charles river

MICROBIAL SOLUTIONS

Bacterial Endotoxin Testing Solutions

Where is bacterial endotoxin testing applicable?

- Sterile compounding or purified water production quality control
- Dialysis (water for dialysis and dialysates)
- Parenterals, injectable drugs and in-process raw materials
- Medical devices (catheters, implants, prosthetics, and surgical material)
- Nuclear medicine for radiopharmaceutical products

Limulus amebocyte lysate (LAL) is an aqueous extract of blood cells (amebocytes) from the horseshoe crab, *Limulus polyphemus*. Comprised of proteins, LAL is used to detect the presence of endotoxins, a cell wall component of gram-negative bacteria that cause a pyrogenic response (fever) and symptoms of septic shock. They are extremely potent, heat stable, and ubiquitous in nature.

Prior to FDA approval of LAL in the 1980s, the rabbit pyrogen test was the standard FDA-approved test for endotoxins. This test, however, was labor intensive, lengthy and expensive. Years of research and application have proven LAL to be unequivocally recognized as the most sensitive method available for the detection of endotoxins. In the 50 years since the discovery of LAL, approximately 70 million bacterial endotoxin tests have been performed each year, and there have been no FDA-confirmed pyrogenic outbreaks due to an LAL false-negative result.

Charles River offers a complete portfolio of bacterial endotoxin testing reagents and technologies, including our innovative cartridge-based testing systems, to help ensure safety in the manufacturing processes. Our FDA-licensed kinetic chromogenic and turbidimetric reagents yield quantitative endotoxin values and feature buffered formulations that provide robust testing with the highest accuracy and precision.

Bacterial Endotoxin Testing Solutions:

- Kinetic chromogenic (KCA) LAL reagents
  - Endosafe®-PTS™ LAL cartridges
  - Endochrome-K™
- Kinetic turbidimetric (KTA) LAL reagents
  - KTA
  - KTA^2
- Endosafe® gel-clot LAL
- LAL accessory products
- EndoScan-V™ endotoxin-specific software
- BioTek® plate readers and support
- Contract endotoxin testing services

EVERY STEP OF THE WAY

Kinetic Chromogenic (KCA) LAL Reagents

Endosafe®-PTS™ LAL cartridges

Our traditional kinetic chromogenic LAL reagent is used in our pre-calibrated, single-use, Endosafe®-PTS™ LAL test cartridge, along with a substrate to provide quantitative endotoxin analysis. These cartridges can be used with any of our Endosafe® rapid testing systems (PTS™, nexgen-PTS™, MCS™ or Nexus™), and offer a 15-minute endotoxin assay. This proven, innovative technology delivers fully quantitative results in a rapid, easy-to-use, self-contained package, eliminating preparation of multiple reagents and reducing the opportunity for technician error.

The disposable cartridge contains four channels — two channels with CSE and LAL, which serve as the positive control channels, and two channels with LAL for testing of samples. To perform the test, simply add 25 μL of sample into all four sample reservoirs. The reader's internal pump moves the sample along the channels' reagent stations for mixing, then into the optical cells of the cartridge to be read kinetically.

Endochrome-K™

A fully quantitative and uniquely stable kinetic chromogenic reagent, Endochrome-K™ features an optimized KCA formulation that offers an unrivaled combination of sensitivity, linearity and interference resistance. Endochrome-K™ delivers quantitative endotoxin values in roughly an hour, depending on the user's desired sensitivity, and the stability of the reconstituted LAL allows for extended bench time and reuse, making it a highly cost-effective solution.

Kinetic Turbidimetric (KTA) LAL Reagents

KTA

KTA is a testing solution that yields quantitative endotoxin values in the same amount of time (or less) that it takes to run a gel-clot assay. Utilizing a buffered reagent that provides significant interference resistance, KTA is licensed for both kinetic and gel-clot analysis and permits direct correlation between the two methods.

KTA^2

A second-generation kinetic turbidimetric reagent, KTA^2 offers faster reaction times over a wider standard curve range (to 0.005 EU/mL) than traditional KTA reagents. The superior formulation of KTA^2 delivers the performance of kinetic chromogenic reagents at turbidimetric prices. Like our KTA reagent, KTA^2 is buffered to provide significant interference resistance.

Endosafe® Gel-Clot LAL

Our FDA-licensed gel-clot assay is a simple qualitative method best used for biologics, dialysis clinics and low-volume laboratories. Our lysate features a firm gel over a wide range of sensitivities as the buffered reagent provides better interference resistance for routine testing.

LAL Accessory Products

A critical part of endotoxin testing is the choice of LAL accessories that enable data collection free of artifacts and sources of interference. The selection of non-interfering accessories for a BET is not only a pharmacopeial directive, but also a regulatory expectation. Accessories play a major role in the quality of results generated in the BET lab. But all too often, cost, not quality, is the driving force in the BET accessory decision-making process. Charles River offers a comprehensive range of accessories, including depyrogenated glass pipettes and tubes, LAL reagent water, LAL buffers and 96-well plates. All accessory products are provided with a certificate of quality certifying appropriate endotoxin levels.

EndoScan-V™ Endotoxin-Specific Software

EndoScan-V™ is a fully validated, verified and 21-CFR-Part-11-compliant endotoxin-specific software package. With flexible setup and intuitive data analysis, the software is compatible with a variety of microplate and tube readers, as well as our complete Endosafe® line of rapid testing systems. EndoScan-V™ features drag-and-drop capability for fast and easy template setup, a user-defined product database, flexible exporting functions and enhanced security features, and is available in English, French and German language versions.

BioTek® Plate Readers and Support

Our partnership with BioTek® allows for a superior level of support for BioTek® plate readers. In addition to selling the BioTek® ELX808IU™ reader, our technical support team qualifies the instrument for compatibility with Endoscan-V™ software and the LAL test. This service provides a smooth transition for replacing or implementing a BioTek® plate reader for BET testing. Our onsite annual qualification of the BioTek® reader and software provides the assurance that the plate reader is operating correctly and fulfills the preventative maintenance requirements recommended by Charles River.

Contract Endotoxin Testing Services

Our technical services laboratory is available to assist with performing critical tests to help streamline the process to final product release. Our experts can help identify which technology is the best fit and assist with product validation programs, regulatory compliance guidance and troubleshooting technical issues.

LAL Techniques and Methods Offered:

Testing techniques:

- Gel-clot technique: based on gel formation
- Turbidimetric technique: based on the development of turbidity
- Chromogenic technique: based on the development of color after cleavage of a synthetic peptide-chromogen complex

Testing methods:

- Method A: Gel-clot method (limit test)
- Method B: Gel-clot method (semi-quantitative test)
- Method C: Turbidimetric kinetic method
- Method D: Chromogenic kinetic method (conventional or rapid micro-method Endosafe®-PTS™/ Endosafe®-MCS™)
- Method E: Chromogenic endpoint method (Not available in North America)

Available LAL testing services:

- Routine testing and test for interfering factors
- Depyrogenation validation
- Protocol and method development (e.g., stability testing)
- SOP and protocol writing
- Product specificity (e.g., resolve interferences, glucan, confirm results with a second method)
- Product release/stability testing
- Product validation programs – one and three lots

Note: Our European facility based in Lyon is COFRAC accredited (April of 2007 [ISO 17025:2005] for gel-clot, kinetic chromogenic and kinetic turbidimetric techniques) and approved to perform the BET in accordance with all methods described in the European Pharmacopoeia (Chapter 2.6.14) and USP (Chapter <85>). The facility is also ISO 9001:2008 certified and FDA-registered as of December 2009.

The Charles River Kinetic Testing Solutions Portfolio*

Kinetic Chromogenic (KCA) LAL	
PTS™	FDA-licensed, USP- and Ph. Eur-compliant LAL test cartridges
	Ultimate in simplicity and speed
	Prevents bottlenecks and hold steps
	Improves sample management and reduces technician errors
	Available in 4 sensitivity ranges: • 0.5–0.005 EU/mL • 1.0–0.01 EU/mL • 5.0–0.05 EU/mL • 10.0–0.1 EU/mL
Endochrome-K™	32 tests per vial
	Can test to 0.001 EU/mL using the appropriate conditions
	Licensed for linear and polynomial regression
	Buffered interference-resistant reagent
	Highly stable reagent available in kit form or bulk packaging
Kinetic Turbidimetric (KTA) LAL	
KTA	50 tests per 5.2 mL vial
	50–0.05 EU/mL standard curve range (other curve ranges may be run under the appropriate conditions)
	Can be used for kinetic and gel-clot analysis
	Buffered interference-resistant reagent
KTA^2	50 tests per 5.2 mL vial
	Can test to 0.005 EU/mL using the appropriate conditions
	Licensed for linear and polynomial regression
	Buffered interference-resistant reagent
	Kinetic chromogenic performance at turbidimetric prices
Software	
EndoScan-V™ (ESV)	Validated endotoxin-specific software
	Enhanced security and audit trail feature
	Drag-and-drop for fast and easy template setup
	Save and reuse templates for improved efficiency
	Full qualification package available
	Available in English, French and German
Accessories	
	Depyrogenated endotoxin-free pipettes, tubes and sampling material
	LAL reagent water
	LAL buffers
	96-well polystyrene plate

* Please contact Customer Service for details.

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