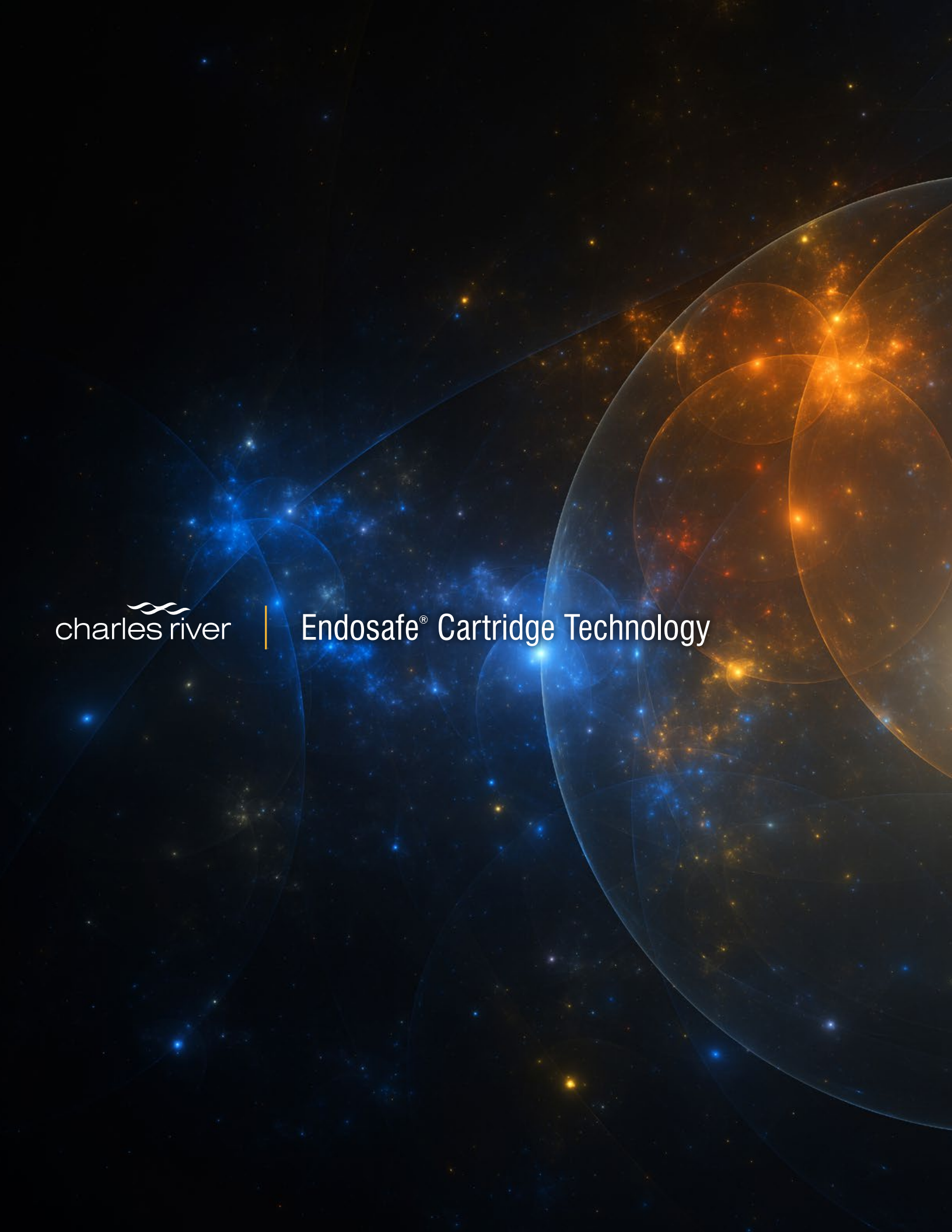

charles river
Endosafe® Cartridge Technology

The most expensive test is the one you have to do twice.

Traditional endotoxin testing has long had pain points including long turnaround times, extensive training requirements, and multiple steps for assay preparation. To make matters worse, an invalid test result can potentially cripple your manufacturing timelines.

There's no mistake that the LAL assay is the gold standard for endotoxin testing, and while conventional kinetic testing is a tried and trusted method, advances in science have allowed for improvement in how it's utilized. The end result is our revolutionary cartridge technology.

Reduce Retest Rates. Decrease Variability.

Endosafe® cartridge technology is our innovative response to our customers' need for higher sensitivity and faster quantitative results. Designed to optimize and refine our use of LAL, the cartridge technology eliminates a significant amount of the raw material and accessories required for traditional LAL methods while reducing time-consuming preparation and technician variability.

Streamlined Design for Compliance

Using 20 times less raw material than what is needed for traditional LAL tests, cartridge technology achieves operational efficiencies and supports our commitment to preserve the blood of the horseshoe crab, an important natural resource.

Each cartridge contains precise amounts of our FDA-licensed LAL reagents, chromogenic substrate, and controls needed to obtain rapid, accurate results. The cartridges automatically perform a duplicate sample and positive product control, thereby satisfying the harmonized BET chapters USP<85> or EP<2.6.14> for LAL testing.

The Archived Standard Curve (ASC)

An ASC is defined as a stored standard curve created by regression analysis from multiple reaction times for specified endotoxin concentrations, and is the critical component of the Endosafe® LAL cartridges. An ASC for a batch of cartridges is created from a statistically sound number of units, and regulatory commitments. All of the data points for a 3-point (2-log) standard curve from primary endotoxin standard (RSE) are used to calculate a correlation coefficient of the standard curve line. A second group of cartridges is taken and subjected to tests for precision and accuracy. The use of an ASC eliminates the variability between analysts when creating a standard curve and rehydrating reagents.

Quality Control

Prior to shipment, we test each lot of cartridges per rigid quality control procedures to ensure test accuracy and stability. Values for the standard reaction times and spike concentration are determined for each lot. These parameters, as well as the lot's archived curve, are expressed in a unique calibration code found on the lot's Certificate of Analysis (CoA). During quality testing, the calibration code is verified with additional cartridges that are challenged with known concentrations of RSE. Reader software calculates the reaction times determined for each well against the known values to give sample value and spike recovery just like with traditional kinetic LAL assays.

Rapid Results. Flexible Applications.

Whether you need to perform standard endotoxin testing or support investigations with Gram identification or Beta-glucan detection, our easy-to-use cartridge technology delivers a robust assay and rapid results.

FDA-Licensed LAL Cartridges

Our LAL cartridges use existing FDA-licensed Endosafe® chromogenic LAL reagent to measure color intensity directly related to the endotoxin concentration in a sample.

- Real-time quantitative endotoxin analysis in 15 minutes
- Proven USP/EP/JP-compliant BET method
- Licensed by the FDA in 2006 for in-process and final product release testing
- Detects between 0.005-10 EU/mL

Gram Identification Cartridges

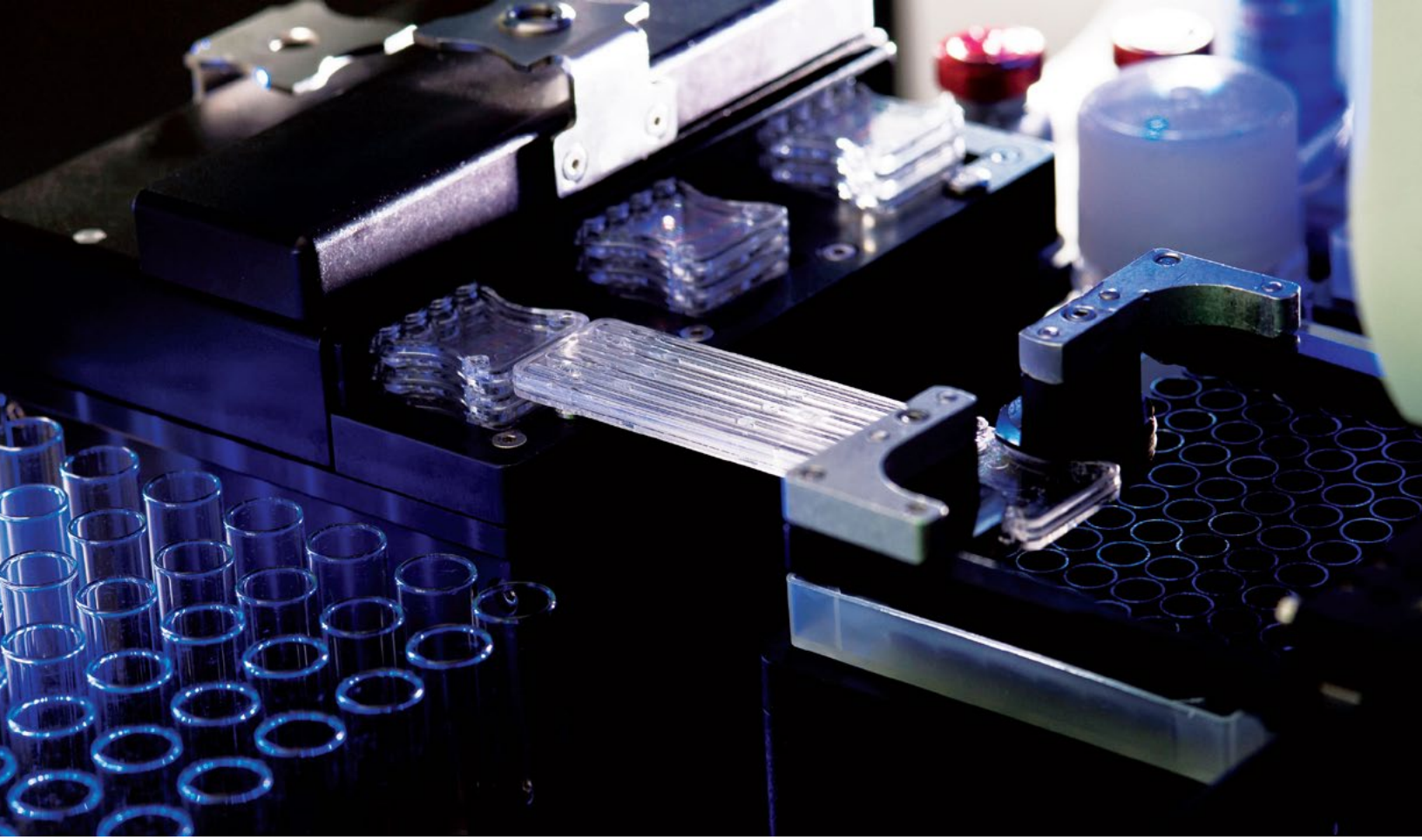
Our Gram ID cartridge technology is a rapid assay that measures differences in the cell walls of microbial isolates. As a stain-free assay, the Gram ID cartridge eliminates procedure variability that occurs in traditional Gram stain determination.

- Results in 3-7 minutes for Gram negative, Gram positive, and yeast and mold confirmation
- Capable of testing organisms <72 hours old
- Reduces the need to subculture

Beta-Glucan Cartridges

The Beta-glucan assay is a rapid, in-process test designed for investigational purposes to ensure that products do not contain (1,3)-β-D glucans. Glucans are known to cause false-positive results in LAL assays, which could trigger an investigation.

- Sensitivity range of 10-1,000 μg/mL
- Results in approximately 30 minutes
- Designed to mimic kinetic chromogenic method by measuring color intensity



Designed for Simplicity. Engineered for Compliance.

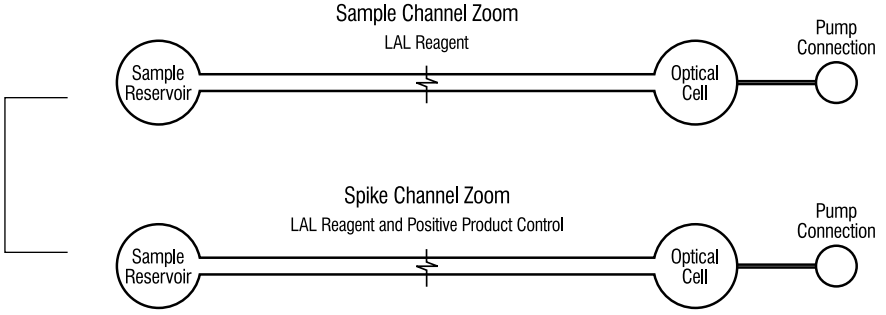
The simplicity of the Endosafe® cartridges eliminates the need for costly specialized training. A user loads the cartridge into one of our Endosafe® readers, pipettes 25 μL of a sample into each of the four cartridge reservoirs, and initiates the test per the chosen reader.

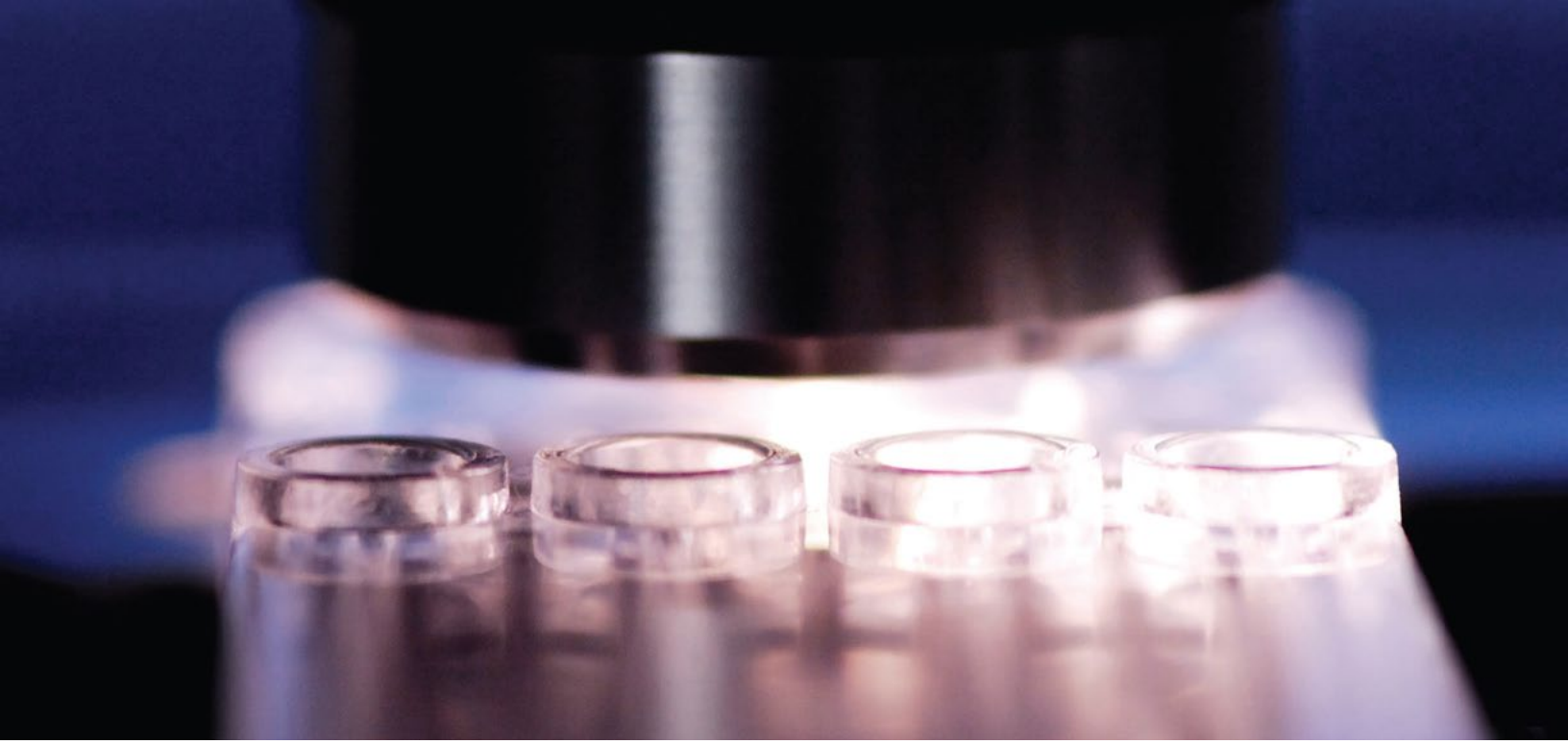
How They Work

The four reservoirs represent two pairs of sample and spike channels that allow the test to automatically run in duplicate (see Figure 1). This design satisfies the harmonized USP/EP BET requirements for LAL testing.

Each channel ends in an optical cell where the samples are analyzed by the reader. In the sample channels, the reader draws and mixes the sample with the LAL reagent. In the spike channels, the sample is mixed with the LAL reagent and positive control. Each sample is then combined with the chromogenic substrate and incubated. After mixing, the reader measures color intensity directly related to the endotoxin concentration and compares the reaction times to the ASC.

Figure 1



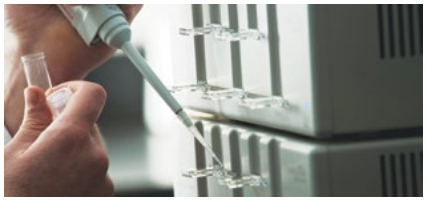


Multiple Platforms. One Robust Technology.

Charles River offers several highly flexible rapid testing platforms to meet the needs of a variety of sample throughput and different lab sizes and configurations. All support the same cartridges for accurate, convenient, and real-time endotoxin testing, glucan concentration determination, and Gram identification. In addition, every system integrates with the Charles River Cortex™ data management software platform, creating a truly robust, optimally controlled endotoxin testing program.

Endosafe® nexgen-PTS™
for point-of-sample testing

- Portable, handheld touch screen spectrophotometer
- Quick read of stat samples and raw materials
- Enhanced reporting functionality for real-time data analysis and optional signature and date lines
- User Management and password protection functionality improves QA oversight on the manufacturing floor and ensures compliance with the FDA's 21 CFR Part 11



Endosafe® nexgen-MCS™
for higher sample throughput

- Multi-cartridge, stackable bench top system
- Test up to five samples simultaneously within 15 minutes
- Samples run independently, allowing for random access, eliminating the need for batch sampling
- Endotoxin measurement and assay acceptance criteria are calculated by EndoScan-V™

Endosafe® Nexus™
for the central QC lab

- Hands-off robotic testing system, with ability to test up to 60 samples per run
- Bar-coding technology enhances data management, reduces input errors, and the need for subsequent investigations.
- Automated dilution and sample handling with the ability to suspend current run
- Fully audit-trailed, with every action recorded to ensure data integrity

Addressing the Impact on the Horseshoe Crab

Limulus amebocyte lysate (LAL) is critical to human health, and so then is the horseshoe crab. It is essential that we balance our need for this valued biomedical resource with a mission to protect the livelihood of its source. As a responsible LAL manufacturer, Charles River is dedicated to conservation and animal welfare practices to protect this important animal. We further these preservation efforts through innovations in our technology.

Our FDA-licensed LAL cartridges (license # 1197) use only 1/20th of the raw material required for a traditional test. If all tests were performed using this optimized technology, today's entire worldwide demand could be met with the blood from less than our current annual quota. Learn more at hsc.criver.com.

Interested in Improving Your Lab's Efficiency?

We're confident there is nothing comparable to the speed, simplicity, and accuracy of the Endosafe® cartridge technology, but you be the judge. Request a demonstration and learn why over 5,000 organizations have adopted this rapid and proven technology to streamline their manufacturing processes.

Contact Us

- 1-877-CRIVER-1
- International Toll Free: +800.3195.3430
- askcharlesriver@crl.com


charles river
www.criver.com