USE OF RECOMBINANT FACTOR C (RFC) IN BACTERIAL ENDOTOXINS TESTING: TRANSITION FROM *LIMULUS* AMEBOCYTE LYSATE (LAL)

Recombinant Factor C (rFC) is a readily available, effective, reliable and environmentally sustainable enzymatic reagent that can alleviate dependence on horseshoe crab blood used to produce the reagent Limulus Amebocyte Lysate (LAL) in quality control testing of parenteral therapies, including the many Covid-19 therapies currently in clinical development. With significant declines in horseshoe crab and related-species populations over the last 20 years, rFC provides a pathway for the biomedical industry to transition from an animal-based test platform.

SUSTAINABILITY

- The American horseshoe crab is considered "Vulnerable" while the tri-spine horseshoe crab in Asia is considered "Endangered" by the International Union for the Conservation of Nature (IUCN).
- rFC is a more sustainable solution to address additional BET capacity needs and supply chain bottlenecks, without adversely affecting horseshoe crabs and related-species populations.
- Implementing rFC is aligned with corporate sustainability efforts including United Nations Sustainable Development Goals and the 3Rs (Reduce-Refine-Replace).

SUPPLY CHAIN

- The safe and reliable supply of medicine is of paramount importance to pharmaceutical manufacturers, patients, and the global health authorities that regulate industry.
- Implementation of rFC ensures business continuity as a hedge against LAL restrictions due to natural resource constraints.

QUALITY

- More than 15 peer-reviewed studies involving head-to-head trials and nearly 200 pharmaceutical products using real-world samples have been published in the primary literature. These studies affirm rFC equivalence or superiority to LAL for the detection of bacterial endotoxins, especially as it relates to specificity for bacterial endotoxins.
- LAL is derived from the blood of wild horseshoe crabs, thus subject to inherent variability from environmental factors experienced by bled individuals. In contrast, rFC is manufactured using modern, reproducible, and validated biotechnology manufacturing processes, and is expected to perform more consistently lot-to-lot.
- The FDA and other global health authorities have approved four Eli Lilly medicines for which rFC is used to release product to the market. Currently, the US Pharmacopoeia is the only such body that has not embraced rFC as an equivalent or superior alternative to LAL.
- Since 2012 the FDA has allowed pharmaceutical companies to perform endotoxin testing using rFC — as long as they demonstrated validity equal to or better than with LAL.

COST

- Eli Lilly reported rFC to be cost-favorable; waste reduction gains have been realized and the test method is amenable to automation.
- A transition to rFC by will help restore horseshoe crabs to ecological carrying capacity and the recovery of threatened shorebird populations and sport fish that depend on horseshoe crab eggs, while maintaining patient safety and the safe supply of medicine. Please take an active role in your organization to facilitate the implementation of rFC as a sustainable alternative to LAL.