

# Conservation initiatives for an invaluable partner



Because endotoxins can be so toxic, any product or device that comes into contact with bodily fluids is screened by *Limulus* amoebocyte lysate (LAL) reagents. John Dubczak, General Manager of Charles River's Microbial Solutions Operations, explains the importance of conserving the source of this valuable reagent.

LAL reagents are produced using the Atlantic horseshoe crab's (*Limulus polyphemus*) only type of blood cell, known as the amoebocyte, which coagulates around endotoxins. The amoebocytes are used in every segment of the quality control process, from testing raw materials to the final products. About 25% of the medical device market is dependent upon LAL for endotoxin detection, and 70 million LAL tests alone are made annually to safeguard the world's supply of injectable medications.

As demand for injectable and other therapeutic and biomedical products increase, the need to conserve the horseshoe crab and its precious blood has never been greater. Biomedical and LAL manufacturers who depend upon LAL to produce safe products have a specific responsibility to protect the crab.

The US state of South Carolina, where Charles River harvests horseshoe crabs, provides one of the best examples of how the biomedical industry and legislators have worked together to conserve the horseshoe crab for nearly 20 years. In the early 1990s, the state passed stringent industry-backed laws, enacted with the help of Charles River, governing the management and regulation of horseshoe crab fisheries, permitting horseshoe crabs to only be used for LAL production and marine biological research, not as bait for the eel and whelk industries. As a result, the crabs in South Carolina are one of the most protected species on the East Coast of the US. Tagging studies, and a multi-year statewide analysis of the crab's genetic pool suggest that the population is stable and growing there.

In Maryland and Delaware, where populations are also stable, fishermen are prohibited from collecting female horseshoe crabs and Delaware has established sanctuaries for horseshoe crabs during the spawning season.

New England is a different story. The collection of horseshoe crabs for bait appears to be thriving there. The horseshoe crab fishery supplies bait for the American eel, conch (whelk) and, to a lesser degree, catfish fisheries, according to the Atlantic States Marine Fisheries Commission (ASMFC). The ASMFC's stock assessments in New England from 1978 to 2008 and New York from 1987 to 2008 show a decline in the abundance of horseshoe crabs. Since 2009, the trend has not reversed itself, according to the ASMFC.

In Asia, with multiple species of *Tachypleus* horseshoe crabs, the situation is even worse. Unlike the US, no restrictions are placed on crab collection for purposes including, but not limited to, biomedical use, medicinal purposes, baiting and even food consumption. Great concern exists for the sustainability of the three Asian horseshoe crab populations. Biomedical companies that manufacture *Tachypleus* Amoebocyte Lysate (TAL) in China are continuously stressing the need for best management practices.

While there is clearly a need in Asia for better conservation laws, concerns about a collapsing TAL market's impact on the wider LAL market are a little overstated. Marketing analyses indicate that Chinese firms perform less than 20% of the world's endotoxin tests, and it is likely that the US could easily absorb the Chinese market. We have also made strides in LAL testing technology that allow us to do more with less LAL. There are FDA-licensed LAL cartridges that use only 5% of the LAL used in a traditional test. Over the past 10 years, this technology has been adopted and has alleviated the pressure on the horseshoe crab.

Recombinant products that use Factor C are also on the horizon. However, their use has been limited. The design



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of this recombinant technology limits the sensitivity of the test, and requires expensive instrumentation; furthermore, this method is not a recognised compendial test in the US or Europe. As an alternative method, its use must undergo extensive validation and approval by the regulatory authorities.

It is essential for both horseshoe crab populations and public health that LAL suppliers remain sensible to conservation practices, including ensuring the preservation of horseshoe crab habitats. ■



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