Lithium (Li) – Serum
Beckman UniCel DxC Systems

Technical Procedure 3141

Principle

Intended Use

Infinity™ Lithium reagent, when used in conjunction with UniCel® DxC 600/800 System(s) and Thermo Lithium Calibrator, is intended for quantitative determination of Lithium concentrations in human serum.

Clinical Significance

Lithium is widely used in the treatment of manic depressive psychosis.(1,2) 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. Lithium is cleared through the kidneys where its 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

Lithium reagent uses a spectrophotometric method which has been 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.

Chemical Reaction Scheme

Specimen

Acceptable Sample Containers

13 x 75 Red Top BD tubes
Red Top BD microtainers

Unacceptable Sample Containers

Serum tubes containing gel, plasma, whole blood, or urine are not recommended for use as a sample. Grossly lipemic samples should be ultra-centrifuged (90,000 x g for 10 minutes) prior to analysis. Grossly hemolyzed samples should be cancelled.

Type of Specimen

Biological fluid samples should be collected in the same manner routinely used for any laboratory test.(2,3) Freshly drawn serum is the preferred specimen.

Specimen Storage and Stability

Tubes of blood are to be kept closed at all times and in a vertical position. It is recommended that the serum be physically separated from contact with cells within four hours from the time of collection.(2,3)

Separated serum should not remain at room temperature longer than 8 hours. If assays are not completed within 8 hours, serum or plasma should be stored at +2°C to +8°C. for one week. If assays are not completed within 1 week, or the separated sample is to be stored beyond 1 week, samples should be frozen at -15°C to -20°C for one year. (2,3)

Sample Volume

The optimum volume, when using a 0.5 mL sample cup, is 0.3 mL of sample. For optimum primary sample tube volumes and minimum volumes, refer to the *Primary Tube Sample Template* for UniCel DxC Systems.

Reagents

Contents

Each kit contains the following items Kit Reorder #A19611:

SYNCHRON Cartridge with diluent
Ready-to-use Thermo Lithium reagent 2 x 18 mL
Thermo Lithium Calibrator (20 mmol/L) 1 x 4 mL

Volumes per Test

Sample Volume	3 µL
Total Reagent Volume	225 µL

Reactive Ingredients

Reagent Constituents

Sodium hydroxide	0.5 mol/L
EDTA	50 µmol/L
Substituted porphyrin	15 µmol/L

Also preservative and surfactant necessary for optimal system performance

CAUTION

Avoid contact with skin and eyes. If this occurs wash immediately with water. Spills should be thoroughly washed with water. Reagent contains sodium azide which may react with copper or lead plumbing. Flush with plenty of water when disposing.

Calibrator Constituents

Lithium carbonate (2.0 mmol/L)	4 mL

Materials Needed But Not Supplied With Reagent Kit

Deionized water (low level calibrator)
At least two levels of control material

Reagent Preparation

Reagent is provided ready-to-use. Transfer entire contents of reagent to Compartment B of the SYNCHRON cartridge.
Document lot number in reagent log, date and initial every cartridge before loading.

Acceptable Reagent Performance

The acceptability of this reagent is determined by successful calibration and by ensuring that quality control results are within acceptance criteria, as defined in the Clinical Chemistry Quality Control Procedure #3000.T.

Reagent Storage and Stability

Li reagent when stored unopened at 2°C to 8°C, will remain stable until the expiration date printed on the kit label. Once transferred to the SYNCHRON cartridge and loaded on the analyzer, the reagent is stable for 14 days unless the expiration date is exceeded.

Indications of reagent deterioration include turbidity, failure to recover control values within the acceptable range, and/or the color of the reagent is light purple.

DO NOT FREEZE.

Equipment

This test is performed on the Beckman UniCel DxC 800 Systems; Beckman-Coulter, Brea, California. For technical assistance, call the Beckman-Coulter hotline: 1-800-854-3633.

Refer to the Beckman *UniCel DxC 800 systems Reference Manual* for detailed instructions.

Calibration

Calibrator Required

Thermo Lithium Calibrator (included in reagent kit)
Deionized water (low calibrator)

Calibrator Preparation

No preparation is required.

Calibrator Storage and Stability

Thermo Lithium Calibrator is stable until the expiration date printed on the label if stored capped in the original container at 2°C to 8°C.

DO NOT FREEZE.

Calibration Information

The system must have a valid calibration curve in memory before control or patient samples can be run.

Under typical operating conditions the Li reagent cartridge must be calibrated every 5 days or with each new lot, and also with certain parts replacements or maintenance procedures, as defined in the UniCel DxC800 System *Instructions For Use* (IFU) manual.

For detailed calibration instructions, refer to the UniCel DxC800 System *Instructions For Use* (IFU) manual.

The system will automatically perform checks on the calibration and produce data at the end of calibration. In the event of a failed calibration, the data will be printed with error codes and the system will alert the operator of the failure. For information on error codes, refer to the UniCel DxC 600/800 System *Instructions For Use* (IFU) manual.

Calibrator Summary

Thermo Lithium Calibrator is prepared in an aqueous solution by weighing the appropriate amount of lithium carbonate to achieve 2.0 mmol/L. The calibrator is designed for generation of a two-point calibration curve using deionized as a low-level calibrator.

Traceability

The Thermo Lithium Calibrator is traceable to NIST SRM 3129.

Quality Control

A minimum of two levels of control material will be analyzed each day of patient testing.

In addition, controls should be run under the following circumstances:

Upon loading a new reagent cartridge.
Following each new calibration.
Following specific maintenance or troubleshooting procedures as detailed in the UniCel DxC800 System *Instructions For Use* manual.

More frequent use of controls or the use of additional controls is left to the discretion of the user based on workload and workflow.

The following controls should be used in accordance with the package instructions for use inserts. Quality control results should be evaluated and handled with respect to the Clinical Chemistry Quality Control Procedure #3000.T. Controls are compiled statistically in the LIS and reagent lot changes are documented on DxC Reagent Log sheets.

Quality Control Material

Control	Storage
MAS ChemTrak 1	2°C to 8°C
MAS ChemTrak 3	2°C to 8°C

Controls are received frozen and stored at –10°C to –20°C.
MAS ChemTrak bottles of controls in use are thawed and stored at 2°C to 8°C and are good for 14 days.

Testing Procedure

1. If necessary, load the reagent onto the system.
2. After reagent load is completed, calibration may be required.
3. Program samples and controls for analysis.
4. After loading samples and controls onto the system, follow the protocols for system operation.

For detailed testing procedures, refer to the UniCel DxC800 System *Instructions For Use* (IFU) manual.

Calculations

UniCel DxC Systems perform all calculations internally to produce the final reported result. The system will calculate the final result for sample dilutions made by the operator when the dilution factor is entered into the system during sample programming.

Reporting Results

Equivalency between the SYNCHRON LX and UniCel DxC 800 Systems has been established. Chemistry results between these systems are in agreement and data from representative systems may be shown.

Reference Intervals

The pharmacological response to serum lithium level is subject to considerable individual variation. (1,2)

The physician should determine the appropriate therapeutic interval for each patient.

Reference intervals

Range	Sample Type	Conventional Units	Level
From literature	Serum/Plasma	1.0 – 1.2 mmol/L	12-hour post dose
	Serum/Plasma	0.6 mmol/L	Minimum effective concentration
UCDHS	Serum/Plasma	0.5 – 1.5 mmol/L	Therapeutic range

Critical Value: Lithium results **≥ 2.5 mmol/L** are critical and should immediately be called to the patient's nurse or physician.

Procedural Notes

Anticoagulant Test Results

If plasma is the sample of choice, EDTA plasma was found to be compatible with this method.

Limitations

The reagent is light sensitive and will absorb atmospheric carbon dioxide, which could affect performance.

Interferences

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. The following substances were tested:

Substance	Level	Observed Effect
Sodium	up to 200 mmol/L	NSI
Potassium	up to 8.00 mmol/L	NSI
Calcium	Up to 16 mg/dL	NSI
Magnesium	Up to 4.86 mg/dL	NSI
Iron	Up to 1117 ug/dL	NSI
Zinc	up to 1625 ug/dL	NSI
Copper	up to 1588 ug/dL	NSI

The following substances were also tested for interference with this methodology:

Substance	Level	Observed Effect
Hemoglobin	up to 2 g/dL	NSI[a]
Free Bilirubin	up to 45 mg/dL	NSI
Conjugated Bilirubin	up to 45 mg/dL	NSI
Lipemia as triglycerides	2000 mg/dL	NSI

[a] NSI = No Significant Interference (less than 10% deviation).

Refer to Reference (3) for other interferences caused by drugs, disease and preanalytical variables.

Performance Characteristics

Analytical Measurement Range

The Infinity Lithium method for the determination of Li provides the following analytical range:

Analytical Measurement Range (AMR)

Sample Type	Conventional Units
Serum or Plasma	0.1 – 3.0 mmol/L
ORDAC[a]	3.0 – 7.0 mmol/L

[a] Over-range Detection and Correction. Refer to the UniCel DxC 800 System Instructions For Use (IFU) manual for more details on this function.

Clinical Reportable Range:

Clinical Reportable Range (CRR) as determined at UCDMC

Sample Type	Conventional Units
Serum or Plasma	0.1 – 7.0 mmol/L

Samples with concentrations below the AMR and CRR (0.1 mmol/L) will be reported as **< 0.1 mmol/L**.

Samples with concentrations greater than the ORDAC AMR (> 7.0 mmol/L) will be reported as **>7.0 mmol/L**.

Sensitivity

Sensitivity is defined as the lowest measurable concentration which can be distinguished from zero with 95% confidence. When run as recommended, the sensitivity for the Infinity Li method is 0.06 mmol/L.

Equivalency

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.

Equivalency determined by Infinity:

Serum or plasma (in the range of 0.3 to 2.7 mmol/L):

Y (Infinity Lithium/LX Systems)	= 0.969X + 0.021
N	= 67
MEAN (Infinity Lithium/LX Systems)	= 0.89
MEAN (Beckman Coulter EL-ISE)	= 0.88
CORRELATION COEFFICIENT (r)	= 0.994

Refer to References (6) for guidelines on performing equivalency testing.

Equivalency determined at UCDMC Specialty Testing Center Toxicology lab (STC) using IL943 Flame and/or Perkin-Elmer 3300 Flame Atomic Absorption Spectrophotometer methods:

Serum or Plasma (in the range of 0.0 – 3.5 mmol/L):

Y (UniCel DxC800-4449)	= 0.9915X – 0.0336
N	= 45
MEAN (Uni Cel DxC800-4449)	= 0.72
MEAN (STC)	= 0.82
CORRELATION COEFFICIENT (R^2)	= 0.9900

Serum or Plasma (in the range of 0.0 – 3.5 mmol/L):

Y (UniCel DxC800-4427)	= 0.9768X – 0.0273
N	= 45
MEAN (UniCel DxC800-4427)	= 0.72
MEAN (STC)	= 0.82
CORRELATION COEFFICIENT (R^2)	= 0.9908

Serum or Plasma (in the range of 0.0 – 3.5 mmol/L):

Y (UniCel DxC800-4118)	= 0.994X + 0.0015
N	= 45
MEAN (UniCel DxC800-4118)	= 0.82
MEAN (STC)	= 0.82
CORRELATION COEFFICIENT (R^2)	= 0.9924

Serum or Plasma (in the range of 0.0 – 3.5 mmol/L):

Y (UniCel DxC800-4449)	= 0.9817X + 0.0080
N	= 45
MEAN (UniCel DxC800-4449)	= 0.72
MEAN (UniCel DxC800-4427)	= 0.72
CORRELATION COEFFICIENT (R^2)	= 0.9978

Serum or Plasma (in the range of 0.0 – 3.5 mmol/L):

Y (UniCel DxC800-4118)	= 1.0188X + 0.0294
N	= 45
MEAN (UniCel DxC800-4118)	= 0.82
MEAN (UniCel DxC800-4427)	= 0.72
CORRELATION COEFFICIENT (R^2)	= 0.9953

Serum or Plasma (in the range of 0.0 – 3.5 mmol/L):

Y (UniCel DxC800-4118)	= 1.0014X + 0.0367
N	= 45
MEAN (UniCel DxC800-4118)	= 0.82
MEAN (UniCel DxC800-4449)	= 0.72
CORRELATION COEFFICIENT (R^2)	= 0.9955

Precision

A properly operating SYNCHRON® System(s) and UniCel DxC System(s) should exhibit imprecision values less than or equal to the following.

As determined by Beckman

Precision Values

Type of Precision	Sample Type	1 SD mmol/L	Changeover Value[a] mmol/L	%CV
Within-run	Serum/Plasma (Values ≤ 3.0)	0.03	1.0	3.0
	ORDAC (Values ≥ 3.0)			5.0
Total	Serum/Plasma (Values ≤ 3.0)	0.045	1.0	4.5
	ORDAC (Values ≥ 3.0)			7.5

[a]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)x100.

Precision established at UCDMC

Type of Precision	Sample Type	n	Mean (mg/L)	1 SD	%CV
DxC800-4118 Within-run	Low Control	20	0.80	0.02	2.5
	High Control	20	2.23	0.03	1.3
DxC800-4427 Within-run	Low Control	20	0.79	0.04	5.1
	High Control	20	2.16	0.01	0.5
DxC800-4449 Within-run	Low Control	20	0.81	0.02	2.5
	High Control	20	2.28	0.04	1.8

Type of Imprecision	Sample Type	n	Mean (mg/dL)	SD	%CV
DxC800-4418 Day to Day	MAS ChemTrak 1	20	0.78	0.01	1.3
	MAS ChemTrak 3	20	2.20	0.05	2.3
DxC800-4427 Day to Day	MAS ChemTrak 1	20	0.79	0.04	5.1
	MAS ChemTrak 3	20	2.20	0.04	1.8
DxC800-4449 Day to Day	MAS ChemTrak 1	20	0.79	0.01	1.3
	MAS ChemTrak 3	20	2.22	0.04	1.8

Comparative Performance

Data for the SYNCHRON LX® System evaluated using the NCCLS Approved Guideline EP5-A appears in the table below.(6)

NCCLS EP5-A Precision Estimate Method

Type of Imprecision	Sample Type	No. Data Points	Test Mean Value (mmol/L)	EP5-T2 Calculated Point Estimates	
				SD	%CV
Within-run	LEVEL 1	80	0.54	0.015	2.71
	LEVEL 2	80	1.44	0.022	1.53
	LEVEL 3	80	2.34	0.034	1.44
Total	LEVEL 1	80	0.54	0.022	4.06
	LEVEL 2	80	1.44	0.042	2.93
	LEVEL 3	80	2.34	0.067	2.88

NOTICE

These degrees of precision and equivalency were obtained in typical testing procedures on the SYNCHRON LX System and are not intended to represent the performance specifications for this reagent.

Additional Information

For more detailed information on UniCel DxC Systems, refer to the *Instructions for Use* and *Reference* manual.

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.
7. Infinity™ Lithium Reagent for Beckman Coulter SYNCHRON Systems Instruction for Use, Fisher Diagnostics, a division of Fisher Scientific Company, a part of Thermo Fisher Scientific Inc., Middletown, Virginia 22645-1905

Prepared By	Date Adopted	Supersedes Procedure #
Kathy Dagang	2016	New Previously run at STC

Revision Date	Type of Revision	Revised by	Review/Annual Review Date	Reviewed By
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