

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

A. 510(k) Number:

k153357

B. Purpose for Submission:

Adding previously cleared sodium assay onto a new instrument platform

C. Measurand:

Sodium

D. Type of Test:

Quantitative, Ion Specific Electrode (Potentiometric method)

E. Applicant:

Abbott Point of Care Inc.

F. Proprietary and Established Names:

i-STAT Alinity System with i-STAT Sodium test

G. Regulatory Information:

| Regulation Name | Classification | Regulation Section | Product Code | Panel |
|--------------------|----------------|--------------------|--------------|----------------|
| Sodium test system | Class II | 21 CFR § 862.1665 | JGS | Chemistry (75) |

H. Intended Use:

1. Intended use(s):

See Indications for use below.

2. Indication(s) for use:

The i-STAT Alinity System with i-STAT Sodium test is intended for use in point of care or clinical laboratory settings. The i-STAT Alinity System with Sodium test is intended for the quantitative measurement of sodium in arterial and venous whole blood. Sodium measurements are used for monitoring electrolyte imbalances.

For *in vitro* diagnostic use.

3. Special conditions for use statement(s):

For prescription use only

For Point-of-Care or clinical laboratory setting

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 point of care or clinical laboratory settings 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 Alinity system has the following components and functions:

- i-STAT Alinity Instrument: Used to perform cartridge testing, reviewing test results, and conducting quality control (QC) testing.
- i-STAT Alinity Base Station: Used to recharge the battery installed in the i-STAT Alinity.
- i-STAT Cartridge: Contains sensors and reagents for all patient and quality testing.
- i-STAT Alinity Rechargeable battery: Provides main power source to the instrument.

- i-STAT Alinity Electronic Simulator: Provides an independent check on the instruments thermal controls and success of software updates.
- i-STAT Alinity Portable Printer: Used to print records stored in the instrument.

The i-STAT cartridge contains test reagents which are located on the biosensors chips. The instrument interacts with the cartridge to move fluid across the biosensors and generate a quantitative result. The biosensor chips, also known as ion selective electrodes, are a transducer which is made from thin film technology microfabricated onto silicon chips. The biosensors are made of chemically sensitive films coated over active regions of the silicon chips. The sodium test generates a potentiometric signal that is read by the instrument and converted into results. Cartridges require two to three drops of whole blood which are typically applied to the cartridge using a syringe. The instrument calibration is a one-point on board calibration and is performed each time a cartridge requiring calibration is used. This one-point calibration adjusts the offset of the stored calibration curve. A five-level calibration verification set is used to verify the calibration of i-STAT cartridges throughout the analyte reportable range.

The sodium test included in the EC3+ cartridge is identical to the assay cleared in k103195 and is representative for the sodium assay found in all i-STAT cartridges that include the sodium assay.

J. Substantial Equivalence Information:

1. Predicate device name(s):

i-STAT 1 Wireless Analyzer

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

k103195

3. Comparison with predicate:

| Similarities | | |
|--------------------------|--|---|
| Characteristics | Predicate Device (k103195) | Candidate Device i-STAT Alinity system with sodium test |
| Intended Use | <p>The i-STAT 1 Wireless Analyzer is used by trained medical professionals for running a variety of clinical chemistry tests and test panels contained in i-STAT test cartridges.</p> <p>The test for sodium, as part of the i-STAT System, is intended for use in the in vitro quantification of sodium in whole blood.</p> | Same |
| Calibration | 1-point on-board (contained within the cartridge) This one-point calibration adjusts the offset of the stored calibration curve. | Same |
| Sodium Reportable Range | Sodium: 100-180 mmol/L (mEq/L) | Same |
| Sample Volume | 65 µL | Same |
| Traceability of Sodium | NIST SRM956 | Same |
| Principle of Measurement | Sodium: Ion selective electrode | Same |
| Reagent Format | Cartridge | Same |
| Reagent Storage | Storage: 2°C to 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 |
| Time to test | ~2 minutes | Same |

| Differences | | |
|-----------------------|--|---|
| Characteristics | Predicate Device (k103195) | Candidate Device i-STAT Alinity system with sodium test |
| Sample type | Fresh arterial, venous or capillary whole blood | Fresh arterial or venous whole blood. |
| Weight | 1.4 lb. (635 grams) | 1.87 lb (850 g) |
| Dimensions | Width 3.0 in. (7.7 cm) Length | Width 5.62 in (14.3 cm) |
| Power | Two 9-volt lithium batteries, or rechargeable battery. | Lithium-Ion rechargeable battery |
| Data Storage | 1,000 patient records | 500 patient records |
| Connectivity | TCP/IP 802.11 (WiFi) b/g | TCP/IP 802.11 a/b/g/n |
| Barcode Technology | Class II laser bar code scanner | Imager that reads 1-D and 2-D barcodes |
| User Interface | 19 keys for data entry | LCD touch screen |
| User Interface Screen | A grey scale LCD (3.5 in.) | A color LCD screen (5 in.) |

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

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 4/ 1/2003

CLSI EP07-A2, Interference Testing in Clinical Chemistry; Approved Guideline-Second Edition 11/23/2015

CLSI EP09-A3, Measurement Procedure Comparison and Bias Estimation Using Patient Samples; Approved Guideline-Third Edition 8/30/2013

CLSI EP 15-A3, User Verification of Precision and Estimation of Bias; Approved Guideline-Third Edition 9/11/2014

CLSI EP 17-A2, Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline-Second Edition 6/18/2012

IEC 62366-1 Edition 1.0 2015-02, Medical Devices- Part 1: Application Of

L. Test Principle:

The i-STAT Alinity Instrument uses internal contact pins to create electrical connections to the cartridge biosensors (ion selective electrode and reference electrode); the electrical system of the instrument measures ion-selective electrodes which are located on the cartridge biosensor chips, the biosensor generate a potentiometric signal that is read by the electrical system of the instrument and converted by the instrument software into a clinically meaningful result.

Ion selective methods are based on the measurement of potential difference (voltage) between the ion selective electrode and the reference electrode (both are found on the biosensors within the cartridge). The biosensor chips convert the activity of the ion dissolved in the patient sample into an electrical signal which can be measured. The concentration of sodium in the patient sample is calculated (derived from the Nernst equation) from the difference between the patient sample and the calibrant solution electrical signals.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

All performance studies for the i-STAT Sodium test were conducted using the i-STAT E3+ cartridge representing the i-STAT cartridges that include the sodium assay.

a. Precision/Reproducibility:

i.) Precision study at internal site for 20-day

The precision of the i-STAT Alinity System with i-STAT Sodium test was evaluated using 5 levels of commercially available i-STAT Calibration Verification materials. The study was conducted using 10 instruments and one cartridge lot over 20 days at one site. The results using the initial runs (including any outlying runs) are shown below.

20-day Precision Study Results Summary:

| Calibration Verification Material Level | N | Mean (mmol/L) | Within-run | | Between Run | | Total | |
|---|----|---------------|------------|------|-------------|-------|-------|------|
| | | | SD | %CV | SD | %CV | SD | %CV |
| CV L1 | 80 | 99.6 | 0.36 | 0.36 | 0.22 | 0.22 | 0.43 | 0.43 |
| CV L2 | 80 | 121.2 | 0.31 | 0.26 | 0.02 | 0.017 | 0.32 | 0.27 |
| CV L3 | 80 | 133.7 | 0.29 | 0.22 | 0.17 | 0.13 | 0.34 | 0.26 |
| CV L4 | 80 | 160.9 | 0.96 | 0.60 | 0.00 | 0.00 | 0.96 | 0.60 |
| CV L5 | 80 | 180.2 | 0.38 | 0.21 | 0.42 | 0.23 | 0.56 | 0.31 |

ii.) Multi-day Precision Study at 3 POC sites (using aqueous materials)

The precision of i-STAT Alinity System with i-STAT Sodium test was evaluated using 5 levels of aqueous materials (i-STAT Calibration Verification Set). This multi-day precision testing was performed at 3 point of care sites and was based on CLSI document EP15-A3: *User Verification of Precision and Estimation of Bias; Approved Guideline-Third Edition*. The study was conducted using 5 instruments and one cartridge lot of i-STAT E3+ cartridges (which contain the i-STAT Sodium test) over 5 days at each of the 3 sites by staff representative of end-users.

Multi-day Precision Results Summary (All Sites Combined):

| Calibration Verification Material Level | N | Mean (mmol/L) | Within-Run | | Within-Site(Total) | |
|---|----|---------------|------------|------|--------------------|------|
| | | | SD | %CV | SD | %CV |
| CV L1 | 75 | 99.7 | 0.43 | 0.43 | 0.50 | 0.50 |
| CV L2 | 75 | 121.5 | 0.45 | 0.37 | 0.53 | 0.44 |
| CV L3 | 75 | 133.9 | 0.37 | 0.27 | 0.41 | 0.31 |
| CV L4 | 75 | 161.3 | 0.45 | 0.28 | 0.48 | 0.30 |
| CV L5 | 75 | 180.8 | 0.55 | 0.30 | 0.58 | 0.32 |

iii.) Precision study at 3 POC sites (using whole blood (WB))

The whole blood precision of the i-STAT Alinity System with i-STAT Sodium test was evaluated using venous whole blood (native and altered) samples targeted to be within a low abnormal, normal and high abnormal sodium levels: At all 3 POC sites, specimens for WB low and WB high were altered; specimens for WB normal were native sample, not altered.

One cartridge lot of i-STAT Sodium test was used across 3 point of care sites at hospitals. Each site collected and tested its own samples. At each site, each sample was tested 3 times on each of 7 i-STAT Alinity Instruments (total of 21 test results per sample).

Whole Blood POC Precision Results Summary:

| Concentration n Lev | Site | N | Mean (mmol/L) | Within- Instrument | | Total | |
|--------------------------------|------|----|------------------|-----------------------|------|-------|------|
| | | | | SD | %CV | SD | %CV |
| <138 mmol/L (abnormal low) | 1 | 21 | 114.6 | 0.50 | 0.43 | 0.50 | 0.43 |
| | 2 | 21 | 115.0 | 0.38 | 0.33 | 0.38 | 0.33 |
| | 3 | 21 | 114.2 | 0.44 | 0.38 | 0.44 | 0.38 |
| 138 to 146 mmol/L (normal) | 1 | 21 | 140.0 | 0.00 | 0.00 | 0.00 | 0.00 |
| | 2 | 21 | 139.8 | 0.31 | 0.22 | 0.45 | 0.32 |
| | 3 | 21 | 141.6 | 0.49 | 0.34 | 0.51 | 0.36 |
| >146 mmol/L (abnormal high) | 1 | 21 | 156.0 | 0.38 | 0.24 | 0.38 | 0.25 |
| | 2 | 21 | 155.1 | 0.36 | 0.23 | 0.36 | 0.23 |
| | 3 | 21 | 165.9 | 0.30 | 0.18 | 0.30 | 0.18 |

b. *Linearity/assay reportable range:*

The linearity study was designed based on CLSI EP06-A: Evaluation of the linearity of quantitative measurement procedures. The linearity of the i-STAT Sodium test was evaluated on the i-STAT Alinity Instruments by preparing a series of sodium concentration levels in venous whole blood that spanned the reportable range of the test. Linearity testing was performed using seven whole blood test samples. Whole blood was obtained from a healthy subject; this whole blood was altered to produce a high sample pool and a low sample pool. Intermediate test samples were created from the high and low pool. Sample range tested from 87 to 204 mmol/L. Linear regression analysis was performed. The first order regression analysis generated the following equation $y = 1.00914x - 0.822$. The linearity results support the claimed reportable range of the sodium assay from 100 – 180 mmol/L.

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

Traceability; Sodium measurement is traceable to the U.S. National Institute of Standards and Technology (NIST) standard reference material SRM956.

The stability of the sodium test was previously cleared in k103195.

The i-STAT Controls and i-STAT Calibration Verification Material were previously cleared in k001387 and stability/value assignment information can be found in k001387.

d. *Detection limit:*

The detection limits are supported by the linearity study (see M.1.b. above). In addition, a LoQ study was performed to verify the low end measuring range claim.

The LoQ study was based on the CLSI EP17-A2 guideline. The LoQ of the i-STAT Sodium test was evaluated on the i-STAT Alinity Instruments using venous

whole blood that was altered to low sodium concentrations (four test samples ranging in sodium concentration from 80.3 mmol/L to 89.7 mmol/L) and two lots of i-STAT E3+ cartridges over four days. The total number of replicates is 154 for the evaluation of the LoQ value. The LOQ of the i-STAT Sodium test on the i-STAT Alinity instrument was determined to be 80 mmol/L.

The sponsor claimed that the sodium assay has a measuring range of 100 to 180 mmol/L.

e. *Analytical specificity:*

The interference performance of the i-STAT Sodium test on the i-STAT Alinity Instrument was evaluated based on CLSI EP07-A2 guideline. The interference performance was evaluated using whole blood samples at two sodium concentrations. The effect of each compound was evaluated by comparing the performance of a test sample spiked to a high concentration of the compound and a control test sample spiked with an equal volume of solvent. A compound was identified as an interferent if the difference between the spiked test sample and the control was >4 mmol/L.

Non-Interfering Compounds and Test Concentrations

| Compound | Tested Concentration mmol/L (unless specified) | Tested Concentration mg/dL* |
|-----------------------|--|-----------------------------------|
| Ascorbic Acid | 0.342 | 6.02 |
| β-Hydroxybutyric Acid | 6.00 | 62.47 |
| Calcium (Total) | 5.0 | 20.04 |
| Lactate | 6.6 | 58.79 |
| Magnesium | 15 | 36.46 |
| Salicylic Acid | 4.34 | 59.94 |
| Ibuprofen | 2.425 | 50.03 |
| Heparin | 3000 U/L | n/a |
| Acetaminophen | 1.33 | 20.10 |
| Acetyl Cysteine | 10.2 | 166.45 |
| Ammonium | 2.0 | 10.70 |
| Lithium | 3.2 | 2.22 |
| Acetyl Salicylic Acid | 3.62 | 65.22 |
| Bilirubin | 0.342 | 20.01 |
| Hemoglobin | 2 g/L | 200.00 |
| Triglyceride | 37 | 3233.80 |
| Uric Acid | 1.4 | 23.54 |

*The molecular weight of the substance tested was used to convert the test concentration from mmol/L to mg/dL. The molecular weight of each substance could vary depending on the form chosen.

Interfering Compounds and Interfering Concentrations

| Compound | Tested Concentration mmol/L | Tested Concentration mg/dL |
|---------------------------------|-----------------------------|----------------------------|
| Bromide | 37.5 | 299.64 |
| Nithiodote (sodium thiosulfate) | 16.7 | 264.04 |

Sponsor has the following limitations in the labeling:

| Substance | Interference |
|---------------------------------|---|
| Bromide | A bromide concentration above 16.65 mmol/L may give a falsely decreased i-STAT sodium test result of more than 4 mmol/L. See Note 1 below. Use another method |
| Nithiodote (sodium thiosulfate) | A sodium thiosulfate concentration above 3.57 mmol/L may give a falsely increased i-STAT sodium test result of more than 4 mmol/L. See Note 2 below. |

“Note 1: Bromide interference testing included two levels: the CLSI recommended level of 37.5 mmol/L and a therapeutic plasma concentration level of 2.5 mmol/L. The latter is the peak plasma concentration associated with halothane anesthesia, in which bromide is released. APOC has not identified a therapeutic condition that would lead to levels consistent with the CLSI recommended level. Bromide at a concentration of 37.5 mmol/L decreased i-STAT sodium results, while a therapeutic range of bromide (2.5 mmol/L) did not significantly interfere with the i-STAT sodium results.”

“Note 2: Nithiodote (sodium thiosulfate) is indicated for the treatment of acute cyanide poisoning. The journal article titled “Falsely increased chloride and missed anion gap elevation during treatment with sodium thiosulfate” indicated that sodium thiosulfate could be used in the treatment of cilciphylaxis indicating that “the highest concentration likely to be seen in plasma [is] after infusion of a 12.5 g dose of sodium thiosulfate pentahydrate. Assuming that the 12.5 g dose of sodium thiosulfate pentahydrate is distributed in a typical blood volume of 5 L with a hematocrit of 40%, the peak sodium thiosulfate plasma concentration expected is 16.7 mmol/L.”

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. *Method comparison with predicate device:*

The method comparison study compared the clinical results of the i-STAT Alinity System with i-STAT Sodium test to the i-STAT Sodium Test performance on the i-STAT 1 Wireless Analyzer (predicate). This study was conducted across 4 point of care sites using whole blood venous or arterial samples prospectively collected or left-over from routine patient care. The study included 174 subjects using lithium heparin whole blood (venous or arterial) samples. A total of 9 specimens out of the 174 method comparison specimens were altered (5.17%). Each site collected and tested approximately 40-55 samples until sufficient samples (both venous and arterial) were collected and tested for study analysis. A total of 91 venous specimens and 83 arterial specimens were tested in this study (Site 1 tested 21 venous and 20 arterial samples, (Site 2 tested 29 venous and 14 arterial samples, Site 3 tested 23 venous and 28 arterial samples, and Site 4 tested 18 venous and 21 arterial samples. One lot of i-STAT E3+ cartridges was used for this testing. Weighted Deming regression analysis comparing the first replicate of the candidate device results to the mean of the predicate device results yielded the following results:

Individual POC Sites

| Site # | n | Sample Range tested | Regression Equation | “r” |
|--------|----|---------------------|---------------------|-------|
| 1 | 41 | 128-156 mmol/L | $y=1.000x-1.0$ | 0.998 |
| 2 | 43 | 117-159 mmol/L | $y=1.000x-1.0$ | 0.999 |
| 3 | 51 | 118-173 mmol/L | $y=1.000x-1.0$ | 0.999 |
| 4 | 39 | 114-166 mmol/L | $y=1.000x + 0$ | 0.999 |

All Sites Combined

| n | Sample Range tested | Regression Equation | “r” |
|-----|---------------------|---------------------|-------|
| 174 | 114-173 mmol/L | $y =1.000x-1.0$ | 0.999 |

b. *Matrix comparison:*

The purpose of this study was to perform a sample matrix comparison study between non-anticoagulated venous whole blood and anti-coagulated venous whole blood (lithium heparin). The comparator condition for this study is the anticoagulated venous whole blood (Lithium Heparin collection tubes) and the test condition is the non-anticoagulated venous whole blood sample collected without anticoagulant. The comparison study was performed using the i-STAT Alinity instrument and 40 venous blood samples across the sodium concentration range (100 – 180 mmol/L). Deming regression analysis between first individual non- anticoagulated result and the heparinized mean result yielded the following regression results.

| n | Sample Range | Regression Equation | “r” |
|----|------------------|---------------------|-------|
| 40 | 103.8-178 mmol/L | $y = 1.000x + 0.83$ | 0.999 |

The sponsor states that lithium heparin is an acceptable anticoagulant in addition to non-anticoagulated whole blood sample collected without anticoagulant.

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:

| Test/Abbreviation | Units | Reference Range* |
|-------------------|-------------------|------------------|
| Sodium/Na | Mmol/L (mEq/L) | 138 - 146 |

* B.E. Statland, Clinical Decision Levels for Lab Tests (Oradell, NJ: Medical Economics Books, 1987).

The reference range shown above is intended to be used as a guide for the interpretation of results. Since reference ranges may vary with demographic factors such as age, gender and heritage, it is recommended that reference ranges be determined for the population being tested. Each facility should establish its own reference range to assure proper representation of specific populations.

N. Instrument Name:

i-STAT Alinity Instrument

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 or No

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

Yes or No

2. Software:

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

Yes or No

The applicant has provided documentation that indicates the device was designed and developed under good software life-cycle processes.

3. Specimen Identification:

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

4. Specimen Sampling and Handling:

The sodium assay 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 sodium cartridge includes an on board calibration that is performed with each cartridge use. The calibrant solution is automatically released from its foil pack and is positioned over the sensors. The signals produced by the sensors' responses to the calibrant solution are measured. This one-point calibration adjusts the offset of the stored calibration curve.

6. Quality Control:

Controls: i-STAT TriControls, 3 levels, previously cleared in k001387 are recommended by the sponsor for use with the i-STAT Sodium test on the i-STAT Alinity Instrument and should be run in accordance with facility protocols and best practices, and according to regulatory requirements.

Calibration verification materials previously cleared in k001387 are recommended by the sponsor for use with the i-STAT Sodium test on the i-STAT Alinity Instrument. The sponsor has provided detailed information regarding when to perform calibration verification in the device operator's manual.

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

Temperature Operating Range:

The purpose of this study was to evaluate the performance of the i-STAT Alinity System with i-STAT Sodium test across the operating temperature range of the i-STAT cartridge 16°C to 30°C. The cartridge temperature operating range of the i-STAT Sodium test was evaluated using a minimum of 20 i-STAT Alinity Instruments, using blood samples at three sodium concentration levels that spanned the range of the test and a temperature chamber set to the minimum and maximum cartridge operating temperatures. The results of this study demonstrate that the performance of the i-STAT Sodium test on the i-STAT Alinity Instrument across the cartridge operating temperature range of 16°C to 30°C is not affected.

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.