510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:

K163342

B. Purpose for Submission:

Migration of the previously cleared i-STAT Hematocrit test (previously cleared for use with the i-STAT 1 Wireless Analyzer; K103195) to the i-STAT Alinity System (K153357; instrument cleared with i-STAT Sodium test).

C. Measurand:

Hematocrit

D. Type of Test:

Quantitative conductivity (electrical) measurement

E. Applicant:

Abbott Point of Care, Inc.

F. Proprietary and Established Names:

i-STAT Hematocrit test with i-STAT Alinity System

G. Regulatory Information:

1. Regulation section:

   21 CFR § 864.6400 – Hematocrit measuring device

2. Classification:

   Class II

3. Product code:

   JPI – Device, hematocrit measuring

4. Panel:

Hematology (81)

H. Intended Use:

1. Intended use(s):

   See Indications for use below.

2. Indication(s) for use:

   The i-STAT Alinity instrument with i-STAT tests is intended for use in point-of-care or clinical laboratory settings. The i-STAT Alinity system is intended for the quantitative measurement of various analytes in arterial and venous whole blood.

   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.

   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.

   For in vitro diagnostic use.

3. Special conditions for use statement(s):

   For prescription use only

   For point-of-care or clinical laboratory settings

4. Special instrument requirements:

   i-STAT Alinity instrument

I. Device Description:

The i-STAT Alinity System is a handheld, *in vitro* diagnostic analytical device designed to run i-STAT test cartridges. The system is designed for use at or near the point of patient care, by trained medical professionals and is for prescription use only.

The i-STAT Alinity System is comprised of the instrument, rechargeable battery, base station, electronic simulator, control material, printer and i-STAT test cartridges. The i-STAT Alinity instrument features a barcode scanner, user interface with touch screen display and wireless capability. The instrument reports quantitative results within approximately 2 minutes.

The i-STAT test cartridge contains sensors which are located on the biosensor chips. The instrument interacts with the cartridge to move fluid across the sensors and generate a quantitative result. Cartridges require two to three drops of whole blood which are typically applied to the cartridge using a syringe.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   i-STAT Hematocrit test with the i-STAT 1 Wireless Analyzer

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

   K103195

3. Comparison with predicate:

Similarities		
Item	Device i-STAT Hematocrit test with i-STAT Alinity System	Predicate i-STAT Hematocrit test with i-STAT 1 Wireless Analyzer (K103195)
Intended Use	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 whole blood. It is intended for use with the i-STAT Alinity instrument 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.	Same
Principle of Measurement	Hematocrit is measured using the conductivity method.	Same
Calibration	1-point on-board calibration (contained within cartridge)	Same
Test traceability	Microhematocrit method	Same
Reportable Range	15–75% packed cell volume (PCV)	Same

Similarities		
Item	Device i-STAT Hematocrit test with i-STAT Alinity System	Predicate i-STAT Hematocrit test with i-STAT 1 Wireless Analyzer (K103195)
Sample Volume	65–95 µL	Same
Time to Test	~ 2 minutes	Same
Test Format	Cartridge	Same
Test Preparation	Ready-to-Use	Same
Test Storage and Stability	Storage: 2–8°C (35–46°F)	Same
Quality Checks	A series of quality checks are automatically run each test cycle prior to the system generating a result. Quality checks verify the analyzer motor, electrical, pressure, and temperature systems and cartridge elements.	Same

Differences		
Item	Device – i-STAT Hematocrit test with i-STAT Alinity System	Predicate – i-STAT Hematocrit test with i-STAT 1 Wireless Analyzer (K103195)
Sample Type	Fresh heparinized arterial or venous whole blood	Fresh heparinized arterial, venous or capillary whole blood

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

CLSI C46-A2: Blood Gas and pH Analysis and Related Measurements; Approved Guideline – Second Edition

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 EP09-A3: Measurement Procedure Comparison and Bias Estimation Using Patient Samples; Approved Guideline – Third Edition

CLSI EP15-A3: User Verification of Precision and Estimation of Bias; Approved Guideline – Third 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

L. Test Principle:

The i-STAT Hematocrit test uses the conductivity method. The measured conductivity of the sample is inversely proportional to the number of 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 i-STAT Hematocrit test is always paired with the i-STAT Sodium test in an i-STAT cartridge.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   For the analytical performance studies described below, the i-STAT Hematocrit test was performed using the EC4+ cartridge, which contains both the hematocrit test and the sodium test, and was run on the i-STAT Alinity instrument.

   a. Precision/Reproducibility:

      i. Internal Site/20-day Precision Study:

         The internal precision study was performed over the course of 20-days using four levels of control material, with duplicates of each sample tested twice a day. This study was performed at one site, using two operators, on 10 i-STAT Alinity instruments, with one lot of test cartridges (type EC4+; 500 cartridges used). The following components of variability for each level of control were determined and are shown below: within-run, between-run, between-day, and total (within-laboratory) precision. The i-STAT Hematocrit test demonstrated acceptable precision when evaluated using control material at four %PCV levels spanning the reportable range of the test.

20-Day Internal Precision Study Results Summary:

Control Material Level	N	Mean (%PCV)	Within-Run		Between-Run		Between-Day		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
CV L2	80	16.9	0.44	2.60	0.09	0.53	0.09	0.53	0.46	2.72
CV L3	80	33.9	0.48	1.42	0.13	0.38	0.11	0.32	0.51	1.50
CV L4	80	55.2	0.47	0.85	0.12	0.22	0.09	0.16	0.49	0.89
CV L5	80	65.0	0.37	0.57	0.10	0.15	0.09	0.14	0.39	0.60

ii. Multi-Site/Multi-Day Precision Study:

A multi-day study was performed at three sites using four levels of control material (i-STAT TriControls Calibration Verification Set) for five days, with one run per day on five instruments and one lot of test cartridges. The results from this study are shown below for all sites combined (within-site/total variability includes within-run and between-run variance components). For all levels of control material evaluated, the within-site SD and overall SD were found to be the same, indicating that there was negligible between-site variability. The i-STAT Hematocrit test demonstrated acceptable precision when evaluated using control material at four %PCV levels spanning the reportable range of the test.

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

Calibration Verification Material Level	N	Min (%PCV)	Max (%PCV)	Mean (%PCV)	Within-Run		Within-Site (Total)		Overall SD
					SD	%CV	SD	%CV	
CV L2	75	17	18	17.7	0.45	2.57	0.46	2.63	0.46
CV L3	75	35	36	35.5	0.48	1.36	0.50	1.42	0.50
CV L4	75	56	58	57.1	0.37	0.64	0.38	0.66	0.38
CV L5	75	67	68	67.3	0.37	0.56	0.47	0.70	0.47

iii. Whole Blood Precision Study

The whole blood precision study was performed using nine venous whole blood patient samples, either native or contrived, to generate the following hematocrit (%PCV) target ranges: < 38%, 38–51%, and > 51%. The study was performed at three POC sites, with each sample tested in triplicate, on seven i-STAT Alinity instruments per site, for a total of 21 test results per sample. One lot of test cartridges (type EC4+) 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. A summary of the results from this study is shown below. The i-STAT Hematocrit test demonstrated acceptable precision when evaluated using fresh venous whole blood at four %PCV levels.

Whole Blood Precision Study Results Summary:

Concentration Level (%PCV)	Site	N	Mean (%PCV)	Within-Analyzer		Total	
				SD	%CV	SD	%CV
< 38	1	21	34.6	0.44	1.26	0.51	1.49
	2	21	35.2	0.44	1.24	0.44	1.24
	4	21	34.4	0.49	1.42	0.50	1.45
38–51	1	21	45.5	0.49	1.07	0.51	1.13
	2	21	42.5	0.44	1.03	0.52	1.22
	4	21	42.2	0.44	1.03	0.44	1.03
> 51	1	21	54.9	0.44	0.80	0.48	0.88
	2	21	53.1	0.30	0.57	0.30	0.57
	4	21	53.0	0.22	0.41	0.22	0.41

b. Linearity/assay reportable range:

The linearity study was performed using heparinized venous whole blood from one subject to make a high hematocrit sample and a low hematocrit sample (via concentration or dilution with plasma, respectively). A series of seven samples with varying hematocrit levels (< 15% PCV to > 75% PCV) were created by mixing different proportions of the low and high hematocrit samples. The low and high samples were (hematocrit) value assigned using 10 i-STAT EC4+ test cartridges on 10 i-STAT 1 Analyzers (model 300). The study was conducted at one site, using a single instrument, and one lot of test cartridges. The regression coefficients for the first, second, and third order polynomial regression models were determined and the non-linear models were assessed for fit. 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 of $\leq$ 0.81 %PCV for samples with expected values < 15 %PCV, or $\leq$ 5.4 %PCV of the expected value for samples with expected values $\geq$ 15.0 %PCV. The linearity of the i-STAT Hematocrit test used with the i-STAT Alinity instrument has been demonstrated over the reportable range of the test of 15–75% PCV. The absolute value of non-linearity for the test ranged from 0.19 to 0.81 %PCV.

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

i. Controls and calibrators:

Control and calibration materials to be used with the i-STAT Alinity System are i-STAT Control Solutions (Levels 1, 2, and 3), i-STAT TriControl Solutions (Levels 1, 2, and 3), i-STAT Calibration Verification material (Levels 1–5), and i-STAT TriControl Calibration Verification material (Levels 1–5). The control and calibration verification materials were cleared under K972868.

ii. Test cartridges:

A number of different cartridges containing a variety of hematological and

clinical chemistry tests in various combinations are currently cleared for use with previous models of the i-STAT instrument. The hematocrit test on the EC4+ test cartridge type was evaluated in the majority of the analytical studies and the method comparison study. The i-STAT Hematocrit test, when evaluated on the i-STAT 1 Analyzer, is directly traceable to the microhematocrit centrifugation reference method. The i-STAT Hematocrit test when run on the i-STAT Alinity has been found to be equivalent to the i-STAT Hematocrit test run on the i-STAT 1 Analyzer.

d. Detection limit:

The limit of quantification (LoQ) study was performed using fresh venous whole blood from four subjects with same-subject plasma added to dilute samples to the target range of 13.5–14.5 %PCV. Each sample was value assigned using the i-STAT EC4+ cartridges run on the i-STAT 1 Analyzer, which is directly traceable to the microhematocrit centrifugation reference method. Determination of the LoQ for the hematocrit test on the i-STAT Alinity instrument used 52 instruments, in which each of the four diluted samples were then tested on two cartridge lots using 50 cartridges from each lot, for a total of 100 test results per sample. The LoQ for each cartridge lot was determined to be the lowest mean/median hematocrit level to meet the calculated total error goal. The LoQ for the i-STAT Hematocrit test was thus determined to be 14.0% PCV, which is the larger of the two LoQ values associated with the two lots evaluated.

The limit of blank (LoB) and limit of detection (LoD) for the i-STAT Hematocrit test on the i-STAT Alinity were determined in a study conducted over four days, using two lots of i-STAT EC4+ cartridges, and 40 i-STAT Alinity instruments. Heparinized venous whole blood samples from four subjects were altered to generate low hematrocrit level samples for the LoD study and used to generate plasma ("zero hematocrit") samples for the LoB study. The LoB was determined to be 3.8 %PCV and the LoD was determined to be 4.5 %PCV for the i-STAT Hematocrit test on the i-STAT Alinity.

e. Analytical specificity:

The interference study was performed using heparinized venous whole blood samples at two hematocrit levels (low and high) tested against six potentially interfering compounds at concentrations indicated by CLSI EP07-A2 to be "toxic" for exogenous compounds or "pathological" for endogenous compounds (or "similarly high" for compounds not specified in CLSI EP07-A2). For compounds identified as interferents at the high concentration, a concentration-response curve evaluating multiple concentrations of the interfering compound was generated. Based on this method of interferent determination, compounds listed in the table below were found not to interfere with the i-STAT Hematocrit test at the concentration indicated:

Non-Interfering Substances:

Compound	Test Concentrations
Bromide*	< 37.5 mmol/L and < 325.69 mg/dL
Bilirubin	≤ 0.342 mmol/L and ≤ 20.01 mg/dL
Sodium Thiosulfate	≤ 16.7 mmol/L and ≤ 264.04 mg/dL
Triglyceride	≤ 37 mmol/L and ≤ 3233.80 mg/dL
Total Protein (Human Serum Albumin)	≤ 12 g/dL and ≤ 12,000 mg/dL
White Blood Cells	21,700 WBC/µL

*Bromide (37.5 mmol/L) is an interferent with the sodium test and it may result in an increased rate of star out (***) for the hematocrit test.

Total protein and high levels of white blood cells (WBC) were identified as interferents to the i-STAT Hematocrit test for samples with certain hematocrit levels, as indicated in the table below:

Interfering Substances:

Compound	Test Concentration (g/dL)	Hematocrit Level (%PCV)	Result
Total Protein (Human Serum Albumin)	>12	26.5 – 31.5	Interfering
Total Protein (Human Serum Albumin)	>12	57.0 – 63.0	Non-interfering
White Blood Cells	> 50,000 WBC/µL	26.5 – 31.5	Interfering

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

The method comparison study was initially performed using 229 heparinized whole blood samples (134 venous and 95 arterial samples). In order to provide better coverage of the reportable range of 15–75 % packed cell volume (PCV), an additional 11 heparinized venous samples (for a total of n = 240 samples) were additionally evaluated to help supplement the samples evaluated in the initial study. Less than 10% of all samples used in the study were contrived to supplement the lowest and highest hematocrit samples. Samples were tested in duplicate on both the i-STAT Alinity instrument and the i-STAT 1 Wireless Analyzer (K103195), using two of each instrument type at each of the three clinical sites. Each site collected specimens from the point-of-care (POC) settings of the intensive care unit and emergency department. Two sites collected specimens from general hospital floors. Specimens were evaluated in blood gas laboratories or in the hospital laboratory by typical POC operators, to include nurses, research technicians, phlebotomists, nursing assistants, clinical site coordinators, and certified clinical research coordinators.

Passing-Bablock (PB) and Weighted Deming (WD) regression analyses were performed on the data separately for each site and for all sites combined, and the

results for arterial and venous samples were combined for the analyses. The results from the Weighted Deming regression analyses comparing the first replicate result from the i-STAT Hematocrit test (EC4+ cartridge) run on the i-STAT Alinity to the mean result of the i-STAT Hematocrit test (EC4+ cartridge) run the i-STAT 1 Wireless Analyzer for each site and all sites combined is shown below. Individual site analyses were performed for the n = 229 samples initially included in the study. The analyses for the cumulative site data includes all samples evaluated in the study (n = 240).

Individual Site Results:

Site	N	Sample Range Tested (%PCV)	r (95% CI)	r^2 (95% CI)	Slope (WD) (95% CI)	Intercept (WD) (95% CI)
1	78	22–62	0.993 (0.989, 0.995)	0.986	1.029 (0.978, 1.080)	-0.769 (-2.775, 1.238)
2	90	21–70	0.997 (0.996, 0.998)	0.995	1.006 (0.987, 1.026)	0.235 (-0.467, 0.938)
4	61	18–55	0.986 (0.977, 0.992)	0.972	1.042 (0.976, 1.108)	-1.356 (-4.102, 1.389)

Combined Sites Results:

N	Sample Range Tested (%PCV)	r (95% CI)	r^2	Method	Slope (95% CI)	Intercept (95% CI)
240	15–75	0.995 (0.994, 0.996)	0.991	PB	1.000 (1.000, 1.000)	0.500 (0.500, 0.500)
				WD	1.016 (1.001, 1.031)	-0.256 (-0.866,0.355)

b. Matrix comparison:

The purpose of this study was to determine if the performance of the i-STAT Hematocrit test on the i-STAT Alinity was comparable for both anticoagulated (heparinized) venous whole blood samples and non-anticoagulated venous whole blood samples. The anticoagulant study was performed using 40 anticoagulated (lithium heparin) and non-anticoagulated whole blood samples spanning the hematocrit reportable range (15–75 %PCV). Performance was assessed using one lot of i-STAT EC4+ cartridges on eight i-STAT Alinity instruments. Deming regression of the results obtained from the two sample types gave a slope of 1.00 and a correlation coefficient of 1.00, which indicates that these two sample types gave comparable results when tested using the i-STAT Hematocrit test on the i-STAT Alinity.

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

5. Expected values/Reference range:

Adult Reference Ranges:

Test	Units	Reference Range – Whole Blood (Stadtland, 1987)
Hematocrit (Hct)	%PCV	Female: 38–46; Male: 43–51
	Fraction	Female: 0.38–0.46; Male: 0.43–0.51
Hemoglobin (Hb)	g/dL	Female: 12–15.6; Male 14–17
	g/L	Female: 120–156; Male: 140–170
	mmol/L	Female: 7–10; Male: 9–11

Pediatric Reference Ranges by Age (and Gender) for Hemotocrit[1]:

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

The i-STAT Hematocrit reference range for whole blood is intended to be used as a guide for the interpretation of results. Reference range may vary with demographic factors such as age, gender and heritage; therefore, it is recommended that reference ranges be determined for the population being tested. Each test facility should establish its own reference range.

N. Instrument Name:

i-STAT Alinity Instrument

[1] Wu, Alan H.B., "Tietz Clinical Guide to Laboratory Tests," Fourth Edition, 2006. W.B. Saunders Company.

O. System Descriptions:

1. Modes of Operation:

   Does the applicant's device contain the ability to transmit data to a computer, webserver, or mobile device?

   Yes ___X_____ or No _____

   Does the applicant's device transmit data to a computer, webserver, or mobile device using wireless transmission?

   Yes ___X_____ or No _____

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:

   The specimen identification may be manually entered or automatically scanned by the device.

4. Specimen Sampling and Handling:

   The i-STAT Hematocrit test is intended to be used with arterial and venous whole blood. The sample type must be selected using the device touchscreen. After the sample type is selected the on-screen help appears and the help graphics on the device screen vary based on the sample type selected. The reagent cartridge contains a sample chamber that includes the sample well and the channel leading from the well up to the fill mark. The cartridge label is intended to help the operator fill the cartridge correctly. When filled, the sample chamber contains sufficient sample for testing. Sample volume and placement are monitored by the instrument and an error message will be generated if filled incorrectly. Either lithium heparin tube or syringe could be used but samples must be analyzed within 30 minutes. Samples should be remixed thoroughly before testing. If plain non-anticoagulated tube or syringes are used then samples must be analyzed within 3 minutes after collection.

5. Calibration:

   The cartridge housing the i-STAT Hematocrit test includes an on-board calibration that is performed with each cartridge use. The calibration solution is automatically released from its foil pack and is positioned over the sensors. The signals produced by the

sensors' responses to the calibration solution are measured. This one-point calibration adjusts the offset of the stored calibration curve. The calibration solution is used to measure a known resistance before the sample resistance is measured. The final hematocrit result is based on a ratio of the known resistance and the unknown (sample) resistance.

6. Quality Control:

   Control and calibration materials to be used with the i-STAT Alinity System are i-STAT Control Solutions (Levels 1, 2, and 3), i-STAT TriControl Solutions (Levels 1, 2, and 3), i-STAT Calibration Verification material (Levels 1–5), and i-STAT TriControl Calibration Verification material (Levels 1–5). The control and calibration verification materials were cleared under K972868.

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

1. Temperature Operating Range Study:

   The purpose of this study was to evaluate the performance of the i-STAT Hematocrit test on the i-STAT Alinity across the operating temperature range of the i-STAT cartridge (16°C to 30°C). Using the i-STAT EC4+ cartridge, the cartridge temperature operating range of the i-STAT Hematocrit test was evaluated using blood samples at four hematocrit levels that spanned the reportable range of the test on 40 i-STAT Alinity instruments. The results of this study demonstrate that the performance of the i-STAT Hematocrit test on the i-STAT Alinity instrument is not affected by operating temperature over the temperature range of 16°C to 30°C.

2. Recovery Study:

   The purpose of this study was to evaluate the i-STAT Hematocrit test recovery (using the i-STAT EC4+ cartridge) on the i-STAT Alinity instrument across the reportable range of 15 – 75% PCV. The recovery study used seven whole blood samples with hematocrit levels ranging from < 15% PCV to > 75% PCV, and the highest and lowest hematocrit were value assigned using the i-STAT EC4+ cartridges run on the i-STAT 1 Analyzer. The i-STAT Hematocrit test on the i-STAT Alinity instrument recovered between 100.1% to 102.8% of the assigned hematocrit value.

3. Altitude Study:

   The purpose of this study was to evaluate the performance of the i-STAT Hematocrit test (using the i-STAT EC4+ cartridge) on the i-STAT Alinity instrument at elevations of up to 10,000 feet above sea level. The altitude study was performed at three altitudes (250, 5,000, and 10,000 feet) using three levels of i-STAT TriControl Control material (L1, L2, and L3) on six i-STAT Alinity instruments. The study was performed using control material to ensure that test results generated on different days at different altitudes were

comparable. The study as performed demonstrated that the Hematocrit test was found to be equivalent from sea level to elevations up to 10,000 feet.

4. Cleaning Robustness Study:

   The purpose of the cleaning robustness study was to evaluate the i-STAT Alinity performance after 10,950 cleaning and disinfection cycles using CaviWipes Disinfecting Towelettes (which corresponds to three years of peak use, with 10 cleaning and disinfection cycles per day). The study design was based on communications with the FDA through Pre-Submission Q130270 and using "Reprocessing Medical Devices in Health Care Settings: Validation Method and Labeling: Guidance for Industry and Food and Drug Administration Staff." The study utilized three i-STAT Alinity instruments and three i-STAT 1 Wireless Analyzers, used three lots of i-STAT E3+ test cartridges, and whole blood samples (from three healthy subjects) at four concentrations of hematocrit spanning the range of the test were evaluated at four testing events: pre-test (before any cleaning/disinfection), after 3650 cycles, after 7300 cycles, and after 10,950 cycles. At each testing event, the i-STAT Alinity was evaluated for its appearance, operational functionality, and performance. Based on the results of this study, performance up to 10,950 cycles (or three years of peak use) was not supported for all sample types tested (samples with different levels of hematocrit).

5. Lot-to-Lot (Cartridge) Imprecision Study:

   The purpose of this study was to evaluate the lot-to-lot component of variability of the i-STAT Hematocrit test on the i-STAT Alinity instrument. Precision was evaluated using three lots of i-STAT EC4+ cartridges over 5 days with test samples spanning the reportable range of the test (15 – 75 %PCV). Each i-STAT EC4+ cartridge lot used in this study was manufactured with an independent lot of hematocrit biosensor chips, thus the three cartridge lots are unique. The precision of the i-STAT Hematocrit test was evaluated on 15 i-STAT Alinity instruments using four levels of commercially available i-STAT TriControl Calibration Verification materials. The lot-to-lot (between-lot) variability for the different levels of control material had %CV values that ranged from 0.20%CV (highest control level) to 0.80%CV (lowest control level). Lot-to-lot imprecision was found to meet the predefined acceptance criteria.

   Lot-to-Lot Variability of i-STAT Hematocrit Test on EC4+ Cartridges

Control Material Level	N	Mean (%PCV)	Within-Run/Day		Between-Lot		Between-Day		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
CV L2	75	17.6	0.36	2.05	0.14	0.80	0.07	0.40	0.39	2.22
CV L3	75	34.6	0.34	0.98	0.10	0.29	0.07	0.20	0.36	1.04
CV L4	75	55.5	0.37	0.67	0.21	0.38	0.11	0.20	0.44	0.79
CV L5	75	65.4	0.35	0.54	0.13	0.20	0.00	0.14	0.38	0.58

6. Operator-to-Operator Imprecision Study:

   The purpose of this study was to evaluate the operator-to-operator component of variability of the i-STAT Hematocrit test on the i-STAT Alinity instrument. Precision was evaluated using one lot of i-STAT EC4+ cartridges over 5 days with test samples spanning the reportable range of the test (15–75 %PCV). Testing was conducted by three operators representative of point of care operators: a medical doctor, a nurse and a phlebotomist. The precision of the i-STAT Hematocrit test was evaluated on i-STAT Alinity instruments using commercially available i-STAT TriControl Calibration Verification materials. The operator-to-operator variability for the different levels of control material had %CV values that ranged from 0.28%CV (lowest control level) to 0.12%CV (highest control level). Operator-to-operator imprecision was found to meet the predefined acceptance criteria.

7. Evaluation of the Effect of Sodium Study:

   Since the measurement of hematocrit by the i-STAT Hematocrit test is based on a conductivity method that relies on the measurement of the sodium concentration in the sample, an evaluation of the effect of physiological levels of sodium on hematocrit measurements made by the i-STAT Hematocrit test was conducted. The performance of the i-STAT Hematocrit test was evaluated on the i-STAT Alinity instrument using whole blood test samples at three hematocrit levels and three sodium concentrations (for a total of nine test conditions). The effect of the sodium concentration was evaluated by comparing the i-STAT Hematocrit test result from an i-STAT EC4+ cartridge to the microhematocrit result of each test sample. An interfering effect was identified if the difference between the results was > 10.8% CV of the microhematocrit result. The microhematocrit (reference) method was used as the comparator in this study because the sodium concentration (ionic strength) of the test sample has a direct effect on the size of the red blood cells and thus the true hematocrit of the sample. The 95% confidence intervals of the observed differences fell within the acceptable differences and the acceptance criteria were met.

8. Interference by total protein:

   Hematocrit measurements may be affected by the level of total protein in the blood sample. The sponsor includes the following limitations in the labeling:

Displayed Result	Total Protein < 6.5 g/dL	Total Protein > 8.0 g/dL
HCT < 40 %PCV	Hematocrit decreased by approximately 1 %PCV for each decrease of 1 g/dL of total protein below the normal range.	Hematocrit increased by approximately 1 %PCV for each increase of 1 g/dL of total protein above the normal range.
HCT > 40 % PCV	Hematocrit decreased by approximately 0.75% PCV for each decrease of 1 g/dL of total protein below the normal range.	Hematocrit increased by approximately 0.75 %PCV for each increase of 1 g/dL of total protein above the normal range.

"Total protein levels may be low in neonatal and burn patient populations, as well as in additional clinical populations listed in Statland (e.g. kidney disease, liver disease, severe malnutrition, and malabsorption conditions)[2]. Total protein levels may also be decreased in patients undergoing cardiopulmonary bypass IV fluids. Care should be taken when using hematocrit results from patients with total protein levels below the adult reference range (6.5 to 8 g/dL)."

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.

[2] B.E. Stadtland, Clinical Decision Levels for Lab Tests (Oradell, NJ: Medical Economics Books, 1987).