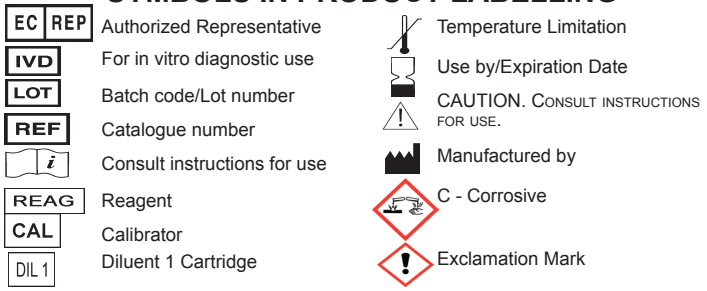
Infinity™ Lithium† (Li) Reagent
for Beckman Coulter™ SYNCHRON ‡Systems‡

PRODUCT SUMMARY

Stability	:	Until Expiry at 2-8°C
Linear Range	:	Up to 7.0 mmol/L
Specimen Type	:	Serum/EDTA plasma
Method	:	Endpoint
Reagent Preparation	:	Supplied ready to use.

IVD

SYMBOLS IN PRODUCT LABELLING



INTENDED USE
Reagent for the quantitative determination of Lithium concentrations in human serum and plasma on Beckman Coulter SYNCHRON LX and UniCel‡ DxC Systems.

CLINICAL SIGNIFICANCE[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.
This Lithium reagent is a spectrophotometric method which has been 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	15 µmol/L
preservative	
surfactant	

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 Reagent Safety Data Sheet.

REAGENT PREPARATION
Reagent is supplied ready to use. Transfer entire contents of reagent to Compartment B of the SYNCHRON cartridge.

STABILITY AND STORAGE
The unopened reagents are stable until the expiration date when stored at 2-8°C. When stored on SYNCHRON Systems, the reagent is stable for 14 days.

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 HANDLING [1,2,3]
Collection: 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. 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.[4]
All samples, calibrators and controls are diluted on-line.
Sample Size 5µL (1:29 dilution: 10 µL neat sample plus 280 µL diluent)
ORDAC sample size 5 µL (1:71 dilution: 4 µL neat sample plus 280 µL diluent)

MATERIALS PROVIDED
- Thermo Lithium reagent for Beckman Coulter SYNCHRON Systems.
- Thermo Lithium Calibrator, 2.0 mmol/L.
- Beckman Coulter SYNCHRON Cartridge with Diluent.

ADDITIONAL EQUIPMENT REQUIRED BUT NOT PROVIDED
- Beckman Coulter SYNCHRON chemistry analyzer.
- Beckman Coulter sample cups.
- Assayed Normal and Abnormal Controls.
- Deionized water (low calibrator).

TESTING PROCEDURES
If necessary, load the reagent onto the system as directed in the Operations Manual. After reagent load is completed, calibration may be required. Refer to the Operations Manual.
Program samples and controls for analysis as directed in the Operations Manual.

CALIBRATION
The system must have a valid calibration curve in memory before control or patient samples can be run. Under typical operating conditions the Lithium reagent cartridge must be calibrated every 5 days.
SYNCHRON Systems are calibrated using a two point calibration with deionized water (low calibrator) and Thermo Lithium Calibrator. 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.

TRACEABILITY
The Thermo Lithium Calibrator is traceable to NIST SRM 3129.

CALCULATIONS
Results are calculated, automatically by the instrument.

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 calibrator, 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 the local distributor.

LIMITATIONS[3]
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

Thermo SCIENTIFIC

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 2 g/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[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].

PERFORMANCE DATA
The following data was obtained using Thermo Lithium reagent on the Beckman Coulter SYNCHRON Systems according to established procedures.

IMPRECISION
Imprecision was evaluated using three levels of commercially available quality control serum following the NCCLS EP5-A procedure[6].

Within Run:	LEVEL I	LEVEL II	LEVEL III
Number of data points	80	80	80
Mean (mmol/L)	0.54	1.44	2.34
SD (mmol/L)	0.015	0.022	0.034
CV (%)	2.71	1.53	1.44

Total:	LEVEL I	LEVEL II	LEVEL III
Number of data points	80	80	80
Mean (mmol/L)	0.54	1.44	2.34
SD (mmol/L)	0.022	0.042	0.067
CV (%)	4.06	2.93	2.88

METHOD COMPARISON
Comparison studies were carried out following the EP9 protocol and using the Beckman Coulter EL-ISE (ion selective electrode) as a reference method. Serum and EDTA plasma samples were assayed in duplicate and the results compared by Deming regression. The following statistics were obtained:

Test Method: Infinity Lithium / LX20

Number of sample pairs	67
Range of sample results	0.3 - 2.7 mmol/L
Mean of reference method results	0.89 mmol/L
Mean of test method results	0.88 mmol/L
Slope	0.969
Intercept	0.021 mmol/L
Correlation coefficient	0.994

MEASURING RANGE
When run as recommended the assay is linear up to 3.00 mmol/L (initial measuring range) and from 3.0 to 7.0 mmol/L (ORDAC*).

*ORDAC is the Over Range Detection And Correction function.

LOWEST DETECTION LIMIT
The lowest detection limit (LDL) for this method was determined by assaying 20 replicates of a serum that does not contain Lithium. The mean and standard deviation were determined and LDL was calculated using the formula:

$$LDL = \overline{X} + (2 \times s)$$

Where: $\overline{X}$ = mean value of replicates
s = standard deviation of replicates (n - 1).
When run as recommended the lowest detection limit is 0.06 mmol/L.

PRECISION
A properly operating SYNCHRON System should exhibit precision values less than or equal to the following:

TYPE OF PRECISION	SAMPLE TYPE	1 SD	CHANGEOVER VALUE*	% CV
		mmol/L	mmol/L	
WITHIN RUN	Serum/Plasma	0.03	1.0 (Values ≤ 3.0)	3.0
		ORDAC	(Values > 3.0)	5.0
TOTAL	Serum/Plasma	0.045	1.0 (Values ≤ 3.0)	4.5
		ORDAC	(Values > 3.0)	7.5

* When the mean of the test precision data is less than or equal to the changeover value, compare the test SD to the SD guideline given above to determine the acceptability of the precision testing. When the mean of the test precision data is greater than the changeover value, compare the test %CV to the %CV guideline given above to determine acceptability. Changeover value = (SD guideline/CV guideline) x 100.

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.
5. Wachtel M et al, “Creation and Verification of Reference Intervals.” Laboratory Medicine 1995; 26:593-7.
6. National Committee for Clinical Laboratory Standards. Precision Performance of Clinical Laboratory Devices, Approved Guideline-NCCLS; 1999, NCCLS Publication EP5-A.

Hazard Symbol: Corrosion
Signal Word: Danger

Hazard Statements
Causes severe skin burns and eye damage

Precautionary Statements - Prevention
Do not breathe dust/fume/gas/mist/vapors/spray
Wash face, hands and any exposed skin thoroughly after handling
Wear protective gloves/protective clothing/eye protection/face protection
Precautionary Statements - Response
Immediately call a POISON CENTER or doctor/physician
Specific treatment (see supplemental first aid instructions on this label)
Eyes
IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing
Immediately call a POISON CENTER or doctor/physician
Skin
IF ON SKIN (or hair): Remove/Take off immediately all contaminated clothing. Rinse skin with water/shower
Wash contaminated clothing before reuse
Inhalation
IF INHALED: Remove victim to fresh air and keep at rest in a position comfortable for breathing
Immediately call a POISON CENTER or doctor/physician
Ingestion
IF SWALLOWED: Rinse mouth. DO NOT induce vomiting
Precautionary Statements - Storage
Store locked up
Precautionary Statements - Disposal
Dispose of contents/container to an approved waste disposal plant

Reorder Information:

REF	REAG	CAL	DIL 1	No. Tests
A19611	2 x 18 mL	1 x 4 mL	2 x 40 mL	130

Contact your local Beckman Coulter representative.

† Patent No.: US 7,241,623 B2

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