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

A. 510(k) Number:

k181201

B. Purpose for Submission:

New Device

C. Measurand:

Sodium, Potassium, Chloride

D. Type of Test:

Quantitative, ion selective electrode technology

E. Applicant:

Infrared Laboratory Systems, LLC (dba Synermed)

F. Proprietary and Established Names:

Synermed ISE Reagents

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
JGS	Class II	21 CFR 862.1665 Sodium Test System	Clinical Chemistry (75)
CEM		21 CFR 862.1600 Potassium Test System	
CGZ		21 CFR 862.1170 Chloride Test System	

H. Intended Use:

1. Intended use(s):

   See Indications for use below.

2. Indication(s) for use:

   The Synermed ISE reagents are intended for the in vitro quantitative measurement of sodium, potassium, and chloride concentrations in serum. This device is for use in clinical laboratories only. Sodium measurements are used in the diagnosis and treatment of aldosteronism, diabetes insipidus and other diseases involving electrolyte imbalance. Potassium measurements are used to monitor electrolyte balance in the diagnosis and treatment of disease conditions characterized by low or high blood potassium levels. Chloride measurements are used in the diagnosis and treatment of electrolyte and metabolic disorders such as cystic fibrosis and diabetic acidosis.

3. Special conditions for use statement(s):

   For in-vitro diagnostic use only.
   For prescription use only.

4. Special instrument requirements:

   Synermed IR-1200 Clinical Chemistry Analyzer

I. Device Description:

The Synermed ISE reagents includes the following:
ISE buffer: Contains triethanolamine preservatives 0.1 M, phosphoric acid 0.3% and non-reactive preservatives; 6x1000mL.
ISE MID-Standard: Contains sodium chloride (2.96mM), potassium chloride (0.12 mM), buffer and non-reactive preservatives; 6x1000mL.
ISE Reference B: Contains 1M potassium chloride; 6x500mL.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Synermed ISE Reagent

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

   k952179

3. Comparison with predicate:

Similarities and Differences		
Item	Candidate Device: Synermed ISE Reagents k181201	Predicate Device: Synermed ISE Reagents k952179
Intended Use	For the quantitative measurement of sodium, potassium and chloride in serum	Same
Use Environment	Clinical laboratory use only	Same
Specimen	Serum	Same
For use with	Synermed IR-1200	Hitachi 717

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

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

L. Test Principle:

The Synermed ISE reagents measures sodium, potassium, and chloride using ion selective electrode technology. Ion-selective electrodes (ISE) for sodium, potassium, and chloride utilize membranes selective to each of these ions. An electrical potential (voltage) is developed across the membranes between the reference and measuring electrodes in accordance with the Nernst equation. The voltage is compared to previously determined calibrator voltages and converted into ion concentration.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Precision testing was performed in accordance with CLSI EP05-A2 guideline. Five levels of serum pools were tested in two replicates per run, two runs per day for 20 days (N=80). The results of the precision studies are summarized below.

Precision results for Sodium:

Sample	N	Mean (mmol/L)	Within Run		Within Lab	
			SD	CV (%)	SD	CV (%)
Serum 1	80	81.1	0.04	0.05	0.03	0.04
Serum 2	80	114.87	0.07	0.06	0.06	0.05
Serum 3	80	134.97	0.06	0.05	0.06	0.04
Serum 4	80	150.02	0.09	0.06	0.07	0.05
Serum 5	80	181.05	0.13	0.07	0.12	0.07

Precision results for Potassium:

Sample	N	Mean (mmol/L)	Within Run		Within Lab	
			SD	CV (%)	SD	CV (%)
Serum 1	80	1.49	0.01	0.52	0.01	0.37
Serum 2	80	2.98	0.01	0.22	0.01	0.19
Serum 3	80	5.79	0.01	0.12	0.01	0.1
Serum 4	80	7.49	0.01	0.11	0.01	0.09
Serum 5	80	10.04	0.06	0.58	0.05	0.46

Precision results for Chloride:

Sample	N	Mean (mmol/L)	Within Run		Within Lab	
			SD	CV (%)	SD	CV (%)
Serum 1	80	60.22	0.31	0.52	0.29	0.48
Serum 2	80	90.08	0.09	0.10	0.07	0.07
Serum 3	80	100.77	0.49	0.48	0.43	0.43
Serum 4	80	112.00	0.09	0.08	0.06	0.06
Serum 5	80	129.98	0.08	0.06	0.48	0.05

b. *Linearity/assay reportable range:*

The linearity studies were performed following the CLSI EP06-A guideline. For the three electrolytes, nine to eleven equally spaced concentrations covering the measurement range were prepared by mixing high and low concentration samples. Four replicates were measured for each sample. The observed values were plotted against the expected values and linear regression analysis was performed. The summary results are provided in the table below.

Measurand	**Slope**	**Intercept**	**R^2**	**Sample Range Tested (mmol/L)**	**Claimed Measuring Range (mmol/L)**
Sodium	0.9987	1.1021	0.9995	80 - 180	80 - 180
Potassium	1.0048	0.0237	0.9999	1.5 - 10	1.5 - 10
Chloride	0.9814	1.3911	0.9998	60 - 140	60 -140

The results of the linearity study support the sponsor's claimed measuring ranges (as described in the table above).

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

Traceability: The Synermed ISE method on the IR-1200 Clinical Chemistry Analyzer is correlated to the same assay on the Hitachi 717 analyzer.

d. *Detection limit:*

Reportable ranges were determined based on the linearity studies (see above, M.1.b).

e. *Analytical specificity:*

Interference studies were performed according to CLSI EP07-A2 guideline to determine the effects from potential interferents on the ISE assays. Various concentrations of interferents were spiked into two levels (low and high) of each analyte in serum. Testing was performed in four replicates per level using one reagent lot on one instrument. The sponsor states that interference is considered to be non-significant if the bias between the tested and control samples are within 10% for Na+, K+ and Cl-, respectively.

The results of the interference study for serum samples are summarized below:

Analyte	Interferent	Highest concentration tested that did not show significant interference
Sodium	Unconjugated Bilirubin	342 µmol/L
	Conjugated Bilirubin	342 µmol/L
	Triglycerides	37 mmol/L
	Hemoglobin	500.0 mg/dL
Potassium	Unconjugated Bilirubin	342 µmol/L
	Conjugated Bilirubin	342 µmol/L
	Triglycerides	37 mmol/L
Chloride	Unconjugated Bilirubin	342 µmol/L
	Conjugated Bilirubin	342 µmol/L
	Triglycerides 37mmol/L	37 mmol/L
	Hemoglobin	500.0 mg/dL

The sponsor includes the following limitation in the labeling: Hemolysis is a known contributing factor to abnormally high potassium levels therefore potassium should not be tested in hemolyzed samples.

f. *Assay cut-off:*

Not Applicable.

2. Comparison studies:

   a. *Method comparison with predicate device:*

      Method comparison studies were performed by testing patient samples in singlet on one candidate device and the results were compared to those obtained on the predicate device (Sodium, Potassium and Chloride ISE methodologies on the Hitachi 717 Analyzer). Among the samples tested for each analyte, 10% of the samples were spiked or diluted to fully span the claimed measuring range of each analyte. The ordinary linear regression analyses for the three electrolytes are summarized below:

Analyte in Serum	Slope	Intercept	r^2	N	Range tested (mmol/L)	Claimed Measuring Range (in mmol/L)
Sodium	0.991	0.944	0.992	106	93-179	80 -180
Potassium	0.986	-0.102	0.993	109	2.3-10.6	1.5 -10
Chloride	0.998	0.123	0.993	110	60-140	60-140

   b. *Matrix comparison:*

      Not applicable, only serum samples are recommended for use with the Synermed ISE Reagents.

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 of Na+, K+, and Cl- are cited from literature:

   Sodium: 136 – 145 mmol/L
   Potassium: 3.5 – 5.1 mmol/L
   Chloride: 98 – 107 mmol/L

   Tietz, N.W.,editor, Fundamentals of Clinical Chemistry, 7th Edition,W.B. Saudner Co., 2015; pp 412-420.

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Parts 801 and 809, as applicable.

O. Conclusion:

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