

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

A. 510(k) Number:

k070987

B. Purpose for Submission:

Clearance of new assay

C. Measurand:

lithium

D. Type of Test:

quantitative spectrophotometric assay

E. Applicant:

Sentinel Diagnostics

F. Proprietary and Established Names:

Multigent Lithium Assay

G. Regulatory Information:

1. Regulation section: 21CFR862.3560, Lithium Test System
2. Classification: Class II
3. Product code: JIH
4. Panel: Toxicology (91)

H. Intended Use:

1. Intended use(s):

The Multigent Lithium is intended to measure lithium levels in serum or plasma. Measurements of lithium are used to aid in the management of individuals taking lithium for the treatment of mental disturbances, such as manic-depressive illness (bipolar disorder). For use on Architect and Aeroset Analyzers.

2. Indication(s) for use:

See intended use.

3. Special conditions for use statement(s):

For prescription use

4. Special instrument requirements:

Aeroset and Architect C8000 Analyzers

I. Device Description:

The ready-for-use reagent contains sodium hydroxide, EDTA and substituted porphyrin (and <1% sodium azide.)

J. Substantial Equivalence Information:

1. Predicate device name(s):

Infinity Lithium Liquid Stable Reagent Assay on the Hitachi 911 Analyzer.

2. Predicate K number(s):

k003583

3. Comparison with predicate:

Both devices have the same intended use and technology. Performance is similar for both assays.

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

CLSI documents: "Evaluation of Precision Performance of Quantitative Measurement Methods" EP5-A; "Method Comparison and Bias Estimation Using Patient Samples" EP9-A; "Protocols for Determination of Limits of Detection and Limits of Quantitation" EP17-A.

L. Test Principle:

The assay is a spectrophotometric method for use on automated clinical chemistry analyzers. Lithium present in the sample reacts with a substituted porphyrin compound at an alkaline pH, resulting in a change in absorbance, proportional to the concentration of lithium in the sample.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

The precision study was performed over 20 days per CLSI EP5-A. The samples evaluated included two commercial control sera (Level 1, Level 2) and a human serum pool (Level 3). The latter was spiked with a solution of lithium-lactate to reach a concentration of 1.5 mMol/L. These samples were tested on the AEROSET and ARCHITECT c8000 in replicates of two, twice per day (separated by a minimum of two hours), for twenty days using one instrument. Results are shown below:

AEROSET 20-days Total Imprecision

Imprecision	Level 1		Level 2		Level 3	
	SD	% CV	SD	% CV	SD	% CV
Mean (mMol/L)	0.839 mMol/L		2.579 mMol/L		1.436 mMol/L	
Within Run	0.022	2.61	0.034	1.31	0.024	1.69
Between Days	0.020	2.38	0.002	0.08	0.030	2.09
Total	0.033	3.98	0.043	1.68	0.038	2.67

ARCHITECT c8000 20-days Total Imprecision

Imprecision	Level 1		Level 2		Level 3	
	SD	% CV	SD	% CV	SD	% CV
Mean (mMol/L)	0.883 mMol/L		2.733 mMol/L		1.519 mMol/L	
Within Run	0.021	2.41	0.031	1.13	0.023	1.50
Between Days	0.017	1.96	0.037	1.37	0.033	2.19
Total	0.029	3.23	0.049	1.78	0.042	2.73

b. *Linearity/assay reportable range:*

Linearity was evaluated with samples prepared from human serum pools. A lithium-spiked aliquot was serially diluted with an un-spiked aliquot to obtain a set of at least eleven samples with proportionally decreased concentrations of lithium. Each dilution point was tested in triplicate. The deviation from the linear model for each sample was determined by dividing the mean observed result by the theoretical value. Results below support the sponsor's linearity

claim extending to 4.2 mMol/L for the Aeroset and 3.9 mMol/L for the Architect. See detection limit (below) for evaluation of 0.1 mM/L as the lower end of the measuring range.

Aeroset Concentration (mMol/L)	Aeroset Absolute difference from linear model	Architect Concentrations (mMol/L)	Architect Absolute difference from linear model
0.074	-0.072	0.052	-0.049
0.281	-0.042	0.267	-0.027
0.487	0.000	0.483	0.004
0.900	0.048	0.913	0.037
1.313	0.070	1.343	0.037
1.726	0.053	1.773	0.047
2.139	0.007	2.203	0.030
2.552	0.023	2.634	-0.040
2.965	-0.016	3.064	-0.034
3.378	-0.069	3.494	-0.004
3.791	-0.131	3.924	-0.158
4.204	-0.168		

c. Traceability, Stability, Expected values (controls, calibrators, or methods): Calibrators and control materials were cleared previously (k070971).

d. Detection limit:

A limit of quantitation evaluation was performed using human serum spiked with low concentrations of lithium. The criteria for limit of quantitation are defined by the manufacturer as the lowest concentration of analyte at which imprecision is < 20% CV and non-linearity within +/- 0.075 mMol/L. Measurements were from 3 runs per instrument, 7 samples per run. Data in the 510(k) support the claim for the low limit of the reportable range of 0.10 mMol/L.

e. Analytical specificity:

The compounds and ions listed below were spiked into a human serum pool containing lithium. A series of samples containing increasing concentrations of the potential interferents were tested in triplicate, and the median was determined. Results were evaluated relative to reference samples (i.e., the lithium samples without the potential interferents). The compounds and the highest concentrations for which bias was less than < +/-0.075 mMol/L, or < +/-5% (manufacturer's criteria) are shown below:

bilirubin 40 mg/dL
 triglycerides (intralipid) 2000 mg/dL
 hemoglobin 1000 mg/dL
 sodium 367 mMol/L
 potassium 13.8 mMol/L
 calcium 6.5 mMol/L
 magnesium 2.6 mMol/L
 iron up to 200 μ Mol/L
 zinc up to 233 μ Mol/L
 copper up to 239 μ Mol/L

f. Assay cut-off:
 Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

The manufacturer performed an in-house evaluation. Measurements from the Aeroset Sentinel, and Architect Sentinel, were compared to the predicate.

Sixty individual specimens were measured. The specimens were measured over 3 runs. No outliers were excluded. The following are results of linear regression analysis (based on singlicate measurements).

Instrument	N	r	Slope (confidence)	Intercept (mMol/L) Confidence)	Sy/x (mMol/L)
AEROSSET vs. Hitachi	60	0.999	1.019 (1.006 to 1.032)	-0.029 (-0.047 to – -0.012)	0.031
ARCHITECT vs. Hitachi	60	0.999	0.993 (0.980 to 1.005)	-0.0061 (-0.0229 to 0.0107)	0.031

b. Matrix comparison:

Collection tubes evaluated by the manufacturer included serum, EDTA, SST, and sodium heparin. Samples obtained from 5 subjects, were tested with each of the collection tubes evaluated. For each pool, 5 replicates were measured for each type of collection tube. Concentrations spanned from 0.2 mMol/L to concentrations exceeding the recommended therapeutic range. Relative to serum, the mean bias for the other anticoagulants did not exceed +/- 5%, or 0.075 mMol/L.

3. Clinical studies:

a. Clinical Sensitivity:

Not typically provided for this device type.

b. Clinical specificity:

Not typically provided for this device type.

c. Other clinical supportive data (when a. and b. are not applicable):

4. Clinical cut-off:

Not applicable. The device is for quantitative measurements.

5. Expected values/Reference range:

The package insert cites the range of 1.0-1.2 mMol/L for specimens 12 hrs post-dose.

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

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