

# Infinity™

## Lithium Liquid Stable Reagent\*

### PRODUCT SUMMARY

Stability	:	Until Expiry at 2-8°C
Measuring Range	:	0.04 - 3.00 mmol/L
Specimen Type	:	Serum/EDTA plasma
Method	:	Endpoint
Reagent Preparation	:	Supplied ready to use.

**IVD**

#### INTENDED USE

This reagent is intended for the in vitro quantitative determination of Lithium (Li) in human serum or EDTA plasma.

#### CLINICAL SIGNIFICANCE<sup>1,2</sup>

Lithium is widely used in the treatment of manic depressive psychosis. Administered as Lithium Carbonate, it is completely absorbed by the gastrointestinal 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<sup>1</sup>

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

This Lithium reagent is a spectrophotometric method which can be readily adapted to automated clinical chemistry analysers. 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 COMPOSITION

Active ingredients	Concentration
Sodium hydroxide	0.5 mol/L
EDTA	50 µmol/L
Substituted Porphyrin preservative surfactant	15 µmol/L

**WARNING:** Do not ingest. Avoid contact with skin and eyes. If spilt thoroughly wash affected areas with water. Reagent contains sodium azide which may react with copper or lead plumbing. Flush with plenty of water when disposing. For further information consult the Infinity Lithium Liquid Stable Reagent Material Safety Data Sheet.

R34	Causes burns
S26	In case of contact with eyes, rinse immediately with plenty of water and seek medical advice.

#### REAGENT PREPARATION

Reagent is supplied ready to use.

#### STABILITY AND STORAGE

Once opened the reagent is stable in the opaque bottle until the expiry date stated, provided that it is capped when not in use and stored at 2-8°C. When stored on board a Hitachi 911® automated analyser, the reagent will remain stable for 1 month. Refer to calibration section for expected calibration frequency.

#### Indications of Reagent Deterioration:

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

### SYMBOLS IN PRODUCT LABELLING

<b>EC REP</b>	Authorized Representative		Temperature Limitation
<b>IVD</b>	For in vitro diagnostic use		Use by/Expiration Date
<b>LOT</b>	Batch code/Lot number		CAUTION. CONSULT INSTRUCTIONS FOR USE.
<b>REF</b>	Catalogue number		Manufactured by
	Consult instructions for use		C - Corrosive

#### SPECIMEN COLLECTION AND HANDLING<sup>1,2,3</sup>

**Collection:** It is recommended that a standardised 12 hour post dose serum Lithium concentration be used to assess adequate therapy. Peak concentration is reached 2 to 4 hours after oral dose. Serum or EDTA plasma should be separated from cells if storage of more than 4 hours is anticipated.

**Serum:** The best specimen is non-haemolysed serum.

**Plasma:** Use EDTA plasma only.

**Storage:** Samples are stable for 1 week at 2-8°C or >1 year at -20°C.<sup>4</sup>

**Sample Preparation:** For analysers which do not have automatic dilution, samples, controls and calibrators should be prediluted 1:10 with distilled or deionized water.

#### ASSAY PROCEDURE

The following system parameters are recommended. Individual instrument applications are available upon request from the Technical Support Group.

#### SYSTEM PARAMETERS

Temperature	37°C
Primary Wavelength	510 nm (505-520nm)
Secondary Wavelength	480 nm (450-480nm)
Assay Type	Endpoint
Direction	Decrease
Reagent Blank	Yes

Dilute samples, calibrators and controls 1:10 prior to assay.(see note 2).

Sample : Reagent Ratio	1:50
eg. Sample Vol	5µL
Diluent Vol	50µL
Dil. Sample Vol	5µL
Reagent Vol	250µL
Incubation Time	120 seconds
Linearity	0.04 - 3.00 mmol/L

#### CALCULATIONS

Results are calculated, automatically by the instrument, as follows:

$$\text{Lithium} = \frac{\Delta\text{Abs of Unknown}}{\Delta\text{Abs of Calibrator}} \times \text{Calibrator Value}$$

#### Example (at 505, 480nm):

Absorbance of calibrator	=	0.116
Absorbance of unknown	=	0.095
Value of Calibrator	=	1.0 mmol/L

$$\text{Lithium} = \frac{0.095}{0.116} \times 1.0 = 0.8 \text{ mmol/L}$$

#### NOTES

1. The reagent and sample volumes may be altered proportionally to accommodate different spectrophotometer requirements.
2. Diluent - distilled or deionized water.

## CALIBRATION

Calibration of this lithium procedure is accomplished by the use of a suitable aqueous lithium standard such as the Thermo Lithium Standard (TR66901) (See standard package insert for traceability). On the Hitachi 911, calibration frequency can be expected to be 1 week. For calibration frequency on other automated instruments, refer to the instrument manufacturers specifications.

However, if during this period any one of the following events occurs, recalibration is recommended:-

- The lot number of reagent changes.
- Preventative maintenance is performed or a critical component is replaced.
- Control values have shifted or are out of range and a new vial of control does not rectify the problem.

## QUALITY CONTROL

To ensure adequate quality control, normal and abnormal control with assayed values should be run as unknown samples:-

- At least once per day or as established by the laboratory.
- When a new bottle of reagent is used.
- After preventative maintenance is performed or a critical component is replaced.
- With every calibration.

Control results falling outside the upper or lower limits of the established ranges indicate that the assay may be out of control. The following corrective actions are recommended in such situations:-

- Repeat the same controls.
- If repeated control results are outside the limits, prepare fresh control serum and repeat the test.
- If results are still out of control, recalibrate with fresh standard, then repeat the test.
- If results are still out of control, perform a calibration with fresh reagent, then repeat the test.
- If results are still out of control, contact Technical Services or your local distributor.

## LIMITATIONS<sup>3</sup>

1. 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).
2. 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:

No significant interference (<5% deviation from assigned Lithium concentration) from

- 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 (1117 µg/dL);
- Zinc:** Up to 250 µmol/L (1625 µg/dL); and
- Copper:** Up to 250 µmol/L (1588 µg/dL);

was observed with this method.

3. Studies to determine the level of interference from Bilirubin, Lipaemia and Haemoglobin in the presence of a lithium concentration of approximately 1 mmol/L were carried out and the following results were obtained:

**Free Bilirubin:** No significant interference from free bilirubin (<10% deviation) up to 769 µmol/L (45 mg/dL).

**Conjugated Bilirubin:** No significant interference from conjugated bilirubin (<10% deviation) up to 769 µmol/L (45 mg/dL).

**Lipaemia:** No significant interference from lipaemia (<10% deviation) measured as triglycerides, up to 22.6 mmol/L (2000 mg/dL).

**Haemoglobin:** No interference from haemoglobin (<5% deviation) up to 2g/L.

Interference (>+10% deviation from 1 mmol/L Lithium concentration) was observed with this method for concentrations of bilirubin and lipaemia greater than those stated above.

## EXPECTED VALUES<sup>1,2</sup>

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<sup>5</sup>.

## PERFORMANCE DATA

The following data was obtained using the Infinity Lithium Liquid Stable Reagent on a well maintained automated clinical chemistry analyser (Hitachi 911). Users should establish product performance on their specific analyser used.

## IMPRECISION

Imprecision was evaluated using two levels of commercially available quality control serum following the NCCLS EP5 procedure<sup>6</sup>.

	LEVEL I	LEVEL II
Number of data points	80	80
Mean (mmol/L)	1.00	2.49
<b>Within Run:</b> SD (mmol/L)	0.019	0.019
CV (%)	1.9	0.8
<b>Total:</b> SD (mmol/L)	0.038	0.09
CV (%)	3.9	3.6

## METHOD COMPARISON

Comparison studies were carried out on an automated clinical chemistry analyser (Hitachi 911) using a commercially available Lithium ISE analyser as a reference. Serum samples, collected from randomly selected patients being treated with Lithium, were assayed in parallel and the results compared by least squares regression. The following statistics were obtained.

Number of sample pairs	67
Range of sample results	0.11 - 2.26 mmol/L
Mean of ISE results	0.85 mmol/L
Mean of Infinity Lithium results	0.80 mmol/L
Slope	0.95
Intercept	-0.02 mmol/L
Correlation Coefficient	0.99

## MEASURING RANGE

When run as recommended the assay is linear from 0.04 to 3.00 mmol/L.

## LOWEST DETECTION LIMIT

The lowest detection limit (LDL) for this method was determined by assaying 11 replicates of a serum substitute material (SeraSub<sup>®</sup>) that does not contain Lithium. The mean and standard deviation were determined and LDL was calculated using the formula:

$$LDL = \bar{x} + (2 \times s)$$

Where:  $\bar{x}$  = mean value of replicates  
s = standard deviation of replicates (n - 1).

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

## REFERENCES

1. Tietz Fundamentals of Clinical Chemistry, Sixth Edition Saunders Elsevier 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. pg 3-360.
4. Tietz NW "Blood Gases and Electrolytes in Fundamentals of Clinical Chemistry, Philadelphia W.B. Saunders Co., 1976 pg 899-901.
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6. National Committee for Clinical Laboratory Standards. User evaluation of Precision Performance of Clinical Laboratory Devices. NCCLS; 1984, NCCLS Publication EP5-T.



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REF	Reorder Information	
	Catalogue No.	Configuration
<b>Lithium Reagent</b>	TR66056 TY66001 (Hitachi)	2 x 28 mL 2 x 28 mL
<b>Lithium Standard</b>	TR66901	1 x 10 mL

\* Patent No. US 7,241,623 B2