Lonza

Limulus Amebocyte Lysate (LAL)
QCL-1000®

Catalog Number: 50-647U, 50-648U

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QCL-1000®

Limulus Amebocyte Lysate

U.S. License No. 1775

For the rapid, chromogenic quantitation of bacterial endotoxin.

IMPORTANT

Read Entire Brochure Before Performing Test

INTENDED USE

This product is intended as an *In Vitro* end-product endotoxin test for human and animal parenteral drugs, biological products, and medical devices. This product is not intended for the detection of endotoxin in clinical samples or as an aid in the diagnosis of human disease. This method utilizes a modified Limulus Amebocyte Lysate and a synthetic color producing substrate to detect endotoxin chromogenically.

In December, 1987, the United States Food and Drug Administration (FDA) published the "Guideline on the Validation and Use of the Limulus Amebocyte Lysate Test as an End-Product Endotoxin Test for Human and Animal Parenteral Drugs, Biological Products, and Medical Devices."[8] This Guideline outlines those procedures which the FDA considers necessary for: 1) establishing endotoxin limits for pharmaceuticals and medical devices, 2) validating the use of LAL as an end-product endotoxin test, and 3) developing a routine testing protocol.

The procedures described herein are based on those described in the FDA Guideline. Similar performance requirements for end point chromogenic assays have been published and are updated regularly in the United States Pharmacopeia.[9]

WARNING

For *In Vitro* Diagnostic Use Only. Not for the *In Vitro* Determination of Endotoxemia in Man. The LAL test may be substituted for the USP Rabbit Pyrogen Test when used according to the FDA Guideline for the end-product testing of human and animal parenteral drugs, biological products, and medical devices.[8]

EXPLANATION OF TEST

The Chromogenic Limulus Amebocyte Lysate (LAL) Test is a quantitative test for gram-negative bacterial endotoxin. A sample is mixed with the LAL supplied in the test kit and incubated at 37°C (±1°C) for 10 minutes. A substrate solution is then mixed with the LAL-sample and incubated at 37°C (±1°C) for an additional 6 minutes. The reaction is stopped with stop reagent. If endotoxin is present in the sample, a yellow color will develop. The absorbance of the sample can be determined spectrophotometrically at 405-410 nm. Since this absorbance is in direct proportion to the amount of endotoxin present, the concentration of endotoxin can be calculated from a standard curve.

The use of LAL for the detection of endotoxin evolved from the observation by Bang[1] that a gram-negative infection of *Limulus polyphemus*, the horseshoe crab, resulted in fatal intra-vascular coagulation. Levin and Bang[2,3] later demonstrated that this clotting was the result of a reaction between endotoxin and a clottable protein in the circulating amebocytes of *Limulus*. Following the development of a suitable anticoagulant for *Limulus* blood, Levin and Bang[4] prepared a lysate from washed amebocytes which was an extremely sensitive indicator of the presence of endotoxin. Solum[5,6] and Young, Levin and Prendergast[7] have purified and characterized the clottable protein from LAL and have shown the reaction with endotoxin to be enzymatic.

The present LAL method utilizes the initial part of the LAL endotoxin reaction to activate an enzyme which in turn releases p-nitroaniline (pNA) from a synthetic substrate, producing a yellow color.

PRINCIPLE

1 Proenzyme $\xrightarrow{\text{Endotoxin}}$ Enzyme

2 Substrate + H_2O $\xrightarrow{\text{Enzyme}}$ Peptide + pNA

Gram-negative bacterial endotoxin catalyzes the activation of a proenzyme in the Limulus Amebocyte Lysate (LAL)[7]. The initial rate of activation is determined by the concentration of endotoxin present. The activated enzyme catalyzes the splitting of pNA from the colorless substrate Ac-Ile-Glu-Ala-Arg-pNA. The pNA released is measured photometrically at 405-410 nm after the reaction is stopped with stop reagent. The correlation between the absorbance and the endotoxin concentration is linear in the 0.1-1.0 EU/ml range. The concentration of endotoxin in a sample is calculated from the absorbance values of solutions containing known amounts of endotoxin standard.

REAGENTS SUPPLIED AND STORAGE CONDITIONS

Kit part number	Lysate vials	Endotoxin vials	Substrate vials	LAL Reagent Water vials
50-647U	5	1	2	2
50-648U	5	2	5	——

Limulus Amebocyte Lysate (LAL)

The LAL reagent contains lyophilized lysate prepared from the circulating amebocytes of the horseshoe crab *Limulus polyphemus*.

Reconstitute immediately before use with LAL Reagent Water per following table:

Kit part number	LAL Reagent Water required
50-647U	1.4 ml/vial lysate
50-648U	3.0 ml/vial lysate

If the contents of more than one vial are required, pool two or more vials before use. Swirl gently to avoid foaming. Lyophilized LAL is to be stored at 2-8°C. Protect from long term exposure to light.

Reconstituted LAL Reagent should be used promptly. Reconstituted lysate can be stored at -10°C or colder up to one week if frozen immediately after reconstitution. Thaw and use only once.

***E. coli* Endotoxin**

Each vial contains approximately 15-40 EU lyophilized endotoxin. Reconstitute by adding 1.0 ml of LAL Reagent Water warmed to room temperature. The actual concentration of the vial will be determined by the value stated on the enclosed Certificate of Analysis. For example, if the value of the vial is 24 EU, when reconstituted with 1.0 ml water it will yield a concentration of 24 EU/ml. Shake vigorously for at least 15 minutes, preferably with a vortex mixer.

Lyophilized endotoxin is to be stored at 2-8°C. Reconstituted stock endotoxin is stable for four weeks at 2-8°C. Prior to use, the solution must be warmed to room temperature and vigorously mixed for 15 minutes. This is important because the endotoxin tends to attach to glass.

This endotoxin is provided for the user's convenience. Other endotoxin preparations may be used to prepare the standards; however, their performance in the chromogenic assay relative to the Reference Standard Endotoxin (RSE) must be determined.

WARNING: Contains human source material

Chromogenic Substrate

Each vial contains approximately 7 mg lyophilized substrate. Reconstitute by adding 6.5 ml of LAL Reagent Water to yield a concentration of ~2mM.

Lyophilized chromogenic substrate is to be stored at 2-8°C. Once reconstituted, the substrate solution is stable for four weeks at 2-8°C, if not contaminated with microorganisms or endotoxin.

PROTECT SUBSTRATE FROM LONG-TERM EXPOSURE TO LIGHT

LAL Reagent Water

Each bottle contains 30 ml and is used in the reconstitution of all reagents and as a negative control (blank). LAL Reagent Water should be stored at 2-8°C. (Note: Not included in 50-648U kit.)

MATERIALS AND EQUIPMENT NOT PROVIDED

1. For 50-648U, LAL Reagent Water #W50-640 (30 ml), #W50-100 (100 ml), #W50-500 (500 ml), or equivalent.
2. Stop reagent (e.g. Acetic acid, 25% v/v glacial acetic acid in water; or sodium dodecylsulfate (SDS) solution, 10g/100 ml in water).
3. Sodium hydroxide, 0.1N, dissolved in LAL Reagent Water, for pH adjustment.
4. Hydrochloric acid, 0.1N, diluted in LAL Reagent Water, for pH adjustment.
5. Disposable endotoxin-free glass dilution tubes (13x100 mm, #N207 or equivalent).
6. Individually wrapped measuring pipettes.
7. Automatic hand-held pipettes with sterile, individually wrapped or racked tips (#25-415, #25-416, #25-417 or equivalent).
8. FOR TUBE METHOD Disposable endotoxin-free glass assay tubes (10x75 mm, #N201, #N205, or equivalent).

9. FOR MICROPLATE METHOD Disposable sterile microplates.
   NOTE: Prior to routine use, microplates should be pre-qualified for each lysate lot by the acceptable performance of the linearity test as described under PERFORMANCE CHARACTERISTICS.
10. 8 channel pipettor.
11. Reagent reservoirs (#25-364 or equivalent).
12. Dry Bath/ Multi-Blok Heater at 37°C ± 1.0°C.
13. Stopwatch.
14. Vortex mixer.
15. Spectro- or filterphotometer with 405-410 nm filter.
16. Microplate reader (ELx808™ IU Reader, #25-315; or equivalent).
    If using a nonincubating reader:
    Tube block for heater, 1 each.
    Microplate adapter for heater (#25-038).

SPECIMEN COLLECTION AND PREPARATION

Careful technique must be used to avoid microbiological or endotoxin contamination. All materials coming in contact with the specimen or test reagents must be endotoxin-free. Clean glassware and materials may be rendered endotoxin-free by heating at 250°C for 30 minutes. Appropriate precautions should be taken to protect depyrogenated materials from subsequent environmental contamination.

From experience, most sterile, individually wrapped, plastic pipettes and pipette tips are endotoxin-free. However, these materials should be tested before regular use.

It may be necessary to adjust the pH of the sample to within the range 6.0-8.0 using endotoxin-free sodium hydroxide or hydrochloric acid. Always measure the pH of an aliquot of the bulk sample to avoid contamination by the pH electrode. Do not adjust unbuffered solutions.

Samples to be tested must be stored in such a way that all bacteriological activity is stopped or the endotoxin level may increase with time. For example, store samples at 2-8°C for less than 24 hours; samples stored longer than 24 hours should be frozen.

If the container of diluent used to rehydrate the reagents has been opened previously or was not supplied by Lonza, the diluent alone must be tested for endotoxin contamination

REAGENT PREPARATION

In each series of determinations, four standard endotoxin solutions should be used. The table below suggests a dilution scheme for the construction of these standards from the endotoxin supplied in the kit. Alternative dilution schemes can be used as well as other endotoxins not supplied in this kit. The initial dilution from the endotoxin stock is 1/X, where X equals the concentration of the endotoxin vial. This yields an endotoxin solution containing 1.0 EU/ml. For example, if the potency is 23 EU/ml, the initial dilution is 1/23 or 0.1 ml of endotoxin stock into 2.2 ml of LAL Reagent Water.

Endotoxin Concentration EU/ml	Endotoxin Stock Solution	Endotoxin Std. Solution 1 EU/ml	LAL Reagent Water
1.0	0.1 ml		(X-1)/10 ml
0.5		0.5 ml	0.5 ml
0.25		0.5 ml	1.5 ml
0.1		0.1 ml	0.9 ml

X = endotoxin concentration of the vial

1. Prepare a solution containing 1.0 EU/ml endotoxin by diluting 0.1 ml of the endotoxin stock solution with (X-1)/10 ml of LAL Reagent Water in a suitable container, where X equals the endotoxin concentration of the vial. This solution should be vigorously vortexed for at least 1 minute before proceeding. For example, if X = 23 EU/ml, then dilute 0.1 ml of the endotoxin stock solution with 2.2 ml, (23-1)/10, LAL Reagent Water.
2. Transfer 0.5 ml of this 1.0 EU/ml solution into 0.5 ml of LAL Reagent Water in a suitable container and label 0.5 EU/ml. This solution should be vigorously vortexed for at least 1 minute before use.
3. Transfer 0.5 ml of the 1.0 EU/ml solution into 1.5 ml of LAL Reagent Water in a suitable container and label 0.25 EU/ml. This solution should be vigorously vortexed for at least 1 minute before use.
4. Transfer 0.1 ml of the 1.0 EU/ml solution into 0.9 ml of LAL Reagent Water in a suitable container and label 0.1 EU/ml. This solution should be vigorously vortexed for at least 1 minute prior to use.

TEST PROCEDURE

The addition of all reagents in the LAL assay must be consistent. All tubes or microplate wells must be treated in exactly the same manner in order to determine the proper endotoxin concentration. It is suggested that, in a series of tests, reagents should be pipetted in the same order from tube to tube or well to well, and at the same rate. The table below outlines the test procedure.

	Sample	Blank
Test sample or standard at 20-25°C	50 µl	
LAL Reagent Water		50 µl
LAL	50 µl	50 µl
Mix and incubate at 37°C ± 1°C	10 min.	10 min.
Substrate solution at 37°C ± 1°C	100 µl	100 µl
Mix and incubate at 37°C ± 1°C	6 min.	6 min.
Stop reagent	100 µl	100 µl
Mix immediately		

Test Tube Method

1. Carefully dispense 50 µl of sample or standard into the appropriate endotoxin-free reaction tube in a 37°C ± 1°C block or waterbath.
   Each series of determinations must include a blank plus the four endotoxin standards run in duplicate. The blank tubes contain 50 µl of LAL Reagent Water instead of sample. All reagent additions and incubation times are identical.
2. At time T = 0, add 50 µl of LAL to the reaction vessel. Begin timing as LAL is added to the first reaction vessel. It is important to be consistent in the order of reagent addition from vessel to vessel and in the rate of pipetting. Thorough mixing of the two solutions is essential, but do not vortex.
3. At T = 10 minutes, add 100 µl of substrate solution (prewarmed to 37°C ± 1°C). Pipette the substrate in the same order as in Step 2. Maintain a consistent pipetting rate. Assure thorough mixing of solutions.
4. At T = 16 minutes, add 100 µl of stop reagent. Maintain the same pipetting order and rate as in Steps 2 and 3. Mix well.
5. Read the absorbance of each reaction tube at 405-410 nm using distilled water to adjust the photometer to zero absorbance.

Microplate Method

1. Pre-equilibrate the microplate at 37°C ± 1°C in the heating block adapter. (NOTE: Do not use a cabinet-style incubator to run this test.)
2. While leaving the microplate at 37°C ± 1°C, carefully dispense 50 µl of sample or standard into the appropriate microplate well.
   Each series of determinations must include a blank plus the four endotoxin standards run in duplicate. The blank wells contain 50 µl of LAL Reagent Water instead of sample. All reagent additions and incubation times are identical.
3. At time T = 0, add 50 µl of LAL to the first microplate well, or first column of microplate wells if using a multi-channel pipettor and reagent reservoir. Begin timing as the LAL is added. It is important to be consistent in the order of reagent addition from well to well or row to row, and in the rate of pipetting. Once the LAL has been dispensed into all microplate wells containing samples or standards, briefly remove the microplate from the heating block adapter and repeatedly tap the side of the plate to facilitate mixing. Return the plate to the heating block adapter and replace cover.
4. At T = 10 minutes, add 100 µl of substrate solution (prewarmed to 37°C ± 1°C). Pipette the substrate solution in the same manner as in Step 3. Maintain a consistent pipetting rate. Once the substrate solution has been dispensed into all microplate wells, briefly remove the microplate from the heating block adapter and repeatedly tap the side of the plate to facilitate mixing. Return the plate to the heating block adapter and replace cover.

5. At T = 16 minutes, add 100 µl of stop reagent. Maintain the same pipetting order as in Steps 3 and 4. Once the stop reagent has been dispensed into all microplate wells, remove the plate and repeatedly tap the side of the plate.
6. Read the absorbance of each microplate well at 405-410 nm using distilled water to adjust the photometer to zero absorbance.
   NOTE: The performance characteristics of certain microplate readers are optimal with sample volumes less than 300 µl. The final reaction volume per well can be reduced by adding only 50 µl of the above suggested stop reagents without adversely affecting the test results.

PERFORMANCE CHARACTERISTICS

Linearity

The linearity of the standard curve within the concentration range used to predict endotoxin values should be verified with each new lot of reagents (known as an Initial Qualification). No less than 4 endotoxin standards spanning the desired concentration range should be assayed along with a blank, in quadruplicate. Under standard assay conditions, endotoxin standards ranging from 0.1 to 1.0 EU/ml may be prepared as described in REAGENT PREPARATION.

The coefficient of correlation, r, for the individual mean Δ absorbance of the standards (at least 16 points) vs. their respective endotoxin concentration (see CALCULATION OF ENDOTOXIN CONCENTRATION, Calculator Method) should be ≥0.980.

Reproducibility

Replicate samples should be run in order to establish good technique and low coefficient of variation. The coefficient of variation (C.V.) equals 100 times the standard deviation of a group of values divided by the mean and is expressed as a percent. The C.V. absorbance should be less than 10%. With experience, values of 3-4% should be attainable when measured on the uncorrected absorbance for the 1 EU standard during the qualification assay.

CALCULATION OF ENDOTOXIN CONCENTRATION

Under the standard conditions, the absorbance at 405-410 nm is linear in the concentration range of 0.1 to 1.0 EU/ml endotoxin (See PERFORMANCE CHARACTERISTICS). There are several methods to determine the endotoxin concentration of samples. Subtract the mean absorbance of the blank from the mean absorbance value of the standards and samples to calculate mean Δ absorbance.

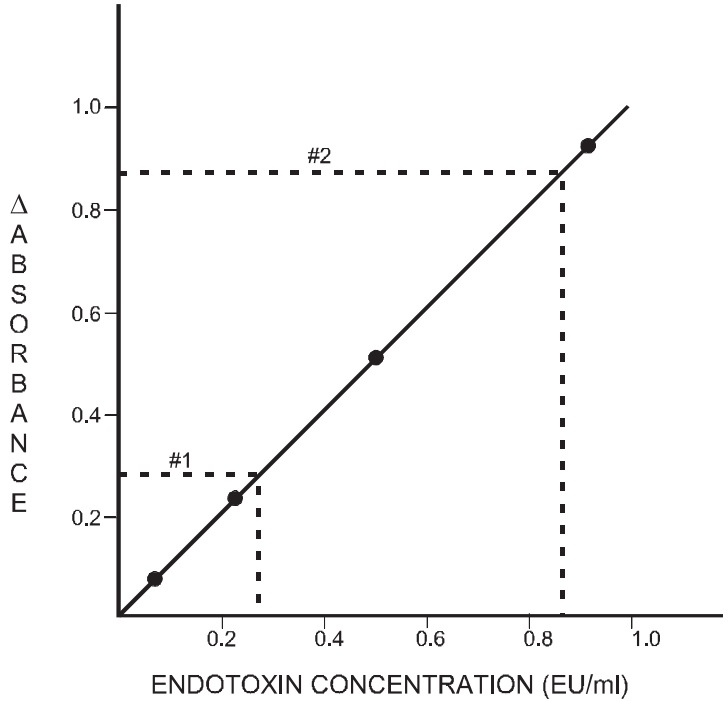
A. Graphic Method
   Plot the mean Δ absorbance for the four standards on the y-axis vs. the corresponding endotoxin concentration in EU/ml on the x-axis. Draw a best fit straight line between these points and determine endotoxin concentrations of samples graphically.

B. Calculator Method
   A calculator equipped with linear regression capability can be used. Enter the mean Δ absorbance and the corresponding concentrations of the four standards. Determine the corresponding endotoxin concentration of the samples from their absorbance by linear regression.

Example Data

Tube Well	Sample	Absorbance at 405 nm	Mean Absorbance	Mean Δ Absorbance
1	LAL Reagent	0.080		
2	Water (Blank)	0.084	0.082	–
3	0.1 EU/ml	0.160		
4	Standard	0.180	0.170	0.088
5	0.25 EU/ml	0.309		
6	Standard	0.325	0.317	0.235
7	0.5 EU/ml	0.570		
8	Standard	0.557	0.564	0.482
9	1.0 EU/ml	1.052		
10	Standard	1.012	1.032	0.950
11	Product	0.372		
12	#1	0.392	0.382	0.300
13	Product	0.916		
14	#2	0.912	0.914	0.832

A. Graphic Method



#1 = 0.32 EU/ml
#2 = 0.87 EU/ml

B. Calculator Method

$$\text{Slope} = \left(\frac{Sy}{Sx}\right) r$$

Y - intercept = $\Sigma y/N - (\Sigma x/N \times \text{slope})$

$$r = \frac{N\Sigma xy - (\Sigma x)(\Sigma y)}{N(N-1)SxSy}$$

$$\text{Endotoxin concentration} = \frac{\Delta Abs. - (y - \text{intercept})}{\text{slope}}$$

x = Endotoxin concentration in EU/ml

y = Mean Δ Absorbance Value

N = Number of standards used

Σx = Summation of concentration of standards used in EU/ml

Σy = Summation of Mean Δ Absorbance Values

Σxy = Summation of the standard concentrations times Mean Δ Absorbance Values

$$Sx = \text{Standard deviation of } x = \sqrt{\frac{N\Sigma x^2 - (\Sigma x)^2}{N(N-1)}}$$

$$Sy = \text{Standard deviation of } y = \sqrt{\frac{N\Sigma y^2 - (\Sigma y)^2}{N(N-1)}}$$

Calculations using example data: (Page 10)
N = 4

$\Sigma x = 1.85 = (0.100 + 0.250 + 0.500 + 1.00)$

$\Sigma y = 1.76 = (0.088 + 0.235 + 0.482 + 0.950)$

$\Sigma xy = 1.26 = (0.100 \times 0.088) + (0.250 \times 0.235) + (0.500 \times 0.482) + (1.00 \times 0.950)$

Sx = 0.394

Sy = 0.378

$$r = \frac{4(1.26) - (1.85)(1.76)}{4(4-1)(0.394)(0.378)} = 1.00$$

$$\text{Slope} = \frac{0.378}{0.394} \times 1.00 = 0.959$$

$$\text{Y-intercept} = \frac{1.76}{4} - \left(\frac{1.85}{4} \times 0.959\right)$$

$$\text{Y-intercept} = 0.440 - (0.463 \times 0.959) = -0.004$$

Product #1

$$\text{Endotoxin concentration (EU/ml)} = \frac{0.300 - (-0.004)}{0.959} = \frac{0.304}{0.959} = 0.317 \text{ EU/ml}$$

Product #2

$$\text{Endotoxin concentration (EU/ml)} = \frac{0.832 - (-0.004)}{0.959} = \frac{0.836}{0.959} = 0.872 \text{ EU/ml}$$

NOTE

If the concentration of endotoxin in the test sample is greater than 1.0 EU/ml, dilute sample 5-fold in LAL Reagent Water and retest. Calculate the concentration of the diluted sample and multiply by 5 to determine the original endotoxin concentration.

PRODUCT INHIBITION

Product inhibition occurs when substances in the test sample interfere with the LAL reaction. In the chromogenic assay, this inhibition results in a lower, final Δ absorbance, indicating lower levels of endotoxin than what may actually be present in the test sample. The lack of product inhibition should be determined for each specific sample, either undiluted or at an appropriate dilution.

To verify the lack of product inhibition, an aliquot of test sample (or a dilution of test sample) is spiked with a known amount of endotoxin (e.g. 0.4 EU/ml). The spiked solution is assayed along with the unspiked samples and their respective endotoxin concentrations are determined. The difference between these two calculated endotoxin values should equal the known concentration of the spike ± 25%.

A spiked aliquot of the test sample (or dilution) may be prepared as follows:

1 . Prepare a 1.0 EU/ml endotoxin solution in the test sample (or dilution) by diluting the endotoxin stock solution 1/X, where X is the endotoxin concentration of stock in EU/ml. Use the test sample (or dilution) as the diluent. This solution should be vigorously vortexed for one minute before proceeding. For example, if the concentration of the endotoxin stock solution is 24 EU/ml, the initial dilution is 1/24 or 0.1 ml of endotoxin stock solution into 2.3 ml of test sample (or dilution).
2. To prepare a 0.4 EU/ml endotoxin solution in test sample (or dilution), dilute the 1.0 EU/ml solution 1/2.5 using the test sample (or dilution) as the diluent. This can be done by combining 1.0 ml of the 1.0 EU/ml solution in test sample (or dilution) with 1.5 ml of test sample (or dilution). This solution should be vigorously vortexed for 1 minute prior to use.

If the test sample (or dilution) is found inhibitory to the LAL reaction the sample may require further dilution until the inhibition is overcome.

Example:
Determination of a Non-Inhibitory Dilution

	Calculated Endotoxin Concentration (EU/ml)		
Sample Dilution	Unspiked	Spiked	Difference
1/10	0.18	0.28	0.10 Inhibitory
1/20	0.11	0.36	0.25 Inhibitory
1/40	<0.1	0.44	0.44 Non-inhibitory

Initially, one may want to screen for product inhibition by testing 10-fold dilutions of test sample. Once the approximate non-inhibitory dilution is determined, the exact dilution can be found by testing two-fold dilutions around this dilution.

LIMITATIONS

The degree of inhibition or enhancement will be dependent upon the concentration of product. If several concentrations of the same product are to be assayed, it is necessary to establish performance characteristics for each independently.

Patterns of inhibition or enhancement different from those seen with the traditional LAL gelation test may be found.

It may be necessary to adjust the pH of the sample to within the range 6.0 to 8.0 using endotoxin-free sodium hydroxide or hydrochloric acid to overcome inhibition.

COLORED SAMPLES

In the Chromogenic assay, samples which possess significant color on their own may require special attention. Also, if using 25% acetic acid as the stop reagent, one must be conscious of products which turn yellow in acid environments, such as certain tissue culture media.

A quick test to determine if a product's intrinsic color is sufficient to be of concern is to construct a mock reaction tube. Add 50 µl of sample, 150 µl LAL Reagent Water and 100 µl appropriate stop reagent without incubation. Read the absorbance at 405-410 nm of this solution. If the absorbance is significantly greater than the absorbance of LAL Reagent Water, then the color of the product must be taken into account.

At the time of assay, prepare a sample blank by combining 50 µl sample, 150 µl LAL Reagent Water, and 100 µl appropriate stop reagent without incubation. In addition, assay the product along with the appropriate standards and LAL Reagent Water blank. To calculate Δ absorbance of the sample, subtract the absorbance of the sample blank as well as the mean absorbance of the LAL Reagent Water blank. However, use only the LAL Reagent Water blank to calculate Δ absorbance for the endotoxin standards and non-colored products.

If the background color is significant (>0.5 absorbance units), the sample should be diluted and reassayed. The dilution factor is then used in the final calculations for determining the concentration of endotoxin.

CORRELATION WITH OTHER METHODS

The FDA regulates the official use of LAL testing in the United States. The FDA has official LAL and endotoxin preparations which have been of great assistance in standardizing LAL testing. The FDA reference LAL is not readily used in this test since it has not been formulated for the chromogenic method. However, the official endotoxin has been used to standardize the endotoxin in this kit. The potency of different endotoxin

preparations vary in both the traditional gel test and the chromogenic method. The endotoxin standard supplied in this kit has been compared to the RSE using the chromogenic assay and the potency is provided on the enclosed Certificate of Analysis. The calibration curve diluted from this standard will yield a range of 0.1 to 1.0 endotoxin units/ml relative to the RSE. It should be remembered, however, that the traditional gel test is standardized by two-fold dilutions, so that variations will appear quite large in comparison to those in the chromogenic test where standardization is continuous and variations are minimal.

A NOTE FOR OUR INTERNATIONAL CUSTOMERS

Other regulatory agencies may adopt other performance standards which need to be satisfied in order to be in compliance in their jurisdictions.

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PATENTS

Various components of this product are protected under the following U.S. Patents:
4510241
4322717

TRADEMARKS

NOTES

Lonza

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P50-648U-9
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