LAL Testing Overview
Any product that is labeled non-pyrogenic must be tested to verify the absence of bacterial components left from pre-sterilization bacterial contamination. Thus, the pharmaceutical industry takes great care to produce drugs, vaccines and medical devices that are non-toxic and sterile-free of microorganisms. For years, pharmaceutical manufacturers have used the Bacterial Endotoxin Test (BET), or LAL (Limulus Amoebocyte Lysate) Test—which uses amoebocyte lysate from the blood of the American horseshoe crab (Limulus polyphemus)—to detect endotoxins of gram-negative origin.

Regulatory authorities require an LAL test for injectable and intravenous drugs, as well as for screening prosthetic devices such as heart valves or hip replacements. Any medical devices with bloodstream or cerebrospinal fluid contact must also be tested for bacterial endotoxins. Many other products, such as dialysis fluids, must be screened to insure the safety of patients as well.

Charles River Technical Services–Lyon, France Laboratory
Charles River Technical Services offers testing and support services to improve the compliance and efficiency of endotoxin detection programs.

History: Charles River has extensive testing experience, dating back to the foundation of Endosafe® in 1987. Our European laboratory—conveniently located on the outskirts of Lyon, France—has been dedicated to bacterial endotoxin testing for more than 18 years.

Services: A wide range of samples can be tested at this site, including end product release, raw material, in-process samples, medical devices, dialysis fluids, and much more. All testing protocols can be requested or viewed during an audit. In addition to testing, we offer results analysis, SOP writing assistance and protocol recommendations. We also offer standard or customized LAL training courses.

Accreditation: Accreditation: Our facility is COFRAC accredited (April of 2007 (ISO17025 v2005) for Gel-clot, kinetic chromogenic and kinetic turbimetric technics) and approved to perform the BET in accordance with all methods described in the European Pharmacopeia (Chapter 2.6.14) and USP (Chapter 85). The facility is also ISO 9001v2008 certified and FDA-registered as of December 2009.
LAL Techniques and Methods Offered

Establishing an LAL testing program requires a large investment in time, resources and space. Initiation requires careful consideration of methods, instruments and technical mastering.

Testing Techniques

- Gel-clot technique–based on gel formation
- Turbidimetric technique–based on the development of turbidity
- Chromogenic technique–based on the development of colour 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 end-point method

Available LAL Testing Services

Routine testing, and test for interfering factors: All testing is performed using the customer-requested method—for each sample submitted. Our optimized formulations provide increased sensitivity, greater linearity and superior interference resistance. Formulations are offered with a comprehensive range of buffers and accessories, providing numerous options for resolving interferences with difficult to test products. Specific sensitivity requests can be met with ranges that include 0.015 to 0.25 EU/mL for gel-clot, and as low as 0.001 EU/mL for the kinetic chromogenic method.

Depyrogenation validation: From oven validation studies, to stopper washing endotoxin reduction studies and syringe cleaning process validation, a wide variety of depyrogenation validation studies are offered. These studies—often performed during production downtime—use specifically contaminated articles to verify a 3-log reduction in endotoxin content.

Charles River can also contaminate specific devices or articles with an adequate contamination value, or provide ready-to-use endotoxin indicators as preferred. With a capacity of more than 200 samples per day, all returned devices, articles or indicators can be assayed within 48 hours of receipt—avoiding production delays.

Benefits of LAL Testing with Charles River

Why use Charles River’s Technical Laboratory?

- Outsource testing
  - Manage unexpected increases in testing activity
  - Quick turnaround on a large number of samples
  - Save on equipment costs
  - Streamline facility for fewer samples
- Product specificity
  - Resolve interferences for difficult products
  - Check for Glucan false positives
  - Confirm results with a second method
- Protocol and method development
  - Perform oven validation studies
  - Methods transfer and specific studies (e.g. transfer existing method to the Endosafe®-MCS™ instrument)
- Stability testing
- Sample preparation
- SOP and protocol writing

What value does Charles River offer?

- High-quality process
  - 48 hour sample testing
  - High capacity—more than 200 samples per day
  - Thorough QA/QC review of report and acceptance criteria before release
  - Results archived for 10 years in secure storage facility
- Dedicated team
  - Specialist recommendations before choice of method
  - Technical expertise and explanation of results
  - Qualified LAL technicians
- Exceptional features
  - Only lab offering the option to transfer from classical method to Next Generation rapid BET with PTS® and MCS® technology
  - Maximum sensitivity—0.001 EU/mL for kinetic chromogenic method and 0.015 EU/mL for gel-clot method
  - Alternative testing solutions for internal methods
  - Experience with a diverse range of samples
  - Variety of certified containers for transportation of samples