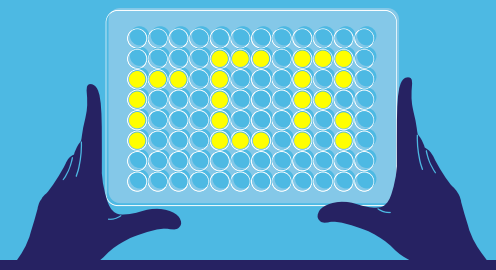
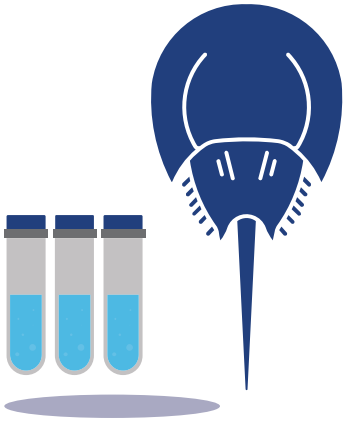


The Future of Bacterial Endotoxin Testing



Conventional LAL Reagents vs Recombinant BET Technology



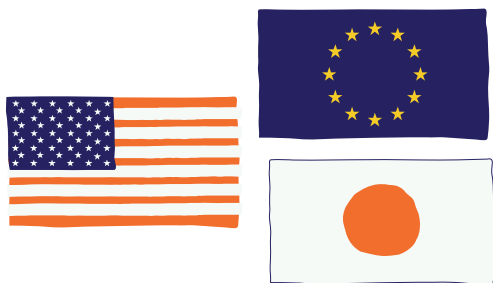
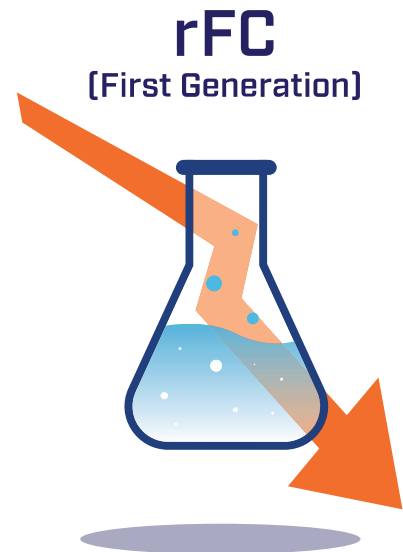
Accepted Test Methods

BET methods using traditional LAL reagents, will continue to have a very important place in the bacterial endotoxin testing space. They are, currently, the only FDA licensed reagents for BET.

Emerging Test Methods

The use of Recombinant Factor C (rFC) reagent as an alternative to LAL reagents (which are derived from the horseshoe crabs) has been implemented by some users, however, failed to achieve a wider industry's adoption over the 20 year period since its introduction.

A new recombinant alternative – Recombinant Cascade Reagent (rCR) was recently introduced providing the sustainable benefits of rFC reagents with none of the drawbacks of the rFC methods (refer to the table below for more information). Many early adopters have already implemented rCR for in house BET testing, especially for in process water samples.



Regulatory Outlook

In order for regulatory bodies such as the USP, EP & JP to incorporate recombinant based reagents for BET fully into their technical standards, it is expected to be documented that they perform equally to or better than the traditional LAL reagents. This is also referred to as comparability studies.

The Path Forward

Technology providers, subject matter experts and pharmaceutical companies have been working on comparability studies for several years. These industry stakeholders are committed to providing scientific evidence of whether the recombinant reagents for BET are equal to or better than the LAL reagents. With a growing body of evidence and a significant increase in adopting sustainable alternatives within the life science industry, the end users are becoming more confident in using recombinant reagents as an alternative to LAL reagents in their effort to convert to sustainably produced reagents. For your reference, the table below highlights the benefits of the rCR reagent compared to the conventional LAL reagent and the rFC reagent.



| ATTRIBUTES EXPECTED FROM BET REAGENTS | TRADITIONAL LAL REAGENT | rFC REAGENT (FIRST GENERATION) | rCR REAGENT (SECOND GENERATION) |
|---|-------------------------|--|---------------------------------|
| Data collection: Kinetic Assay? | ✓ | ✗ Endpoint only | ✓ |
| Assay Setup: single step reconstitution? | ✓ | ✗ rFC requires three reagents in a 1:4:5 ratio and a 10 min. pre-incubation step | ✓ |
| Instrumentation: Standard Absorbance Readers? | ✓ | ✗ Fluorescent reader required | ✓ |
| Sourcing: Derived From Limulus polyphemus (e.g. LAL)? | ✓ | ✗ Recombinantly prepared from <i>Carcinoscorpilus</i> or <i>Tachypleus</i> Amebocyte Lysate (CAL/TAL) | ✓ rCR is recombinant LAL |
| Multi-step Cascade Pathway Mechanism? | ✓ | ✗ | ✓ |
| Endotoxin Specific? | ✗ | ✓ | ✓ |
| Sustainable Reagent (animal free)? | ✗ | ✓ | ✓ |