TO: Horseshoe Crab Management Board April 27, 2023

FROM: James F. Cooper

Re: Prompt approval of revised Best Management Practices as submitted

At this very moment, in almost every hospital bed worldwide, millions of patients are receiving intravenous solutions and injectable medications for healing. These medications are assured of being free of bacterial endotoxin because of the remarkable work of Levin and Bang, 60 years ago, when they invented the LAL reagent to detect its presence. We soon proved that LAL could replace the current animal assay because of its greater sensitivity, specificity and simplicity. Today, a handful of American LAL firms bear the awesome responsibility of providing sufficient LAL reagent to test the world's supply of injectable drugs. This obligation must be the focus of the Board's deliberations today.

When I first set up a LAL production lab in Chincoteague VA in 1971, I had the honor of a visit from Carl Shuster, the father of horseshoe crab (HSC) science. Carl was fascinated by the bleeding process and procedures. He pointed out that HSC lived for days out of water as long as their environs were cool and gills were kept moist. We devised specific procedures for collection, cleaning, bleeding and prompt return safely to sea. Carl continued to follow HSC abundance during summer visits to Delaware Bay in the 1990s where he worked with Swan and Finn to found the DB Spawning Survey. Continued study of HSC recovery from diverse commercialization during the previous century, led to Carl's confident in their ability for resilience. One of his last pieces of advice to this Board was the following:

"The record of horseshoe crabs contradicts the untruthful comments by environmentalist, birders, and the media on the plight of the horseshoe crabs in Delaware Bay. If the media and environmental protagonists keep misrepresenting the fate of the horseshoe crab, can we be sure of what they are telling us about migratory shorebirds? However, all these regulations, prohibiting the harvesting of horseshoe crabs, are not necessary to protect the crabs. The best current judgement is that no further tinkering with management regulations is needed. It is time to let the crabs and Mother Nature resolve the local migratory bird problem." *Delaware Bay Horseshoe Crabs are Thriving* by Carl N. Shuster Jr.

The ASMFC has ably protected and managed the use of the horseshoe crab for the past 25 years. It completed a thorough stock assessment of the HSC in 2019 and found that LAL processing had no significant detrimental impact on HSC or migratory birds and that HSC populations were stable or increasing in most US waters. Furthermore, ASMFC recently tasked a group of LAL experts, technical committee, natural resource managers, and advisory panel members with expertise in horseshoe crab biology, ecology, and biomedical processing to revisit the Best Management Practices (BMPs, 2011). An updated set of BMPs is presented to the Board that reflects procedures applied in their respective firms to assure humane treatment of crabs during their collection, processing and return to sea. The GMP revision comprehensively address all of the critical steps and processes for managing HSC in biomedical hands. Reasonable compromises were made to accommodate regional differences. In my opinion, as a scientist and co-founder of LAL industry, the proposed new GMPs should be adopted as written. An alternative GMP by the HCRC group has an agenda other than patient safety and should not be considered. The biomedical LAL firms are developing recombinant LAL reagents, but unqualified equivalence to natural LAL is not confirmed.

It's the FDA's opinion that current LAL used by the pharmaceutical industry is a fool-proof test for endotoxin and that there is no urgency for an alternative LAL test. FDA's acceptance is essential.

The large HSC population in Delaware Bay is believed to be a consequence of the bay's long sandy shoreline, favorable hydrographic features (e.g.. moderately large tidal range, ideal temperature and salinity), abundant areas of intertidal sand flats that serve as juvenile nursery habitats, and the abundance of food resources in the bay and nearby continental shelf (Shuster 2015; Botton, Loveland, Munroe, Bushek, and Cooper, Springer, 2022). The Virginia Tech Survey indicates about 50 million adult HSC. Although numbers are undocumented, large populations of horseshoe crab are observed in other parts of the American east coast, including Cape Cod, and the barrier islands of Delmarva Peninsula, South Carolina, and Georgia (Smith, et al. 2016). Only Delaware Bay populations have been assessed over the past two decades. Coastal habitats in the Sea Islands of South Carolina offer the same favorable features to HSC as do Delaware Bay, leading to the notion that tens of millions of HSC also inhabit SC waters. Spawning habitats include salt water marshes and sandy beaches (Kendrick *et al*. 2023, DOI: 10.1086/714277) It is reasonable to assume that at least 100 million adult HSC are in Atlantic waters and billions of immature specimen are progressing to maturity. Clearly, there is no urgency to alter ASMFC's comprehensive and effective policies for managing the HSC.

The ASMFC is urged to accept the revised BMPs, as written, and continue its partnership with the biomedical industry in assuring the quality of the world's supply of parenteral drugs and medical devices.

Thank you