levels of commercially available calibration verification samples were tested using one lot of i-STAT CHEM8+ (blue) cartridges and eight 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 approximately 80 test results per level. The results are summarized below.

20-Day Internal Precision Study Results Summary:

Level	N	Mean (%PCV)	Within-Run		Between-Run		Between-Day		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
L2	80	20.5	0.20	1.0	0.08	0.4	0.06	0.3	0.22	1.1
L3	80	32.4	0.29	0.9	0.08	0.2	0.07	0.2	0.31	1.0
L4	81	53.2	0.94	1.8	0.26	0.5	0.30	0.6	1.02	1.9
L5	80	63.9	0.79	1.2	0.31	0.5	0.18	0.3	0.87	1.4

Point of care precision (aqueous control material)
A three-site precision study using four concentration levels of aqueous control solutions were tested using one lot of i-STAT CHEM8+ (blue) cartridges and six i-STAT 1 analyzers. Each sample was tested at each site once per day for five days on six i-STAT 1 analyzers for a total of 90 measurements. The same operator conducted all testing at a given site, with a different operator at each site. The results were analyzed for within-day (contains between-analyzer) variance, within-site (contains within-day and between-day variance components) variance, and overall (summation of within-site and between-site variance components) variance and is provided in the table below for all sites combined.

Multi-Day Precision Study Results Summary (all sites combined):

Level	N	Min (%PCV)	Max (%PCV)	Mean (%PCV)	Within-Day		Within-Site		Overall	
					SD	%CV	SD	%CV	SD	%CV
L2	90	20	22	20.7	0.47	2.3	0.58	2.8	0.62	3.0
L3	90	33	34	33.1	0.22	0.7	0.28	0.8	0.28	0.8
L4	90	52	55	53.7	0.68	1.3	0.68	1.3	0.69	1.3
L5	90	62	65	63.7	0.71	1.1	0.71	1.1	0.74	1.2

Point of care precision (whole blood)
A venous whole blood precision study was performed using venous whole blood from patients collected in lithium heparin tubes, with samples either native or contrived, to generate the following hematocrit (%PCV) target ranges: < 38%, 38–51%, and > 51%. The study was performed at three point of care sites, by one operator at each site, with each sample tested in triplicate, on seven i-STAT 1 analyzers, for a total of 21 test results per sample. One lot of i-STAT CHEM8+ (blue) cartridges was used for the study. The abnormal low hematocrit specimens were contrived by adding plasma and the abnormal high hematocrit specimens were contrived by removing plasma. Within-analyzer (repeatability) variance and total (summation of between-analyzer and within-analyzer variance components) variance was determined for each sample at each site. Summaries of the results from this study are shown below.

Venous Whole Blood Precision Results by Sample Summary:

				Within-analyzer		Total	
HCT range (%PCV)	**Site**	**N**	**Mean (%PCV)**	**SD**	**%CV**	**SD**	**%CV**
< 38	01	21	34.2	1.09	3.2	1.09	3.2
	02	21	36.8	0.62	1.7	0.71	1.9
	03	21	37.7	0.53	1.4	0.56	1.5
	03	21	33.9	0.85	2.5	0.85	2.5
38 – 51	01	21	41.1	0.49	1.2	0.58	1.4
	01	21	42.5	0.62	1.5	0.62	1.5
	02	20*	42.2	0.51	1.2	0.51	1.2
	02	14*	47.2	1.22	2.6	1.22	2.6
	02	21	43.1	0.49	1.1	0.49	1.1
	02	21	38.9	0.38	1.0	0.38	1.0
	02	21	38.1	0.44	1.2	0.44	1.2
	03	21	43.9	0.69	1.6	0.69	1.6
	03	21	40.8	0.49	1.2	0.54	1.3
	03	21	41.5	0.53	1.3	0.53	1.3
	03	21	45.9	0.62	1.4	0.63	1.4
> 51	01	21	55.1	0.38	0.7	0.44	0.8
	02	21	55.0	0.53	1.0	0.53	1.0
	03	21	55.0	0.44	0.8	0.45	0.8

*excluded measurements for samples not tested within protocol-specified timeframe

Arterial whole blood repeatability was assessed using data collected across two point of care sites. An additional assessment of venous whole blood repeatability was determined using data collected at a single point of care site. Sixty-seven arterial samples, and 123 venous samples, collected during the method comparison study were measured in duplicate and repeatability estimates were calculated for each pair of duplicate results within three hematocrit ranges, $\leq$ 35%PCV, 35 – 50%PCV, and >50%PCV. Less than 10% of samples were contrived to cover the high hematocrit range. Only samples with duplicate measurements were included in the assessment. The study included measurements from one lot of i-STAT CHEM8+ (blue) cartridges run on seven i-STAT 1 analyzers by multiple point of care operators at each site.

Venous Whole Blood Precision Results Summary:

HCT Range (%PCV)	N	Mean (%PCV)	SD	%CV
≤ 35	48	28.6	0.44	1.6
35 – 50	66	42.5	0.60	1.4
> 50	9	60.0	0.47	0.8

Arterial Whole Blood Precision Results Summary:

HCT Range (%PCV)	N	Mean (%PCV)	SD	%CV
≤ 35	40	27.2	1.93	7.1
35 – 50	21	39.9	0.82	2.0
> 50	6	62.9	0.65	1.0

2. Linearity:

The linearity of the hematocrit test on the i-STAT CHEM8+ (blue) cartridge was evaluated following the recommendations in CLSI EP06-A – *Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline*. Venous whole blood was collected in a lithium heparin tube obtained from a healthy subject and the specimen was altered to produce a high hematocrit sample and a low hematocrit sample (via concentration or dilution with plasma, respectively). A series of 11 samples with varying hematocrit levels (< 15% PCV to > 75% PCV) were created by mixing different proportions of the high and low hematocrit samples. The low and high samples were value assigned for hematocrit using 20 i-STAT CG8+ (white) cartridges on i-STAT 1 analyzers. Each sample was measured in replicates of 20 using five lots of i-STAT CHEM8+ (blue) cartridges on i-STAT 1 analyzers. An assessment of linearity was performed and polynomial regression analyses for first-, second-, and third-order polynomials were determined. The third-order model was determined to have the best fit and was used for the assessment of the degree of non-linearity. For all test samples, the absolute value of the degree of non-linearity met the pre-defined acceptance criteria and linearity was demonstrated over the reportable range of 15 – 75% PCV.

3. Analytical Specificity/Interference:

The analytical specificity of the hematocrit test on the i-STAT CHEM8+ (blue) cartridge was established by conducting interference testing following the recommendations in CLSI EP07-A2 - *Interference Testing in Clinical Chemistry; Approved Guideline – Second Edition*. Interference from certain exogenous and endogenous substances was assessed using lithium heparin venous whole blood samples at two hematocrit levels: low hematocrit (26.5% – 31.5% PCV) and high hematocrit (57 – 63% PCV). Each low and high sample was further divided into two aliquots: control (with no added interferent) and test (with added interferent). Each sample was measured in replicates of 10 using one lot of i-STAT CHEM8+ (blue) cartridges. A substance was identified as an interferent if the point estimate of the difference between the test sample and the control sample was outside of the pre-defined allowable error of ±10.8% PCV. For any substances identified as an interferent, a dose-response analysis was performed to determine the degree of interference as a function of the substance concentration. Based on this method of interferent determination, substances listed

in the table below were found not to interfere with the hematocrit test on the i-STAT CHEM8+ (blue) cartridge at the concentration indicated.

Non-Interfering Substances:

Substance	Highest concentration at which no interference was observed
Bilirubin	0.342 mmol/L and 20.01 mg/dL
Nithiodote (Sodium Thiosulfate)	16.7 mmol/L and 264.04 mg/dL
Triglyceride	37.0 mmol/L and 3233.80 mg/dL
White Blood Cells (WBCs)	50,000 cells/µL
Intralipid	5296 mg/dL

Lithium bromide, total protein and high levels of white blood cells (WBC) were identified as interferents to the hematocrit test for samples with certain hematocrit levels, as summarized in the table below:

Interfering Substances:

Substance	Concentration	Interference
Lithium bromide	≥ 14.0 mmol/L	Decreased HCT results
Total Protein	≥ 10.2 g/dL	Increased HCT results
Total Protein	≤ 5.3 g/dL	Decreased HCT results
White Blood Cells	> 50,000 cells/µL	Increased HCT results

Additionally, factors that affect the sodium measurement on the i-STAT CHEM8+ (blue) cartridge will also affect hematocrit measurements, as the electrolyte concentration from the sample is used to correct the measured conductivity prior to reporting hematocrit results.

4. Assay Reportable Range:

   See Section A.2 Linearity

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

   For the measurement of hematocrit, the i-STAT 1 System can be customized to agree with methods calibrated by the microhematocrit reference method using either K_3EDTA or K_2EDTA anticoagulant. Mean cell volumes of K_3EDTA anticoagulated blood are approximately 2 – 4% less than K_2EDTA anticoagulated blood (CLSI H7-A3: *Procedure for Determining Packed Cell Volume by the Microhematocrit Method; Approved Standard – Third Edition*). While the choice of sample anticoagulant affects the result of the microhematocrit method (to which all hematocrit methods are calibrated), results on hematology analyzers are independent of the anticoagulant used because these methods dilute the sample. Since most clinical hematology analyzers are calibrated by the microhematocrit method using K_3EDTA anticoagulant, the i-STAT 1 System default customization is K_3EDTA.

6. Detection Limit:

Detection capability studies of limit of blank (LoB), limit of detection (LoD), and limit of quantitation (LoQ) for the hematocrit test on the i-STAT CHEM8+ (blue) cartridge with the i-STAT 1 analyzer were conducted following the recommendations in CLSI EP17-A2 – *Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline – Second Edition*.

LoB
The LoB study was conducted over three days using two lots of i-STAT CHEM8+ (blue) cartridges and whole blood samples collected in lithium heparin tubes from four unique subjects. The whole blood from each subject was altered to create a 'blank' hematocrit level sample for LoB testing. Since whole blood is not stable over time, each of the three days, a fresh whole blood blank sample was created from a unique specimen. Each of the four LoB samples was measured in 20 replicates on each of the two cartridge lots for a total of approximately 80 measurements per cartridge lot. The LoB was determined based on the maximal LoB value obtained for the cartridge lots tested. The LoB for the hematocrit test on the i-STAT CHEM8+ (blue) cartridge was determined to be 0.66% PCV.

LoD
The LoD study was conducted over three days using two lots of i-STAT CHEM8+ (blue) cartridges and evaluated whole blood samples collected in lithium heparin tubes from four unique subjects. The whole blood from each subject was altered to create four low-level hematocrit samples. Since whole blood is not stable over time, each of the three days, four fresh whole blood low-level hematocrit samples were created from a unique specimen. Each of the four low-level samples from each of the four subjects was measured in 10 replicates on each of the two cartridge lots for a total of approximately 160 measurements per cartridge lot. The LoD was determined based on the maximal LoD value obtained for the cartridge lots tested. The LoD for the hematocrit test on the i-STAT CHEM8+ (blue) cartridge was determined to be 1.38% PCV.

LoQ
The LoQ for hematocrit was evaluated using lithium heparin venous whole blood collected on each day, over the course of three days, from unique healthy subjects. The whole blood was altered to produce four low-level hematocrit samples below the lower limit of the reportable range (< 15% PCV). Each of the four samples was measured in 15 replicates on each of two i-STAT CHEM8+ (blue) cartridge lots for a total of 60 measurements per cartridge lot. The LoQ was determined to be 12.4 %PCV, which is below the lower limit of the i-STAT Hematocrit test reportable range (15 – 75 %PCV).

7. Assay Cut-Off:

Not applicable

B Comparison Studies:

1. Method Comparison with Predicate Device:

A method comparison study was performed comparing the performance of the hematocrit test on CHEM8+ (blue) cartridges run on the i-STAT 1 analyzer compared to the hematocrit test on the EC4+ cartridge run on the i-STAT Alinity analyzer (K163342). A total of 194 specimens from subjects ≥ 19 years old were tested across three point of care sites by operators representative of point of care operators. Specifically, 124 lithium heparin venous whole blood specimens and 70 lithium heparin arterial whole blood specimens were evaluated in the study. Less than 10% of all specimens used in the study were contrived to supplement the lowest and highest hematocrit specimens. The data was analyzed separately for venous whole blood and arterial whole blood specimens by Passing-Bablok regression analyses comparing the first replicate from the candidate device to the mean of duplicate measurements from the predicate device for each specimen. Data was also analyzed for venous and arterial whole blood specimens combined, as the data was demonstrated to be poolable. Results are presented in the tables below.

Passing-Bablok Regression Analyses Summary

Specimen Type	N	HCT Range Tested (%PCV)	r (95% CI)	Slope (95% CI)	Intercept (95% CI)
Venous + Arterial (All Sites Combined)	194	16 – 75	1.00 (1.00, 1.00)	1.030 (1.000, 1.043)	-0.530 (-1.087, 0.750)
Venous (Site 1)	124	16 – 75	1.00 (1.00, 1.00)	1.032 (1.000, 1.048)	-0.597 (-1.238, 1.000)
Arterial (All Sites Combined)	70	19 – 74	1.00 (0.99, 1.00)	1.033 (1.000, 1.064)	-0.617 (-1.733, 1.000)
Arterial (Site 2)	31	23 – 74	1.00 (1.00, 1.00)	1.000 (1.000, 1.051)	1.000 (-1.368, 1.000)
Arterial (Site 3)	38	19 – 40	0.99 (0.97, 0.99)	1.056 (1.000, 1.125)	-1.254 (-3.375, 0.750)

Predicted biases at medical decision points for hematocrit (33% PCV, 53% PCV, 56% PCV, and 70% PCV) were also determined for venous and arterial whole blood, with results demonstrating acceptable performance.

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 the hematocrit test on the i-STAT CHEM8+ (blue) cartridge are cited from literature.

Adult Reference Ranges

Analyte	Unit	Adult Reference Ranges† Arterial and Venous	
	%PCV (packed cell volume)	**Female**	**Male**
Hematocrit/HCT**		38−46	43−51
	Fraction	0.38−0.46	0.43−0.51

Pediatric Reference Ranges by Age (and Gender)

Age	Reference Range, %PCV‡
1 month	33–55
2 months	28–42
4 months	32–44
6 months	31–41
9 months	32–40
12 months	33–41
1-2 years	32–40
3-5 years	32–42
6-8 years	33–41
9-11 years	34–43
12-14 years	Female: 34–44; Male: 35–45
15-17 years	Female: 34–44; Male: 37–48

†B.E. Statland, Clinical Decision Levels for Lab Tests (Oradell, NJ: Medical Economics Books, 1987).
‡Wu, Alan H.B. Tietz, Clinical Guide to Laboratory Tests – Fourth Edition (St. Louis, MO: W. B. Saunders Elsevier, 2006).

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.