Bacterial Endotoxins Testing Using Non-Animal Derived Reagents and Innovative Microfluidic Technology on Real World Samples

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Background

Annex 1 encourages pharmaceutical companies to adopt new and innovative technologies in order to streamline their manufacturing processes. As well, companies are continually looking to create more sustainable laboratories. More recently, the USP announced the upcoming publication of a new chapter, USP <86> related to the use of recombinant reagents for endotoxin testing.

For these reasons, Veolia Water Technologies & Solutions-Sievers Instruments, in partnership with Eli Lilly, conducted a comparison study using a novel Bacterial Endotoxins Testing (BET) Platform to compare results between traditional Limulus Amebocyte Lysate (LAL) and newer recombinant cascade reagents (rCR). The Platform utilizes microfluidics and centripetal force; allows for assay set up in 85% of the time it takes to set up a traditional 96-well microplate; uses up to 90% less LAL or rCR; and is automated. It also increases efficiency and assures precise and accurate results, allowing manufacturers to meet Annex 1 and sustainability goals while remaining in full compliance with regulations to assure patient safety.

This poster presentation outlines the results of the endotoxin tests with data obtained from real-world samples, providing a practical comparison between the two reagent types.

Comparison Study

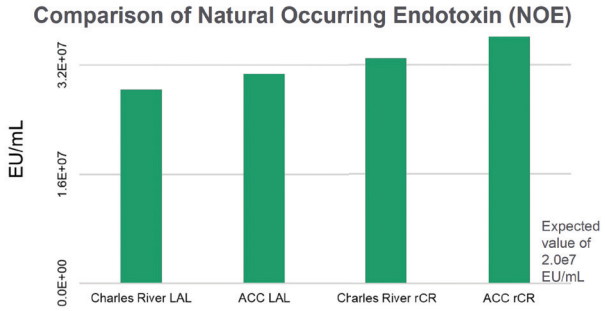
Compared recombinant cascade reagents (rCR) against traditional Limulus Amebocyte Lysate (LAL) reagents from two different vendors with a wide range of pharmaceutical samples and components from Eli Lilly

- Samples were diluted to non-interfering test dilutions to evaluate the PPC recoveries and sample suitability
- Testing was conducted using the Sievers Eclipse Bacterial Endotoxins Testing Platform
- The purpose of the study was twofold:
- To test naturally occurring endotoxins (NOE) as well as purified water with RSE to show endotoxins were recoverable with both LAL and rCR
- To challenge the Sievers Eclipse with both reagents to prove suitability for real-world samples utilizing 90% less lysate as well as recombinant reagents for sustainability

Samples

The following samples were used in the comparison study between Limulus Amebocyte Lysate (LAL) and recombinant cascade reagents (rCR):

- Two monoclonal antibodies
- Insulin
- Peptide
- NOE (see chart)
- Histidine and Sodium Acetate
- LRW
- Purified Waters
- Purified Waters with RSE spikes
- Polysorbate 80
- Counterfeit products
- Components (stopper, cartridge)
- Yeastolate



Conclusion

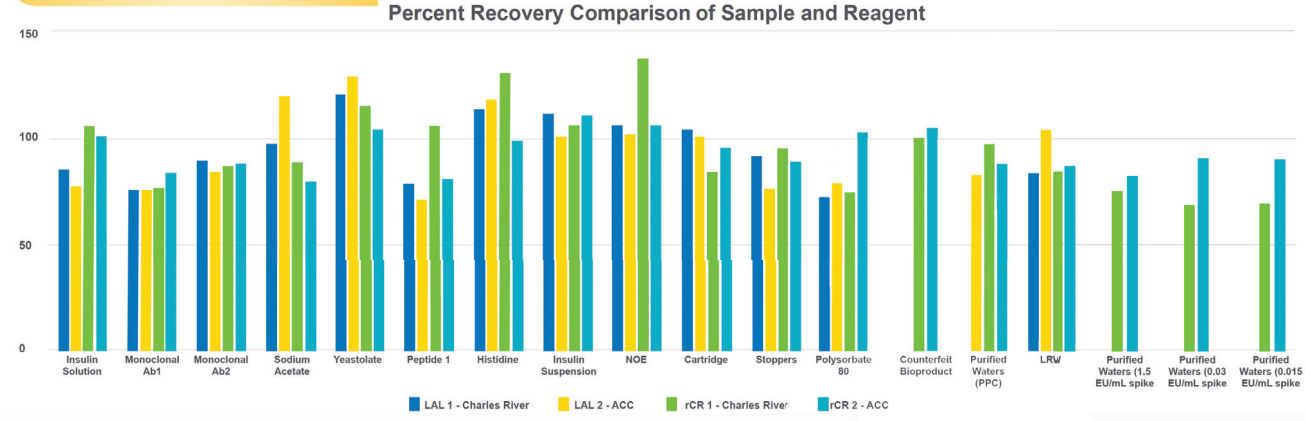
This study showed equivalent performance between LAL and rCR using the Sievers Eclipse for the detection of bacterial endotoxins in real-world samples, as well as naturally occurring endotoxins. Based on the evidence, it can be determined that the Sievers Eclipse Bacterial Endotoxins Testing Platform is able to successfully utilize recombinant cascade reagents, provided that the sample's compatibility has been verified.

Automation via the Eclipse's centripetal microfluidic platform offers the simplest form of BET automation available, providing significant time savings and reducing opportunities for error. With the availability of this innovative technology, BET assays can be automated while remaining fully compliant with compendia.

Benefits include:

- USP <85> and future <86> compliant
- Proven to work with both LAL and rCR reagents
- Up to 90% less reagent needed; aids in sustainability initiatives
- 27 total pipetting steps for 21 samples for increased efficiency
- Innovative technology aligned with Annex 1 guidelines

Results



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Resources:

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