

Best Management Practices for Handling Horseshoe Crabs for Biomedical Purposes



May 2023



Sustainable and Cooperative Management of Atlantic Coastal Fisheries

Biomedical Best Management Practices Work Group

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Summary

The Atlantic States Marine Fisheries Commission (Commission) has maintained primary management authority for horseshoe crabs in state and federal waters since it adopted the Interstate Fishery Management Plan for Horseshoe Crabs (FMP) in 1998. The goal of the FMP includes management of horseshoe crab populations for continued use by current and future generations of the fishing industry and non-fishing public, including the biomedical industry, scientific and educational researchers, migratory shorebirds, and other dependent fish and wildlife. The Commission also assesses the horseshoe crab population through periodic stock assessments; the most recent assessment was the Horseshoe Crab Stock Assessment and Peer Review Report completed in 2019¹.

In 2022, the Horseshoe Crab Management Board (Board) appointed a work group to review and update the best management practices (BMPs) for handling biomedical catch, given over a decade has passed since the BMPs were originally developed. The work group included technical committee and advisory panel members with expertise in horseshoe crab biology, ecology, and biomedical processing. The purpose of the BMPs is to recommend broadly applicable industry standards that are expected to minimize mortality and injury of horseshoe crabs associated with the biomedical process. This document includes the modified BMPs, as recommended by the work group. It also provides background on the horseshoe crab biomedical fishery, information on current regulations in the Commission's Horseshoe Crab Fishery Management Plan (FMP) related to biomedical collections, descriptions of general processes used to collect and transport horseshoe crabs for biomedical purposes, and research recommendations that could further inform the BMPs and potentially further reduce mortality or injury of biomedical horseshoe crabs.

Background

Coastwide, horseshoe crabs are harvested for use as bait, and are an important resource for research and human health. In 1964, researchers discovered that horseshoe crab blood coagulates in the presence of very small quantities of bacterial endotoxin. By 1979, the U.S. Food and Drug Administration (FDA) issued draft guidelines for the use of Limulus ameobocyte lysate (LAL), the product derived from horseshoe crab blood, as a test for detecting pathogens in patients, medical devices, and injectable drugs. The LAL test is the compendial standard² currently used domestically and internationally for screening injectable and indwelling medical products for endotoxin contamination. Vaccines, IV fluids, medications, artificial joints, and internal devices (e.g., stents, pacemakers, catheters) are just some examples of products

¹ Horseshoe crab stock assessment reports and information can be found on the Commission's webpage here: <http://www.asmfc.org/species/horseshoe-crab#stock>

² "Compendial standard" refers to a pharmaceutical standard of the United States Pharmacopeia, or other international pharmacopeia, meaning it is the official quality standard to be used for all pharmaceutical products sold in the U.S. or international marketplace. Testing and compliance to these standards is a basic requirement for global manufacturing, release, and distribution of pharmaceutical products.

tested. LAL is also used in medical research for human health and most recently, it has been approved for use as a clinical diagnosis of invasive fungal infections in patients.

To manufacture LAL, horseshoe crabs are collected by fishermen and provided to biomedical companies, which take a portion of their blood. The blood is then separated, and the proteins within the white blood cells are processed for more precise results. There are currently five FDA-licensed LAL manufacturers along the Atlantic Coast that process horseshoe crab blood for use in manufacturing LAL: Associates of Cape Cod Inc.; Lonza, Limuli Laboratories; FujiFilm Wako Chemicals; and Charles River Microbial Solutions. Horseshoe crabs are currently collected for biomedical purposes in Massachusetts, Rhode Island, New Jersey, Maryland, Virginia, and South Carolina.

As required for the reporting for biomedical horseshoe crabs, both the total number of horseshoe crabs collected and the number bled are reported. The number of bled horseshoe crabs has averaged 92.6% of the total number collected for the years since 2011 when the BMP document was developed. Some crabs are not bled due to damage, health (slow movements) and mortality. Horseshoe crabs collected solely for biomedical use are required to be released alive, however, there is a low level of mortality associated with biomedical processing. The overall biomedical mortality reported by the Commission includes any horseshoe crabs that are observed dead between the point of capture and release, plus the estimated number of horseshoe crabs that die from the biomedical bleeding process. Biomedical companies are required to record and report numbers of horseshoe crabs that are observed dead between the point of capture and release, however, there are differences in how this information is collected by different biomedical collectors, companies, and facilities. Since this reporting began in 2004, the observed number of biomedical mortalities per year has averaged about 1.5% of the total number of horseshoe crabs collected for biomedical purposes coastwide (ASMFC 2022). The estimated mortality rate is 15% of all horseshoe crabs processed and released alive by the biomedical industry, which was determined through a review of all available literature on mortality, including studies that were not representative of standard biomedical handling practices, nor the practices described in the 2011 BMPs. This mortality rate has been reassessed and maintained in recent stock assessments (ASMFC 2019). Some states also have a dual use program where horseshoe crabs destined for the bait market can be loaned to a biomedical facility to be bled, before being returned to the bait market. These horseshoe crabs are not subject to the reporting described above; instead, they are counted against the state's bait quota as they have a 100% mortality rate.

The relative mortality of horseshoe crabs from the biomedical fishery is small when compared to the bait fishery. The number of horseshoe crabs harvested for bait on an annual basis typically accounts for over 85% of the total fishing mortality (bait fishery harvest plus estimated and observed biomedical mortality). Additionally, the Commission does not have regulatory authority over biomedical companies; they are subject to regulation by the FDA. Nevertheless, the Board strives to minimize the impact of biomedical collections on Atlantic horseshoe crab populations. In 2011, an *ad-hoc* work group drafted a BMP document including BMPs for the various steps throughout the biomedical process, from harvest to release. Many of the practices identified as BMPs had been historically used by the biomedical companies to sustain

the horseshoe crab population and ensure a steady and reliable product supply to the pharmaceutical market. The work group recommended biomedical facilities follow the BMPs and monitor their suppliers. Recognizing the potential for future changes in the industry and the status of the resource, the WG also recommended meetings be held periodically to identify opportunities for improvements and minimize mortality.

In 2022, the Board formed a new work group to review and update the 2011 BMPs for handling biomedical catch. Over several meetings in early 2023, the work group evaluated each of the BMPs and identified areas that are out of date or could be improved with additional information. This document reflects the recommendations of the 2023 work group. Its purpose is to establish broadly applicable industry standards that are expected to minimize mortality and injury of horseshoe crabs associated with the biomedical process. This document also serves to educate the public about the biomedical industry, processes, and practices.

Horseshoe Crab Biomedical Regulations

Biomedical LAL manufacturers are regulated by the FDA and are permitted to obtain horseshoe crabs for blood collection by individual states. Collections of horseshoe crabs for biomedical use are subject to state regulations, separate from those placed on harvest and landing of horseshoe crabs for bait. The Commission's Horseshoe Crab FMP and subsequent Addenda include some regulations that states must comply with related to the biomedical collection of horseshoe crabs, which are summarized below.

FMP Requirements:

Interstate Fishery Management Plan for Horseshoe Crab (ASMFC 1998):

- States must issue a special permit, or other specific authorization, for harvests³ for biomedical purposes.
- Horseshoe crabs taken for biomedical purposes shall be returned to the same state or federal waters from which they were collected.
- If horseshoe crabs are captured for biomedical use, all states must monitor and report monthly and annual harvest of horseshoe crabs by biomedical facilities (i.e., numbers), identify percent of mortality up to the point of release (including harvest, shipping⁴, handling, and bleeding mortality), and certify that harvested horseshoe crabs are being used by biomedical facilities and not for other purposes.

³ The FMP refers to the collection of horseshoe crabs for biomedical purposes as "harvest." However, for the purposes of this document the term "collection" will be used because it more accurately represents the practices of the industry.

⁴ The FMP refers to the transport of horseshoe crabs for biomedical purposes from where they are collected to a biomedical facility as "shipping." However, in this document the term "transport" is used because it more accurately represents the practices of the industry.

Addendum III (ASMFC 2004):

- All states where horseshoe crabs are captured for biomedical use must monitor and report monthly and annual harvest of horseshoe crabs by biomedical facilities. All states must identify percent mortality up to the point of release (including harvest, shipping, handling and bleeding mortality), harvest method, number or percent of males and females, disposition of bled crabs, and condition of holding environment of bled crabs prior to release.

Best Management Practices for Handling Biomedical Collections

The following presents the biomedical process broken down into steps (Figure 1), with the best management practices associated with each step, as well as overarching practices applicable to all steps.

The general steps in the process are collection, transport to facility, holding at facility, inspection, blood collection, transport for return to sea, and release. "Collection" refers to removing horseshoe crabs from their natural environment, using methods such as trawl netting, or by hand from shore or shallow water. Some states use the practice of in-water holding, which involves keeping horseshoe crabs in coastal ponds or pens between capture and transport to the facility for blood collection. "Transport" refers to moving horseshoe crabs from the point of collection, landing, or holding to a biomedical facility, typically in containers by truck. "Holding at Facility" and "Blood Collection" refers to keeping the horseshoe crabs at the facility until they are inspected and then collecting blood from horseshoe crabs that pass inspection. Once blood is collected, the horseshoe crabs are held at the facility (along with those that were rejected) until they can be transported to the same state or federal waters from which they were collected and released.

The BMPs presented in this document represent standard practices used by the licensed manufacturers, and serve as recommendations for the best handling practices to minimize mortality and injury of horseshoe crabs. They are geared toward collections of horseshoe crabs for biomedical purposes, however these practices may be utilized by LAL manufacturers participating in a dual use program. The Work Group recommends that states review the BMP recommendations periodically to continue to minimize rates of mortality and injury of horseshoe crabs collected for biomedical purposes. The work group recognized the potential for changes in industry practices, increased knowledge related to the impacts associated with the various aspects of the biomedical process, and other factors that could affect the BMPs. Therefore, periodic review of the BMPs will be necessary to ensure their positive impact into the future.

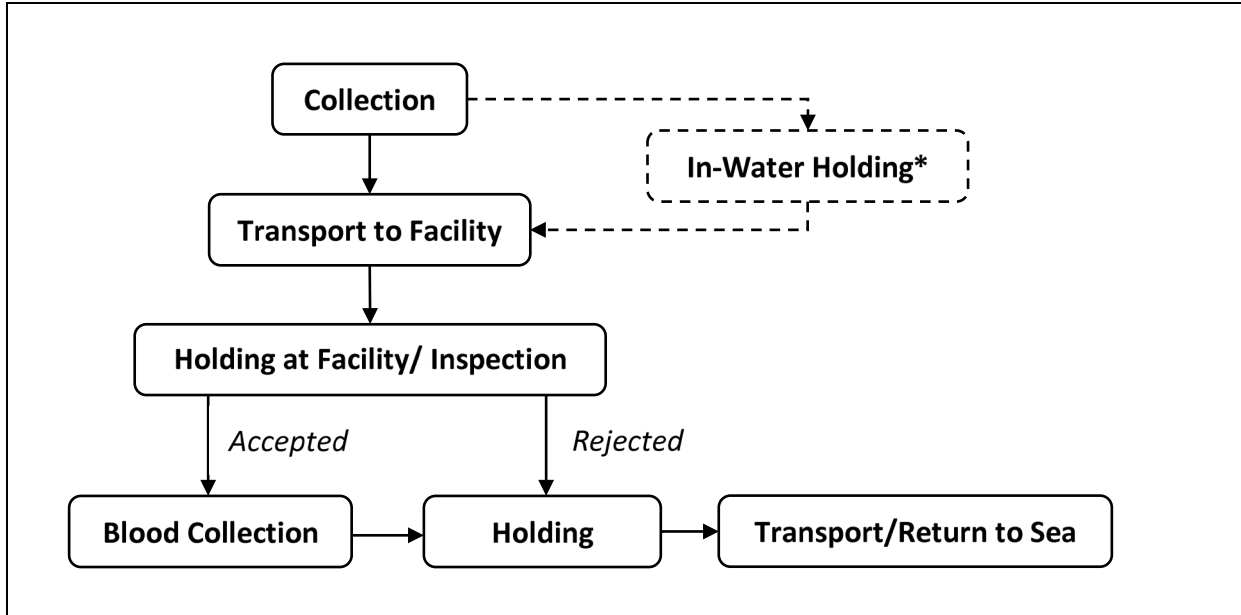


Figure 1. Diagram illustrating the general flow of horseshoe crabs through the biomedical process, from collection until return. *In-water holding is not utilized in all states.

Overarching practices for all steps

- Keep horseshoe crabs cool and moist, and minimize exposure to direct sunlight and anoxic conditions
- Avoid prolonged exposure of gills to fresh water
- Establish a dialogue among collectors, the biomedical company, and the state regulatory agency to address concerns and challenges
- Have a written agreement between collectors and the biomedical company, outlining practices and expectations
- Perform reviews of the various steps and contractors/employees throughout the process
- Ensure proper monitoring and recording of mortality at each step in the chain of custody
- Return horseshoe crabs taken for biomedical purposes to the same state or federal waters from which they were collected
- Avoid keeping horseshoe crabs out of the water for longer than 36 hours in total

Collection

- Minimize tow times for targeted horseshoe crab trawl tows,
- Handle horseshoe crabs carefully to minimize injury (e.g., avoid dropping/tossing horseshoe crabs, etc.)
- Minimize exposure to direct sun, avoid extreme temperatures and rapid temperature changes
- Night collection is recommended, especially during periods of excessive heat, when permitted by state regulation
- Sort out and return immediately to the water individuals that do not appear to be healthy (damaged, slow movement), soft shelled, or undersize horseshoe crabs (based on state regulations)
- Educate collectors in BMPs
- Specify expectations of collectors in written agreements
- Periodically observe horseshoe crab collectors' adherence to BMPs
- Horseshoe crabs marked as having been bled during the calendar year should be immediately released

In-Water Holding

- Minimize holding time
- Avoid overcrowding
- Monitor water conditions (e.g., temperature, dissolved oxygen, salinity) and minimize exposure to stressful conditions
- Follow state guidelines on holding conditions, where applicable

Transport to Facility

- Limit number of horseshoe crabs to a suitable number dependent on container size and shape to minimize damage to horseshoe crabs

- Minimize travel time
- Keep transport containers protected against direct sunlight and heat
- Secure containers in transport vehicle

Holding at Facility/ Blood Collection

- Minimize holding time at the facility, ideally to less than 24 hours
- Follow written procedures for proper care and handling when sorting horseshoe crabs and moving them between bins and within the facility
- Inspect horseshoe crabs for health and damage, selecting only undamaged and healthy individuals for blood collection
- Maintain clean, sanitary conditions during blood collection
- Maintain same level of care for rejected horseshoe crabs while they are being held until release back to state or federal waters
- Avoid collecting blood from individual horseshoe crabs more than once per year (e.g., by marking, tagging, etc.)
- If horseshoe crabs are marked, ensure that the mark is residual and not harmful
- Cease blood collection once blood flow rate slows
- Do not use suction to collect blood
- Perform internal audits to maintain quality control over written procedures

Post-Blood Collection Holding

- Maintain the same level of care that is used prior to blood collection
- Return to the state or federal waters from where they were collected as soon as possible, following state guidance when applicable
- Keep horseshoe crabs in low-light areas to minimize movement and injury

Return to Sea

- Use same care in handling and transporting horseshoe crabs being returned to the water
- Include written instructions and requirements for return within agreements with collectors, if applicable
- Periodically observe horseshoe crab collectors on implementation of BMPs and/or other criteria

Research Recommendations

The Work Group compiled the following list of research recommendations, which would enhance the understanding of impacts of the biomedical process on horseshoe crab populations. The work group recommends future experimental research related to biomedical practices using horseshoe crabs adhere to the applicable BMPs to more accurately reflect industry practices.

- *Study survival rates of horseshoe crabs collected for biomedical purposes over time when kept in in-water holding ponds or pens*

- *Compare survival of horseshoe crabs at different holding durations to determine standard maximum holding times for different systems and water conditions*
- *Study the impacts of biomedical collection processes on spawning of horseshoe crabs, including the differential impacts of various collection and holding methods*
- *Compare mortality rates across different collection methods*
- *Estimate horseshoe crab discard mortality associated with trawling collection methods*
- *Review and summarize the findings of current literature on horseshoe crab mortality associated with blood collection, and compare across experiments that more closely reflect BMPs and do not reflect BMPs*
- *Quantify mortality rates of horseshoe crabs post-blood collection, applying the BMPs and other standard biomedical industry practices*
- *Study conditions that minimize movement and injury of horseshoe crabs during biomedical processes (e.g., light, density, etc.)*

References

- Atlantic States Marine Fisheries Commission (ASMFC). 2022. [Review of the Interstate Fishery Management Plan for Horseshoe Crab \(*Limulus polyphemus*\): 2021 Fishing Year](#). Arlington, VA. 31 pp.
- ASMFC. 2019. [2019 Horseshoe Crab Benchmark Stock Assessment](#). Arlington, VA. 271 pp.
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