REF	OSRT056
REAG 1	2 x 16 mL
STD	1 x 3 mL

Infinity™ Lithium Reagent for Beckman Coulter AU Chemistry Analyzers

Rx ONLY

IVD

INTENDED USE

Reagent for the quantitative determination of Lithium concentrations in human serum and plasma for use on the Beckman Coulter AU Chemistry Analyzers.

SUMMARY[1,2]

Lithium is widely used in the treatment of manic depressive psychosis. Administered as Lithium Carbonate, it is completely absorbed by the gastro- intestinal tract, peak serum levels occur 2 to 4 hours after an oral dose. The half life in serum is 48 to 72 hours and it is cleared through the kidneys (excretion parallels that of sodium). Reduced renal function can prolong clearance time.

Lithium acts by enhancing the uptake of neurotransmitters which produces a sedative effect on the central nervous system. Serum Lithium concentrations are carried out essentially to ensure compliance and to avoid toxicity.

Early symptoms of intoxication include apathy, sluggishness, drowsiness, lethargy, speech difficulties, irregular tremors, myoclonic twitchings, muscle weakness and ataxia. Levels higher than 1.5 mmol/L (12 hours after a dose) indicate a significant risk of intoxication.

METHODOLOGY[1]

Lithium can be determined by atomic absorption spectrophotometry, flame emission photometry or ion - selective electrode. These methods require specific and often dedicated instrumentation.

The Infinity™ Lithium reagent is a spectrophotometric method which can be readily adapted to 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 which is directly proportional to the concentration of Lithium in the sample.

REAGENT AND STANDARD COMPOSITION

Lithium Reagent

Sodium Hydroxide	0.5 mol/L
EDTA	50 µmol/L
Substituted Porphyrin	15 µmol/L Preservative
Surfactant	

Lithium Standard

Lithium Chloride	1.00 mmol/L

WARNING AND PRECAUTIONS

1. For in vitro diagnostic use only. Do not ingest. Harmful if swallowed. Avoid contact with skin and eyes. If spilled, thoroughly wash affected areas with water.
2. Contains sodium azide (0.1% W/V). Sodium azide preservative in diagnostic reagents may react with lead joints in copper drain lines to form explosive compounds. Even though the reagent contains minute quantities of sodium azide, drains should be well flushed with water when discarding the reagent. For further information consult the Safety Data Sheet.

DANGER

Skin corrosion/irritation	Category 1
Serious eye damage/eye irritation	Category 1

H314	Causes severe skin burns and eye damage.
P260	Do not breathe dust/fume/gas/mist/vapors/spray.
P264	Wash face, hands and any exposed skin thoroughly after handling.
P280	Wear protective gloves/protective clothing/eye protection/face protection.
P310	Immediately call a POISON CENTER or doctor/physician.

REAGENT PREPARATION

Reagent and standard are supplied ready to use.

STABILITY AND STORAGE

1. The unopened reagents and standard are stable until the expiration date when stored at 2 - 8°C.
2. Once opened the reagents and standard are stable in the bottles provided until the expiry date stated, provided that they are capped when not in use and stored at 2 - 8°C. When stored on board the reagent is stable for 2 weeks.

Indications of Reagent Deterioration

- Turbidity;
- Failure to recover control values within the assigned range; and/or
- Color of reagent is light purple.

SPECIMEN COLLECTION AND PREPARATION[1,2,3]

It is recommended that a standardized 12-hour post dose serum Lithium concentration be used to assess adequate therapy. Peak concentration is reached 2 to 4 hours after oral dose.

Use only serum or EDTA plasma. Serum or EDTA plasma should be separated from cells if storage of more than 4 hours is anticipated.

For analyzers which do not have automatic dilution, samples, controls and calibrators must be prediluted 1:10 with distilled or deionized water [1 part sample plus 9 parts water].

Sample Storage and Stability:

Samples are stable for one week at 2 - 8°C or > 1 year at -20°C.[4]

LIMITATIONS

The reagent is light sensitive and will absorb atmospheric carbon dioxide. It is recommended that the reagent be stored capped and in a dark container when not in use for prolonged periods of time (eg. overnight).

Interfering Substances

1. Studies to determine the level of interference from other cations normally present in serum were carried out in the presence of a lithium concentration of approximately 1 mmol/L and the following results were obtained:

Sodium:	Up to 200 mmol/L
Potassium:	Up to 8.00 mmol/L
Calcium:	Up to 4.00 mmol/L (16 mg/dL)
Magnesium:	Up to 2.00 mmol/L (4.86 mg/dL)
Iron:	Up to 200 µmol/L (1,117 µg/dL)
Zinc:	Up to 250 µmol/L (1,625 µg/dL)
Copper:	Up to 250 µmol/L (1,588 µg/dL)

   No significant interference (<5% deviation from assigned Lithium concentration) were observed with this method.

2. Studies to determine the level of interference from Bilirubin, Lipemia (Triglyceride) and Hemoglobin in the presence of a lithium concentration of approximately 1 mmol/L were carried out and the following results were obtained:

Free Bilirubin:	Interference is less than 10% at 45 mg/dL
Conjugated Bilirubin:	Interference is less than 10% at 45 mg/dL
Lipemia:	Interference is less than 10% at 2000 mg/dL (Triglyceride)
Hemoglobin:	Interference is less than 5% at 2 g/L

Lithium

ASSAY PROCEDURE

Materials Provided

- Infinity™ Lithium Reagent
- Infinity™ Lithium Standard

Suggested Analytical Parameters

Refer to the User Guide accompanying Instrument.

Calibration

The calibration frequency for this procedure is 7 days. Calibration of this lithium procedure is accomplished by use of the Infinity™ Lithium standard provided in the kit. The Infinity™ Lithium standard is traceable to NIST SRM3129.

Recalibration of this procedure is required when a reagent lot number has changed or there is an observed shift in control values, if a critical part of the analyzer is replaced or, if a major preventative maintenance procedure was performed on the analyzer.

Quality Control

Two levels of chemistry control sera should be analyzed routinely with each group of unknown samples, at least once per day.

Results

Results in mmol/L will be automatically printed for each sample assayed.

EXPECTED VALUES[1,2]

- 12 hour post dose trough concentration: 1.0 - 1.2 mmol/L
- Minimum effective concentration: 0.6 mmol/L
- Values > 1.5 mmol/L 12 hours after dose indicates a significant risk of intoxication.

The quoted values should serve as a guide only. It is recommended that each laboratory verify this range or derives a reference interval for the population it serves[5].

SPECIFIC PERFORMANCE CHARACTERISTICS

The following data was obtained using the Beckman Coulter AU analyzers according to established procedures. Results obtained in individual laboratories may vary.

Dynamic Range

The Infinity™ Lithium procedure is linear from 0.1 mmol/L to 5.0 mmol/L.

Precision[6]

Estimates of precision, based on CLSI recommendations[7], are less than 3% within run and total precision is less than 5% on the AU Chemistry Analyzers. Assays of control sera products were performed and the data produced following the CLSI guidelines above.

N= 80	Within Run		Total	
Mean (µmol/L)	SD	CV%	SD	CV%
1.00	0.017	1.6	0.024	2.3
1.50	0.019	1.2	0.027	1.7
2.00	0.035	1.7	0.048	2.3

Method Comparison[6]

The following data below demonstrates representative performance on Beckman Coulter AU Chemistry Analyzers. A comparison of this Infinity™ Lithium Reagent method (Method 1) vs. an on-market method (Method 2) was run per CLSI EP09-A2 utilizing 86 patient serum samples. The resulting data is as follows:

Correlation Coefficient:	r = 0.998
Regression equation:	Method 1 = 0.921x -0.003
Range of patients:	0.27 to 2.11 mmol/L

Lower Limit of Detection[9]

The lower limit of detection was determined using CLSI EP17-A2[8] where:

LOD = LOB + 2SDWR

LOB = Limit of Blank

SDWR = Within Run standard deviation of a low level sample

When run as recommended the lowest limit of detection is 0.04 mmol/L.

REFERENCES

1. Tietz Fundamentals of Clinical Chemistry, Sixth Edition Saunders Elservier Inc., 2008 pg 555, 556, 868.
2. Amdisen A. “Serum Lithium determinations for Clinical use.” Scand Jnl Clin Lab Invest. 1967; 20:104-8.
3. Young DS. “Effects of Preanalytical Variables on Clinical Laboratory Test” 2nd Ed. 1997, pg 3-360.
4. Tietz NW “Blood Gases and Electrolytes in Fundamentals of Clinical Chemistry, Philadelphia W.B. Saunders Co., 1976 pg 899-901.
5. Wachtel M et al, “Creation and Verification of Reference Intervals”, Laboratory Medicine 1995; 26:593-7.
6. Data is on file for specific AU analyzers.
7. Clinical and Laboratory Standards Institute. User evaluation of Precision Performance of Clinical Laboratory Devices. CLSI: 2004, CLSI Publication EP5-A2.
8. Clinical and Laboratory Standards Institute. Protocols for Determination of Limits of Detection and Limits of Quantitation. CLSI:2012, CLSI publication EP17-A2.

SYMBOLS

Rx ONLY	Prescription Use Only
IVD	*In Vitro* Diagnostic Medical Device
EC REP	Authorized Representative in the European Community
LOT	Batch Code / Lot Number
REF	Catalogue Number
	Consult Instructions for Use
REAG	Reagent
STD	Standard
	Temperature Limitation
	Use by / Expiration Date
	Manufacturer
	Corrosive

Fisher Diagnostics
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EC REP

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