

Intended Use

The Akers Biosciences, Inc. Lithium[®] System is intended to measure lithium blood levels. 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). The test may be used with whole blood, serum, or EDTA-plasma.

Summary and Explanation

Lithium has a narrow therapeutic range and therefore requires routine, ongoing clinical monitoring of patient lithium levels. Periodic monitoring of serum lithium levels has helped to assure the safe and effective use of the drug, and aid in assessing a patient's adherence to treatment. Optimal use depends on achieving the correct balance within a target therapeutic range. The amount of lithium needed to treat or prevent manic and depressive symptoms effectively differs greatly from one patient to another. Therefore, it is recommended that clinicians frequently order serum lithium blood levels to determine optimized treatment. Clinicians requiring a patient's lithium blood level have normally required extensive, time-consuming hospital or reference laboratory tests. Given the variation in hospital and/or laboratory operations, time spent waiting for, and receiving, the blood draw, and potential revisits to the physician, patients who are prescribed lithium tend to incur a high burden. As a result, many patients become non-compliant to testing, resulting in less than optimal therapeutic outcome.

The new point-of-care lithium test option is easy to use in a moderate complexity laboratory setting and provides the physician with a convenient monitoring solution for personalizing patient treatment with lithium. Monitoring lithium levels can be completed simply and quickly in a qualified office, clinic, or hospital. Dosage management, if required, can be initiated at point-of-treatment. This simple two (2) minute test will require only 50 µL of blood obtained via a finger stick (or venipuncture) to determine accurate and reliable lithium blood levels for patients who are prescribed lithium.

Principle of Test

The Akers Biosciences, Inc. Lithium[®] System is a colorimetric method based upon the sensitive and specific binding of lithium to a modified porphyrin compound.

The system consists of three key components, starting with the Blood Cell Separator. The Blood Cell Separator (referred to as the Separator) is a sample preparation aid to *in vitro* diagnostic testing systems, where a precise, micro-volume sample of serum or plasma is acquired from whole blood, serum or an EDTA-plasma specimen. This is achieved through the attraction and capture of blood cells from a whole blood specimen by a membrane impregnated with agents designed to bind to both red and white blood cells. The residual liquid continues to flow laterally to the tip of the membrane at which time the bulb pipette that has been inserted into the designated hole in the Separator, fills to the pipette's fixed volume and is ready to use.

The precise volume (0.2 µl) of cell-free sample that is captured using the Separator is introduced to the second key component of the system, the lithium reagent. The lithium reagent is a colorimetric reagent whose active ingredient is a porphyrin compound that is highly specific and sensitive to lithium. Absorbance of light at 510 nm is decreased by lithium concentration, and is linear from 0.1 to 2.0 mEq/L of lithium. Lithium results greater than 2.0 mEq/L are reported as ">2.0 mEq/L."

The third key component of the system is the Akers Lithium[®] System's photometric reader, which is designed to measure the absorbance at 510 nm of a solution contained in a cuvette and report concentrations from 0.1 to 2.0 mEq/L of lithium on the reader's display system.

Commercial kits available for purchase include:

- Test Kit
- Control Kit

Test Kit - Materials Provided

Quantity	
25	Blood Cell Separators
25	Bulb Pipettes
25	Reagent – filled cuvettes in an individually sealed foil pouch (aqueous based solution that contains 0.5 mol/L sodium hydroxides, 50µmol/L EDTA, 20 µmol/L substituted porphyrin, and 0.1% w/v sodium azide)
1	Lithium Control Test Packet (see contents below)
1	Package Insert
1	Pictorial Guide

Control Kit - Materials Provided

Quantity

5	Lithium Control Test Packs (see contents below)
1	Package Insert

Note: Lithium Control Test Packs Include on (1) each of the following:

- Reagent - filled cuvette in an individually sealed foil pouch (aqueous based solution that contains 0.5 mol/L sodium hydroxides, 50 µmol/L EDTA, 20 µmol/L substituted porphyrin, and 0.1% w/v sodium azide)
- Blood Cell Separator
- Bulb Pipette
- 300 µL control reagent pipette. The control reagent is quantitatively measured lithium (1.00 mEq/L) in physiological saline with 0.1% w/v sodium azide.

Materials Required But Not Provided

Akers Lithium System Reader
Disposable Lab Gloves
50 µL Blood Collection Tube

Storage Instructions

The reagent kits may be stored at room temperature: 18° to 27°C (64° to 81°F).

Warnings and Precautions

- All specimens should be handled in accordance with good laboratory practices, including Universal Precautions for the handling and proper disposal of potentially bio-hazardous materials.
- Use only fingerstick whole blood, venous whole blood (EDTA), serum, or EDTA plasma. Lithium heparin should not be used as an anticoagulant, and sodium heparin has not been evaluated. Venous samples should be tested within 4 hours of collection. **Do not use frozen specimens.**
- Do not expose the test kit to temperatures greater than 40°C (104°F) or below 0°C (32°F).
- During operation, the Lithium Reader **must** be located on a level surface.
- Never look directly into the light located on the right side of the reader.
- Do not ingest. Avoid contact of lithium reagent with skin and eyes. Wash thoroughly with water.
- The test and control reagents contain low levels of sodium azide. If containers are emptied into a sink, the plumbing should be flushed with copious amounts of water.

Specimen Collection

- The Lithium System should only be used with 50µl of **Fresh** whole blood, serum, or EDTA-plasma.
- Whole blood may be obtained through finger stick or routine venipuncture.

Test Procedure

For diagrams, see the Pictorial Guide included with this Package Insert.

Preparing Reader

1. Turn the Reader on by pressing the switch located on the side of the unit. Reader will display **“Remove Cuvette Press Run”**. Remove Cuvette Cover and check that the Cuvette Holder is empty. Replace Cuvette Cover and press down to ensure that it is firmly seated. Press the Run button. Confirm that the Reader display reads **“Insert Reagent Blank/Press Run”**.
2. Gather together a Separator, Bulb Pipette and a Reagent Pouch.
3. Place the Separator on a level surface, parallel to the right side of the Reader. Ensure that the yellow blood well is facing front. Gently place the Bulb Pipette into the hole just behind the yellow blood well. The Bulb Pipette will remain upright. Position the Separator approximately 2 to 3 inches from the Reader, making sure that the Bulb Pipette is positioned directly in line with the Side Light.

4. Open the Reagent Pouch and grasp the Cuvette from the top portion only throughout the procedure (this will avoid any marks on the cuvette that will be in the light path and could affect the result).
5. Tap the cuvette on the table to ensure all reagent is down to the bottom. Peel back and remove the seal on the cuvette. Remove the Cuvette Cover and insert the Cuvette into the Reader by aligning the flange on the Cuvette with the slot located in the front of the Cuvette Holder and pushing down firmly until seated.
6. Replace Cuvette Cover and press down to ensure that it is firmly seated. Press the Run button. In about 15 seconds the display will read ***“Insert Sample/Press Run.”***

Obtain Patient Test Sample

1. Add 50 µL of patient sample to the yellow well on the Separator.
2. Wait approximately 1 minute, then press and hold the Check button on the Reader. A light will shine from the side of the Reader onto the shaft of the Bulb Pipette. **Do not look directly at the light.** Be sure that the green indicator reaches the black mark before removing the Bulb Pipette. Continue to press the Check button at 5 – 10 second intervals until the green indicator reaches the black mark. (This step is complete when the green indicator reaches the black mark on the Bulb Pipette shaft.)
Note: Visibility of the green indicator can be enhanced by moving the separator closer to the light, lifting the separator assembly directly into the light path or tilting the reader to angle the light path onto the lower end of the bulb pipette shaft.

Process the Sample

1. Remove Cuvette Cover and Cuvette from the Reader. Remove the Bulb Pipette from the Separator and completely immerse the tip into the reagent solution in the Cuvette.
2. Hold the Cuvette from the top at about eye level. Firmly squeeze and hold the Bulb to add the sample to the Cuvette. Bubbles will appear. Keep squeezing the Bulb and withdraw the Pipette from the Cuvette to ensure that none of the reagent is drawn back into the Pipette.
3. Shake the Cuvette from side-to-side vigorously to ensure mixing.
4. Insert the Cuvette into Reader by aligning the flange on the Cuvette with the slot located in the front of the Cuvette Holder and pushing down until firmly seated.
5. Replace Cuvette Cover and press down to ensure that it is firmly seated. Press the Run button. The Reader will display the calculated lithium level in mEq/L. Record the value. Once the result is recorded, simply press the Run button to prepare the Reader for the next test cycle.

Quality Control

Controls (also known as "quality control materials") are solutions for which an expected analyte concentration ranges have been established. Good Laboratory Practices necessitate the use of Controls to test and verify the performance of the test system. You should also follow State and local guidelines concerning the use of controls. Quality control samples will check the function of the lithium reagent and the Reader. They also check that the Separator is delivering the correct volume.

It is recommended that controls be run if any of the following circumstances occur: 1) initially use of a new on a new Lithium[®] System Reader, prior to running any patient samples; 2) starting a new shipment of Reagent Cuvettes; and/or 3) whenever Lithium[®] System results do not correspond to clinical symptoms. Lithium controls are included in the Test Kit and Control Kit sold by Akers Biosciences, Inc. For further information, please contact Akers Biosciences at 1-800-451-TEST.

Controls should be run in the same manner as clinical samples, including the use of the Separator. The controls will check for the function of the Reader and the Reagent Cuvettes. They also check that the Separator is delivering the correct volume. To run controls, simply substitute two (2) drops of control solution for blood or serum/plasma. The control solution is contained in a pipette. Using the supplied ampoule crusher, squeeze the pipette to break the ampoule located inside. Tap the pipette a few times to move the liquid to the tip. Remove the cap and dispense the two (2) drops into the yellow well. Follow the remainder of the sample testing procedure. Do not use after the expiration date on the label.

Performance Characteristics

Therapeutic Range:

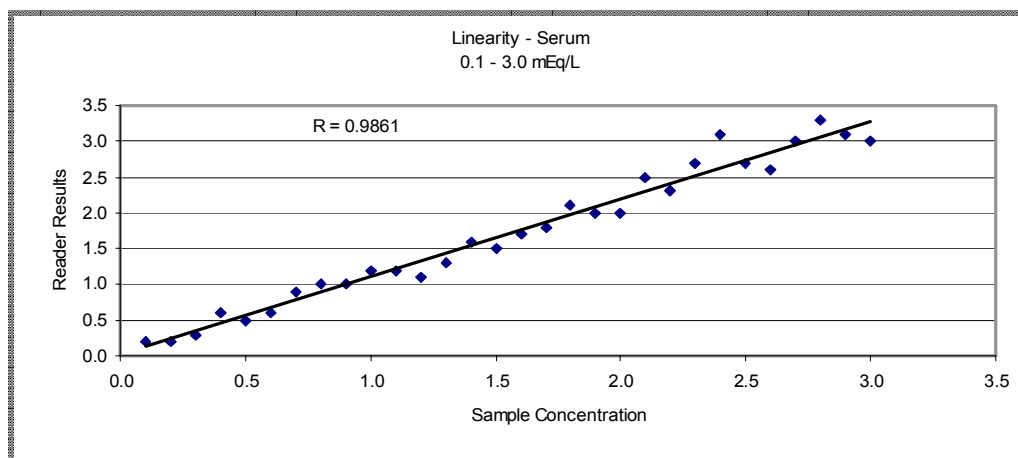
Clinicians should make their own individual patient assessments regarding patient status and lithium concentrations. Appropriate levels may vary among patients, and may depend slightly on the specific assay used. However, a therapeutic range of 0.6 to 1.2 mEq/L has been reported (Lithobid® package insert [PI], Solvay Pharmaceuticals, Inc., 2002). Mild to moderate adverse events may occur at concentrations between 1.5 and 2.5 mEq/L, and moderate to severe reactions may be seen at concentrations from 2.0 mEq/L and above. These values are based on measurements 8-12 hours post-dose (Lithobid PI). Lithium values should be interpreted in conjunction with other clinical findings and values above 1.5 mEq/L should be corroborated.

Sensitivity:

Serum, plasma, and whole blood samples, containing no exogenous lithium, were each assayed in 20 separate runs with the Lithium® System. The data showed that the lowest limits of detection, using two standard deviations above the mean, were 0.14, 0.06, and 0.14 mEq/L for serum, EDTA plasma, and whole blood, respectively.

Linearity:

Thirty (30) serum samples, spiked with lithium ranging from approximately 0.1 to 3.0 mEq/L, were assayed in singleton with the Lithium® System using serum. The data showed that the assay is linear throughout this range. The claimed linearity range for the Lithium® System is 0.1 to 2.0 mEq/L. Graphic representation of the linearity plot is provided below.



Precision:

Two levels of controls, “Low” and “High,” containing approximately 0.5 and 1.3 mEq/L lithium respectively, were each assayed in 2 runs over 20 days (n = 40 per level). The percent coefficients of variation (%CVs) were 8.1% for the Low sample, and 4.4% for the High sample.

Two spiked EDTA plasma samples, “Low” and “High” containing approximately 0.3 and 0.7 mEq/L lithium, respectively, were each assayed in 10 separate runs over three days (n = 30 per level). The standard deviations for each day of testing, and for all days combined, ranged from 0.04 to 0.11.

Two spiked whole blood samples, “Low” and “High” containing approximately 0.5 and 1.2 mEq/L lithium, respectively, were each assayed 20 times on one day by each of two operators and two different InstaRead readers. The %CVs ranged from 9.4% to 12.7% for the Low sample, and from 5.3% to 6.8% for the High Sample.

Specificity (Interference Testing):

NOTE: specificity results are based on the primary reagent manufacturer’s package insert

- No significant interference (<5% deviation from assigned lithium concentration of approximately 1 mEq/L) was observed from the following substances at their described concentrations:

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

- Studies to determine the level of interference from bilirubin, lipemia and hemoglobin in the presence of a lithium concentration of approximately 1 mEq/L were carried out, and the following results were obtained:

Free Bilirubin:	No significant interference from free bilirubin (<10% deviation) up to 769 μ mol/L (45 mg/dL).
Conjugated Bilirubin:	No significant interference from conjugated bilirubin (<10% deviation) up to 769 μ mol/L (45 mg/dL).
Lipemia:	No significant interference from lipemia (<10% deviation) measured as 22.6mmol/L (2000 mg/dL).
Hemoglobin:	No significant interference from hemoglobin (<5% deviation) up to 1000 mg/dL. Significantly higher levels may interfere with the assay; this could be recognized by the user by coloration of the sample.

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

- Studies to determine the level of interference from various therapeutic agents in the presence of a lithium concentration of approximately 1 mEq/L were carried out, and the following results were obtained:

Compound	Concentration	Result
N-Acetylcysteine	90 mg/dL	<10% Bias
Carbamazepine	12 ug/mL	<10% Bias
Procainamide	8 ug/mL	<10% Bias
Quinidine	6 ug/mL	<10% Bias
Valproic Acid	100 ug/mL	<10% Bias

Accuracy:

The Lithium[®] System was clinically evaluated in several studies. In the first study, 200 spiked serum samples (100 at each of two sites) were assayed with both the Lithium[®] System and a conventional laboratory instrument. The data appear below.

SERUM STUDY LINEAR REGRESSION

SITE	N	SLOPE		Y-INTERCEPT		S _{v/x}	“r”
		slope	95% CI*	y-intercept	95% CI*		
1	100	0.970	0.918 to 1.022	0.03	-0.04 to 0.10	0.14	0.966
2	100	1.025	0.966 to 1.085	-0.07	-0.15 to 0.02	0.17	0.961
Total	200	0.998	0.958 to 1.038	-0.02	-0.07 to 0.04	0.16	0.962

*CI = Confidence Intervals

In a second study, 29 spiked whole blood samples were assayed by the Lithium[®] System at a doctor’s office, and the corresponding plasma samples were assayed by a routine chemistry analyzer. The data appear below.

WHOLE BLOOD STUDY LINEAR REGRESSION

n	SLOPE		Y-INTERCEPT		S _{v/x}	“r”
	slope	95% CI	y-int	95% CI		
29	0.833	0.772 to 0.895	0.05	-0.03 to 0.13	0.10	0.983

Two separate studies were conducted to evaluate Lithium[®] System performance with fingerstick whole blood samples. One study included 40 native fingerstick samples, and the second study included 20 samples. In each study, fingerstick samples were assayed by the Lithium[®] System at a doctor’s office, and venous blood was collected into a neutral tube and processed to serum. The serum was assayed by atomic absorption at a reference laboratory. The data from the two studies appear below.

FINGERSTICK STUDY #1 LINEAR REGRESSION

n	SLOPE		Y-INTERCEPT		S _{v/x}	“r”
	slope	95% CI	y-int	95% CI		
40	0.847	0.735 to 0.958	0.02	-0.07 to 0.11	0.14	0.928

FINGERSTICK STUDY #2 LINEAR REGRESSION

	SLOPE		Y-INTERCEPT			

n	slope	95% CI	y-int	95% CI	S _{y/x}	"r"
20	1.194	1.129 to 1.258	0	-0.06 to 0.06	0.06	0.994

Limitations










- **The reagent is light sensitive and will absorb atmospheric carbon dioxide. Keep each Reagent Cuvette in its foil pouch until ready for use.**
- For best results, the user must follow the directions.

References

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Visit us on the web at
www.akersbiosciences.com

For technical support:
USA 1-800-451-TEST

Index of Symbols			
	Attention, see instructions for use		Tests per kit
	For <i>in vitro</i> diagnostic use only		Use by
	Store between 2-30°C		Lot Number
			Manufacturer
			Do not reuse
			Catalog #



"Auth. Rep."
acc.to IVDD 98/79/EC
MDSS
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30163 Hannover,

Manufacturer:

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201 Grove Road
Thorofare, NJ 08086 USA

Part Number 1390053 Rev 2 07/05
Patent Pending