

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

A. 510(k) Number:

k070057

B. Purpose for Submission:

New device

C. Measurand:

Glucose, Sodium, Potassium, Chloride and Lithium

D. Type of Test:

Quantitative photometric and ion-selective electrode

E. Applicant:

Medica Corp.

F. Proprietary and Established Names:

EasyRA Clinical Chemistry Analyzer

G. Regulatory Information:

1. Regulation section:

21CFR862.1345 - Glucose test system

21CFR862.1665 - Sodium test system

21CFR862.1600 - Potassium test system

21CFR862.1170 - Chloride test system

21CFR862.3560 - Lithium test system

21CFR862.1150 - Calibrator

21CFR862.2160 - Discrete photometric chemistry analyzer for clinical use

21CFR862.1660 – Quality control material

2. Classification:

Class 2, 2, 2, 2, 2, 2, 1, and 1, respectively

3. Product code:

CGA- Glucose Oxidase, Glucose

JGS - Electrode, Ion Specific, Sodium

CEM - Electrode, Ion Specific, Potassium

CGZ - Electrode, Ion-Specific, Chloride

JIH - Flame Photometry, Lithium

JIT – Calibrator, secondary

JJE - Analyzer, Chemistry (Photometric, Discrete), for clinical use

JJY – Multi-analyte controls

4. Panel:
Chemistry (75), toxicology (91)

H. Intended Use:

1. Intended use(s):
See indication(s) for use below.
2. Indication(s) for use:
The EasyRA clinical analyzer is designed for clinical laboratory use, making direct quantitative measurements of Na⁺ (sodium), K⁺ (potassium), Cl⁻ (chloride), Li⁺ (lithium) and Glucose (Trinder method) in human serum samples. Additionally, other various chemistry assays may be adaptable to the analyzer depending on the reagent used to induce a photometric reaction.

Sodium measurements are used in the diagnosis and treatment diseases involving electrolyte imbalance.

Potassium measurements monitor electrolyte balance and in the diagnosis and treatment of diseases conditions characterized by low or high blood potassium levels.

Chloride measurements are used in the diagnosis and treatment of electrolyte and metabolic disorders.

Glucose measurements are used in the diagnosis and treatment of carbohydrate metabolism disorders including diabetes mellitus, neonatal hypoglycemia, and idiopathic hypoglycemia, and of pancreatic islet cell carcinoma.

Lithium measurements are used to assure that the proper drug dosage is administered in the treatment of patients with mental disturbances, such as manic-depressive illness (bipolar disorder).

3. Special conditions for use statement(s):
Prescription use
4. Special instrument requirements:
EasyRA Clinical Chemistry Analyzer

I. Device Description:

The EasyRA (EZRA) is a random-access clinical chemistry analyzer with positions for 24 photometric tests on-board as well as 4 additional tests performed by ion-selective electrode technology. The EZRA accommodates up to 24 samples and processes these using 72 disposable optical cuvettes. Typical test throughput is 150 tests per hour. These may include photometric and potentiometric tests. The user interface software has been designed to make operation as simple and intuitive as possible.

J. Substantial Equivalence Information:

1. Predicate device name(s):
 Diagnostic Chemicals Limited, Glucose (Trinder) assay
 Medica Corporation, EasyElectroLyte Na+, K+, Li+ Analyzer
 Medica Corporation, EasyElectroLyte Na+, K+, Cl- Analyzer
 Roche Diagnostic Systems, Inc., COBAS MIRA Chemistry System
2. Predicate 510(k) number(s):
 k875211, k002407, k000926, and k920402, respectively
3. Comparison with predicate:

| Similarities | | |
|--------------------------|---|--|
| Item | Device | Predicate |
| <u>Glucose</u> | | <u>Diagnostic Chemicals Limited on the COBAS MIRA</u> |
| <u>Intended use</u> | Quantitative determination of glucose in serum | Quantitative determination of glucose in serum |
| <u>Method</u> | Photometric-end point reaction using the Trinder glucose oxidase method | Photometric-end point reaction using the Trinder glucose oxidase method |
| <u>Formulation</u> | | |
| pH (buffered) | 7.40 units | 7.25 units |
| 4-aminoantipyrine | 0.30 mM/L | 0.25 mM/L |
| phenol | 10 mM/L | 20.0 mM/L |
| glucose oxidase | >10,000 U/L | >40,000 U/L |
| peroxidase (horseradish) | >700 U/L | >2,000 U/L |
| <u>Sample Volume</u> | 3µl | 3µl |
| <u>Analysis time</u> | 10.4 minutes for 1st result | 5.4 minutes for 1st result |
| <u>ISE Assays</u> | | |
| <u>Intended use</u> | Quantitative determination of Na,K,Cl and Li in serum | Quantitative determination of Na,K,Cl and Li in serum, plasma, whole blood and urine (urine not applicable for Li) |

| Similarities | | |
|----------------------|-------------------------|-------------------------|
| Item | Device | Predicate |
| <u>Method</u> | Ion Selective Electrode | Ion Selective Electrode |
| <u>Sample Volume</u> | 70µl | 55µl |
| <u>Analysis time</u> | 35 seconds | 35 seconds |

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

CLSI - Evaluation of Precision Performance of Clinical Chemistry Devices - EP05-A2

CLSI - Evaluation of the Linearity of Quantitative Analytical Methods - EP06-A

CLSI - Interference Testing in Clinical Chemistry - EP07-A2

CLSI - Method Comparison and Bias Estimation Using Patient Samples - EP09-A2

L. Test Principle:

Photometric Chemistries

The analyzer utilizes up to 6 wavelengths in conjunction with reagents, which are mixed with samples by the EZRA to perform up to 24 tests including Glucose-Trinder (Glu-T). The analyzer is adaptable to test methods based on rate and endpoint monitoring using monochromatic or bi-chromatic measurements. The photometer measures the light of a selected wavelength passing through optical cuvettes in which reagents react with a sample. This amount of light is then compared with that which occurred when on-board calibration standards were previously run to produce final results. Values for the parameters used with each test measurement, including wavelength, time of reaction and liquid volumes are stored on an RFID chip which is mounted on each reagent vessel. This insures that the correct photometric method is used by the EZRA with each reagent.

Potentiometric Chemistries

Additional tests, including Na, K, Cl, and Li are measured using ion-selective electrodes using the exact same technology with the EasyElectroLytes predicate devices cleared by the FDA under k002407 (for Cl-) and k000926 (for Na+, K+, Li+). The Ion Selective Electrode (ISE) technology measures changes in voltages (potentiometric measurement) which are a function of Na, K, Cl or Li ion activity in the sample. These changes are then compared with those obtained during a single point calibration to produce the final results.

Glucose-Trinder Reagent

The glucose oxidase in the reagent oxidizes the glucose in a serum sample to gluconic acid and releases hydrogen peroxide (H₂O₂). The H₂O₂ generates a quinoneimine dye, the absorbance of which at 520nm is directly proportional to the amount of glucose in the serum sample. Medica's Glu-T reagent is packaged in a 40ml bottle

(wedge) that fits the reagent tray of the EZRA. The shelf-life of the Glu-T reagent in the wedge has been established to be 36 months. The wedge label includes an RFID chip that has pre-programmed information about the reagent, which is automatically uploaded to the computer for the analysis to commence. The above reaction principle is the same with the one used by the “Diagnostic Chemicals Limited” (DCL) dye, cleared by the FDA under K875211, and utilized routinely with the Cobas-Mira predicate device.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:
 - a. *Precision/Reproducibility:*

Glucose

Within run imprecision: Twenty replicates of each of three levels of commercial human serum based QC material were tested 5 replicates per day over 4 days.

| QC Level | Within Run SD | Within Run CV |
|----------|---------------|---------------|
| mg/dL | Mg/dL | % |
| 272 | 1.94 | 0.71% |
| 109 | 0.87 | 0.79% |
| 60 | 1.00 | 1.69% |

Total Imprecision: Duplicate measurements of each of three levels of QC material were tested over 20 days.

| QC Level | Total SD | Total CV |
|----------|----------|----------|
| mg/dL | mg/dL | % |
| 263.93 | 4.39 | 1.66% |
| 105.86 | 1.62 | 1.53% |
| 60.43 | 1.30 | 2.16% |

ISE chemistries

Within Run Imprecision was evaluated on the EZRA Chemistry Analyzer using two levels of human-based QC material (A, B) in five replicates per day over 5 days.

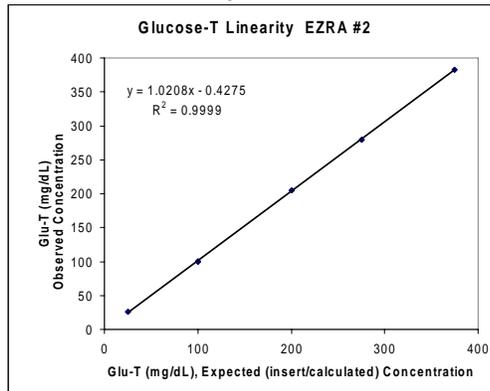
| | Level Mean | | Within Run SD | | CV | CV |
|-----------|------------|----------|---------------|----------|-------|-------|
| | A mmol/L | B mmol/L | A mmol/L | B mmol/L | A % | B % |
| Na | 144.56 | 161.78 | 0.61 | 0.71 | 0.42% | 0.44% |
| K | 4.18 | 6.19 | 0.035 | 0.06 | 0.84% | 0.97% |
| Li | 0.97 | 1.92 | 0.00 | 0.01 | 0.00% | 0.52% |
| Cl | 99.41 | 117.35 | 0.55 | 0.49 | 0.55% | 0.41% |

Total Imprecision was evaluated on the EZRA Chemistry analyzer using two levels of human-based QC material (A,B) in duplicate, twice a day (am and pm) over 20 days.

| | Mean | | Total SD | | Total CV | Total CV |
|-----------|-------------|-------------|-------------|-------------|----------|----------|
| | A mmol/L | B mmol/L | A mmol/L | B mmol/L | A % | B % |
| Na | 143.50 | 159.98 | 2.02 | 1.51 | 1.41% | 0.95% |
| K | 4.15 | 6.10 | 0.06 | 0.06 | 1.41% | 1.00% |
| Li | 0.95 | 1.90 | 0.01 | 0.02 | 1.48% | 1.29% |
| Cl | 99.0 | 117.1 | 1.00 | 1.02 | 1.01% | 0.87% |

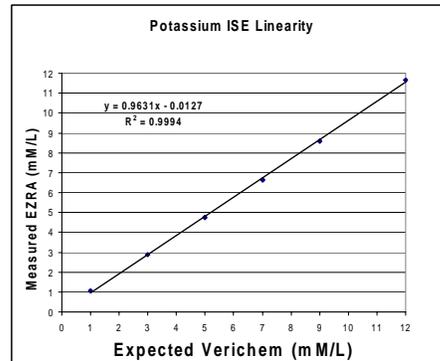
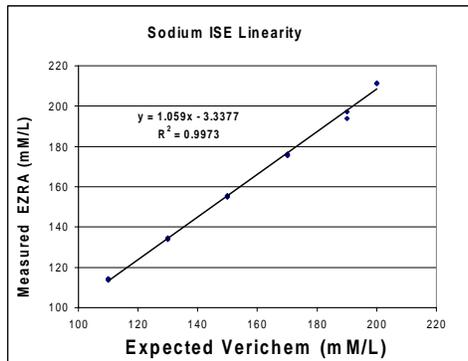
b. *Linearity/assay reportable range:*

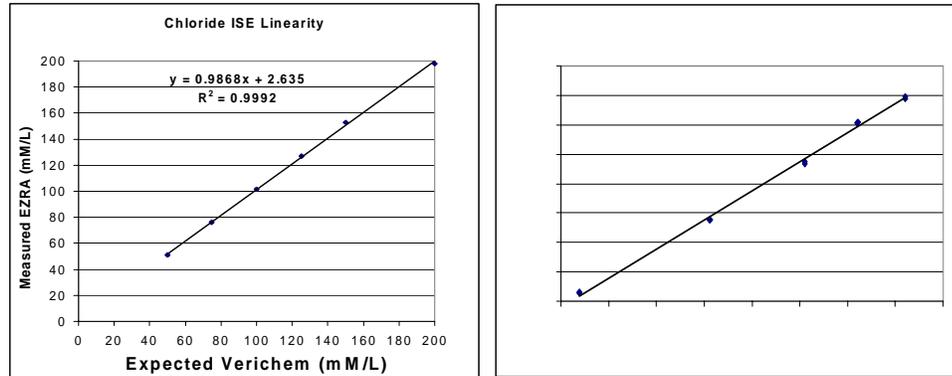
The Glucose assay is linear from 25 to 375 mg/dL



The linearity of ISE assays are as follows:

- Sodium 110 to 200 mmol/L
- Potassium 1.0 to 10.0 mmol/L
- Chloride 50 to 150 mmol/L
- Lithium 0.2 – 3.5 mmol/L





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

The Glu-T calibrator is provided by and is traceable to a commercially available secondary calibrator. The calibrator material was value-assigned using a primary glucose aqueous standard. Twenty replicates of the lyophilized human serum based calibrator to be assigned were tested interspersed with samples of the primary standard used for the calibration. The resulting calibrator assigned value was tested by:

- Evaluating linearity using NIST-traceable standards
- Evaluating CAP results
- Evaluating method comparison results in-house vs. the predicate device.

All data obtained supported the validity of the value assignment. The shelf life of this material was established by the manufacturer for 3 years.

ISE calibrator is manufactured at Medica and was 510(k) cleared for use as calibrator in Electrolyte Analyzers per k000926 and k002407. Medica will repackage the original solutions to fit the EZRA and re-label as “ISE Module Reagent Pack.” Medica identifies each manufacturing lot using a unique lot numbering system that identifies materials, methods, date and personnel used. The aqueous calibrator material in the reagent pack is tested at Medica prior to release to ensure compliance with Medica’s specifications. Each analyte in the calibrant material is tested on pre-qualified analyzers against secondary primary standard solutions prepared gravimetrically.

The current claim for shelf life of these reagents has been established to be 24 months via an accelerated shelf life study, and supported by a real time study.

The shelf life of this material is 3 years from date of manufacture as established by the original manufacturer. Medica will use the same expiration date on the Medica label.

Quality Control

The quality control materials to be used with the EZRA analyzer are manufactured by and traceable to a commercially available control material. At Medica, the mean values for each lot are established using Medica's Calibrator "EasyCal", and the EasyRA chemistry analyzer. The ranges are then adjusted around the new mean values.

d. Detection limit:

The lower limit of detection (LOD) of the Glucose assay is 0.34 mg/dL. The functional sensitivity (the lowest concentration that can be measured with 20% CV) is 1.3 mg/dL.

See linearity study above for ISE methods.

e. Analytical specificity:

Glucose

No significant interference was found with levels up to 300 mg/dL of hemoglobin. No significant interference was found with levels up to 5 mg/dL of bilirubin. No significant interference was found with levels up to 5 mg/dL of Ascorbic Acid. Ascorbic Acid above 5 mg/dL produces a negative bias in glucose levels. There is a significant interference to lipemia (Intralipid) at 200 mg/dL. Intralipid produces a positive bias in glucose values.

ISE

There was no interference with sodium, potassium, lithium and chloride sensors by bilirubin up to 20 mg/dL. There was no interference with sodium, chloride and lithium sensors to hemoglobin at 500 mg/dL. There was no interference with sodium, potassium and chloride sensors by Intralipid up to 2000 mg/dL. There appeared to be a small dose-related effect on the lithium sensor results that may be inherent in the Intralipid formulation. Despite this trend, there was no interference up to 800 mg/dL Intralipid.

To test for drug-related interferences, serum was spiked with a potentially interfering substance to the test concentration shown in the following tables.

The interference was calculated using the difference between the medians of the spiked and unspiked samples.

There was no interference with sodium, potassium, lithium and chloride sensors by the following chemicals at the corresponding levels:

| Chemical | Level tested (mg/dL) |
|-----------------------|----------------------|
| Imipramine | 0.1 |
| Procainamide | 10 |
| Nortyptylene | 0.15 |
| Hydroxytyramine | 40 |
| Chlorpromazine | 5 |
| Erythromycin | 5 |
| Ethosuximide | 20 |
| Acetaminophen | 20 |
| Ampicillin | 5 |
| Potassium thiocyanate | 20 |
| Salicylic acid | 20 |
| Acetylsalicylic acid | 50 |
| Ibuprofen | 40 |

The following results are for substances found to significantly interfere with one or more sensors.

| Chemical | Level tested (mg/dL) | Effect |
|-----------------------|----------------------|--|
| Valproic acid | 50 | Decreases Sodium by 5.7 mM |
| Benzalkonium Chloride | 8 | Increases Sodium by 14 mM and Potassium by 1mM |

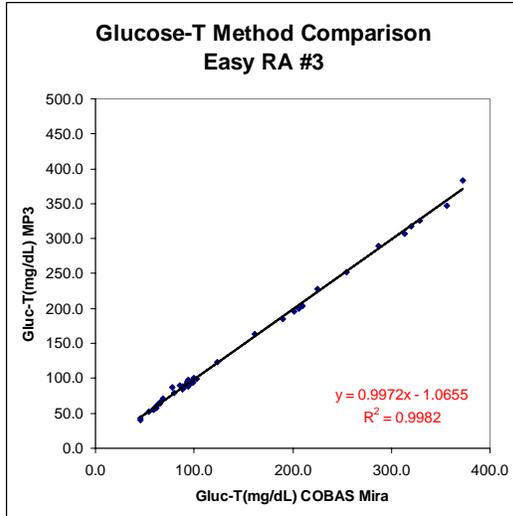
f. *Assay cut-off:*
Not Applicable

2. Comparison studies:

a. *Method comparison with predicate device:*

The following lists the data obtained in a comparison of the Medica Glucose Trinder reagent on the Medica EZRA Chemistry Analyzer (y) to the performance of a similar Glucose reagent (x) on the Roche COBAS MIRA Analyzer. Values ranged from 45 to 373 mg/dL. The data shown below are the results for single results obtained on the Medica EZRA Chemistry Analyzers vs. the average of 2 replicate values obtained on the Roche COBAS MIRA Analyzer.

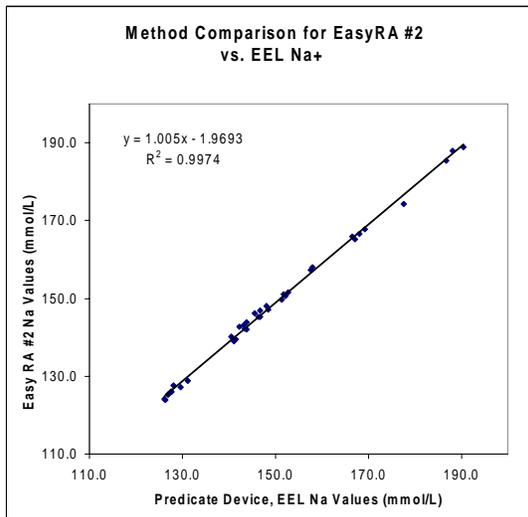
| | |
|-------------------------|-------|
| Number of Samples | 43 |
| Slope | 0.997 |
| Y Intercept | -1.06 |
| Correlation Coefficient | 0.998 |



The performance of the Medica Na/K/Cl/Li ISE module (y) on an EZRA Chemistry Analyzer was compared with the performance of the Na/K/Li Medica ISE module (x) in a Medica EasyElectrolytes analyzer. The following table lists the data obtained in the comparison. Values for x and for y ranged from 126.1 to 190.5 mmol/L for sodium, 2.66 to 8.93 mmol/L for potassium, 0.24 to 3.34 mmol/L for lithium and 59 to 153 mmol/L for chloride.

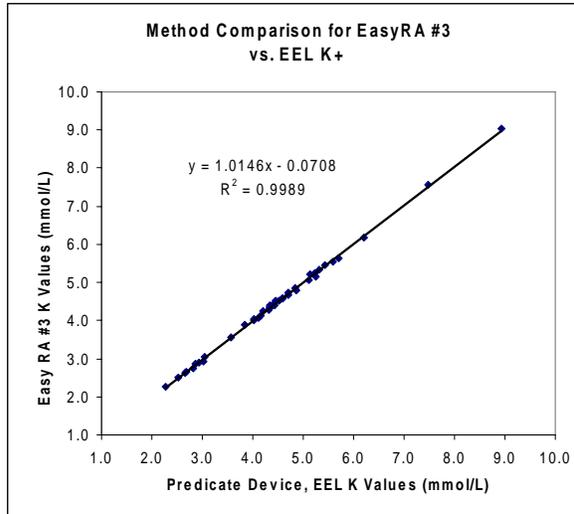
Sodium:

| | |
|-------------------------|--------|
| Number of Samples | 40 |
| Slope | 1.01 |
| Y Intercept | -1.97 |
| Correlation Coefficient | 0.9974 |



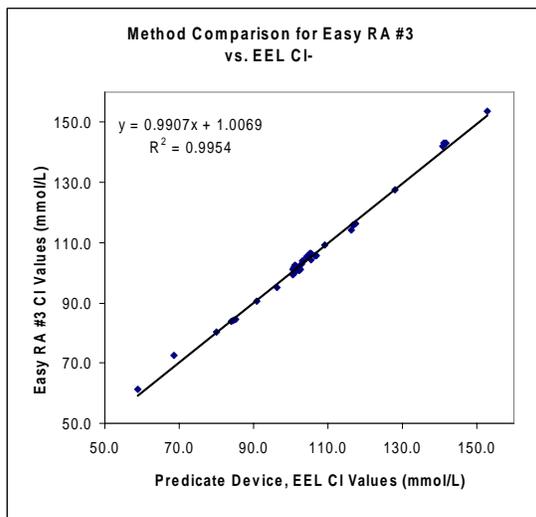
Potassium:

| | |
|-------------------------|--------|
| Number of Samples | 42 |
| Slope | 1.01 |
| Y Intercept | -0.07 |
| Correlation Coefficient | 0.9989 |



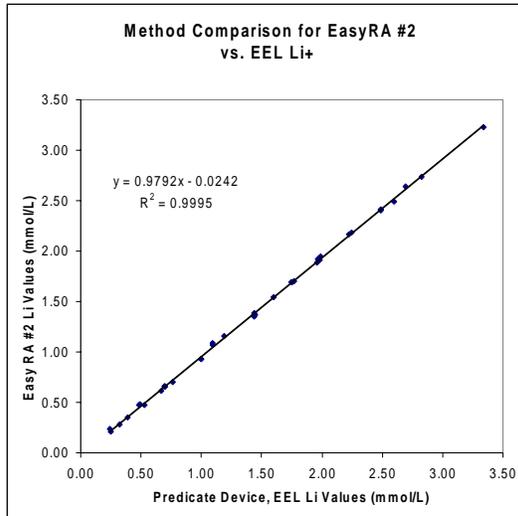
Chloride:

| | |
|-------------------------|--------|
| Number of Samples | 41 |
| Slope | 0.991 |
| Y Intercept | 1.01 |
| Correlation Coefficient | 0.9954 |



Lithium:

| | |
|-------------------------|--------|
| Number of Samples | 40 |
| Slope | 0.98 |
| Y Intercept | 0.02 |
| Correlation Coefficient | 0.9995 |



- b. *Matrix comparison:*
Not Applicable (serum only)
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:
Reference ranges are provided in the labeling from literature as follows:

Glucose 70 - 105 mg/dL
 Sodium 136.0 – 146.0 mmol/L
 Potassium 3.5 – 5.1 mmol/L
 Chloride 98 – 106 mmol/L
 Lithium* 0.6 – 1.2 mmol/L

*Therapeutic Range

Tietz NW. Clinical Guide to Laboratory Tests 3rd ed. WB Saunders and Co., Philadelphia, PA, 1995: p268.
 Statland, B. Clinical Decision Levels for Lab Tests, 2nd ed., Oradell, NJ, Medical Economics Books, p. 22 – 209; 1987
 Tietz, N.W. Fundamentals of Clinical Chemistry, 5th ed., Philadelphia, PA, WB Saunders and Co., p. 961 – 1027 (2001)

N. Instrument Name:

EasyRA Clinical Chemistry Analyzer

O. System Descriptions:

1. Modes of Operation:

Random access routine and stat mode

2. Software:

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

Yes or No

3. Specimen Identification:

Barcode capability with LIS connectivity

4. Specimen Sampling and Handling:

Direct tube sampling or sample cup

5. Calibration:

Photometric calculations are made on sample blanks, reagent blanks, bi-chromatic endpoints, rate or enzyme reactions, and kinetic reactions. ISE calculations use the Nernst equation determined by the voltage difference resulting from a 2 point calibration.

6. Quality Control:

The instrument has a quality control program.

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

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.