BLUE BLOOD MONEY: DRAINING HORSESHOE CRABS FOR PROFIT

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ABSTRACT

Most Americans, even those that consider themselves vegan, are implicated in the morally deplorable practice of harvesting and bleeding horseshoe crabs. In the U.S., the biomedical industry collects the distinctive blue blood of horseshoe crabs to test the safety of most injectable medicines, vaccines, and implantable medical devices. In 2022, the industry harvested more than 900,000 horseshoe crabs from the Atlantic coast and bled them for biomedical purposes. While most are returned to the sea afterwards, an estimated 20-35% of horseshoe crabs perish from the bleeding process, and the released survivors often suffer lasting health consequences after the removal of up to half of their blood. Currently, there is only a patchwork of federal, state, and interstate regulation addressing the taking, treatment, and use of horseshoe crabs collected for biomedical purposes. These anthropocentric regulations fall drastically short of protecting horseshoe crabs' interest in living free from human exploitation.

Fortunately, recent developments may soon encourage an industry shift to a non-animal-derived alternative toxicity test. This paper argues the replacement of the horseshoe crab-dependent test, rather than improved welfare regulations, would best protect the interests of horseshoe crabs. The latter only further entrenches the exploitative biomedical horseshoe crab industry.

> Horseshoe crabs are not charismatic animals like cats, dogs or orcas. As arthropods, they will rank quite low on the scale of moral worth for many. Even conservation efforts may be more informed by their toxicological utility than their status as a keystone species. But ethics at its best requires us to move beyond charisma, convenience, or utility and respond to what ethically matters.[1]

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1. Andrew Fenton & Lori Marino, *The Blood Harvest of Horseshoe Crabs is a Moral Fiasco*, KIMMELA CTR. FOR ANIMAL ADVOC., https://www.kimmela.org/wp-content/uploads/2020/08/The-Blood-Harvest-of-Horseshoe-Crabs-is-a-Moral-Fiasco.pdf (last visited Nov. 29, 2023).

INTRODUCTION

Every American has benefited from the eerily invisible yet ubiquitous industry that annually removes nearly one million horseshoe crabs from the Atlantic shores.[2] This industry extracts the crabs from their environment before strapping them to metal tables in sterilized facilities, plunging a thick syringe directly into their hearts, draining them of up to half of their blood, and (usually) releasing them back to the sea.[3] Due to its unique ability to detect toxins, the blue blood of horseshoe crabs has become a lucrative commodity in the U.S. biomedical industry.[4] The industry uses the fluid to test the safety of most injectable medicines, vaccines, and implantable medical devices, from which Americans collectively benefit.[5] Unfortunately, federal, state, and interstate law anthropocentrically and inadequately regulates the exploitation of horseshoe crabs for biopharmaceutical purposes. Consequently, these ancient creatures, to which we owe the development of many lifesaving medicines, suffer greatly as individuals and as a species.[6] We cannot ignore this reality any longer.

After all, every American is implicated in the industrialized harvesting and bleeding of horseshoe crabs for biomedical use. Even vegans ethically opposed to animal exploitation are not exempt if they use insulin, have a pacemaker, receive vaccines (including COVID-19 vaccines), or, if vaccine-free, reap the benefits of herd immunity.[7] Nonetheless, horseshoe crabs carry intrinsic value and an interest in living free from human exploitation, which society and the law fail to consider.[8] Especially given that there is an available animal-free alternative to the horseshoe crab-derived toxicity test, ethical obligations to promptly end the biomedical horseshoe crab industry exist.[9] Despite existing regulatory barriers, measures can be implemented to

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2. Ben Levitan, *A Pathway to End the Medical Harvest of Horseshoe Crabs*, EARTH JUST. (July 29, 2024), https://earthjustice.org/experts/ben-levitan/a-pathway-to-end-the-medical-harvest-of-horseshoe-crabs.

3. Chiara Eisner, *Coastal biomedical labs are bleeding more horseshoe crabs with little accountability*, NAT'L PUB. RADIO, https://www.npr.org/2023/06/10/1180761446/coastal-biomedical-labs-are-bleeding-more-horseshoe-crabs-with-little-accountabi (last visited Nov. 09, 2024).

4. *See* Sebastian B. Okun, *Mating in the Moonlight: The Battle to Save the American Horseshoe Crab*, 18 OCEAN & COASTAL L.J. 195, 201 (2012) (discussing how horseshoe crabs are a lucrative commodity in the U.S. biomedical industry).

5. Jordan Krisfalusi-Gannon et al., *The Role of Horseshoe Crabs in the Biomedical Industry and Recent Trends Impacting Species Sustainability*, 5 FRONTIERS MARINE SCI. 1, 2 (2018).

6. *Id.* at 2–5.

7. *See* Ariel Wittenberg, *Got Your COVID-19 Vaccine? Thank a Horseshoe Crab*, E&E NEWS (Jan. 8, 2021), https://www.eenews.net/articles/got-your-covid-19-vaccine-thank-a-horseshoe-crab/ (last visited May 14, 2024) (noting that injectable medicine and implantable devices necessitate endotoxin testing—for which the horseshoe crab-derived test has become standard).

8. Fenton, *supra* note 1.

9. *Id.*

incentivize biopharmaceutical manufacturers to transition away from an antiquated test dependent on extracting horseshoe crab blood.[10]

Part I provides background information on the horseshoe crab species related to their biology and use by humans. Part II discusses how the biomedical industry uses and abuses horseshoe crabs. Part II also covers the development of the horseshoe crab-derived toxicity test, as well as the structure and impacts of the multi-million-dollar industry that is bleeding horseshoe crabs dry. Part III reveals a regulatory failure to acknowledge and protect the well-being of horseshoe crabs. Part IV describes the development, availability, and recent approval of an animal-free alternative. Finally, Part V argues that anything short of completely phasing out the horseshoe crab-dependent test contravenes our moral obligation to protect these ancient mariners' interests. It also presents recommendations for accomplishing industry-wide change. The paper concludes by reflecting on the U.S.'s moral obligations owed to horseshoe crabs.

I. BACKGROUND ON HORSESHOE CRABS

Horseshoe crabs are "living fossils" that have inhabited Earth for over 450 million years.[11] Contrary to their common name, these aquatic invertebrates are more closely related to scorpions and spiders than crabs.[12] They belong to the arthropod family.[13] There are four species of horseshoe crabs, three of which inhabit the coastal waters of Asia.[14] This paper focuses upon the "American" horseshoe crab: *Limulus polyphemus*.[15] This species ranges along the North American Atlantic coast but is most prolific around the central Atlantic coast.[16] These animals are particularly abundant in the Delaware Bay region straddling New Jersey and Delaware.[17] Hereinafter, "horseshoe crab" refers to the American variety.

Studies estimate that these animals have a natural life expectancy of at least 14-18 years, with females reaching reproductive maturity around 10 years.[18] Due to the large size and tough exoskeleton of horseshoe crabs,

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10. Fenton, *supra* note 1.

11. Mark L. Botton et al., *Horseshoe Crabs: "Living Fossils" Imperiled in the Anthropocene*, IMPERILED: THE ENCYCLOPEDIA OF CONSERVATION 1, 1 (2021).

12. *Id.*

13. CHESAPEAKE BAY PROGRAM, *Horseshoe Crab: Limulus polyphemus*, https://www.chesapeakebay.net/discover/field-guide/entry/horseshoe-crab (last visited Oct. 26, 2024).

14. These three species are the *Tachypleus tridentatus*, *Tachypleus gigas*, and *Carcinoscorpius rotundicauda*. *Id.*

15. *Id.*

16. *Id.* at 8.

17. *Id.*

18. *Id.* at 3.

natural predation of adults is relatively rare.[19] However, various animals rely on horseshoe crab eggs as a vital food source, making them a keystone species.[20] In fact, the limited conservation measures for horseshoe crabs are typically driven not by the intrinsic value of the horseshoe crabs themselves, but rather to safeguard the threatened Rufa Red Knot shorebirds that rely on protein-rich horseshoe crab eggs for their annual migration.[21] The horseshoe crab is classified as "vulnerable" by the International Union for the Conservation of Nature (IUCN).[22]

Humans have historically and contemporarily exploited horseshoe crabs in a myriad of ways.[23] Once harvested for fertilizer and livestock feed, today, these creatures are now collected primarily for use as commercial bait and for biomedical purposes.[24]

Horseshoe crabs' dogged survival over hundreds of millions of years, through multiple mass extinction events, can be attributed in part to their being "ecological generalists."[25] These creatures can tolerate wide ranges in water salinity, temperature, and other environmental variables.[26] However, these "living fossils" are not invincible.[27] Like many other species that have survived until the Anthropocene,[28] their well-being and existence are now threatened by human greed.[29] A team of international scientists suggested that "[p]erhaps the best-known factor contributing to commercial

19. CHESAPEAKE BAY PROGRAM, *supra* note 13.

20. To get an idea of just how intense this egg predation is, consider that "it has been estimated that as few as one out of 100,000 American horseshoe crab eggs survive to the end of their first summer of life." *Id.*

21. *See* Okun, *supra* note 4, at 203 (stating that "[i]t is largely due to the tireless efforts of those interested in protecting the feeding grounds of migratory shorebirds that great measures have been taken to protect horseshoe crabs"); *see generally* Lawrence J. Niles, *Effects of Horseshoe Crab Harvest in Delaware Bay on Red Knots: Are Harvest Restrictions Working*, 59 BIOSCIENCE 153, 155–60 (2009) (analyzing the effects of overharvesting horseshoe crabs on the *Rufa* population, and suggesting increased protection of horseshoe crabs to meet the "[r]ecovery goal that is a 'restored' *rufa* population").

22. The IUCN is an international environmental organization that maintains the IUCN Red List of Threatened Species, "the world's most comprehensive information source on the global extinction risk status of animals, fungus and plant species." *IUCN Red List of Threatened Species*, IUCN, https://iucn.org/resources/conservation-tool/iucn-red-list-threatened-species (last visited Nov. 21, 2023).

23. Krisfalusi-Gannon et al., *supra* note 5, at 2.

24. *Id.*

25. Botton, *supra* note 11, at 1–3; AM. MUSEUM NAT. HIST., *Horseshoe Crabs are One of Nature's Greatest Survivors*, PHYS. ORG. (Jan 24, 2012), https://phys.org/news/2012-01-horseshoe-crabs-nature-great-survivors.html (last visited Oct. 26, 2024).

26. Botton, *supra* note 11, at 1–3.

27 *Id.* at 10.

28. The Anthropocene generally refers to the "human-dominated geological epoch" that we currently live in, marked by human-induced ecological crises. *See generally* Simon Lewis & Mark Andrew Maslin, *Defining the Anthropocene*, 519 NATURE 171, 171 (2015) (assessing competing perspectives on what the Anthropocene Epoch is and when it began).

29. *See* Botton, *supra* note 11, at 1 ("Our current human-dominated era, the Anthropocene, poses a unique set of challenges for horseshoe crabs that stem from overexploitation and habitat loss.").

exploitation of horseshoe crabs comes from their biomedical importance."[30] In 2022 alone, the biomedical industry captured nearly one million horseshoe crabs off the Atlantic coast and drained up to half of their blue blood[31]—nearly double the "blood harvest" in 2017.[32]

II. THE BIOMEDICAL HORSESHOE CRAB INDUSTRY AND ITS IMPACTS

Before analyzing the regulations pertaining to the biomedical exploitation of horseshoe crabs—or the lack thereof—it is important to first understand several things: (1) the biomedical value of horseshoe crab blood; (2) the structure of the multi-million-dollar industry erected around this blue substance; and (3) this industry's drastic welfare impacts on horseshoe crabs, both on the individual and species levels. This section explores each facet in turn.

A. The LAL Test

While the biomedical industry has capitalized on horseshoe crabs for several decades,[33] this paper focuses on the discovery of a novel application for the animals' blue blood in the late 20th century.[34] Horseshoe crabs' 450 million years of survival on Earth can partly be attributed to their "innate immunity" arising from their unique blood, which contains only one type of cell: the amoebocyte.[35] When a horseshoe crab suffers an injury and bacteria enters their bloodstream, these amoebocyte cells coagulate and form a blood clot.[36] This reaction, one of the earliest evolutionary immune systems, transformed the biomedical industry in the 1960s and 1970s.[37] The scientific community's discovery of this ancient immune response led to the development of the *Limulus* amebocyte lysate (LAL) test, which relies on horseshoe crab blood to detect endotoxins.[38]

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30. Botton, *supra* note 11, at 1.

31. Levitan, *supra* note 2.

32. *Lawsuit Demands Maryland's Crucial Horseshoe Crab Death, Injury Data*, CTR. FOR BIOLOGICAL DIVERSITY (May 22, 2024), https://biologicaldiversity.org/w/news/press-releases/lawsuit-demands-marylands-crucial-horseshoe-crab-death-injury-data-2024-05-22/.

33. *See, e.g.,* Okun, *supra* note 4, at 199 ("For over seventy years, horseshoe crab eyes have been considered valuable experimental models in vision research.").

34. *Id.* at 200.

35. Krisfalusi-Gannon, *supra* note 5, at 2; Okun, *supra* note 4, at 199; AM. MUSEUM NAT. HIST. *supra* note 25. For comparison, mammals have two: red and white blood cells. Laura Dean, *Blood Groups and Red Cell Antigens*, NAT'L CTR. FOR BIOTECHNOLOGY INFO., 1 (2005), https://www.ncbi.nlm.nih.gov/books/NBK2263/.

36. Okun, *supra* note 4, at 199.

37. *Id.* at 199–200.

38. Krisfalusi-Gannon, *supra* note 5, at 2.

Endotoxins are highly toxic molecules existing in bacterial cells that can sicken and kill humans—even after the bacteria that produced them have been eliminated.[39] The LAL test relies on horseshoe crab blood, which is centrifuged to amass the amebocytes before water is added to break apart the invaluable coagulation proteins for quick and accurate endotoxin testing.[40] The LAL clots around the endotoxins on pharmaceuticals and medical devices.[41] This reaction reveals any endotoxin contamination and, if so, to what extent.[42]

The Food & Drug Administration (FDA) requires that endotoxin levels are tested in injectable drug products (e.g., vaccines and insulin), and implantable medical devices.[43] Prior to FDA approval of LAL in 1983 for endotoxin testing, pharmaceutical and biomedical companies tested intravenous drugs and medical devices for these harmful endotoxins on live rabbits.[44] These companies were more than happy to transition to the LAL test, given that the rabbit method was "costly, sometimes inaccurate, and created poor publicity."[45] Today, the LAL test is the primary method used in the U.S. for endotoxin testing.[46] It is also increasingly used to assess environmental quality, as the test can detect endotoxins in freshwater, sea water, and surrounding sediment.[47] The biopharmaceutical sector's reliance on the LAL test has fueled a lucrative industry that profits off the capture and bleeding of horseshoe crabs.

B. The Structure of the Biomedical Horseshoe Crab Industry

Once composed of family businesses that owned smaller facilities, today, there are only five federally licensed manufacturers that process horseshoe crab blood.[48] These are owned by giant multinational firms like Fujifilm and Charles River Laboratories (Charles River Lab).[49] These five facilities are located along the East Coast in South Carolina, New Jersey, Massachusetts,

39. James Gorman, *Tests for Coronavirus Vaccine Need This Ingredient: Horseshoe Crabs*, N.Y. TIMES (June 3, 2020), https://www.nytimes.com/2020/06/03/science/coronavirus-vaccine-horseshoe-crabs.html.

40. *Id.*

41. Chris Iovenko, *Horseshoe Crabs are in Danger Because Everyone Wants Their Blood*, THE VERGE (Dec. 17, 2021), https://www.theverge.com/2021/12/17/22840263/horseshoe-crab-blood-medical-industry-controversy.

42. *Id.*

43. Sarah A. Robinson et al., *Bacterial Endotoxin Testing of Drugs and Biologics in the US: Ensuring Patient Safety*, REGUL. FOCUS (Aug. 18, 2023), https://rapsprod.blob.core.windows.net/rapsk13/raps/media/news-images/23-8_robinson-et-al_rev-2.pdf.

44. Okun, *supra* note 4, at 200.

45. *Id.*

46. *Id.*

47. Krisfalusi-Gannon, *supra* note 5, at 2.

48. Eisner, *supra* note 3.

49. *Id.*

Virginia, and Maryland, where they enjoy convenient proximity to horseshoe crab habitat.[50] These facilities obtain the horseshoe crabs through various means before siphoning their precious blood.[51] Depending on the state, fishermen either harvest the creatures directly from the sea with trawling nets or pluck them off the beaches by hand.[52] A blend of middleman and bounty hunter, these fishermen then deliver the horseshoe crabs to the bleeding facilities.[53]

In recent years, there has been controversy over Charles River Lab's practice of allowing its suppliers to store captured horseshoe crabs in holding ponds before bleeding them, a practice legal only in South Carolina.[54] In 2022, Defenders of Wildlife and the Coastal Conservation League filed a lawsuit against Charles River Lab seeking to enjoin the use of these "temporary containment ponds" during the horseshoe crab spawning season.[55] Plaintiffs argued that Charles River Lab violated the Endangered Species Act (ESA) through impermissibly "taking" the threatened Rufa Red Knot.[56] This alleged taking included depriving the threatened shorebirds of their "critical food source"—horseshoe crab eggs.[57] In August 2023, the parties reached a settlement.[58] The settlement ended the placement of female horseshoe crabs in holding ponds prior to their bleeding, which allows them to lay their eggs on beaches.[59] The resulting protection to horseshoe crabs, but notably only females, evidences the limited protections afforded to horseshoe crabs are often secondary effects of Rufa conservation efforts.

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50. Eisner, *supra* note 3; Patrick Whittle, *There's a Growing Conflict Over Horseshoe Crab Blood Harvesting. Find Out Why*, DEL. ONLINE (Aug. 1, 2023), https://www.delawareonline.com/story/news/2023/08/01/horseshoe-crabs-blue-blood-harvesting-medicine/70506964007.

51. Eisner, *supra* note 3.

52. *Id.*

53. *Id.*

54. *Historic Limits on Horseshoe Crab Harvest Will Protect Threatened Shorebirds*, S. ENV'T L. CTR. (May 5, 2023), https://www.southernenvironment.org/news/historic-limits-on-horseshoe-crab-harvest-will-protect-threatened-shorebirds.

55. *Defenders of Wildlife and Conservation Groups Sue Regulators, Pharmaceutical Company Over Crab Pens*, DEFS. OF WILDLIFE (Jan. 13, 2022), https://defenders.org/newsroom/defenders-of-wildlife-and-conservation-groups-sue-regulators-pharmaceutical-company-over; Defs. of Wildlife v. Boyles, No. 2:22-CV-112-RMG, slip op. at 1 (D.S.C. Apr. 4, 2023) (Westlaw).

56. Defs. of Wildlife v. Boyles, No. 2:22-CV-112-RMG, slip op. at 1 (D.S.C. Apr. 4, 2023).

57. *See id.* (describing the lawsuit's basis in denying the defendant's motion to strike expert evidence).

58. *Charles River Labs Signs Joint Agreement for Protection of Crabs Used in Medical Tests*, REUTERS (Aug. 25, 2023), https://www.reuters.com/business/healthcare-pharmaceuticals/charles-river-lab-signs-joint-agreement-protection-crabs-used-medical-tests-2023-08-24 (last visited Nov. 21, 2023).

59. *Id.*

Society and the legal community fail to acknowledge the intrinsic value and interests of horseshoe crabs to be free from exploitation.[60]

Regardless, whether temporarily kept in a facility holding pond or not, all captured horseshoe crabs meet the same fate during the bleeding process. Lab technicians puncture the crabs' hearts with syringes before draining them alive.[61] The bleeding process can last up to eight minutes and extract over half the volume of horseshoe crabs' blue blood.[62] After the bleeding process, the biomedical industry delivers most bled horseshoe crabs back to the fishermen and harvesters.[63] As investigative reporter Chiara notes:

> [This] makes the bleeding business unique among the [fishing and biomedical] industries it straddles. It's an unusual fishery, because the animals are not sold to be eaten. It's an atypical utilization of animals in medicine, since the crabs are not bled in the research stage . . . . The business is also different from extractive industries like mining and logging, because the harvested natural resource is often supposed to be returned to the environment alive.[64]

The uniqueness of the biomedical horseshoe crab industry allows it, in part, to occupy a profitable legal gray area with little regulatory oversight.[65]

Unfortunately, secrecy and a lack of transparency marks the bleeding companies.[66] State governments can also play a role in shielding the industry from the public eye, evidenced by a lawsuit filed by the Center for Biological Diversity (CBD) in May 2024 against the Maryland Department of Natural Resources.[67] CBD sued the agency for violating the state's public records law when the agency failed to disclose "exactly how" the thousands of horseshoe crabs are harvested, bled, killed, or injured by the biomedical industry and fishermen each year.[68] In a press release concerning its lawsuit, CBD asserted that "because Maryland shrouds in secrecy the process it uses to determine

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60. There has been scientific research that examines the physiological and mortality impacts of time spent in holding ponds on harvested horseshoe crabs. *See* Kristin Linesch Hamilton et al., *Physiological Impacts of Time in Holding Ponds, Biomedical Bleeding, and Recovery on Atlantic Horseshoe Crab, Limulus Polyphemus*, 239 COMPAR. BIOCHEMISTRY & PHYSIOLOGY 1, 1 (2020).

61 . Eisner, *supra* note 3.

62. *Id.*

63. Eisner, *supra* note 3; Tom Maloney et al., *Saving the Horseshoe Crab: A Synthetic Alternative to Horseshoe Crab Blood for Endotoxin Detection*, PUB. LIBR. OF SCI. BIOLOGY, 2 (2018).

64. Eisner, *supra* note 3, at 4.

65. Eisner, *supra* note 3.

66. Eisner, *supra* note 3, at 2; *see also* Caren Chesler, *Medical Labs May Be Killing Horseshoe Crabs*, SCI. AM. (June 9, 2016), https://www.scientificamerican.com/article/medical-labs-may-be-killing-horseshoe-crabs/ (reporting that four of the five harvesting facilities did not respond to requests to be interviewed).

67. CTR. FOR BIOLOGICAL DIVERSITY, *supra* note 32.

68. *Id.*

when crabs can be harmed, the Center [for Biological Diversity] and other parties can't meaningfully participate in protecting the imperiled animals" from corporate interests.[69]

Behind closed doors, industry actors are raking in an exorbitant amount of money from the blood of horseshoe crabs.[70] The high demand for horseshoe crab blood for endotoxin testing can price a quart of LAL at $15,000.[71] Economic revenue gained from the biomedical use of horseshoe crabs "far out-shadows" all other methods of exploiting these animals for profit (such as for bait harvesting).[72] More specifically, the biomedical industry captures an estimated $220 million of the $260 million generated annually by horseshoe crab-related industries.[73] The harvesters who comb the beaches and seas for horseshoe crabs can earn ten times more by selling their live catches to the biomedical industry as opposed to selling dead horseshoe crabs as bait.[74] With the profit margin so vast for both the horseshoe crab harvesters and five industry bleeders, it is no wonder that the number of horseshoe crabs exploited for biomedical use only increases each year.[75] This exploitation is perpetually sustained by the biopharmaceutical industry's insatiable demand for the LAL test. But the use and abuse necessarily entangled with extracting the crab's precious blue blood takes a toll on these prehistoric creatures.

C. The Biomedical Industry's Severe Impact on Horseshoe Crabs

The profits to be made off the horseshoe crab-derived LAL test have led to increasing harvests each year that devastate horseshoe crabs as individuals and as a species.[76] One researcher notes that "[g]iven the high use of [horseshoe crabs], it is surprising that so little empirical evidence about sentience [and pain] is available."[77] However, horseshoe crabs do possess a central nervous system.[78] Consequently, these animals may very well suffer

69. CTR. FOR BIOLOGICAL DIVERSITY, *supra* note 32.
70. Iovenko, *supra* note 41, at 5.
71. *Id.* at 2.
72. Okun, *supra* note 4, at 201.
73. *Id.*
74. *Id.*
75. Eisner, *supra* note 3.
76. *Id.*
77. Robert W. Elwood, *Behavioural Indicators of Pain and Suffering in Arthropods and Might Pain Bight Back*, 13 ANIMALS 2602, 8 (2023).
78. *Basic Anatomy*, DEL. BAY HORSESHOE CRAB SURV., https://www.delawarebayhscsurvey.org/anatomy (last visited Nov. 22, 2023).

during every step of their industrialized biomedical exploitation: from harvest, to bleeding process, to after their post-bleed release.[79]

At the beginning of the cycle, harvesters, by hand or net, remove live horseshoe crabs from their habitat.[80] Then, they stack the animals on top of one another by the hundreds for delivery to the bleeding facilities—an undoubtedly jarring experience for these creatures.[81] The horseshoe crabs are transported "not in tanks of cold salt water, but in the back of open pickup trucks" that are "dry and hot."[82] They may experience hypoxia[83] after just five minutes out of the water, which reduces their survival time by an average of 74%.[84] Research indicates that picking horseshoe crabs up by their tails can prevent their ability to right themselves when flipped over, which can prove fatal for the animals post-release.[85] Despite this, lifting horseshoe crabs by their tails is a common harvesting practice.[86] Further, before Charles River Labs ended its use of holding ponds, bleeding facilities left captured horseshoe crabs to languish in confinement with no requirement that they be fed prior to their bleeding.[87] Charles River Labs self-reported that the mortality rate of its horseshoe crabs was "just 4%" during the handling and transportation of crabs to and from the facility.[88] From 2004 to 2012, the percentage of horseshoe crabs that perished prior to bleeding jumped by 75%, which scientists attribute to potential "deleterious harvest and transportation practices."[89]

Horseshoe crabs' circumstances do not improve during the bleeding process, which exposes them to more time outside water, rough handling,

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79. There is a lack of research into horseshoe crabs' capacity to feel pain, which would better illuminate the welfare impacts of their biomedical use. Elwood, *supra* note 77, at 8. However, given the ever-growing research unsettling long-held assumptions that many non-human animals do not feel pain, such as crustaceans, fish and insects, it would be prudent to adopt the precautionary principle and proceed as if the horseshoe crabs do experience pain. Andrew Crump et al., *Is It Time for Insect Researchers to Consider Their Subjects' Welfare?*, PUB. LIBR. OF SCI. BIOLOGY, at 3 (2023); Seth Millstein, *Fish Feel Pain, Science Shows—But Humans Are Reluctant To Believe It*, SENTIENT (Jan. 12, 2024), https://sentientmedia.org/do-fish-feel-pain/; Robert W. Elwood, *Potential Pain in Fish and Decapods: Similar Experimental Approaches and Similar Results*, 8 FRONTIERS VETERINARY SCI. 1, 6 (2021).

80. Eisner, *supra* note 3, at 4.

81. *Id.*

82. Bill Schutt, *How Horseshoe Crab Blood Became One of the Most Valuable Liquids in Medicine*, BIG THINK (Oct. 3, 2022), https://bigthink.com/health/horseshoe-crab-blood-clott/.

83. Hypoxia is a state of low-oxygenated blood, which can cause long-term physiological impairments. Beenish S. Bhutta et al., *Hypoxia*, STATSPEARLS, https://www.ncbi.nlm.nih.gov/books/NBK482316/ (Mar. 4, 2024).

84. Krisfalusi-Gannon, *supra* note 5, at 4.

85. Eisner, *supra* note 3.

86. *Id.*

87. *Id.*

88. Chesler, *supra* note 66, at 4.

89. Krisfalusi-Gannon, *supra* note 5, at 4.

and extreme temperatures.[90] Lab technicians scrub the crabs with disinfectant, strap the crabs to metal tables, and bend their hinged shells back,[91] all before piercing the horseshoe crabs' hearts with a large-gauge syringe and removing 5–400 mL of their blood.[92]

The harm inflicted upon horseshoe crabs continues after the blood extraction procedures. Typically, the horseshoe crabs are released far from where they were initially picked up one to three days prior.[93] While this practice is intended to prevent the animals from being recaptured and re-bled,[94] it disrupts the horseshoe crabs' autonomy over their lives and movements. Research suggests that because horseshoe crab harvest often occurs during spawning season, and egg production is energy intensive, the bleeding process takes a greater physiological toll on the already-weakened females.[95] An estimated 15-30% of horseshoe crabs die because of biomedical bleeding after their release.[96] Of course, the mortality rate for the 13% of horseshoe crabs bled before being later sold as bait is 100%, as their use as bait necessitates their killing.[97]

The industrial bleeding of horseshoe crabs not only affects the health and well-being of individual animals, but it also likely impairs the survivability of the species. Research indicates females that survive blood extraction exhibit diminished spawning activity, with some failing to spawn completely.[98] The bleeding process also likely takes its toll on males' ability to produce the next generation of horseshoe crabs.[99] Thus, research suggests that post-bleeding impairs horseshoe crabs' spawning abilities, which could

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90. Krisfalusi-Gannon, *supra* note 5, at 3.

91. Schutt, *supra* note 82.

92. Eisner, *supra* note 3.

93. Alexis C. Madrigal, *The Blood Harvest*, ATLANTIC (Feb. 26, 2014), https://www.theatlantic.com/technology/archive/2014/02/the-blood-harvest/284078/.

94. *Id.*

95. Sami B. Ghubril, *Saving the Horseshoe Crab: The Case for the Oft-forgotten, Critically Important Living Fossil*, VA. ENV'T L.J. 272, 278–79 (2019).

96. *Id.* at 278 (estimating that up to 30% of horseshoe crabs may die following bleeding). The Atlantic States Marine Fisheries Commission (ASMFC), the interstate body charged with regulating the take of horseshoe crabs for the biomedical industry, maintains the 15% mortality rate at the lowest end of the range, despite research indicating otherwise. ATL. STATES MARINE FISHERIES COMM'N, STOCK ASSESSMENT OVERVIEW: HORSESHOE CRAB, at 3 (2019).

97. Maloney et al., *supra* note 63, at 2; *See also* Barbara Moran, *Mass. Proposes New Protections for Horseshoe Crabs*, WBUR NEWS (Feb. 14, 2024), https://www.wbur.org/news/2024/02/15/mass-proposes-new-protections-for-horseshoe-crabs (noting that bait harvest of horseshoe crabs results in 100% mortality).

98. Ghubril, *supra* note 95, at 279.

99. *See* David R. Smith et al., *The Long-Term Effect of Bleeding for Limulus Amebocyte Lysate on Annual Survival and Recapture of Tagged Horseshoe Crabs*, 7 FRONTIERS MARINE SCI. 1, 11 (noting that bleeding may have a greater negative effect on the spawning activity of male rather than female horseshoe crabs, even if the impact on individuals is "short-lived").

potentially impair the reproduction rate at a species level[100]—the species' spawning has decreased by a staggering 72% in the past three decades.[101] Case studies indicate that human predation is the primary cause of collapsing horseshoe crab populations[102] and climate change will cause even greater strain on the horseshoe crab population.[103] In February 2024, CBD, the Humane Society of the United States, and the American Bird Conservancy petitioned the National Oceanic and Atmospheric Administration's National Marine Fisheries Services (NOAA Fisheries) to list the horseshoe crab as an endangered species under the ESA.[104]

However, based on current trends related to horseshoe crab mortality and population, the demand for LAL over the next two decades is likely to reach "unsustainable levels."[105] U.S. regulatory response has been grossly insufficient to protect horseshoe crabs.

III. THE ANTHROPOCENTRIC REGULATORY FRAMEWORK OF THE BIOMEDICAL HORSESHOE CRAB INDUSTRY

The federal government, an interstate compact known as the Atlantic States Marine Fisheries Commission (ASMFC), and the individual states all play a role in regulating the biomedical horseshoe crab industry. The FDA regulates the LAL test manufacturing process to ensure product safety.[106] The regulation of the biomedical horseshoe crab fishery, concerning the harvest and bleeding processes, largely occurs within a cooperative federalism framework.[107] FDA approval of the LAL test resulted in a substantial uptick in horseshoe crab harvesting; the ASMFC began regulating the commercial harvesting of horseshoe crabs in the late 1990s with support from the federal government.[108] This section discusses three things: (1) FDA

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100. Smith, *supra* note 99, at 11 (noting the scientists' research "*could* indicate reduced spawning activity and, in turn, reduced population productivity" but also that "an effect at the population level would require sufficient numbers relative to abundance to reduce their fecundity or spawning activity") (emphasis added).

101. *Petition to List the American Horseshoe Crab (Limulus Polyphemus) under the U.S. Endangered Species Act as an Endangered or Threatened Species and to Concurrently Designate Critical Habitat*, CTR. FOR BIOLOGICAL DIVERSITY (Feb. 27, 2024), https://www.biologicaldiversity.org/species/invertebrates/pdfs/20240212-American-horseshoe-crab-petition.pdf.

102. Krisfalusi-Gannon, *supra* note 5, at 5.

103. NOAA, *Horseshoe Crab—Limulus polyphemus* 143 (2016), https://www.st.nmfs.noaa.gov/Assets/ecosystems/climate/images/species-results/pdfs/Horseshoe_Crab.pdf (last visited Sept. 25, 2024).

104. CTR. FOR BIOLOGICAL DIVERSITY, *supra* note 101.

105. Krisfalusi-Gannon, *supra* note 5, at 5.

106. *See* Okun, *supra* note 4, at 204–13 (providing an overview of the regulatory framework for horseshoe crabs from a conservation perspective).

107. *Id.*

108. *Id.* at 200–06.

oversight of LAL test manufacturing; (2) the cooperative federalism model that involves the ASMFC and federal agencies in regulating the biomedical horseshoe crab fishery; and (3) individual states' ability to supplement the few regulations mandated by the ASMFC. However, current regulations neglect horseshoe crabs' well-being and interest in freedom from human exploitation. Rather, these laws emphasize an anthropocentric objective of managing these ancient creatures as an exploitable "fishery resource" across all regulatory levels.

A. FDA Regulation of LAL Test Manufacturing

Honoring the states' traditional exercise of primary regulatory authority over their wildlife and natural resources,[109] the federal government generally plays a secondary role in regulating biomedical use of horseshoe crabs.[110] An exception is the FDA, which maintains primary oversight of LAL test manufacturing because the process implicates consumer safety rather than fishery management.[111] Naturally, the limited federal regulations in place related to LAL test production are strictly anthropocentric, revolving around consumer safety rather than horseshoe crab welfare. There are no federal standards providing for horseshoe crab welfare during their capture and bleeding for biomedical use.[112]

The FDA oversees the manufacture of the LAL test to protect public health.[113] In 1983, the FDA first approved the LAL test for endotoxin detection after extensive testing and validation by U.S. Pharmacopeia (USP), a scientific nonprofit.[114] The FDA relies on USP to set federal quality

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109. Jean O. Melious, *Enforcing the Endangered Species Act Against the States*, 25 WM. & MARY ENV'T L. & POL'Y R. 605, 609 (2001).

110. *See* David Favre, *American Wildlife Law—An Introduction*, ANIMAL LEGAL & HIST. CTR., https://www.animallaw.info/article/american-wildlife-law-introduction (last visited Nov. 28, 2023) (describing how states have primary jurisdictional authority over fish and wildlife on state lands).

111. *See What Does FDA Regulate*, U.S. FOOD & DRUG ADMIN., https://www.fda.gov/about-fda/fda-basics/what-does-fda-regulate (last visited Nov. 28, 2023) (providing an overview of FDA's broad regulatory authority, inclusive of drugs, and biologics).

112. Notably, the Animal Welfare Act entirely excludes horseshoe crabs from the Animal Welfare Act's purview by narrowly defining "animal. " *See* Animal Welfare Act, 7 U.S.C. § 2132(g) ("The term "animal" means any live or dead dog, cat, monkey (nonhuman primate mammal), guinea pig, hamster, rabbit, or such other warm-blooded animal").

113. Allen L. Burgenson, *Confidence for Adopting the rFC Method in Your Lab*, LONZA, 1 (2022), https://bioscience.lonza.com/lonza_bs/US/en/download/content/asset/35191; *See also* Status of Biological Substances Used for Detecting Bacterial Endotoxins, 38 FED. REG. 1371, 1404 (Jan. 12, 1973) (announcing FDA would regulate LAL as a biologic under the Public Health Service Act); Reyes Candau-Chacon, FDA, *FDA Perspectives on Recombinant Endotoxin Detection Systems*, 31 (Nov. 16, 2021), https://www.usp.org/sites/default/files/usp/document/events-training/03-fda-perspective-on-recombinant-reyes-candau-chacon-final.pdf (explaining why FDA licenses LAL).

114. Okun, *supra* note 4, at 200.

standards for pharmaceuticals.[115] Thus far, USP—and thereby the FDA—has only approved the rabbit and LAL tests for endotoxin assessment for which the industry can forgo additional validation.[116]

Due to LAL's "animal nature" and "intrinsic variability,"[117] the FDA licenses LAL manufacturers.[118] By licensing only five processors throughout the U.S.,[119] the federal government has effectively created a "federally mandated monopoly" of LAL production.[120] Further, FDA regulations offer no guidance for treating bled horseshoe crabs—despite stipulating baseline manufacturing practices for pharmaceutical processing[121] and finished pharmaceuticals to ensure the safety, quality, and purity of LAL tests for human benefit.[122]

No federal animal welfare standards apply to the biomedical use of horseshoe crabs. The Animal Welfare Act (AWA) sets minimal standards for the "humane handling, care, treatment, and transportation" by "research facilities."[123] Yet, bled horseshoe crabs fall outside the scope of AWA regulations for two reasons. First, bleeding facilities, occupying a legal gray space between the fishery and biomedical research domains,[124] likely do not fit the "research facilities" definition as they do not use live animals in "research, tests, or experiments."[125] Second, and more importantly, the AWA narrowly defines those animals afforded its protections to the exclusion of non-warm-blooded animals and invertebrates.[126] Considering the welfare concerns implicated in the biomedical exploitation of horseshoe crabs, the lack of federal regulation is troublesome.

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115. In fact, "[t]he USP-FDA relationship dates back to the 1906 Pure Food and Drug Act, which deemed the United States Pharmacopeia and the National Formulary official compendia under federal law." *USP and FDA Working Together to Protect Public Health*, USP, https://www.usp.org/public-policy/usp-fda-roles (last visited Nov. 28, 2023).

116. *Bacterial Endotoxins/Pyrogens*, FDA (Nov. 11, 2014), https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/inspection-technical-guides/bacterial-endotoxinspyrogens; *See also Guidance for Industry Pyrogen and Endotoxins Testing: Questions and Answers*, FDA (June 2012), https://www.fda.gov/regulatory-information/search-fda-guidance-documents/guidance-industry-pyrogen-and-endotoxins-testing-questions-and-answers.

117. Candau-Chacon, *supra* note 113, at 31.

118. *Id.*; Maribeth Donovan Janke & Allen L. Burgenson, *The FDA Withdrew the LAL Guidance Document, What Are the Implications?*, LONZA, 1 (2011); *See also* ATL. STATES MARINE FISHERIES COMM'N, *Best Management Practices for Handling Horseshoe Crabs for Biomedical Purposes*, 3 (2023) (referring to "FDA-licensed LAL manufacturers") [hereinafter *Best Management Practices*].

119. *Best Management Practices*, *supra* note 118, at 3.

120. Brendan Tindall & Kevin Williams, *The Impact of Supply Chain Risks and LAL Reliance*, EUR. PHARM. REV. (June 26, 2020), https://www.europeanpharmaceuticalreview.com/article/121766/the-impact-of-supply-chain-risks-and-lal-reliance/ (explaining that existence of the monopoly might hamper industry innovation and transition to animal-free alternatives).

121. 21 C.F.R. §§ 210.1–210.3 (2023).

122. 21 C.F.R. §§ 211.1–211.208 (2023).

123. 7 U.S.C. § 2143 (1985).

124. Eisner, *supra* note 3.

125. 7 U.S.C. § 2132(e) (2014).

126. 7 U.S.C. § 2132(g) (2014).

In sum, the federal government plays a peripheral role in regulating the biomedical use of horseshoe crabs. Though the FDA ensures the safety of the LAL test manufacturing process to benefit consumers, the federal government largely lets states take the lead when it comes to the harvest and handling of the bled horseshoe crabs through a cooperative federalism model.

B. Cooperative Federalism and Interstate Regulation

In contrast to the management of the LAL manufacturing process discussed previously, Congress has spoken more directly to the management of horseshoe crab fisheries. In 1993, Congress passed the Atlantic Coastal Fisheries Cooperative Management Act (ACFCMA or "Act")[127] with the stated purpose "to support and encourage the development, implementation, and enforcement of effective interstate conservation and management of Atlantic coastal fishery resources."[128] More specifically, the Act charges NOAA Fisheries and United States Fish and Wildlife Service (USFWS) with "supporting the interstate fisheries management efforts of the Atlantic States Marine Fisheries Commission (ASMFC)."[129]

The ASMFC is an interstate compact predating the ACFCMA by over five decades.[130] The ASMFC member states recognized the need for "cooperative stewardship" when managing shared migratory fishery resources on the Atlantic seaboard.[131] As such, they formed the ASMFC in the 1940s before its approval by Congress in 1942.[132] Today, its member states are: Maine, New Hampshire, Massachusetts, Rhode Island, Connecticut, New York, New Jersey, Pennsylvania, Delaware, Maryland, Virginia, North Carolina, South Carolina, Georgia, and Florida.[133] Despite the biomedical harvest of horseshoe crabs constituting "an unusual fishery, because the animals are not sold to be eaten," the industry's regulation still falls primarily to this ASMFC fishery management body.[134]

The 1993 ACFCMA created a cooperative federalism model for the management of many Atlantic fishery species. The Act directs ASMFC to "prepare and adopt coastal fishery management plans to provide for the

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127. 16 U.S.C. §§ 5101–5108 (2018); NOAA FISHERIES, ATLANTIC COASTAL FISHERIES COOPERATIVE MANAGEMENT ACT: FY 2017–2018 REPORT TO CONGRESS, 1 (2018) [hereinafter NOAA FISHERIES FY 2017–2018 REPORT].

128. 16 U.S.C. § 5101(b) (2018).

129. NOAA FISHERIES FY 2017–2018 REPORT, *supra* note 127, at 1.

130. *About Us*, ATL. STATES MARINE FISHERIES COMM'N, https://asmfc.org/about-us/program-overview (last visited Nov. 28, 2023).

131. *Id.*

132. *Id.*

133. *About Us, ASMFC Member States*, ATL. STATES MARINE FISHERIES COMM'N, http://www.asmfc.org/about-us/links (last visited Nov. 28, 2023).

134. Eisner, *supra* note 3.

conservation of coastal fishery resources," like the horseshoe crab, that the federal government then helps implement through enforcement, funding, and other means.[135] After the ASFMC adopts a fishery management plan for a given coastal fish "resource," member states implement and enforce the fishery management plan on the state level.[136] The ASMFC, in turn, annually reviews each state for fishery management plan compliance and reports its findings to the Secretary of Commerce.[137] Thus, through the ASFMC, states retain primary regulatory authority over commercial horseshoe crab industries—whether horseshoe crabs are harvested for bait or for bleeding.

FDA approval of LAL in 1983 drove increasing commercial use of horseshoe crabs, devastating migratory shorebird populations.[138] To address this issue, the ASMFC adopted the Horseshoe Crab Fisheries Management Plan (Horseshoe Crab FMP) in 1998.[139] The Horseshoe Crab FMP and its Addenda are the main regulations governing the commercial harvest of horseshoe crabs in the U.S. for bait and biomedical use. Despite the 1998 FMP's establishment of an annual biomedical mortality limit of 57,500 horseshoe crabs, this threshold has been exceeded every year since 2008.[140]

Pursuant to the ACFCMA, states must comply with specified ASMFC FMP regulations.[141] Currently the biomedical industry harvests horseshoe crabs in six states: Maryland, Massachusetts, New Jersey, Rhode Island, South Carolina, and Virginia.[142] First, the ASMFC requires states to issue special permits for the biomedical harvesting of horseshoe crabs.[143] Second, permit holders must return bled horseshoe crabs to the same state or federal waters from where they were collected.[144] Finally, states must monitor and report the following: the number of biomedically harvested horseshoe crabs, harvest-to-release mortality rate, [145] harvest method, harvested male-to-female ratio, bled horseshoe crabs' disposition, and condition of bled horseshoe crabs' holding environment prior to their release.[146] Notably, there is no requirement to report post-release numbers, where upper mortality rate estimates hover around 30%.[147]

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135. 16 U.S.C. § 5104(a)(1) (2018).
136. 16 U.S.C. § 5104(b)(1) (2018).
137. 16 U.S.C. § 5104(c) (2018).
138. Okun, *supra* note 4, at 205.
139. *Id.*
140. *Review of the Interstate Fishery Management Plan—Horseshoe Crab (Limulus Polyphemus): 2022 Fishing Year*, ATL. STATES MARINE FISHERIES COMM'N, 16 (Oct. 2023) http://www.asmfc.org/uploads/file/6539318aHSC_FMP_Review_FY2022.pdf.
141. 16 U.S.C. § 5104(a)(1) (2018).
142. *Best Management Practices*, *supra* note 118, at 3.
143. *Id.*
144. *Id.*
145. *Id.* at 5.
146. *Id.*
147. *See supra* note 96.

Federal agencies like NOAA Fisheries and USFWS fulfill their role in the ACFCMA cooperative federalism model by supporting ASMFC's Horseshoe Crab FMP through enforcement, funding, and other measures.[148] While some parts of the Horseshoe Crab FMP are mere suggestions for states, much of it is binding upon states under federal law.[149] A state's failure to comply with a fishery management plan allows the Secretary of Commerce to instate a moratorium on the subject fishery within the noncompliant state's waters.[150] In addition, federal agencies distribute funds to ASMFC member state fisheries to support their management programs; presumably, the federal government helps implement the ASMFC's Horseshoe Crab FMP through funding.[151]

The cooperative federalism model has prompted a few notable federal actions regarding horseshoe crab conservation. ASMFC recommended action to protect "local stocks" of horseshoe crabs and the declining population of migratory shorebirds relying on horseshoe crab eggs for sustenance.[152] Honoring the states' primary regulatory authority, in 2001, NOAA Fisheries created the Carl N. Shuster, Jr. Horseshoe Crab Reserve, which closed off 1,500 square nautical miles north of Delaware Bay to all horseshoe crab harvesting, including biomedical collection.[153] Responding to an August 2023 lawsuit brought by environmentalists, the USFWS banned horseshoe crab harvesting in the Cape Romaine National Wildlife Refuge during their spawning season to better protect the Rufa Red Knot.[154] Nevertheless, these federal limits on biomedical horseshoe crab harvesting, tailored to specific habitats or spawning periods, ignore the horseshoe crabs' interest to be free from human exploitation regardless of time or place. Instead, these protective measures serve as proxies for anthropocentric concerns, aiming to conserve natural resources like the threatened Rufa or the horseshoe crabs themselves for sustainable use.

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148. 16 U.S.C. §§ 5104–5106 (2018); NOAA FISHERIES, ATLANTIC COASTAL FISHERIES COOPERATIVE MANAGEMENT ACT: FY 2021-2022 REPORT TO CONGRESS 1 (2023), https://www.fisheries.noaa.gov/s3//2023-09/ACA-FY21-22-Report-combined-508compliant.pdf.

149. Okun, *supra* note 4, at 206.

150. 16 U.S.C. § 5106(c)(1) (2018).

151. *About Us*, *supra* note 130.

152. *Id.* (quoting Michelle Baldwin et al., *A Review of Developments in Ocean and Coastal Law 2000–2001*, 6 OCEAN & COASTAL L.J. 413, 429 (2001)).

153. Okun, *supra* note 4, at 211.

154. Victoria Hansen, *Federal Agency Limits Horseshoe Crab Harvesting in National Wildlife Refuge Near Charleston*, S.C. PUB. RADIO (Aug. 10, 2023, 2:50 PM), https://www.southcarolinapublicradio.org/sc-news/2023-08-10/federal-agency-limits-horseshoe-crab-harvesting-in-national-wildlife-refuge-near-charleston. However, the South Carolina Attorney General is challenging the federal agency's jurisdiction over the refuge and authority to ban the horseshoe crab harvest. *Horseshoe Crab Harvest Stopped in Cape Romain National Wildlife Refuge*, DEFENDERS OF WILDLIFE (Aug. 7, 2023), https://defenders.org/newsroom/horseshoe-crab-harvest-stopped-cape-romain-national-wildlife-refuge.

Last, but certainly not least, the ASMFC also recently promulgated non-binding Best Management Practices for Handling Horseshoe Crabs for Biomedical Purposes (BMP) in May 2023.[155] The ASMFC created the BMP "to recommend broadly applicable industry standards that are expected to minimize mortality and injury of horseshoe crabs associated with the biomedical process."[156] Among other suggestions, the BMP recommends keeping collected horseshoe crabs cool and moist, minimizing exposure to direct sunlight, avoiding overcrowding, handling them to minimize injury, ceasing blood collection once blood flow rate slows, and returning bled horseshoe crabs to the ocean as quickly as possible to minimize holding time.[157] The guidelines are not enforceable laws, and they are vague by design to help shield the industry from scrutiny.[158] However, some state fishery bodies, like Massachusetts of Marine Fisheries (Massachusetts DMF), have voluntarily codified the BMP through regulations.[159] The BMP claims its recommendations "represent standard practices used by the licensed manufacturers."[160] However, biomedical horseshoe crab industry participants "often disregard[]" the guidelines at every step of the process.[161] The BMP does not adequately address the absence of federally applicable animal welfare standards for horseshoe crabs collected and drained for biomedical purposes.

The cooperative federalism model, established by the ACFCMA and primarily carried out by the ASMFC, affirms state regulatory power over the horseshoe crab fishery. However, managing the horseshoe crab biomedical industry as a "fishery" inadequately protects horseshoe crabs as a species and as individuals. Both at the federal and state level, there are no binding regulations protecting horseshoe crab welfare during the invasive—and sometimes lethal—bleeding process.

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155. *Best Management Practices*, *supra* note 118, at 1–9.

156. *Id.* at 2.

157. *Id.*

158. Eisner, *supra* note 3 (describing a meeting where the best practices were being formulated, at which an industry participant stated that "if we give too much detail [in the guidelines], we're opening ourselves up for scrutiny").

159. Press Release, MASS. DEP'T OF FISH & GAME, Division of Marine Fisheries Announces New Conservation and Management Measures for the Commercial Horseshoe Crab Fishery, (Jul. 10, 2023), https://www.mass.gov/news/division-of-marine-fisheries-announces-new-conservation-and-management-measures-for-the-commercial-horseshoe-crab-fishery [hereinafter Press Release].

160. *Best Management Practices*, *supra* note 118, at 5.

161. Eisner, *supra* note 3.

C. Minor Variances in State Regulations

Under the ACFCMA cooperative federalism framework, the ASMFC first designs the Horseshoe Crab FMP.[162] Next, states implement that FMP within their borders, and finally, the federal government helps support and enforce the FMP.[163] Horseshoe crabs are currently harvested for biomedical use in six states.[164] Of those six, Massachusetts uniquely administers a "rent a crab program" where harvesters collecting horseshoe crabs under bait permits can "lease" captured crabs to a biomedical facility before returning them to the bait market.[165] For these horseshoe crabs, their last moments alive will consist of being seized from their habitats, stabbed, and siphoned of their blood, then killed to be sold as bait.[166]

Some states, like South Carolina in 1991 and New Jersey in 2008, have completely banned harvesting horseshoe crabs for bait, but allow biomedical harvesting to continue in their waters.[167] In August 2023, Connecticut went a step further.[168] The state passed a total ban on harvesting horseshoe crabs and their eggs.[169] Similarly, the New York legislature passed a landmark bill prohibiting all commercial and biomedical harvesting in the state in July 2024.[170] The drafters cited the species' imperiled "unique ecological role" as justification for the measure.[171] As of September 2024, the legislation still awaits the Governor's signature.[172] However, the Connecticut law and New York bill's impact on horseshoe crabs appears negligible, given the historical lack of biomedical harvesting in these states.[173] At the very least, however,

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162. Okun, *supra* note 4, at 205–06.

163. *Id.* at 205–13.

164. *Best Management Practices*, *supra* note 118, at 3.

165. Memorandum from Daniel J. McKiernan, Mass. DMF Director, to MASS. MARINE FISHERIES ADVISORY COMM'N (Feb. 8, 2023), https://www.mass.gov/doc/2023-dmf-horseshoe-crab-memo/download.

166. *See* Moran, *supra* note 97 (noting that bait use of horseshoe crabs results in 100% mortality).

167. Deborah Cramer, *When the Horseshoe Crabs are Gone, We'll Be in Trouble*, N. Y. TIMES (Feb. 16, 2023), https://www.nytimes.com/2023/02/16/opinion/drug-safety-horsehoe-crab.html.

168. Tricia Ennis, *Harvesting Horseshoe Crabs is Now Illegal in Connecticut*, INSIDE INVESTIGATOR (Aug. 11, 2023), https://insideinvestigator.org/harvesting-horseshoe-crabs-is-now-illegal-in-connecticut/.

169. CONN. GEN. STAT. ANN. § 26-292d (2023).

170. S.B. S3185--A, 2023–2024, 638 Legis. Sess. (N.Y. 2023).

171. *Id.*

172. *Id.*

173. Before Connecticut and New York progressed on their harvesting ban laws, ASMFC published a report listing the six states hosting biomedical collection of horseshoe crabs. Connecticut and New York were not among them. *See Best Management Practices*, *supra* note 118, at 3. Further, a survey of ASMFC Horseshoe Crab FMP Reviews from the past decade (2014–22) demonstrates that Connecticut and New York were consistently exempted from the biomedical harvest reporting required of states permitting biomedical harvest per FMP Addenda III. Each of the eight annual reviews designate the biomedical harvesting requirement to be "not applicable" to Connecticut and New York

these states are taking a step in the right direction. By flatly prohibiting the horseshoe crab harvest, they preemptively prevent the biomedical industry from establishing a foothold within their waters. At bottom, no state actively facilitating the biomedical horseshoe crab trade has outright banned the harvesting practice.[174]

Where the biomedical harvesting of horseshoe crabs persists, states must issue special harvesting permits as required under the ASMFC Horseshoe Crab FMP—separate from those permits issued for bait harvesting.[175] States are free to attach more stringent permit restrictions beyond those mandated by the Horseshoe Crab FMP. For example, Rhode Island requires biomedical horseshoe crabs to be returned to the waters from which they were taken within 72 hours of their bleeding.[176] However, enforcement is a separate issue. If violated, Rhode Island may revoke the holder's biomedical harvesting permits for, at most, the current and subsequent year.[177] Virginia requirements go beyond the Horseshoe Crab FMP, mandating that owners of biomedical facilities participate in the state's tagging program to evaluate the post-release mortality of bled horseshoe crabs.[178] Typically, state regulations do not stray far from one another or the Horseshoe Crab FMP—and certainly not with regards to affording greater welfare protections to the horseshoe crabs exploited for biomedical use within their borders.

However, in July 2023, Massachusetts DMF implemented the country's "first-ever biomedical harvest quota" of 200,000 horseshoe crabs per year, to cap total harvest and mortality across both bait and biomedical industries.[179] Massachusetts distributes this quota equally among active biomedical processors, but the previous year's biomedical harvest—

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for the relevant year. ATL. STATES MARINE FISHERIES COMM'N, ADDENDUM III TO THE INTERSTATE FISHERY MANAGEMENT PLAN FOR HORSESHOE CRAB 7 (2024), http://www.asmfc.org/uploads/file//56d7670dAddendumIII.pdf (imposing monitoring and reporting requirements on states facilitating biomedical harvesting). All ASMFC Horseshoe Crab FMP Reviews are available for download at ATL. STATES MARINE FISHERIES COMM'N, *Horseshoe Crab*, http://www.asmfc.org/species/horseshoe-crab. *See also* CITIZENS CAMPAIGN FOR ENV'T, *Protect Horseshoe Crabs Before It's Too Late* (June 20, 2024), https://www.citizenscampaign.org/whats-new-at-cce/protect-horseshoe-crabs-before-its-too-late (stating New York has not issued biomedical harvest permits in "over a decade"). One final note: Even if harvesters illicitly collected horseshoe crabs for biomedical use in Connecticut, the state ban's efficacy is doubtful. Violations rack up a measly $25 fine per unlawfully harvested "specimen." CONN. GEN. STAT. ANN. § 26-292d. The New York bill lacks any penalty provision whatsoever. N.Y. S.B. S3185–A.

174. Cramer, *supra* note 167.

175. *Best Management Practices*, *supra* note 118, at 4.

176. 250 R.I. CODE R. 90-00-5.7(C)(2)(c)(1) (2023).

177. 250 R.I. CODE R. 90-00-5.7(C)(2)(c) (2023).

178. 4 VA. ADMIN. CODE § 20-900-35(G) (2023) (supporting that such tagging programs are voluntary.) *See, e.g.*, *Horseshoe Crab Cooperative Tagging Program*, U.S. FISH & WILDLIFE SERV., https://www.fws.gov/project/horseshoe-crab-cooperative-tagging-program (last visited Nov. 29, 2023) (describing the voluntary federal horseshoe crab tagging program).

179. Press Release, *supra* note 159.

175,000—undercuts the quota's significance.[180] That is, the quota does not set a meaningful limit on biomedical use; it still allows for increased biomedical harvest over the current baseline.[181] In addition, Massachusetts DMF formally codified the otherwise non-binding ASMFC BMP in its regulations, and began requiring "daily reporting by all commercial harvesters to improve accountability and prevent quota overages." [182] Massachusetts DMF's new regulations increase transparency and accountability within a biomedical industry that has been described as a "black box of information."[183] However, Massachusetts DMF enacted these measures to "eliminate[] the potential for uncontrolled growth in the biomedical fishery, which could negatively impact the resource moving forward."[184] Thus, these regulations maintain an anthropocentric framework under which horseshoe crabs continue to be viewed as a "resource" to be conserved and managed for human benefit.

In April 2024, responding to public outcry about unsustainable harvesting of breeding horseshoe crabs, Massachusetts DMF promulgated regulations prohibiting the harvest of horseshoe crabs for both bait and biomedical use during the animals' spawning season. [185] Although a commendable step, the harvesting ban was not motivated by concern for the animals' inherent right to live free of human exploitation, but by a desire to efficiently manage a fishery resource for sustainable use. Massachusetts DMF's director stated that the agency focuses on conserving fisheries, and the spawning closures intend to "sustain[] [horseshoe crab] populations into the future."[186] But for whom? It is certainly not horseshoe crabs in their own right. Massachusetts DMF serves the recreational and commercial fishing industries—not the fished.[187] Even the group that spearheaded the advocacy for the spawning ban noted, while announcing its victory, that they will "keep fighting for stronger protections until shorebirds can once again feed on horseshoe crab eggs at beaches all over Massachusetts."[188] The horseshoe crab is, once again, missing.

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180. Press Release, *supra* note 159.

181. *Id.* (noting that the biomedical use quota is offset through a reduction—of 25,000 horseshoe crabs—in the state's bait crab quota).

182. *Id.* at 2.

183. Eisner, *supra* note 3.

184. Press Release, *supra* note 159.

185. 322 Mass. Code Regs. § 6.34(3)(b); *See also* MASS. AUDUBON*, We Won! Harvest of Spawning Horseshoe Crabs Banned in Massachusetts* (Mar. 22, 2024), https://www.massaudubon.org/news/latest/we-won!-harvest-of-spawning-horseshoe-crabs-banned-in-massachusetts (last visited May 23, 2024) (detailing, in brief, the history of the campaign that contributed to stronger regulations on horseshoe crab harvesting in Massachusetts) [hereinafter MASS. AUDOBON].

186. Moran, *supra* note 97.

187. Press Release, *supra* note 159.

188. MASS. AUDUBON, *supra* note 185.

Without a doubt, Massachusetts stands out in its implementation of biomedical regulations that surpass ASMFC FMP requirements and codifying the otherwise unenforceable BMP.[189] Though these welfarist measures better protect the well-being of horseshoe crabs within Massachusetts' borders, they remain anthropocentric and fail to fundamentally challenge the biomedical exploitation of these creatures. Massachusetts is more concerned with ensuring the sustained exploitation of horseshoe crabs as a fishery resource rather than safeguarding these animals' interest in avoiding capture, bleeding, and death for human benefit. Especially given that there exists an animal-free alternative to the LAL test, there should be a stronger push to replace, rather than refine, the biomedical use of horseshoe crabs. This shift would challenge the prevailing anthropocentric regulations and policies related to the biomedical horseshoe crab industry.

IV. REPLACING BIOMEDICAL HORSESHOE CRAB USE WITH AN EXISTING ANIMAL-FREE ALTERNATIVE: THE RFC TEST

The Reduction, Refinement, and Replacement (3Rs) framework, internationally accepted for governing "ethical" animal-dependent science, emphasizes reducing, refining, and replacing animal use "where possible."[190] Oftentimes, this triad of objectives are pursued simultaneously.[191] However, unlike many other instances of animal-based science and research, an available alternative to the horseshoe crab-dependent LAL test currently exists: the recombinant factor C (rFC) test.[192] This section first describes the development of the rFC test and explains the recently overcome bureaucratic roadblocks hindering widespread adoption of rFC for endotoxin testing within the U.S. biopharmaceutical industry.[193] Next, this section argues that due to an existing animal-alternative, efforts to improve horseshoe crab welfare should focus solely on replacing the LAL test with this alternative, rather than concurrently advocating for reduction or refinement—which risks legitimizing anthropocentricism and further entrenching the biomedical horseshoe crab industry.[194]

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189. Press Release, *supra* note 159.

190. Melanie L. Graham & Mark J. Prescott, *The Multifactorial Role of the 3RS in Shifting the Harm-Benefit Analysis in Animal Models of Disease*, 759 EUR. J. PHARMACOLOGY 19, 19 (2015).

191. *See* Paolo Verderio et al., *3Rs Principle and Legislative Decrees to Achieve High Standard of Animal Research*, 13 ANIMALS 277, 277 (2023) (explaining that the 3Rs principle requires a researcher to pay attention to all three prongs when planning an animal experiment).

192. Maloney et al., *supra* note 63, at 6.

193. *Id.* at 2.

194. In contrast, many other environmental or wildlife advocacy groups adopt the traditional 3Rs framework in their approach to the biomedical use of horseshoe crabs. For example, the Horseshoe Crab

A. Regulatory Roadblocks of rFC Development

In the 1990s, scientists synthesized a protein called rFC that can detect endotoxins, similar to the horseshoe crab blood-derived LAL.[195] Despite rFC's commercial availability since 2003, it has yet to displace the LAL test in the U.S.[196] Initially, concerns over its efficacy or a lack of data hindered the widespread adoption of this animal-free alternative for many years.[197] However, a 2018 review of multiple studies concluded that rFC tests identify endotoxins "equivalent to or better than LAL," and that rFC shows "strong efficacy across a range of uses and demonstrated high sensitivity [and] strong reliability."[198]

Notwithstanding the scientific community's endorsement of the rFC test's efficacy, U.S. pharmaceutical companies remain unlikely to switch over to the animal-free alternative. However, change appears to be just around the corner. All FDA-approved drugs must undergo endotoxin testing due to the significant public health concerns posed by these contaminants.[199] Naturally, biopharmaceutical manufacturers prioritize selecting a reliable and affordable endotoxin detection method to ensure product safety and obtain FDA approval for their products.[200] The intense federal regulation of endotoxin testing disincentivizes pharmaceutical manufacturers from innovating and deviating from recognized and tested methods.[201]

The FDA relies on the scientific nonprofit U.S. Pharmacopeia (USP) to develop national quality standards for pharmaceuticals.[202] As of September

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Recovery Coalition, which is "dedicated to ensuring the future of the American Horseshoe Crabs." *Our Goals*, HORSESHOE CRAB RECOVERY COAL., https://hscrabrecovery.org/goals/ (last visited May 23, 2024). While the coalition seeks to speed up adoption of synthetic alternatives to the LAL test, it also advocates for ending the harvest of *female* horseshoe crabs (but not male) so that their eggs can sustain other wildlife populations and *reforming* (but not ending) the horseshoe crab bleeding industry to require transparency and reduce mortality to zero. *Id.* These measures condone the *refinement* and *reduction* of the biomedical horseshoe crab industry, and therefore the industry's endurance. *Id.*

195. Maloney et al., *supra* note 63, at 2–3. Interestingly, a University of Pennsylvania Student, Aravind Krishnan, is developing a plant-based technology that might serve as an additional LAL test alternative. Dubbed "ToxiSense," the technology relies on a plant that, like horseshoe crab blood, reacts to endotoxins. Zoë Read, *'Blue-Blood' Horseshoe Crabs Suffer from Commercial Bloodletting. One Penn Student Says He Has an Answer*, NJ SPOTLIGHT NEWS (Mar. 28, 2024), https://www.njspotlightnews.org/2024/03/horseshoe-crabs-suffer-from-commercial-bloodletting-this-student-is-developing-an-alternative/ (last visited May 23, 2024).

196. Maloney et al., *supra* note 63, at 4, 6.

197. *Id.*

198. *Id.* at 4–5.

199. *Id.* at 2.

200. *Id.* at 6.

201. *Id.*

202. *Legal Recognition—Standards Categories*, USP, https://www.usp.org/about/legal-recognition/standard-categories (last visited Nov. 29, 2023); *USP and FDA Working Together to Protect Public Health*, USP, https://www.usp.org/public-policy/usp-fda-roles (last visited Nov. 28, 2023). In fact,

2024, U.S. biopharmaceutical companies that use a LAL alternative still must expend greater resources during the FDA approval process.[203] They must undergo a more burdensome and expensive process to validate their use of rFC in contrast to the "streamlined method of verification" for those means already endorsed by USP.[204] This extra regulatory hurdle discourages pharmaceutical companies from using available animal-free alternatives like rFC.[205] Casting itself as an "industry leader," Eli Lilly began transitioning to rFC in 2016 and currently tests 80% of its medicines using rFC rather than LAL.[206]

B. USP Approval of rFC

In August 2023, the USP Microbiology published a proposal on using animal-free alternatives, which included the rFC test and other similar synthetic reagents, in addition to current methods for endotoxin testing.[207] A year later, on July 26, 2024, USP finally approved the inclusion of these alternative endotoxin detection methods in the USP compendia via Chapter <86>.[208] The USP announced that this update to the USP compendia aligned with the organization's "commitment to expanding the use of animal-free methods and materials."[209] Prior to July 2024, the live rabbit and LAL tests were the only USP-endorsed methods of endotoxin testing in the U.S.[210] However, these animal-free endotoxin tests will merely supplement, not replace, Chapters <85> and <151> of the USP compendia, which respectively reflect USP endorsement of the horseshoe crab-derived LAL test and live rabbit-reliant pyrogen test.[211] USP will publish Chapter <86> for

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USP "sets standards for drug manufacturing in 150 countries." Freda Kreier, *Is an End to Using Imperiled Horseshoe Crabs for U.S. Drug Testing in Sight*, SCI. (Aug. 25, 2023), https://www.science.org/content/article/end-using-imperiled-horseshoe-crabs-u-s-drug-testing-sight (last visited Nov. 29, 2023).

203. Maloney et al., *supra* note 63, at 6.

204. *Id*.

205. *Id*.

206. Eli Lilly, *Sustainability Report: Biodiversity*, 42 (2023), https://sustainability.lilly.com/environmental/biodiversity (last visited Sept. 26, 2024).

207. *Expert Committee Proposes Chapter for Endotoxin Testing Using Non-Animal Derived Reagents*, USP (Aug. 22, 2023), https://www.usp.org/news/expert-committee-proposes-chapter-for-endotoxin-testing-using-non-animal-derived-reagents. This was not the first effort by USP to approve animal-free endotoxin tests. Two previous proposals were rejected due to insufficient data and committee infighting. Kreier, *supra* note 202; Cramer, *supra* note 167.

208. *Expert Committee Proposes Chapter for Endotoxin Testing Using Non-Animal Derived Reagents*, *supra* note 207.

209. *Id.*

210. Okun, *supra* note 4, at 200.

211. *Bacterial Endotoxin Test*, USP-NF/PF (May 1, 2018), https://online.uspnf.com/uspnf/document/1_GUID-F9D9BFA5-099F-452C-9711-47674B37C1CC_2_en-US; *Pyrogen Test*, USP-NF/PF (May 1, 2017),

early adoption in November 2024 and officially add it to the USP compendia in May 2025.[212]

Once USP formally includes rFC in the USP compendia, it is likely that the FDA will no longer require additional validation for biopharmaceutical manufacturers' use of rFC for endotoxin detection.[213] USP's approval effectively provides guidance that "will help place recombinant testing on equal footing with LAL."[214] Thus, biopharmaceutical companies will be more apt to transition to a horseshoe crab-free alternative when testing their medical drugs and devices for endotoxins.[215] However, placing rFC "on equal footing" as the LAL test fails to absolve us of our moral obligations owed towards horseshoe crabs.

V. RECOMMENDATIONS: DISRUPTING ANTHROPOCENTRICISM BY REPLACING LAL WITH RFC

Horseshoe crabs have an intrinsic interest in avoiding human exploitation, and their biomedical use blatantly violates this principle and upholds anthropocentricism. Particularly in light of rFC's pending approval, USP or government actors should implement measures strongly incentivizing drug manufacturers to fully replace LAL endotoxin testing with existing and reliable animal-free alternatives. Such affirmative means are preferable to merely allowing market forces to promote change, which reinforces anthropocentric logic.

A. Request USP Retract Its Endorsement of LAL

The approved chapter merely sets out "additional techniques" for endotoxin testing, namely, the LAL test laid out in Chapter <85>.[216] When announcing rFC's approval, USP makes it clear that "[m]anufacturers that currently use [LAL] for endotoxin testing can continue to do so and Chapter <86> has no impact on them."[217] The compendia update falls short of

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https://online.uspnf.com/uspnf/document/1_GUID-162C7E78-8A02-4423-970C-5DF047F57DC2_1_en-US.

212. *Expert Committee Proposes Chapter for Endotoxin Testing Using Non-Animal Derived Reagents*, *supra* note 207.

213. *See Guidance for Industry Pyrogen and Endotoxins Testing: Questions and Answers*, *supra* note 116, at 5 (noting that manufacturers using alternatives endotoxin methods "to those *in a USP compendial article*" must undergo additional validation measures) (emphasis added).

214. *Horseshoe Crab Recovery Coalition Celebrates U.S. Pharmacopeia Recognition of Synthetic Alternatives to Horseshoe Crab Blood*, HORSESHOE CRAB RECOVERY COAL. (July 27, 2024), https://hscrabrecovery.org/wp-content/uploads/2024/07/HCRC.USP_.pdf.

215. *Id.*

216. *Expert Committee Proposes Chapter for Endotoxin Testing Using Non-Animal Derived Reagents*, *supra* note 207.

217. *Id.*

mandating the complete replacement of the LAL test with animal-free alternatives. Instead, it condones the continued use of LAL, despite the LAL test's anthropocentric undergirding and severe negative impact on horseshoe crabs. In short, USP's guidelines fail to meaningfully encourage U.S. biopharmaceutical companies to transition away from LAL, and it is likely that the FDA will uncritically adopt USP's approach.[218]

Instead of approving synthetic reagents like rFC in addition to LAL, USP should instead remove LAL from the USP compendia to better align with its stated objective of "expanding the use of animal-free methods and materials."[219] In addition, the FDA should update its industry guidance for endotoxin testing to include rFC as an approved endotoxin test, subject to the same verification method that the LAL test has long benefited from. In its guidance, the FDA should put forth a recommendation, albeit nonbinding, that the industry transition away from LAL to rFC endotoxin testing. These measures would, in effect, turn the current regime on its head—switching out the long-held inferior status of animal-free endotoxin tests like rFC and the horseshoe crab-dependent LAL test. Biopharmaceutical manufacturers that use USP-endorsed toxicity tests during the FDA product-approval process save significant time and resources. By not only approving rFC but also delisting LAL, USP could create extra regulatory and financial hurdles for biopharmaceutical companies continuing to use LAL endotoxin testing. This would nudge the industry toward animal-free alternatives while avoiding harsher top-down measures (like an outright federal LAL ban) that would be more vulnerable to backlash.

B. Extend ESA Protections to Horseshoe Crabs

The federal government should also leverage the ESA to strongarm the industry into transitioning to animal-free endotoxin methods. As expressed by the Supreme Court, the ESA "represent[s] the most comprehensive legislation for the preservation of endangered species ever enacted by any nation."[220] While indisputably grounded in anthropocentric values,[221] the ESA can shield wildlife from human greed and exploitation. In the case of horseshoe crabs, an ESA listing could hasten the biomedical industry's adoption of rFC.

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218. *See* Candau-Chacon, *supra* note 113, at 20, 22 (demonstrating influence of USP compendia on FDA's regulatory approach to endotoxin testing).

219. *Expert Committee Proposes Chapter for Endotoxin Testing Using Non-Animal Derived Reagents*, *supra* note 207.

220. Tenn. Valley Auth. v. Hill, 437 U.S. 153, 180 (1978).

221. 16 U.S.C. § 1531(a)(3) (justifying the ESA on the basis that endangered and threatened "species of fish, wildlife, and plants are of esthetic, ecological, educational, historical, recreational, and scientific value *to the Nation and its people*") (emphasis added).

The ESA authorizes federal wildlife services to protect "any subspecies of fish or wildlife," (which expressly includes arthropods) that are endangered or threatened.[222] NOAA Fisheries is responsible for most marine species, while USFWS implements the ESA for terrestrial and freshwater species.[223] When determining whether a species warrants listing, the statute requires the services evaluate the following five factors: (1) "the present or threatened destruction, modification, or curtailment of its habitat or range;" (2) "overutilization for commercial, recreational, scientific, or educational purposes;" (3) "disease or predation;" (4) "the inadequacy of existing regulatory mechanisms;" and (5) "other natural or manmade factors affecting its continued existence."[224]

The ESA affords listed species robust protections. Crucially, ESA § 9 prohibits the "take" of endangered species from the wild.[225] Here, "take" means "to harass, harm, pursue, hunt, shoot, wound, kill, trap, capture, or collect, or to attempt to engage in any such conduct."[226] Regulations extend the "take" prohibition to most threatened species as well.[227]

NOAA Fisheries retains the authority to list horseshoe crabs under the ESA, and these creatures certainly merit either an endangered or threatened listing.[228] Various advocacy groups have already petitioned NOAA Fisheries to list the horseshoe crab. Friends of Animals filed their petition in December 2023, while a broader CBD-led coalition of animal and environmental groups filed theirs in February 2024.[229] Notwithstanding NOAA Fisheries' statutory obligation to respond to petitions within 90 days (at least "[t]o the maximum extent practicable"[230]), both petitions remain pending as of September 2024.[231]

CBD's petition compellingly presents data supporting the species listing, with an emphasis on the following statutory considerations: (1) the present or threatened destruction, modification, or curtailment of the horseshoe

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222. 16 U.S.C. §§ 1532(8), (16), 1533. "Endangered species" are those "in danger of extinction throughout all or a significant portion of its range," while "threatened species" are those "likely to become an endangered species within the foreseeable future throughout all or a significant portion of its range." 16 U.S.C. §§ 1532(6), (20).

223. NOAA, *Endangered Species Conservation: ESA Implementation*, https://www.fisheries.noaa.gov/topic/endangered-species-conservation/endangered-species-act-implementation (last visited Sept. 26, 2024).

224. 16 U.S.C. § 1533(a)(1)(A)–(E).

225. 16 U.S.C. § 1538(a)(1)(B).

226. 16 U.S.C. § 1532(19).

227. 50 C.F.R. § 17.31(a).

228. *See Endangered Species Conservation: ESA Implementation*, *supra* note 223.

229. NOAA, *Petitions Awaiting 90-Day Findings*, https://www.fisheries.noaa.gov/national/endangered-species-conservation/petitions-awaiting-90-day-findings (last visited Sept. 26, 2024).

230. 16 U.S.C. § 1533(b)(3)(A).

231. *Petitions Awaiting 90-Day Findings*, *supra* note 229.

crabs' habitat or range; (2) the overutilization for commercial purposes, particularly by the biomedical industry; (3) the inadequacy of existing regulatory mechanisms; and (4) other factors affecting the species' continued existence, such as climate change.[232] With the listing process already set in motion and the best available science conveniently compiled before it by the petitioners, [233] NOAA Fisheries must extend the ESA's protections to horseshoe crabs before it is too late.

By listing horseshoe crabs pursuant to the ESA, the federal government could undercut the biomedical industry's unjustified reliance on LAL for endotoxin detection. The ESA's blanket prohibition on the "take" of listed species would surely prevent the devastating collection and bleeding of horseshoe crabs. While the ESA allows exceptions for educational, scientific, and incidental take, the biomedical use of horseshoe crabs does not appear to fall under any of these categories.[234] By listing horseshoe crabs as either threatened or endangered and thereby prohibiting their "take," NOAA Fisheries could—and should—implement an immediately enforceable federal ban on their biomedical harvest. This would force the industry to rapidly transition to animal-free endotoxin methods like rFC.

C. Push for State Harvesting Bans

Under the cooperative federalism framework governing fishery management, states can leverage their primary regulatory authority to drive change by imposing blanket bans on horseshoe crab harvesting for biomedical use within their waters. For the six states steadfastly engaged in biomedical harvesting and others along the Atlantic coast, state legislatures should implement similar bans to those passed in Connecticut and sitting before New York's governor.

Some states can build upon existing efforts to protect horseshoe crabs by completely outlawing harvesting in their waters. South Carolina and New Jersey, which already prohibit bait harvesting, should expand their bans to encompass biomedical harvesting. Finally, in the wake of rFC's recent approval by USP, Massachusetts should replace its newly enacted biomedical

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232. CTR. FOR BIOLOGICAL DIVERSITY, *supra* note 101, at 54–120.

233. *Id.* at 3.

234. 16 U.S.C. § 1539(a)(1)(A)–(B). Although the biomedical use of horseshoe crabs could arguably fall within the "scientific purposes" exception to unlawful take, a distinction can be drawn between biomedical purposes as opposed to scientific purposes. Even if the biomedical use of horseshoe crabs *could* be exempted, NOAA Fisheries would retain *discretion* over whether to permit such scientific take. 16 § U.S.C. § 1539(a)(1). Hopefully, should horseshoe crabs achieve listing status, the existence of a USP-approved animal-free alternative to LAL would deter NOAA Fisheries from permitting any biomedical harvest to continue. *See also* Ghubril, *supra* note 95, at 298–301 (arguing listing horseshoe crabs under ESA would cause "production of LAL [to] cease").

harvesting quota with an outright ban on the practice. Legislatures in other states bordering horseshoe crab habitat should initiate similar bans.

While state-by-state efforts may curb the biomedical exploitation of horseshoe crabs within their borders, this approach risks reinforcing the ineffective patchwork of regulations that has long plagued the industry. Without uniform regulations, some states—including those along the Eastern seaboard that currently do not facilitate any biomedical harvest—stand to benefit economically by attracting more harvesting activity as others impose stricter protections. That is, states that resist bans could see increased biomedical harvesting in their waters, to the detriment of horseshoe crabs and their interests.

D. A Method of Last Resort: Leave it to the Market

If the above three measures fail, the subsequent challenge will be convincing the biopharmaceutical industry to uniformly shift from LAL to non-animal-derived toxicity tests without external pressure from either USP or the government. Though the ultimate goal is complete replacement, even a gradual transition driven by market changes would decrease demand for horseshoe crab blood and potentially undermine the biomedical horseshoe crab industry. Already, rFC pricing "is competitive with horseshoe crab-derived products and . . . likely to become even more advantageous [as] new suppliers enter[] the field."[235] The FDA's position that it will not license rFC suppliers, unlike LAL where only five suppliers are federally licensed,[236] also encourages healthy market competition that will further drive down rFC costs.[237]

On the bright side, biopharmaceutical industry leadership appears open to converting to animal-free endotoxin testing due to the potential for financial savings once USP approval removes bureaucratic barriers.[238] Yet, relying solely on market forces to drive change presents a drawback: the transition will likely be slow and motivated primarily by a desire to cut costs. The interests of horseshoe crabs are conspicuously absent—lost in the shadows of profit margins.

In sum, with USP's pending finalization of rFC standards in 2025, the biopharmaceutical industry must completely replace LAL with animal-free endotoxin testing. Ideally, USP can incentivize this shift by withdrawing its endorsement of LAL. Alternatively, NOAA Fisheries could list horseshoe

235. Maloney et al., *supra* note 63, at 7.

236. *Best Management Practices*, *supra* note 118, at 3.

237. Candau-Chacon, *supra* note 113, at 31.

238. *See* Maloney et al., *supra* note 63, at 7–8 ("rFC presents potential cost savings, and these are expected to become more significant now that patent protections have expired and more rFC manufacturers are expected to enter the market").

crabs pursuant to the ESA and effectively make the biomedical industry's "take" of horseshoe crabs in all federal waters unlawful. This would force a rapid industry-wide adoption of rFC. At a minimum, states should enact biomedical harvesting bans and take a clear stance to protect horseshoe crabs in their waters. Absent these top-down measures, market dynamics will likely promote a gradual industry shift. However, allowing the anthropocentric desire to cut costs to drive the replacement of LAL neglects our ethical duty to recognize the interests of horseshoe crabs and accelerate the shift via affirmative means.

As a team of scientists imploring an industry-wide transition to animal-free endotoxin testing methods stated, "[t]he move from rabbits to crabs occurred in the late 1970s; it is now time for the industry to modernize its methods and embrace a more humane and ecologically sustainable method of endotoxin testing."[239] This time, instead of merely changing the species and method of animal use, a transition to animal-free endotoxin testing like rFC fundamentally disrupts the anthropocentric assumption that animals can be harmed and exploited for toxicity testing. Mere refinement of the innately cruel, anthropocentric, exploitative, and wholly unnecessary biomedical horseshoe crab industry is insufficient. Rapid replacement of the antiquated horseshoe crab-derived LAL test is presently feasible and ethically mandatory.

CONCLUSION

Ever since scientists discovered the unique endotoxin-detecting properties of horseshoe crab blood during the late 20th century, the assumption that these prehistoric creatures can be used, abused, and drained of their blood for human benefit has rarely been questioned. Existing regulations remain hopelessly anthropocentric and insufficient in addressing the animal welfare concerns implicated in the multi-million-dollar industry that is raking in—quite literally—blood money.

We are fortunate that the biomedical exploitation of horseshoe crabs presents no ethical quagmire pitting the interests of humans against those of animals, which then must be balanced to arrive at an imperfect compromise. Here, humans can both forgo animal exploitation *and* continue advancing biomedical objectives. We already possess an animal-free alternative that is commercially available and as effective as the LAL test at detecting endotoxins. Although USP's recent approval of alternatives may spur widespread LAL replacement, USP and government actors should assume a

239. Maloney et al., *supra* note 63, at 7.

greater role in compelling industry-wide abandonment of LAL to adequately safeguard horseshoe crabs' interests.

For too long, we have forcibly extracted blue blood from live horseshoe crabs, and from that blood, we have developed countless life-saving medicines for human benefit. Now we have the opportunity to respond in kind—though unlike these living fossils (which are now dying), we have the distinct luxury of agency over the matter. Let us not squander this privilege, or this power. We gave horseshoe crabs no choice but to relinquish their blue blood. We, however, can choose to save the lives and honor the interests of these ancient mariners.