IT'S NOT EASY BEING GREEN: THE FDA'S DUTIES UNDER NEPA AND ESA WHEN APPROVING NEW DRUGS AND BIOLOGICAL PRODUCTS

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The Earth is in the midst of its sixth mass extinction event. While previous mass die-offs were caused by cosmic collisions, extraordinary geological events, or other dramatic natural occurrences, the current mass extinction is driven by one clever animal: humans. In particular, species such as amphibians, fish, and coral have been particularly devastated by the anthropogenic changes wreaking havoc on ecosystems, and it is estimated that thirty-two percent of all amphibians are likely to go extinct in the near future. One partial cause of amphibians and other aquatic species' global decline is pollution caused by the manufacturing, use, and disposal of human drug and biological products. While these compounds are essential to keeping humans healthy, they nonetheless result in severely harmful outcomes for aquatic life and thus need to be regulated more stringently in order to prevent deleterious impacts on fragile ecosystems and wildlife. In light of this grave situation, I argue that the Food and Drug Administration (FDA) must do better at meeting its obligations under the National Environmental Policy Act (NEPA) and the Endangered Species Act (ESA) when approving new drugs and biological products. Historically, the FDA has been lax about its obligations under these laws, but the urgency of this mass-extinction event requires a comprehensive commitment to the statutory obligations and goals of these laws. This paper begins with an analysis of why the FDA must be the one to undertake this obligation and then turns to a summary of NEPA, the ESA, and the FDA's relationship to NEPA and the ESA. Next, the paper argues for a more robust implementation of FDA's current NEPA regulations and an increased commitment to completing Section 7 consultations, before concluding with other actions the FDA should take to slow the global loss of certain species. While these actions may not have previously been a priority for the FDA, the FDA must ensure that it gathers the information necessary to prevent grievous harm to ecosystems, animals, and the people who reside in and rely on those ecosystems and animals.

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Introduction

Are your drugs environmentally friendly? It's possible that no one knows the answer to this question: not the companies inventing and producing pharmaceuticals in the first place, not the consumer taking their medications, and not the Food and Drug Administration ("FDA"), the agency "responsible for protecting the public health by ensuring the safety, efficacy, and security of human and veterinary drugs, biological products, and medical devices."[1] In fact, even the Environmental Protection Agency ("EPA") likely does not know the full environmental consequences of manufacturing, using, and disposing of the countless human drugs and biologics which have become integral to the health and daily well-being of most Americans.

This lack of environmental information is surprising and concerning; the pharmaceutical industry is massive, especially in the United States, and it has the potential to significantly impact the environment. On average, Americans use far more medication than people in other developed countries.[2] Over sixty-six percent of adults in America use prescription drugs,[3] and it's estimated that there were 194 billion daily doses of prescription drugs administered in 2021.[4] The FDA has approved or otherwise regulates over 20,000 prescription drugs, hundreds of biological products,[5] and somewhere between 100,000 and 300,000

1. *FDA Basics*, U.S. Food & Drug Admin. (Mar. 3, 2018), https://perma.cc/DTW5-4HHT.
2. Jessica Glenza, *Americans spend too much on pharmaceuticals, health outcomes lag behind*, PBS NewsHour (August 29, 2017), https://perma.cc/W7MJ-LN48.
3. Emily Ihara, *Challenges for the 21st Century: Chronic and Disabling Conditions: Prescription Drugs*, Geo. Health Pol'y Inst. (2022), https://perma.cc/6R9T-S8YH.
4. The Use of Medicines in the U.S. 2022, IQVIA Inst. for Human Data Sci., 2 (2022).
5. *Fact Sheet: FDA at a Glance*, U.S. Food & Drug Admin. (Aug 17, 2022), https://perma.cc/7QLR-5E4M.

over-the-counter drugs.[6] It is also estimated that one out of ten pharmaceutical products have a notable environmental risk,[7] and one major global study found that over twenty-five percent of all river sites sampled worldwide had pharmaceutical contamination at levels dangerous to aquatic wildlife due to either toxicity or risk of antibiotic resistance.[8] Various environmental groups, including EPA,[9] the European Environment Agency,[10] and advocacy groups like the Environmental Working Group[11] and the Natural Resources Defense Council[12] have raised alarms about the growing threat of pharmaceutical pollution in water.[13]

Moreover, there is undeniable evidence that the global environment is increasingly at risk of catastrophe due to climate change, pollution, and biodiversity collapse.[14] Notably, one component of the biodiversity crisis may be linked with pharmaceuticals and drug residues released into the ecosystem: global amphibian species decline.[15] More than seventy percent of amphibian

6. *Over-the-Counter (OTC) Drugs Branch: The OTC Drug Review*, U.S. Food & Drug Admin. (Feb. 2, 2015), https://perma.cc/4EML-M5K7.
7. Anette Küster & Nicole Adler, *Pharmaceuticals in the environment: scientific evidence of risks and its regulation*, 369 (1656); Phil. Transactions Royal Soc'y London B: Biological Sci. 1, 3 (2014).
8. John L. Wilkinson et al., *Pharmaceutical pollution of the world's rivers*, 119 PNAS 1, 1–6 (2022).
9. *See Contaminants of Emerging Concern including Pharmaceuticals and Personal Care Products*, EPA (Feb. 21, 2013), https://perma.cc/V9S8-38CY.
10. *See generally* European Environment Agency, *Pharmaceuticals in the environment—results of an EEA workshop*. EEA Tech. Rep. no. 1/2010 (2010).
11. *Pharmaceuticals Pollute U.S. Tap Water*, Env't Working Group (June 1, 2009), https://perma.cc/DCB5-Q4QC.
12. *See* Mae Wu et al., NRDC, Dosed Without Prescription: Preventing Pharmaceutical Contamination of Our Nation's Drinking Water, 3–6 (2009).
13. *See id.* at 1 ("The presence of pharmaceuticals in our waterways and drinking water is a complex and potentially serious problem that has gained national attention with the public, lawmakers, and regulators.").
14. *See* Owen Dyer, *Global ecological disaster predicted in next 50 years*, 330 BMJ 809, 809 (2005).
15. *See* Andrés Egea-Serrano et al., *Understanding of the impact of chemicals on amphibians: a meta-analytic review*, 2(7) Ecol. Evol. 1382, 1382, 1392 (2012) (stating that pollution, including certain wastewater pollutants sourced from drugs, such as acetaminophen, is "a major threat to amphibians by having large effects on abnormality frequency and medium effects on survival and mass" and that "the impact of pollutants is even higher" than their meta-analysis suggested because other factors significant to survival like "activity level, habitat use, courtship, and swimming performance are all affected by pollution."); Moa Säfholm et al., *Risks of hormonally active pharmaceuticals to amphibians: a growing concern regarding progestagens*, 369 Phil. Transactions Royal Soc'y London B: Biological Sci. 1, 1–5 (2014) (finding adverse impacts to reproduction in amphibians but noted a lack of information on the toxicity of many pharmaceuticals); Eliana Ibrahimi et. al., *Mixed modeling of the effect of pharmaceutical pollution on the metamorphosis of amphibians from incomplete trajectory data*, Rsch. Square, 14 (Jan. 4, 2023) (finding that over-the-counter painkillers like ibuprofen impact tadpole growth); Jake M. Martin et al., *Evidence of the impacts of pharmaceuticals on aquatic animal behaviour: a systematic map protocol*, 10 Env't Evidence 26 (2021) (summarizing how "pharmaceuticals specifically designed to modify behaviour are present

species globally are in decline, and extinction rates for amphibians are over 200 times the background rate of extinction, with up to thirty-two percent of all amphibians facing extinction.[16] Currently, close to fifty different amphibian species are listed by the U.S. Fish and Wildlife Service ("USFWS") as endangered or threatened under the Endangered Species Act ("ESA").[17]

The dramatic decrease in amphibian populations has led some scientists to declare another mass extinction event, comparable to the death of the dinosaurs in the Triassic and the emptying of the oceans during the Permian extinction.[18] Although other factors, such as climate change and habitat loss, are also contributing to this crisis, environmental contaminants, including the pollution from drug manufacturing, use, and disposal, nonetheless play a role in this disturbing decline in amphibian species.[19] It is also becoming obvious that other aquatic species, such as fish[20] and coral,[21] which are also in global decline, are negatively affected by pharmaceuticals entering the aquatic environment.[22]

Given the severity of global biodiversity loss in aquatic animal species, especially amphibians, the dearth of information on how regulated substances impact the environment and imperiled species is striking when agencies like the FDA and EPA have been regulating pharmaceuticals and the environment for decades. In theory, EPA-administered environmental laws such as the Clean

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in the aquatic environment and the tissues of aquatic animals (e.g. antidepressants, anxiolytics, antipsychotics" and that these pharmaceuticals "have the potential to modify or disrupt animal behaviour, or may change behaviour as side-effects differing from their principal course of treatment."); OECD, P*harmaceutical Residues in Freshwater: Hazards and Policy Responses*, OECD Studies on Water (2019), (noting that pharmaceutical pollution causes reproductive changes in fish and amphibians and calling for an increased understanding of environmental impacts, which as of the time of publication were inadequate); James P. Collin et al., Extinction in Our Times: Global Amphibian Decline 101 (2009).

16. T.B. Hayes et al., *The cause of global amphibian declines: a developmental endocrinologist's perspective,* 213(6) J Exp. Biol. 921, 921 (2010).
17. U.S. Fish and Wildlife Service, *Listed Animals*, Env't Conservation Online System, https://perma.cc/9V92-48W5.
18. David B. Wake & Vance T. Vredenburg, *Are we in the midst of the sixth mass extinction? A view from the world of amphibians*, 105 PNAS 11466, 11466–667 (2008), (comparing current amphibian declines to the other 5 mass extinction events); Jacopo Dal Corso et al., *Environmental crises at the Permian–Triassic mass extinction*, 3 Nature Rev. Earth & Env't 197,197 (2022).
19. Wake & Vredenburg, *supra* note 18, at 11466; T.B. Hayes et al., *supra* note 16, at 921; Christopher Regnault, *Unexpected metabolic disorders induced by endocrine disruptors in Xenopus tropicalis provide new lead for understanding amphibian decline*, 115 PNAS E4416, E4420 (2018).
20. Wilfried Sanchez et al., *Adverse effects in wild fish living downstream from pharmaceutical manufacture discharges*, 37 Env't Int'l 1342, 1347 (2011) ("These effects . . . [severe signs of endocrine disruption as shown by high level of circulating VTG concentrations, high proportion of intersex fish and a male-biased sex-ratio] . . . were associated to fish population disturbances with a decrease of occurrence of sensitive fish species and fish density.").
21. Eileen M. Nalley, *Water quality thresholds for coastal contaminant impacts on corals: A systematic review and meta-analysis*, 794 Sci. Total Env't 148632, 148640 (2021).
22. *See id.*; *see generally* Sanchez, *supra* note 20.

Water Act,[23] the Toxic Substances Control Act (TSCA),[24] or the Resource Conservation and Recovery Act (RCRA),[25] should be sufficient to regulate pharmaceutical pollution, especially once it becomes waste or enters waterways, but in practice the EPA has been unable to meaningfully address pharmaceutical pollution using these laws.[26] Relatedly, the FDA has largely ignored the environmental harms of the products it has jurisdiction over, leading some scholars to criticize the FDA for shirking environmental responsibility.[27]

While FDA's organic statute, the Federal Food, Drug, & Cosmetics Act ("FDCA"),[28] as amended, contains no specific environmental mandate related to drugs and biologics and instead charges the FDA only with the responsibility to "promote the public health by promptly and efficiently reviewing clinical research and taking appropriate action on the marketing of regulated products in a timely manner" and to ensure that "human and veterinary drugs are safe and effective,"[29] the FDA is nonetheless obliged to consider the environment in some of the actions it takes related to human drugs and biologics because of the National Environmental Policy Act ("NEPA").[30] NEPA requires all agencies, including the FDA, to conduct an environmental analysis of all "major federal actions" that significantly affect the "quality of the human environment."[31] Additionally, all federal agencies are required, under Section 7(a)(2) of the Endangered Species Act, to consult with the USFWS or the National Marine Fisheries Service ("NMFS") to "insure that…any action authorized… is not

23. Clean Water Act, 33 U.S.C. §§ 1251–1387.
24. Toxic Substances Control Act, 15 U.S.C. §§ 2601–2697.
25. Resource Conservation and Recovery Act, 42 U.S.C. §§ 6901–6992k.
26. *See infra* Part I.. This paper uses the term "pharmaceutical pollution" to describe pollution caused by human drugs and biologics. Other papers may include personal care products and cosmetics in the scope of pharmaceutical pollution, but those topics are beyond the scope of this analysis.
27. Margot J. Pollans & Matthew F. Watson, *FDA as Food System Steward*, 46 Harv. Envtl. L. Rev. 1 (2022); Gabriel Eckstein, *Drugs on Tap: Managing Pharmaceuticals in Our Nation's Waters*, 23 N.Y.U. Env't. L.J. 37, 80 (2015); John Wood, *Can We Teach Old Laws a New Risk: Federal Environmental Law, Risk Management Theory, and Contamination of U.S. Water Supplies with Pharmaceutical and Personal Care Products*, 21 N.Y.U. Env't. L.J. 193, 230–34 (2014); Christopher T. Nidel, *Regulating the Fate of Pharmaceutical Drugs: A New Prescription for the Environment*, 58 Food & Drug L. J. 81 (2003); Zoe M. Grant, *The Plastic Pollution Crisis: Combatting Plastics Through NEPA Challenges to FDA's Food Contact Substance Regulations*, 35 J. Env't L. & Litig. 371 (2020); Joseph A. Gorman, *Drugs in Our Water: A Legal Proposal for Responsible Nationwide Pharmaceutical Consumption*, 26 J. Land Use & Env't. L. 147, 164 (2010).
28. Federal Food, Drug, and Cosmetic Act, 21 U.S.C. §§ 301–399i.
29. 21 U.S.C. § 393(b)(1)–(b)(2)(B); *see also* Pollans & Watson, supra note 27, at 7 ("The FDCA contains no express mention of environmental issues.").
30. Note that the Food Safety Modernization Act, does require the consideration of the environment as well, but these provisions do not relate to human drugs and biologics. 21 U.S.C. § 350h(a)(3)(D).
31. National Environmental Policy Act of 1969, 42 U.S.C. §§ 4332(c).

likely to jeopardize the continued existence of any endangered species or threatened species or result in the destruction or adverse modification of habitat of such species."[32] Based on the requirements found in these two statutes, the FDA has the authority to consider the environmental consequences of the drugs and biologics it approves. Therefore, the question of why the environmental harms caused by FDA-regulated human drugs and biologics are so poorly regulated can be answered by analyzing the FDA's lackluster implementation of NEPA and the ESA.

This paper proceeds in four parts. Part I explains the statutory and regulatory background which has created the need for the FDA to take a more active role in regulating the environmental impacts of drugs and biologics. Part II introduces NEPA and Section 7 of the ESA generally. Part III discusses FDA's current regulations, informal guidance, and some history related to NEPA procedures and Section 7 consultations for agency actions involving human drugs and biologics. Part IV argues that while FDA's current NEPA regulations, especially the "extraordinary circumstances" exemption, and Section 7 of the ESA, may actually be adequate to protect the environment as they are written, those regulations are not being implemented robustly enough in light of the biodiversity crisis. The paper then concludes with a summary of why the FDA should more fully implement the "extraordinary circumstances" exemption in its NEPA regulations and more frequently utilize the Section 7 consultation process in light of anthropogenic climate change and the sixth mass extinction event.

I. Why the FDA?

The FDA is a closely scrutinized agency; the actions it takes impact the daily lives of most Americans, and so it is regularly in the public eye.[33] After all, Americans spend an estimated 20 cents out of every dollar for FDA-regulated products.[34] Because of this public visibility, the FDA is frequently in the news and receives substantial congressional oversight.[35] It has been subject to countless congressional hearings since the 1960s, in light of the precedent set by Senator Estes Kefauver, who launched a relentless attack on the FDA and the pharmaceutical industry in "hearing after hearing," and it is unlikely

32. Endangered Species Act, 16 U.S.C. § 1536(a)(2); 50 C.F.R. §§ 402.12–402.16.

33. Peter Barton Hutt, *Turning Points in FDA History*, *in* Perspectives on Risk and Regulation: The FDA at 100 14, 22 (Arthur A. Daemmrich, Joanna Radin, Chemical Heritage Foundation, eds. 2007). For an example of FDA in the news, *see* Matthew Perrone, *Speedier drug approvals hit slowdown as FDA faces scrutiny*, APNews, Dec. 7, 2022, https://perma.cc/M98Y-2YMD; Rachel Roubein, *The Makena controversy puts FDA's accelerated drug approval program under scrutiny*, Wash. Post, Oct. 22, 2022, https://perma.cc/V6MK-743Z.

34. *Fact Sheet: FDA at a Glance*, U.S. Food & Drug Admin. (Aug 17, 2022), https://perma.cc/7QLR-5E4M.

35. Hutt, *supra* note 33, at 14, 22.

that this scrutiny will soon cease given the agency's importance.[36] Therefore, it is unsurprising that this oft-scrutinized agency has also been criticized for its environmental impact, given the precedent of general media and congressional interest. However, perhaps it is nonetheless shocking that part of the reason for these environmental critiques is that other agencies are actually incapable of monitoring the environmental impacts of FDA-approved products. This section explains why this is by exploring the relationship between the FDA, EPA, and state environmental agencies.

A. Jurisdictional Scope of the FDA

To explain why other agencies lack jurisdiction to regulate the environmental impacts of drugs and biologics, it is first useful to define the scope of FDA's jurisdiction over products which contribute to pharmaceutical pollution. The FDA has jurisdiction over foods, drugs, biologics, medical devices, electronic products giving off radiation, cosmetics, veterinary products, and tobacco products.[37] For the purposes of this paper, two definitions are of note—drugs and biologics—because these substances are a significant component of pharmaceutical pollution or may otherwise have the potential to cause pharmaceutical pollution in the future.[38] The FDCA drug definition is capacious: it includes, at least in part, something which is "intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease" and "articles (other than food) intended to affect the structure or any function of the body of man or other animals."[39] Biologics, or biological products, like drugs,[40] are intended for use in the "prevention, treatment, or cure of a disease or condition of human beings," but they are regulated under the Public Health Services Act, which defines a biological product as a drug consisting of "virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, or analogous product."[41] The FDA must approve both drugs and biologics before they may be marketed.[42] Drugs are subject to the pre-market approval process,

36. *Id* at 22 ("As a result all who have served at the FDA subsequently have spent a lot of time testifying on Capitol Hill, and the FDA has received daily coverage by the news media. The FDA's tenure as an obscure federal agency will never return.").
37. 21 U.S.C. § 301 et seq; *What does FDA regulate?*, U.S. Food & Drug Admin. (Jan 1, 2018), https://perma.cc/7CSV-757Z.
38. Maite Ortúzar et al., *Pharmaceutical Pollution in Aquatic Environments: A Concise Review of Environmental Impacts and Bioremediation Systems*, 13 Frontiers Microbiology 1, 2 (2022), (describing the pharmaceutical pollution as most commonly including "non-steroidal anti-inflammatory drugs (NSAIDs), b-blockers, psychoactive compounds, analgesics, antibiotics, endocrine disruptors, antiretroviral drugs, and drugs to treat cancer").
39. 21 U.S.C. § 321(g)(1).
40. *See* Peter Barton Hutt et. al., Food and Drug Law 90 (5th ed. 2022); 21 C.F.R 600.3(h).
41. 42 U.S.C. § 262(i); 21 C.F.R 600.3(h).
42. 21 U.S.C § 355(a); 42 U.S.C. § 262(a)(1)(A).

which consists of a New Drug Application (NDA), and biologics apply for approval through an analogous process called a biologics licensing application.[43]

Although other FDA-regulated products, like cosmetics and veterinary products, may also contribute to pharmaceutical pollution, the scope of this paper is limited to drugs and biologics since those categories have received less attention in legal scholarship but have been extensively identified as potentially problematic by scientific literature.[44] Drugs and biologics compose a significant proportion of the FDA's activities, as the regulatory activities related to drugs and biologics compose just over forty percent of the FDA's total budget.[45] Additionally, the "FDA has plenary authority over the approval, prescription, and distribution of all drug products,"[46] making the FDA well-positioned to regulate the environmental consequences of drug products.

B. Other Agencies Lack Jurisdiction or Capability to Address This Problem

Neither federal nor state agencies apart from the FDA are suited or are otherwise permitted to address the problem of pharmaceutical pollution caused by drugs and biologics.

EPA has authority to regulate pollution under several environmental statutes such as the Clean Water Act, the Clean Air Act,[47] RCRA, and TSCA.[48] However, this jurisdiction over pollutants once they enter the environment or are disposed of does not mean EPA intrudes into the regulation of the chemicals that the FDA has primary jurisdiction over, such as drugs and biologics.[49] Rather, EPA defers to the FDA on the regulation of drugs and biologics, including those which may contribute to pharmaceutical pollution.[50] In general, prevention of pollution is preferable to the control of pollution once it has entered the environment; this alone should incentivize the FDA to help manage

43. *Frequently Asked Questions About Therapeutic Biological Products*, U.S. Food & Drug Admin. (July 7, 2015), https://perma.cc/T58C-H2NL.

44. *See, e.g.*, Pollans & Watson, *supra* note 27, at 27, 39–48 (analyzing the FDA's relationship with environmental laws in the food context but only briefly in the drug context); Wood, *supra* note 27, 200, 228–36 (analyzing why the FDA should comply with NEPA in the drug approval context, but not the biologics context); Roger Collier, *Swallowing the pharmaceutical waters*, 184 Can. Med. Assoc. J. 163, 163–64 (2012).

45. *Fact Sheet: FDA at a Glance*, U.S. Food & Drug Admin. (Aug 17, 2022), https://perma.cc/7QLR-5E4M.

46. Peter Grossi & Daphne O'Connor, *FDA preemption of conflicting state drug regulation and the looming battle over abortion medications*, 10 J. L. and the Biosciences 1, 5 (2023).

47. Clean Air Act, 42 U.S.C. §§ 7401–7671.

48. Clean Water Act, 33 U.S.C. §§ 1251–1387; Clean Air Act, 42 U.S.C. §§ 7401–7671; Resource Conservation and Recovery Act, 42 U.S.C. §§ 6901–6992k; Toxic Substances Control Act, 15 U.S.C. §§ 2601–2697.

49. Jennifer A. Staman, Cong. Rsch. Serv., R43609, Enforcement of the Food, Drug, and Cosmetic Act: Select Legal Issues (2018).

50. Wood, *supra* note 27, at 208.

pharmaceutical pollution at the point of use and disposal.[51] However, due to complications and gaps within the main federal pollution control laws administered by EPA, even if EPA regulated more aggressively in this area, it would be insufficient to solve this dire problem without some actions taken by the FDA as well.[52]

The Clean Water Act applies only to "navigable waters," or "waters of the United States."[53] The Supreme Court interprets "waters of the United States" to include only "geographic[al] features that are described in ordinary parlance as 'streams, oceans, rivers, and lakes'" and "adjacent wetlands that are 'indistinguishable' from those bodies of water due to a continuous surface connection."[54] This narrow definition does not apply to many ecologically significant wetlands and other water features, such as ephemeral streams and non-navigable waters, where amphibians and fish reside,[55] meaning that the Clean Water Act could not protect large swaths of aquatic habitat even if EPA sought to strictly regulate pharmaceutical pollution in waterways.[56] More significantly, though, the Clean Water Act almost exclusively regulates point-source pollution, which would not prevent the majority of pharmaceutical pollution, which generally derives from non-point sources.[57] Point source pollution is defined by the Clean Water Act as:

> "[A]ny *discernible, confined and discrete conveyance*, including but not limited to any pipe, ditch, channel, tunnel, conduit, well, discrete fissure, container, rolling stock, concentrated animal feeding operation, or vessel or other floating craft, from which pollutants are or may be discharged. This term does not include agricultural storm water discharges and return flows from irrigated agriculture."[58]

Anything which is not a point source is a non-point source.[59]

Drugs and biologics rarely enter waterways via a discernible, confined, and discrete conveyance. Rather, drugs and biologics enter the environment by several means, including "usage by individuals, pets, and livestock; excretion

51. Vinish Kathuria, *Pollution: Prevention vs Control: Is EOP Treatment the Solution?*, 36 Econ. & Pol. Wkly. 2745, 2745 (Jul. 21, 2001).
52. Joseph A. Gorman, *Drugs in Our Water: A Legal Proposal for Responsible Nationwide Pharmaceutical Consumption*, 26 J. Land Use & Env't. L. 147, 163–64 (2010) ("An effective resolution to the dilemma must address the root of the problem.").
53. 33 U.S.C. § 1362(7); 33 U. S. C. §§ 1311(a), 1362(12)(A).
54. Sackett v. EPA, 598 U.S. 651, 671 (2023) (citing Rapanos v. United States, 547 U.S. 715, 755 (2006)).
55. E.A. Crunden, *Post-Sackett, chaos erupts for wetlands oversight*, E&E News (June 2, 2023), https://perma.cc/DFR5-DUCD.
56. Revised Definition of "Waters of the United States", 40 C.F.R. § 120 (2023).
57. 33 U. S. C. §§1311(a), 1362(12)(A); Wood, *supra* note 27, at 244–47, 269–70.
58. 33 U.S.C. § 1362(14) (emphasis added).
59. *Basic Information About Nonpoint Source (NPS) Pollution*, EPA (Dec. 22, 2022), https://perma.cc/F4VD-B36R .

of un-metabolized drugs; drain disposal of unused medication; sewage system infrastructure leakage . . . and direct releases from bathing and swimming," making them non-point sources generally.[60] This means that the Clean Water Act cannot address the environmental impacts of drugs and biologics after they have already become pollutants in the water because the Act simply does not authorize EPA to directly regulate nonpoint sources. The few point sources that release drugs and biologics into waterways––hospital effluent, domestic sewage treatment plants, and untreated sewage overflow––are also either not amenable to federal regulation under the Clean Water Act due to the practical and technological limitations of conventional wastewater treatment methods or otherwise have not yet been regulated effectively.[61] For example, EPA has only required point-source hospitals that directly discharge wastewater into waterways to implement the lowest standard of pre-treatment technology, known as "best practicable control technology… practically applied,"[62] to remove conventional pollutants, such as biochemical oxygen demanding materials, total suspended solids, and pH-altering wastewater.[63] If a hospital discharges wastewater indirectly, meaning that the hospital's waste is connected to a wastewater treatment facility, there are no federal pollution limitations or pretreatment requirements imposed whatsoever under the Clean Water Act,[64] despite the fact that many wastewater treatment facilities do not have the proper technologies to fully remove any pharmaceutical waste released by these facilities from

60. Wood, *supra* note 27, at 200.

61. *See id.* at 245; *see also* Nadeem Khan et al., *Recent trends in disposal and treatment technologies of emerging-pollutants- A critical review*, 122 Trends In Analytical Chemistry 115744, 115744 (2020) ("In case of pharmaceutical residues, it has been observed that only 18–32% of the pharmaceutical residues could be degraded by the secondary treatment of these seven technologies and it has been increased to 30–65% by tertiary treatment. As far as the pharmaceutical residues are concerned, it has been observed that MBR [membrane bioreactors] removes the residues with the efficiency of 28–100%, varying for each pharmaceutical."); Emad K. Radwan et al., *Recent trends in treatment technologies of emerging contaminants*, Env't Quality Mgmt., 10 (2022) ("The complex molecular structure, nonbiodegradability, and low concentration of ECs are the main factors that limit their removal by the conventional methods. Most of the ECs have complex molecular structure that not only cannot be metabolized by microorganisms but may even impede their activity. Moreover, the oxidant and/or disinfectant used during the treatment processes reacts with some ECs resulting in the generation of a group of ECs known as emerging DBPs. Thus, *conventional treatment methods not only ineffective in removing ECs* but also aggravate the problem via generation of metabolites and transformation by-products which are usually more harmful, toxic, and persistent, than their precursors.") (internal citations omitted) (emphasis added).

62. Off. of Water, EPA, EPA-821-R-22-004, Effluent Guidelines Program Plan 15, 20–22 (2023), https://perma.cc/3G6G-FKD4.

63. 40 C.F.R. § 460.12.

64. *See* Management Standards for Hazardous Waste Pharmaceuticals and Amendment to the P075 Listing for Nicotine, 84 Fed. Reg. 5816, 5893 (2019).

the water.[65] Likewise, effluent limitations for pharmaceutical manufacturing facilities under the Clean Water Act do not actually set any discharge limits on pharmaceutical substances and instead only regulate other industrial pollutants such as benzene, acetone, and ammonia.[66] And there is evidence to suggest that the lack of discharge limits results in significantly higher than normal concentrations of pharmaceutical pollution, even in treated wastewater effluent from wastewater treatment facilities that receive water from pharmaceutical manufacturing plants; such treated wastewater effluents have been found to have up to 1000 times more pharmaceutical pollution than standard treated wastewater effluent does.[67]

Other federal statutes, such as TSCA and RCRA, which could theoretically be used to regulate hazardous or environmentally risky substances like pharmaceuticals before they enter the environment or harm vulnerable populations,[68] cannot be used to effectively promulgate drug and biologics pollution regulations, either. TSCA includes an "FDA exemption"; both the text of the statute[69] and the legislative history[70] make it clear that EPA lacks jurisdiction under TSCA to regulate "any food, food additive, drug, cosmetic, or

65. *Id*; *See also* Off. of Water, EPA, EPA–821–R–09– 009, Occurrence of Contaminants of Emerging Concern in Wastewater from Nine Publicly Owned Treatment Works 5–6, 27 (2009).

66. *See* Pharmaceutical Manufacturing Point Source Category, 40 C.F.R. § 439.14 (2003).

67. Patrick J. Phillips et al., *Pharmaceutical Formulation Facilities as Sources of Opioids and Other Pharmaceuticals to Wastewater Treatment Plant Effluents*, 44 Env't Sci. and Tech. 4910, 4910, 4913 (2010).

68. This is particularly significant for the type of pollution caused by drugs and biologics due to technological limitations in removing them from the environment once they have been released. *See* Nadeem A. Khan et al., *Recent trends in disposal and treatment technologies of emerging-pollutants- A critical review*, 122 Trends in Analytical Chemistry 115744, 115744 (2020) ("In case of pharmaceutical residues, it has been observed that only 18–32% of the pharmaceutical residues could be degraded by the secondary treatment.").

69. *See* 15 U.S.C. § 2602(2)(B)(vi). The definition of "chemical substances" specifically excludes FDA-regulated substances, and the other operative portions of TSCA *only* apply to chemical substances, meaning that if something is not a chemical substance, it is outside of TSCA's jurisdiction. *See, e.g.*, 15 U.S.C. § 2603 et seq ("if the Administrator finds that the manufacture, distribution in commerce, processing, use, or disposal of a chemical substance or mixture, or that any combination of such activities, may present an unreasonable risk of injury to health or the environment. . ."); 15 U.S.C. § 2604 ("no person may manufacture a new chemical substance . . .").

70. H.R. Rep. No. 94-1341, at 418 (1976) ("The intent of the Committee in excluding these items . . . [drugs and other FDA regulated items] . . . is to exclude from coverage under the bill items which may be regulated under the Federal Food, Drug, and Cosmetic Act. By adopting the definitions given the items by that Act the Committee has made the exclusion of these items from the bill coextensive with the authority to regulate them under the Federal Food, Drug, and Cosmetic Act. Thus, if an item cannot be regulated as a food, food additive, drug, cosmetic, or device under that Act because it does not come within the definitions in that Act, it is not the intent of the Committee to exclude it from coverage under the bill.").

device . . . when manufactured, processed, or distributed in commerce for use as a food, food additive, drug, cosmetic, or device."[71] Moreover, when describing TSCA's jurisdictional reach, EPA has explicitly acknowledged its limited authority over drugs under the "FDA exemption" and "has consistently taken the position that if the chemical substance is being exclusively manufactured, processed, distributed in commerce, and used for uses falling within the Food and Drug Administration's (FDA's) jurisdiction" then EPA lacks authority to regulate the substance under TSCA.[72]

RCRA, unlike TSCA, does not explicitly prevent EPA from regulating pharmaceutical pollution, but nonetheless RCRA does not meaningfully grant EPA the authority to solve this problem, either. For one, RCRA bifurcates responsibility for regulating solid waste between the federal government and the states; states have primary responsibility over "solid waste,"[73] whereas the federal government takes responsibility for regulating, from "cradle to grave," only "hazardous" solid waste.[74] Because most pharmaceuticals do not fit under the definition of hazardous waste,[75] EPA can only regulate the disposal of a small subset of pharmaceutical substances under RCRA.[76] RCRA's inadequacies in mitigating pharmaceutical pollution are illustrated best by the limited and historically unenforced[77] regulations applicable to pharmaceutical waste. The current pharmaceutical-specific hazardous waste regulations *only* apply to healthcare facilities and reverse distributors, which essentially are large retail pharmacies and healthcare facilities that retain waste pharmaceuticals in order to receive a credit from that pharmaceutical's manufacturer.[78] This excludes other facilities, such as domestic drug users disposing of medications or pharmaceutical manufacturers, who may otherwise be disposing of pharmaceuticals in significant quantities.[79]

71. 15 U.S.C. § 2602(2)(B)(vi). *See also* Letter from Mark A. Greenwood, EPA Director of Pollutions Prevention and Toxics, to David J. Hayes, Latham & Watkins (June 10, 1994), https://perma.cc7AHJ-MGUX.
72. Letter from Mark A. Greenwood, *supra* note 71, at 1.
73. 42 U.S.C. § 6902(a)(1).
74. *Resource Conservation and Recovery Act (RCRA) Overview*, EPA (Feb. 21, 2024), https://perma.cc/KX8E-EXHS; 42 U.S.C. § 6903.
75. Thomas Brugato et al., EPA's Final Hazardous Waste Pharmaceuticals Rule Has Significant Implications for Pharmaceuticals and Product Recalls, Covington Client Alerts 1–2 (Jan. 8, 2019).
76. *See* 40 C.F.R. § 261.2, 261.3, 261.33.
77. EPA Office of Inspector General, Report No. 12-P-0508, EPA Inaction in Identifying Hazardous Waste Pharmaceuticals May Result in Unsafe Disposal 9, 11 (2012).
78. Management Standards for Hazardous Waste Pharmaceuticals and Amendment to the P075 Listing for Nicotine, 84 Fed. Reg. 5816, 5817, 5820, 5835, 5895 (2019).
79. 40 C.F.R. 266.501(f).

Moreover, under this rule, EPA puts the burden on the healthcare facility to determine what is and is not hazardous waste,[80] a notoriously convoluted activity,[81] something which raises serious compliance concerns, even for the narrow category of pharmaceuticals covered by this rule.[82] Despite calls for EPA to identify in greater detail which pharmaceuticals are hazardous waste in order to help healthcare facilities comply with the rule,[83] EPA has been reluctant to do so. The agency has even declared that "it is difficult to provide a precise number of pharmaceuticals that are considered hazardous waste" because of how many drugs are approved for sale in the United States.[84]

In sum, the Clean Water Act could only be used to regulate pharmaceutical pollution coming from a narrow subset of pollution sources and over a limited percentage of waterways, TSCA functionally does not apply to pharmaceuticals at all, and RCRA at best could only be used to regulate a small class of pharmaceuticals at the federal level. Thus, based on these limitations, EPA's actions under the major federal environmental statutes are not likely to sufficiently address the pollution problems caused by products regulated by the FDA.

Agencies other than EPA similarly lack influence in this field. For example, the Drug Enforcement Administration can regulate the disposal of controlled substances,[85] but controlled substances only represent a small portion of all prescription and over-the-counter drugs.[86] Likewise, the Agency for Toxic Substances and Disease Registry, which protects the public from hazardous wastes, cannot regulate hazardous pharmaceuticals because it is a purely advisory agency lacking independent rulemaking authority.[87]

State agencies are similarly incapable of managing the environmental consequences of the manufacturing, use, and disposal of drugs and biologics.

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80. *See* 84 Fed. Reg. 5816, 5819, 5942 (codified at 40 C.F.R. 266.502(c)).
81. Even EPA itself admits that hazardous waste identification can be "a difficult and confusing task," since "the RCRA regulations establish a complex definition of the term 'hazardous waste'" EPA, EPA530-K-05-012, Introduction to Hazardous Waste Identification 1 (2005), https://perma.cc/Q5VG-V2NJ. For an illustration of how many factors are involved with the hazardous waste determination, *see* Robert V. Percival, et al., Env't Regul.: Law, Sci., And Pol. 329–31 (Aspen Publishing 9th. ed. 2021).
82. 84 Fed. Reg. 5816, 5843.
83. *See* EPA Off. of Inspector General, *supra* note 77, at 1.
84. EPA, EPA 530-F-22-003, EPA's Ban On Sewering Pharmaceuticals: Introductory Fact Sheet 2 (2022), https://perma.cc/3D5A-JA5Z.
85. 21 U.S.C. § 822(g)(1)(B)–(g)(5); 21 C.F.R. § 1317.
86. Over 19,000 prescription drugs are approved for marketing, whereas there are a few hundred substances on the DEA's controlled substance list. FDA, FDA at a Glance (2018), https://perma.cc/F9QG-43QF; *see* U.S. Dep't of Just., Lists of: Scheduling Actions, Controlled Substances Regulated Chemicals (2023).
87. *See ATSDR Background and Congressional Mandates*, Agency for Toxic Substances and Disease Registry (July 5, 2018), https://perma.cc/QQ4N-BU4V; *ATSDR Frequently Asked Questions*, Agency for Toxic Substances and Disease Registry (May 27, 2020), https://perma.cc/4HQN-S49A; 42 U.S.C. § 9604(h)(i).

For one, states cannot approve or ban the marketing and distribution of prescription drugs used in interstate commerce themselves; the FDCA preempts state law in this domain.[88] Additionally, while states may regulate non-point source pollution per the Clean Water Act by setting Total Maximum Daily Loads (TMDLs),[89] or "the maximum amount of a pollutant allowed to enter a waterbody so that the waterbody will meet and continue to meet water quality standards for that particular pollutant,"[90] it seems that no states so far have set limits on pharmaceutical pollution in waterways.[91] However, given that states have struggled in the past to set TMDLs for more traditional sources of pollution because of scientific uncertainty and fears about the difficulty of implementing

88. The FDA has been vested with responsibility for approving new drugs before they are used in interstate commerce. 21 U.S.C. § 355; Catherine M. Sharkey, *States v. FDA*, 83 Geo. Wash. L. Rev. 1609, 1614–15 (2015). At least one federal court case has prohibited a state from banning a drug when it disagreed with FDA's determination of that drug's safety and efficacy by holding that the FDCA preempted such an action. *Zogenix, Inc. v. Patrick*, No. 14-11689-RWZ, 2014 WL 1454696 at *1–2 (D. Mass. Apr. 15, 2014). For over-the-counter drugs, states' actions are expressly preempted by 21 U.S.C. § 379r(a). 21 U.S.C. § 379r(a). Preemption doctrine is generally muddled, but it nonetheless stands to reason that a state cannot directly second-guess the FDA's determination that a drug is safe and effective by, for example, banning it altogether. *See* Catherine M. Sharkey, *States v. FDA*, 83 Geo. Wash. L. Rev. 1609, 1614–15. 1628 (2015).

89. *See* 33 U.S.C. § 1313.

90. *Overview of Total Maximum Daily Loads (TMDLs)*, EPA (Nov. 30, 2022), https://perma.cc/3WKH-UMKA.

91. For example, a report describing novel strategies for managing pharmaceutical pollution mentions that states may implement TMDLs, but the article included no references to any already promulgated state water quality standards. Gabriel Eckstein & George W. Sherk, Alternative Strategies for Managing Pharmaceutical and Personal Care Products in Water Resources 19 (2011). Otherwise, though, this determination was based on a review of the following state TMDL's and impaired water listings: Florida, New York, New Jersey, Maine, Nevada, Virginia, North Carolina, South Carolina, Minnesota, Nebraska, Iowa, Missouri, Massachusetts, California, Oregon. *See* Fla. Admin. Code § 62-304; N.Y. Dep't Env't. Conservation, Final New York State 2018 Section 303(d) List of Impaired/TMDL Waters (2020); *New Jersey TMDLs*, State of N. J. Dep't Env't Prot., https://perma.cc/J9F9-JKL9; *TMDLs approved by the Federal Environmental Protection Agency (EPA)*, Me. Dep't of Env't Prot., https://perma.cc/Q9J2-N4VV (non-point sources do not include pharmaceuticals); *Total Maximum Daily Loads (TMDLs)*, Nev. Div. of Env't Prot., https://perma.cc/F6Y2-G6KN; *Approved TMDLs*, Va. Dep't of Env't Quality, https://perma.cc/V6LP-S8DE (list of TMDLs by pollutants does not include any pharmaceuticals); *Draft and Approved TMDLs*, N.C. Dep't of Env't Quality, https://perma.cc/4WLC-YL3E; South Carolina: *Approved TMDLs*, S.C. Dep't of Health and Env't Control, https://perma.cc/374G-9V4A; Minnesota's Impaired Waters and TMDLs Approved TMDLs and WRAPS (2023), https://perma.cc/5MAF-RPZK; *A List of TMDLs in Nebraska*, Neb. Dep't of Env't and Energy, https://perma.cc/A3X6-HWUH; *Water Quality Assessments Impaired Waters List*, Iowa Dept. of Nat. Res., https://perma.cc/VM97-UG9Q; Mo. Dept. of Nat. Res., 2022 EPA Approved Section 303(d) Listed Waters (2024), https://perma.cc/GLD3-KN9U; *Integrated Lists of Waters & Related Reports*, Mass. Dep't of Env't Prot., https://perma.cc/UWZ3-ZUMZ; *Or. TMDLs Approved by EPA*, https://perma.cc/C7VV-LWBF.

TMDLs,[92] it is unlikely that states will soon move to meaningfully regulate pharmaceutical pollution under the Clean Water Act given the complexity and uncertainty involved with such a task. And, as noted, prevention of pollution is better than control of pollution,[93] and a state TMDL standard would thus be a suboptimal regulatory path, especially considering the widespread impacts of pharmaceutical pollution.[94]

Therefore, since the FDA is the only agency that can meaningfully address the environmental impacts of drugs and biologics,[95] it has a unique and important responsibility to consider the environment in actions it takes related to those substances. In fact, it is required by law in some cases to conduct environmental reviews, even if it has infrequently done so in the past, which has led some critics to declare that the FDA may be violating federal environmental laws.[96] Regardless of whether the FDA is unlawfully abrogating its duties under environmental laws, at the very least, the FDA must take its duties more seriously given the gravity of this issue; pharmaceutical pollution is contributing to a mass-extinction event, and action must be taken to slow the ongoing biodiversity crisis.[97]

II. NEPA and the ESA

Under NEPA and Section 7 of the ESA, the FDA must consider the environment and endangered species. Accordingly, the scope of the FDA's authority to take environmentally protective actions is broader than the agency's traditional mission would imply.

A. NEPA

NEPA is a powerful information-gathering environmental statute[98] which requires the government to consider, "to the fullest extent possible"[99] the

92. Paula J. Lebowitz, *Land Use, Land Abuse and Land Re-Use: A Framework for the Implementation of TMDLs for Nonpoint Source Polluted Waterbodies*, 19 Pace Env't L. Rev. 97, 100 (2001).

93. *See supra* note 51, and accompanying text.

94. *See supra* notes 7–13, and accompanying text.

95. *See supra* Part I; *see also* Eckstein, *supra* note 27, at 77.

96. *See* Nidel, *supra* note 27, at 101 (stating that the FDA is "willfully blind" to environmental consequences and that "[i]t is an arbitrary and capricious abdication of . . . [the FDA's] duty under the federal scheme, if the agency fails, in light of new evidence, to consider all of the relevant indicators of the environmental impact of its actions."); *see also* Pollans & Watson, supra note 27, at n. 74 ("Some commentators argue that FDA regularly violates, if not the letter, then at least the spirit of, NEPA.").

97. *See supra* notes 14–22, and accompanying text.

98. *See* Bradley C. Karkkainen, *Toward a Smarter NEPA: Monitoring and Managing Government's Environmental Performance*, 102 Colum. L. Rev. 903, 909–16 (2002).

99. Calvert Cliffs' Coordinating Comm., Inc. v. U.S. Atomic Energy Comm'n, 449 F.2d 1109, 1114 (D.C. Cir. 1971).

environmental impact of "major Federal actions significantly affecting the quality of the human environment."[100] NEPA is an ambitious-sounding statute, as it could theoretically alter or impact most federal activities (what federal activities are not major or do not somehow impact the environment at least indirectly, after all?), but it is a surprisingly brief law and is much shorter on details than it is on grandiose language about environmental protection.[101] While NEPA "declares that it is the continuing policy of the Federal Government . . . to use all practicable means and measures . . . to create and maintain conditions under which man and nature can exist in productive harmony,"[102] the main significance of the Act comes only from the requirement to create a "detailed statement" analyzing the "environmental impact" of any proposed major federal actions which "significantly [impact] the human environment."[103] That "detailed statement" is commonly known as an environmental impact statement (EIS).[104] An EIS must include a description of any "adverse environmental effects" and "alternatives to the proposed action."[105] One other notable component of NEPA is that it created the Council on Environmental Quality (CEQ), an executive office that primarily promulgates regulations directing agencies' NEPA compliance.[106] Since NEPA is such a short statute, CEQ regulations are crucial to expound the sparse details present in the text and shape how agencies implement their own NEPA procedures.[107]

In 2023, Congress substantially amended NEPA for the first time since it was signed into law in 1970.[108] Many of these amendments focused on streamlining NEPA review, for example, by imposing time limits for agencies to complete environmental analyses and setting page limits.[109] Other amendments moderately narrowed NEPA's reach to focus on a more limited range of environmental impacts and alternatives to the proposed federal action[110] and codified previous judicial interpretations of NEPA which held that the law only

100. 42 U.S.C. § 4332.
101. David G. Burleson, *NEPA at 21: Over the Hill Already?*, 24 Akron L. Rev. 623, 623–46 (1991) (describing how some have called NEPA as being lofty but having no substance).
102. 42 U.S.C. § 4331.
103. 42 U.S.C. § 4332(C).
104. 40 C.F.R. § 1502.
105. 42 U.S.C. § 4332(C).
106. Percival, et al., *supra* note 81, at 815.
107. *See id.* at 814–15.
108. Michael D. Smith et al., Highlighting Key Changes to the National Environmental Policy Act, WSP (July 31, 2023), https://perma.cc/YK9V-H8HX.
109. Hina Gupta et al., The Fiscal Responsibility Act's Modest NEPA Amendments to Streamline Project Review, JD Supra (June 14, 2023), https://perma.cc/XM2R-FLPM.
110. *Id.*

applies when an agency has discretion in taking a certain action.[111] Additionally, the amendments likely limited NEPA's scope by formally defining "major federal action" to mean actions that are subject to "*substantial* federal control and responsibility," as determined by the agency taking said action.[112]

Previously, the definition of "major federal action" was found only in CEQ's interpretations of the law,[113] and for decades CEQ held that the definition of "major" was not linked to the level of involvement the federal government had but instead depended on the likelihood that the action would have significant effects on the environment.[114] In short, from the 1970s until 2020, when the Trump Administration significantly overhauled CEQ's NEPA regulations,[115] "major" did not have a meaning independent from "significantly affecting"[116] meaning that the level of federal involvement did not matter as much as how much the activity affected the environment. Yet even the Trump administration's narrowing of the regulatory definition of "major federal action," which stayed in effect after the Biden Administration rolled back some of the significant changes in the Trump-era NEPA regulations,[117] was broader than this new statutory definition, due to the inclusion of the word "substantial."[118] The term "substantial," as used to modify "major federal action," is a wholly new addition to the statutory text of NEPA[119] and has not yet been clearly defined, either in the new statutory text[120] or in the proposed CEQ regulations implementing the amendments to the law, which as of writing are not final.[121] However,

111. *See* 42 U.S.C. § 4336(e)(10)(vii); Dep't of Transp. v. Pub. Citizen, 541 U.S. 752, 769 (2004) (holding that it would violate an internal 'rule of reason' to require an agency to prepare a full EIS due to the environmental impact of an action it could not refuse to perform).
112. 42 U.S.C. § 4336e(10)(a) (emphasis added).
113. *Compare* Nina M. Hart & Linda Tsang, Cong. Rsch. Serv., IF11549, The Legal Framework of the National Environmental Policy Act 1 (2021), *with* 42 U.S.C. § 4336e(10) (2023).
114. The 1978 NEPA regulations defining major federal action were in effect until the Trump administration. 85 Fed. Reg. 43,304, 43304, 43345; Hart & Tsang, *supra* note 113, at 1; 87 Fed. Reg. 23,453, 23,454; *see also* 40 C.F.R. § 1508.18 (1978).
115. 85 Fed. Reg. 43,304, 43304, 43345; Lisa Friedman, Trump Weakens Major Conservation Law to Speed Construction Permits, NYTimes (July 15, 2020), https://perma.cc/MM6X-83G4.
116. 85 Fed. Reg. 43,304, 43345.
117. *See* 87 Fed. Reg. 23,453, 24,469–70 (note how the definition of "major federal action" was not changed in this rulemaking).
118. *See* Jayni Hein, *Amendments to the National Environmental Policy Act (NEPA): Permitting Reform in Context*, Inside Energy and Env't (June 7, 2023), https://perma.cc/SC4S-ZSYJ.
119. *See id.*; *compare* National Environmental Policy Act of 1969, P.L. 91-190 (1970), *with* 42 U.S.C. § 4331 et. seq., *and* 42 U.S.C. § 4336e.
120. *See* 42 U.S.C. § 4336e; Hannah Perls, *Key Changes in CEQ's Proposed Phase 2 Regulations Implementing NEPA*, Harv. L. Sch. Env't & Energy L. Prog. (August 23, 2023), https://perma.cc/AJ2Z-Z5RZ.
121. National Environmental Policy Act Implementing Regulations Revisions Phase 2, 88 Fed. Reg. 49,924.

the proposed CEQ regulations do at least attempt to outline general categories of "major federal actions" and include many of the same activities described in previous iterations of NEPA regulations, such as "[g]ranting authorizations, including permits, licenses, rights-of-way, or other authorizations," adopting official policies, rules, and regulations, "[c]arrying out specific projects," and "[p]roviding financial assistance."[122]

The full consequences of this definitional change on NEPA's implementation are uncertain for now, though it undoubtedly has the potential to limit NEPA's scope,[123] because whether something is a "major federal action" is a key threshold question that determines whether the statute applies to an agency's activities at all.[124]

The other major threshold question which determines whether NEPA applies to a certain agency action is whether an action significantly impacts the environment;[125] indeed, even under the prior, more expansive definition of "major federal actions," few federal agency activities resulted in an EIS,[126] in part because under NEPA each agency may determine for itself when actions *significantly impact the environment*.[127] Thus, if something is a "major federal action," even under NEPA's previous, more broad definition, an agency may nonetheless bypass NEPA's EIS requirements by determining that the activity does not have a "reasonably foreseeable" significant effect on the environment.[128] The significance of the effect on the environment is based on an analysis of both the "context" and "intensity" of the activity.[129]

An agency has two main ways to formally declare that an activity does not significantly impact the environment and is thus not subject to NEPA's EIS requirements; it may either declare that certain activities are de facto exempted

122. *Id.* at 49,924, 49,987; 40 C.F.R. § 1508.1(u)(1) (2023).

123. Stephen M Siros & Arie Feltman-Frank, *Avoiding Default and Streamlining NEPA—Can the Fiscal Responsibility Act of 2023 Accomplish Both Objectives?*, Jenner & Block Corporate Env't Lawyer Blog (May 31, 2023), https://perma.cc/Q8CC-EK3R.

124. Douglas S. Cram et al., *An Introduction to NEPA: The National Environmental Policy Act of 1969*, N.M. State Coll. Agric. Consumer and Env't Sci. 2 (Mar. 2017).

125. Madeline June Kass, *A NEPA Climate Paradox: Taking Greenhouse Gases into Account in Threshold Significance Determinations,* 42 Ind. L. Rev. 47, 55 (2009).

126. U.S. Gov't Accountability Off., GAO-14-369, National Environmental Policy Act: Little Information Exists On NEPA Analyses 7 (2014) ("CEQ estimates that… less than 1 percent [of NEPA analyses] are EISs.").

127. 42 U.S.C. § 4332(2)(C).

128. 42 U.S.C. § 4336(b)(1); 42 U.S.C. § 4336(e)(10); 42 U.S.C. § 4332(2)(C).

129. Both the historical definitions of significance, from 1978 until 2020, and the proposed regulations implementing the new NEPA amendments state that the significance determination is based on context and intensity; *see* Kass, *supra* note 125, at 56; 40 C.F.R.1501.3(d) (proposed regulation, in 88 Fed. Reg. 49,925, 49,969).

from NEPA analyses by designating them as "categorical exclusions," or it may issue Findings of No Significant Impacts (FONSIs) on a case-by-case basis.[130]

Categorical exclusions are defined as categories of actions which normally do not have a significant effect on the human environment and "therefore do not require preparation of an environmental assessment or environmental impact statement."[131] Lawfully under NEPA, an agency can designate broad categories of actions that it concludes do not warrant an EIS or an environmental assessment by identifying them as categorically excluded in their NEPA procedures and regulations.[132] Actions categorically excluded impose few, if any, legal requirements related to environmental review and do not require the production of the environmental documents that make up the core of NEPA—that is, environmental assessments and EIS's.[133] The most recently proposed NEPA regulations even suggest that an agency does not need to publicly post any documentation supporting its decision to apply a categorical exclusion, unless an "extraordinary circumstance" exists.[134]

FONSIs, on the other hand, are issued after a shortened, preliminary environmental review known as an environmental assessment (EA).[135] EAs are conducted for major federal actions that are not subject to categorical exclusions but also either "do[] not have a reasonably foreseeable significant effect on the quality of the human environment" or have an unknown significance to the environment.[136] An EA results in either the agency later conducting a complete EIS or a FONSI, but most commonly EAs conclude with a FONSI.[137]

In sum, due to the use of categorical exclusions and the interim step of EAs, agencies typically only complete an EIS if: (1) an activity is not categorically excluded; (2) an EA is completed; and (3) that EA concludes there will be a significant environmental impact. If any one of these requirements is not met, then an agency will not have to complete a full EIS. Of course, if it is obvious

130. Previously, categorical exclusions and FONSIs were creatures of regulation. The 2023 NEPA amendments formally codified them. 42 U.S.C. § 4336e(1), (7).

131. 40 C.F.R § 1501.4 (2022); *see* 42 U.S.C. § 4336e(1) ("The term "categorical exclusion" means a category of actions that a Federal agency has determined normally does not significantly affect the quality of the human environment").

132. 40 C.F.R § 1501.4 (2022). Note that certain categorical exclusions are statutorily established. U.S. Gov't Accountability Off., GAO-14-369, National Environmental Policy Act: Little Information Exists On NEPA Analyses, 3(2014)

133. Kevin H. Moriarty, *Circumventing the National Environmental Policy Act: Agency Abuse of the Categorical Exclusion*, 79 N.Y.U. L. Rev. 2312, 2321 (2004).

134. *See* 40 C.F.R. § 1501.4(b) (proposed 2023); 88 Fed. Reg. 49924, 49970.

135. 40 C.F.R. § 1501.6 (2020).

136. 42 U.S.C. § 4336(b)(2).

137. *See* U.S. Gov't Accountability Off., GAO-14-369, National Environmental Policy Act: Little Information Exists On NEPA Analyses 3, 7 (2014) (finding that only 1% of projects require an EIS, even though 5% of projects require an EA, suggesting that a significant portion of the EA-projects do not complete an EIS later); 42 U.S.C. § 4336(b)(2).

that an action will affect the human environment, then an agency may begin with an EIS, instead of first conducting an EA, but under the new amendments to NEPA, unless the effects of the action are "reasonably foreseeable," the agency may simply first conduct an EA or rely on a categorical exclusion.[138]

These procedural requirements—to either complete an EIS or an EA and subsequent FONSI, or to issue categorical exclusions—are essentially all NEPA requires.[139] Even in cases where a full EIS must be produced, NEPA does not actually mandate any substantive result based on that EIS.[140] As long as an agency shows that it at least considered the environment and alternatives to the proposed action, it has fulfilled its obligations under the statute.[141] An agency can make the environmentally-worst decision out of all the alternatives, and a court likely will uphold that decision.[142] Because of this, NEPA has received a significant amount of criticism. It has been declared to be only "essentially procedural" by the courts and referred to as a "paper tiger,"[143] "bureaucratic red-tape,"[144] and a "weakling in search of a reason to live."[145]

Nonetheless, NEPA is an important environmental statute. NEPA has been called the nation's environmental law "Magna Carta" because it greatly increases the ability of the public to learn of and potentially influence various federal activities that impact the environment through a public participation process.[146] Since an EIS must go through a public notice and comment period, individuals and groups interested in a proposed project may directly share their

138. 42 U.S.C. § 4336(b).

139. *See* Strycker's Bay Neighborhood Council, Inc. v. Karlen, 444 U.S. 223, 227 (1980).

140. *Id.*

141. *Id.* Some courts have even found EIS's to be acceptable when they only consider two alternative actions in total, one of which being a no-action alternative. *See North Idaho Community Action Network v. U.S. Dept. of Transp.*, 545 F.3d 1147, 1153–54 (9th Cir. 2008); *Citizens Against Burlington, Inc. v. Busey*, 938 F.2d 190, 193 (D.C. Cir. 1991).

142. Many courts are hesitant to deeply analyze the adequacy of an EIS, which has resulted in little attention to NEPA's substance. *See, e.g.*, *Trout Unlimited v. Morton*, 509 F.2d 1276, 1283 (9th Cir. 1974) (stating that the adequacy of an EIS depended on compliance with procedural rules and that "an EIS is in compliance with NEPA when its form, content, and preparation substantially (1) provide decision-makers with an environmental disclosure sufficiently detailed to aid in the substantive decision whether to proceed with the project in the light of its environmental consequences, and (2) make available to the public, information of the proposed project's environmental impact and encourage public participation in the development of that information."); *see also* Karkkainen, *supra* note 98, at 910.

143. Calvert Cliffs' Coordinating Comm., Inc. v. U.S. Atomic Energy Comm'n, 449 F.2d 1109, 1114 (D.C. Cir. 1971).

144. Michael C. Blumm & Keith Mosman, *The Overlooked Role of the National Environmental Policy Act in Protecting the Western Environment: NEPA in the Ninth Circuit*, 2 Wash. J. Env't L. & Pol'y 193, 193, 195 (2012).

145. Burleson, *supra* note 101, at 638.

146. *See* Daniel R. Mandelker, *The National Environmental Policy Act: A Review of Its Experience and Problems*, 32 Wash. U. J. L. & Pol'y 293, 293 (2010); Amanda Jahshan, *NEPA: The Magna Carta of Environmental Law*, NRDC (July 26, 2013), https://perma.cc/53BM-HBXR.

opinions on it.[147] Additionally, NEPA, when combined with the Administrative Procedure Act, makes it possible for people to challenge agency actions that do not adequately take the environment into consideration.[148] If, for example, an agency does not produce an EIS when it should have done so, an environmental plaintiff can bring suit against that agency claiming their decisions were "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law."[149]

NEPA has also had positive impacts insofar as it obliges agencies to consider environmental values in their decision-making, even if they ultimately do not make the most environmentally-conscious decision,[150] something which many scholars believe has generated a more robust and better decision-making process overall.[151] NEPA also serves as a powerful information-gathering tool, and research surveys conducted by CEQ suggest that the public's understanding of environmental law has grown increasingly sophisticated as the information NEPA reviews provide is disseminated and publicized.[152] At the very least, NEPA forces agencies to be more transparent and gives more people more information on the environmental ramifications of the government's actions.[153] In the context of the biodiversity crisis, this information may be especially important for environmental regulators, local government agencies, and advocates who are trying to ensure that sensitive ecosystems and species are sufficiently protected.

B. Section 7 of the ESA

Section 7(a)(2) is a critical provision of the ESA[154] that requires federal agencies to consult with the appropriate mission agency, either the USFWS

147. *National Environmental Policy Act Review Process*, EPA, https://perma.cc/V95D-N256.

148. Ilyssa Birnbach, Note, *Newly Imposed Limitations on Citizens' Right to Sue for Standing in a Procedural Rights Case*, 9 Fordham Env't L. J. 311, 311 (1998).

149. 5 U.S.C. § 706(2)(a).

150. *Strycker's Bay Neighborhood Council, Inc. v. Karlen*, 444 U.S. 223, 228 (1980) (concluding the agency "considered the environmental consequences of its decision . . . NEPA requires no more").

151. Karkkainen *supra* note 98, at 910–11; Mandelker, *supra* note 145, at 294.

152. Council on Env't Quality, The National Environmental Policy Act: A Study of Its Effectiveness After Twenty-five Years 17, 43 (1997); Todd S. Aagaard, *A Functional Approach to Risks and Uncertainties Under NEPA*, 1 Mich. J. Env't & Admin. L. 87, 88, 93 (2012) (referring to NEPA as having "information-forcing" requirements).

153. Aagaard, *supra* note 151, at 93.

154. Fla. Key Deer v. Stickney, 864 F. Supp. 1222, 1226 (S.D. Fla. 1994) ("The heart of the Endangered Species Act lies in Section 7, 16 U.S.C. § 1536, which sets forth certain requirements for all federal agencies whose activities may impact endangered species or their critical habitats."); *see generally* Theodore Z. Wyman, *Construction and Application of the Consultation Requirement Under Section 7 of the Endangered Species Act, 16 U.S.C.A. § 1536(a) to (d)*, 1 A.L.R. Fed. 3d Art. 4 (Originally published in 2015).

or NMFS, before taking discretionary actions.[155] The goal of Section 7(a)(2) consultation is to ensure that an agency's actions are not likely to jeopardize the continued existence of any endangered or threatened species or result in the destruction or adverse modification of critical habitat.[156] The definition of agency action under Section 7 is much broader than the definition of major federal action under NEPA—it encapsulates any discretionary action an agency takes, funds, or authorizes, including "all activities or programs of any kind,"[157] and therefore covers actions that would not be subject to environmental review under NEPA.[158] Section 7 review may be consolidated with an EA completed under NEPA, streamlining the process, but a NEPA EA or EIS alone is insufficient to meet the obligations an agency has under Section 7 of the ESA.[159]

The Section 7 process begins with an informal consultation initiated by the agency that is taking the action which may adversely impact an endangered or threatened species.[160] This is an informal communication period between the action agency and USFWS or NMFS about actions that are likely to adversely affect endangered or threatened species.[161] At this time, USFWS or NMFS may provide a list of species or critical habitats that may be present in the area that will be impacted by the proposed action.[162] After the informal consultation, the federal agency determines whether or not the proposed action is actually likely to adversely impact an endangered or threatened species or their critical habitats. If the agency determines that adverse impacts are unlikely, and USFWS or NMFS concurs, then the Section 7 process concludes.[163]

However, if an agency determines that an action is likely to adversely impact an endangered or threatened species or their habitats, then the ninety-day formal

155. 16 U.S.C. § 1536(a); 50 C.F.R. §§ 402.12–402.16; 50 C.F.R. §§ 402.03. Note that Section 7 of the ESA also has language imposing obligations on all federal agencies to promote the conservation of species and to "utilize their authorities in furtherance of the purposes of this chapter by carrying out programs for the conservation of endangered species and threatened species listed." 16 U.S.C. § 1536(a)(1). However, this provision has not been widely used or interpreted. *See* Sarah Krakoff & Shawn Finley, U.S. Fish and Wildlife Serv., Memorandum on Federal Agency Obligations under Section 7(a)(1) of the Endangered Species Act 1 (Feb. 6, 2024).

156. 16 U.S.C. § 1536(a)(2).

157. 50 C.F.R. §402.02; 16 U.S.C. § 1536(a)(2). Note that the "discretionary" requirement is not part of the definition of action, but rather comes from 50 C.F.R. §402.03.

158. *See* 42 U.S.C. § 4332; 40 C.F.R. § 1508.18.

159. 50 C.F.R. § 402.06.

160. 50 C.F.R. § 402.13(a); *Endangered Species Act Section 7 Consultation*, U.S. Fish and Wildlife Serv., https://perma.cc/MPY6-GWSS.

161. 50 C.F.R. § 402.13(a)-(b); Erin Ward & Pervaze A. Sheikh, Cong. Rsch. Serv. IF12423, Endangered Species Act (ESA) Section 7 Consultation 1 (June 7, 2023), https://perma.cc/KSV7-QXQE.

162. *Endangered Species Act Section 7 Consultation*, U.S. Fish and Wildlife Serv., https://perma.cc/MPY6-GWSS.

163. 50 C.F.R. § 402.13(c).

consultation process begins.[164] At this time, USFWS or NMFS and the action agency continue to share information regarding the environmental impacts of the proposed action. Per federal regulations, "[f]ormal consultation is terminated with the issuance of the biological opinion," and typically USFWS and NMFS have forty-five days to complete a biological opinion.[165] A biological opinion includes either conservation measures and any other measures needed to reduce harm to endangered or threatened species if USFWS or NMFS find the action is "[l]ikely to jeopardize the continued existence of a listed species or result in the destruction or adverse modification of critical habitat," or otherwise only contains a finding that an action is not likely to jeopardize endangered species.[166]

III. FDA's Implementation of NEPA and Section 7(a)(2) of the ESA in the Drug and Biologics Context

Since the FDA does not consider itself an agency with environmental authority and seemingly believes that its actions rarely impact the environment, the FDA's implementation of its duties under NEPA and Section 7(a)(2) of the ESA have been extraordinarily limited.[167] The FDA rarely completes an EIS under NEPA or conducts a Section 7 consultation under the ESA,[168] and in fact, the FDA has only completed one EIS itself in connection with approving a pharmaceutical,[169] though it has participated as a cooperating agency in at least one other EIS.[170] Likewise, there is little case law interpreting either NEPA or the ESA as applied to the FDA, since the agency is rarely sued under either statute. In a CEQ survey of NEPA litigation between the years 2001 and 2013, the

164. 50 C.F.R. §§ 402.14(a), (e).
165. 50 C.F.R. § 402.14(m)(1); 50 C.F.R. § 402.14(e)(3).
166. 50 C.F.R. §§ 402.14(h).
167. Pollans & Watson, *supra* note 27, at 1, 3, 14.
168. *Id.* at 17. FDA Section 7 consultations are so rare that the author can only find one instance of the FDA conducting an informal consultation, based on a search of the Federal Register. This one instance was related to the salmon litigation discussed later in this paper. *See* Draft Amended Environmental Assessment for Production of AquAdvantage Salmon at the Bay Fortune and Rollo Bay Facilities on Prince Edward Island, Canada; Availability; Request for Comments, 87 Fed. Reg. 69032, 69034 (stating "FDA intends to initiate an informal consultation with the services after the close of the public comment period if the current conclusions with respect to the ESA are not altered").
169. Pollans & Watson, supra note 27, at 27.
170. Michael Liftik, Food, Drugs, And The Environmental: How The Food And Drug Administration Has Interacted With The National Environmental Policy Act Of 1969, 29–34 (Apr. 7, 2000).

FDA was only sued for alleged NEPA violations one time,[171] and the National Association of Environmental Professionals' ("NAEP") yearly reports from 2013 through 2022 on appellate NEPA case law do not list any cases against the FDA.[172] The National Agricultural Law Center's Endangered Species Case Law Index, which compiles major ESA cases, only lists one case alleging ESA violations against the FDA.[173]

A. The FDA's Limited Use of Section 7 Consultations

Currently, the FDA has no guidance documents or regulations prescribing when it considers a Section 7 consultation necessary.[174] FDA's Investigations Operations Manual, which lists a comprehensive description of all cooperative efforts with all other federal and state agencies for FDA personnel, does not include any reference to collaborating with USFWS or the NMFS to fulfill its obligations under Section 7 of the ESA.[175] Moreover, a search of the Federal Register reveals that the FDA has never completed a Section 7 consultation in connection with the approval of a new human drug or biological product.[176] Seemingly the only time the FDA came close to conducting a Section 7 consultation in connection with the approval of a new drug or biologic was in the early nineties, after the discovery that a cancer drug, taxol, could be derived from the

171. Council on Env't Quality, NEPA Litigation Surveys: 2001-2013, 13 (2014), https://perma.cc/NS5M-8C9Z.

172. *See generally* James Gregory et al., Nat'l Assoc. of Env't Professionals, 2022 Annual NEPA Report 25–26 (Charles P. Nicholson ed. 2022), (listing all agencies which were defendants under NEPA, none of which were the FDA); James Gregory et al., Nat'l Assoc. of Env't Professionals, 2022 Annual NEPA Report 28–29 (Charles P. Nicholson ed. 2021), (same); Betty Dehoney et al., Nat'l Assoc. of Env't Professionals, 2020 Annual NEPA Report 28–29 (Charles P. Nicholson ed. 2020); Betty Dehoney et al., Nat'l Assoc. of Env't Professionals, 2019 Annual NEPA Report 31–32 (Charles P. Nicholson ed. 2019); Marie Campbell et al., Nat'l Assoc. of Env't Professionals, 2018 Annual NEPA Report 41 (Charles P. Nicholson ed. 2018); Marie Campbell et al., Nat'l Assoc. of Env't Professionals, 2017 Annual NEPA Report 28–29 (Charles P. Nicholson ed. 2017); Charles P. Nicholson et al., Nat'l Assoc. of Env't Professionals, 2016 Annual NEPA Report 33 (Charles P. Nicholson ed. 2016); Ron Lamb et al., Nat'l Assoc. of Env't Professionals, 2015 Annual NEPA Report 45–75 (Karen Johnson ed. 2015); Ron Lamb et al., Nat'l Assoc. of Env't Professionals, 2014 Annual NEPA Report 45–74 (Karen Johnson ed. 2014); Ron Lamb et al., Nat'l Assoc. of Env't Professionals, 2013 Annual NEPA Report 26–27 (Karen Johnson ed. 2013).

173. *Case Law Index Endangered Species Act*, Nat'l Agric. L. Ctr. (Mar. 2023), https://perma.cc/D7S2-G47B.

174. Based on a review of the literature on this topic, FDA's website, the Federal Register, and Hutt et. al., *supra* note 40.

175. Food & Drug Admin., Investigations Operations Manual (2023), https://perma.cc/S3MR-VQPE.

176. *Supra* note 173.

bark of the Pacific Yew Tree.[177] However, at the time the FDA approved taxol, the Pacific Yew Tree was not a listed species, even though there had been a petition to USFWS to list it as threatened,[178] and therefore the approval did not require a Section 7 consultation.[179]

The only documented Section 7 consultation the FDA has initiated was an informal consultation sparked by a legal challenge to the FDA's approval of a genetically-engineered salmon, which was categorized as a new animal drug approval.[180] In *Institute for Fisheries Resources v. United States Food & Drug Administration*, a federal district court remanded without vacatur FDA's approval of a genetically-engineered salmon, ordered the agency to "reconsider its 'no effect' determination under the ESA together with its revised NEPA evaluation," and required the agency to initiate an informal Section 7 consultation.[181] In a Notice of Availability of an updated draft EA released in response to this ruling, the FDA stated its intent to initiate a consultation with both USFWS and NMFS to determine whether the genetically-modified salmon was likely to adversely affect endangered or threatened species.[182] The final results of the consultation have not been completed at the time of writing.[183]

B. The FDA's Implementation of NEPA

In contrast to its implementation of the ESA, the FDA has substantially more guidance, regulations, and history concerning its duties under NEPA, but in general the agency has still issued very few EIS's when approving new drugs

177. Douglas O. Heiken, *The Pacific Yew and Taxol: Federal Management of an Emerging Resource*, 7 J. Env't L. and Litig. 175, 183 (1992).

178. *Id.* at 182.

179. The petition to list the Pacific Yew Tree was ultimately denied because of "insufficient scientific information," meaning that the FDA had no requirement to engage in a Section 7 Consultation, since the species was unlisted and remained unlisted after the petition was denied. *See* Vivien Walsh & Jordan Goodman, *Cancer chemotherapy, biodiversity, public and private property: the case of the anti-cancer drug Taxol*, 49 Social Science & Medicine 1215, 1220 (1999); *see also* Taxol; Environmental Assessments and Findings of No Significant Impact, 58 Fed. Reg. 3954, 3954 (1993).

180. Josh Long, *FDA Ordered to Reassess Environmental Impacts of Genetically Engineered Salmon,* Food & Beverage Insider (Mar. 16, 2021), https://perma.cc/B7EL-VS7F. Inst. for Fisheries Res. v. United States Food & Drug Admin., 499 F. Supp. 3d 657 (N.D. Cal. 2020).

181. *Inst. for Fisheries Res.*, 499 F. Supp. 3d at 668.

182. 87 Fed. Reg. 69032, 69034.

183. Though in a Public Meeting on the Draft Environmental Assessment in January 2023, the FDA did mention it was still intending to undergo consultation with USFWS and NMFS and that consultation had not yet started. *See* Food & Drug Admin., Transcript of CVM's Virtual Public Meeting - Public Meeting on Draft Amended Environmental Assessment for Production of AquAdvantage Salmon at the Bay Fortune and Rollo Bay Facilities on Prince Edward Island, Canada 4, 12 (Jan. 9, 2023).

and biologics.[184] The reason the FDA has completed so few EIS's is that it relies heavily on categorical exclusions or otherwise concludes the NEPA process with FONSIs.[185] As previously mentioned, in the pharmaceutical context, the FDA alone has completed only one EIS, meaning all of its other actions must have resolved NEPA responsibilities through a categorical exclusion or a FONSI.[186]

The FDA's current NEPA regulations declare that approvals of new drug applications, applications for approval of biologics, and actions on investigational new drugs require an environmental assessment unless they constitute a categorical exclusion.[187] However, the regulations categorically exclude many activities related to approving new drugs or biologics, including new drug approvals and applications to market biologics, "if the action does not increase the use of the active moiety" or "if the action increases the use of the active moiety, but the estimated concentration of the substance at the point of entry into the aquatic environment will be below 1 part per billion."[188] Active moiety refers to the core molecule or ion of a drug that is "responsible for the physiological or pharmacological action of the drug substance."[189] It can encompass groups of related pharmaceutical substances with slightly different molecular configurations, such as a specific substance, any esters or salts of that substance, and any variations of that substance with noncovalent appendages.[190] This definition means that a wholly new substance (which necessarily will increase the use of the active moiety given its novelty) would be categorically excluded from NEPA review as long as it enters the aquatic environment in quantities below one part per billion.[191]

The calculation of the quantity of active moieties introduced into the environment is based on a calculation known as the "expected introduction concentration" (EIC), and the EIC normally is based only on a quantification of the consumer's use of a drug, since the FDA assumes that either state or EPA disposal procedures for waste prevent the drug from entering the aquatic

184. Gabriel Eckstein, *Drugs on Tap: Managing Pharmaceuticals in Our Nation's Waters*, 23 N.Y.U. Env't L. J. 37, 66–67 (2015); Pollans & Watson, *supra* note 27, at 27.

185. Pollans & Watson, *supra* note 27, at n. 100.

186. Eckstein, *supra* note 183, at 66–67.

187. 21 C.F.R. § 25.20(l).

188. 21 C.F.R. § 25.31 (active moiety is the "molecule or ion, excluding those appended portions of the molecule that cause the drug to be an ester, salt (including a salt with hydrogen or coordination bonds), or other noncovalent derivative (such as a complex, chelate, or clathrate) of the molecule, responsible for the physiological or pharmacological action of the drug substance"); 21 C.F.R. § 314.3(b).

189. 21 C.F.R. § 314.3(b); *see* Pub. L. No. 117-9, 135 Stat. 256 (2021).

190. Erin H. Ward, Cong. Rsch. Serv., R46110, Defining Active Ingredient: The U.S. Food and Drug Administration's Legal Interpretation of Regulatory Exclusivities 11 (2023).

191. Food & Drug Admin., Center for Drug Evaluation and Research, Guidance for Industry: Environmental Assessment of Human Drug and Biologics Applications 3–4 (July 1998).

environment from other sources.[192] This estimate is notably conservative insofar as it assumes that there is no metabolism of the quantity drug estimated to be used for human consumption, meaning that all of the consumed substance is expected under this calculation to pass directly into wastewater,[193] but in light of evidence about EPA's difficulties in adequately regulating disposal of pharmaceutical waste,[194] this estimate may miss potentially significant sources of pharmaceutical wastes entering the aquatic environment.

The regulations also categorically exclude activities related to drugs and biologics which involve naturally occurring products.[195] The FDA's regulations clarify that there are "no categories of agency actions that routinely significantly affect the quality of the human environment and that therefore ordinarily require the preparation of an EIS."[196]

However, the FDA's NEPA regulations provide an "extraordinary circumstances" exception to its categorical exclusions.[197] This provision requires at least an EA in situations where the FDA believes there is a potential for significant harm to the environment or where an action will "adversely affect a species or the critical habitat of" endangered or protected species.[198] The FDA has clarified that this exception should be applied sparingly and in very "limited instances."[199]

Non-binding recommendations issued via guidance documents clarify the scope of the FDA's NEPA regulations and their applicability to certain types of drugs and biologics.[200] In these documents, the FDA gives significant attention

192. *Id.* at 17–19.

193. *Id.* at 18.

194. See *supra* notes 60–84 and accompanying text.

195. 21 C.F.R. § 25.31(c) (excluding "[a]ction on an NDA, abbreviated application, application for marketing approval of a biologic product, or a supplement to such applications, or action on an OTC monograph, for substances that occur naturally in the environment when the action does not alter significantly the concentration or distribution of the substance, its metabolites, or degradation products in the environment").

196. 21 C.F.R. § 25.22.

197. 21 C.F.R. § 25.21.

198. 21 C.F.R. § 25.21(a)–(b). This provision defined endangered based on a determination "under the Endangered Species Act or the Convention on International Trade in Endangered Species of Wild Flora and Fauna to be endangered or threatened or wild flora or fauna that are entitled to special protection under some other Federal law."

199. 62 Fed. Reg. 40570, 40573 ("[T]herefore application of the extraordinary circumstances provision should be limited. Since 1985, in implementing its NEPA procedures, FDA has invoked the extraordinary circumstance exception to categorical exclusions in limited instances and in a manner consistent with CEQ regulations.").

200. Guidance documents represent the "current thinking" of the FDA and are not binding on FDA or the public. *See, e.g.*, Food & Drug Admin., Center for Drug Evaluation and Research, Guidance for Industry: Environmental Assessment: Questions and Answers Regarding Drugs With Estrogenic, Androgenic, or Thyroid Activity 1 (March 2016).

to categorical exclusions and the extraordinary circumstances exception[201] and explains how to apply for categorical exclusions, clarifies that the extraordinary circumstances exception can apply to the product, use, or disposal of a drug or biologic,[202] and states that the industry should consider circumstances that impact endangered species both directly (for example, in a case where a drug is derived from an endangered species) and indirectly (for example, due to manufacturing emissions) when determining whether the extraordinary circumstances exception applies.[203]

Moreover, with increasing awareness of the harm caused by certain types of drugs in aquatic environments,[204] the FDA recently altered its position on whether categorical exclusions apply to specific drug types.[205] The FDA accounted for the change on two grounds: a citizen petition asking the FDA to repeal the categorical exclusion for substances entering aquatic environments at concentrations below 1 part per billion,[206] and EPA's research on the harm caused by certain types of drugs.[207] Notably, this change in FDA's position on the implementation of its categorical exclusions was not precipitated by litigation, at least not at the appellate level.[208] The NAEP comprehensively summa-

201. *See* Food & Drug Admin., Center for Drug Evaluation & Rsch., Guidance for Industry: Environmental Assessment of Human Drug and Biologics Applications 6–9 (July 1998); Food & Drug Admin., Center for Drug Evaluation & Rsch., Guidance for Industry: Environmental Assessment: Questions and Answers Regarding Drugs With Estrogenic, Androgenic, or Thyroid Activity 3 (March 2016).

202. Food & Drug Admin., Center for Drug Evaluation & Rsch., Guidance for Industry: Environmental Assessment of Human Drug and Biologics Applications 9 (July 1998).

203. *Id.* at 7.

204. Note that some of this growing awareness of the harms of aquatic pollution has been co-opted by anti-abortion advocates. *See* Alice M. Ollstein, *Anti-abortion group launches new pill challenge as SCOTUS mulls sweeping restrictions*, Politico (Apr. 20, 2023), https://perma.cc/444C-EAFN. While there are significant harms related to pharmaceutical pollution, alarm over abortifacients, a necessary form of healthcare, is "completely disingenuous" according to environmental practitioners and experts and distracts efforts from "more widely used pharmaceuticals that pose a confirmed environmental threat." Samantha Putterman, *Anti-abortion advocates turn to the environment: Is mifepristone in wastewater a threat?*, PolitiFact (May 31, 2023), https://perma.cc/X3WD-4BQX.

205. *See* Environmental Assessment: Questions and Answers Regarding Drugs With Estrogenic, Androgenic, or Thyroid Activity; Draft Guidance for Industry; Availability, 80 Fed. Reg. 23802, 23803 n.1 (2015).

206. Great Lakes Environmental Law Center & The Natural Resources Defense Council, Citizen Petition, FDA-2010-P-0377-0001 1 (2010).

207. FDA, in its announcement of a new draft guidance, identified the EPA's Endocrine Disruptor Screening Program as providing core scientific evidence for the updated guidance document. *See* Environmental Assessment: Questions and Answers Regarding Drugs With Estrogenic, Androgenic, or Thyroid Activity; Draft Guidance for Industry; Availability, 80 Fed. Reg. 23802, 23803 n.1 (2015).

208. *See supra* note 171.

rizes appellate NEPA case law each year, and a review of NAEP reports from 2013 through 2022 reveals no cases reaching appellate courts and involving categorical exclusions were brought against the FDA.[209]

In this guidance document, the FDA warned the industry that, even if a proposed drug that has potential estrogenic, androgenic, or thyroid pathway activity enters the aquatic environment at concentrations *below* the regulatory threshold (1 part per billion), then its new drug application may nonetheless not be eligible to receive categorical exclusion due to environmental risks.[210] Because the categorical exclusions may not apply, the guidance document encourages companies seeking approval of such a drug to consult with the FDA early in the new drug approval process.[211] However, this guidance document, as a nonbinding regulation, does not formally change the scope of categorical exclusions and cannot actually force the industry to stop using categorical exclusions.[212]

It is unclear if this guidance document has resulted in any substantial changes to the implementation of the FDA's categorical exclusions or the behavior of the regulated industry; some food and drug law scholars have commented that it is highly ambiguous whether the FDA has ever even invoked the extraordinary circumstances exception by name.[213] This comports with FDA's assertion that the extraordinary circumstances exception should be used sparingly.[214]

In sum, the FDA's implementation of NEPA is, at best, a case of institutional avoidance,[215] if not outright neglect, due to the agency's reliance on categorical exclusions and FONSIs. This avoidance is consistent with the agency's frustrating lack of consultations under the ESA, too. Based on how rarely the FDA has even informally consulted with either USFWS or NMFS, the FDA does not seem to believe that it has the responsibility to comply with Section 7 of the ESA. The rest of this paper discusses how and why the FDA should change this approach.

209. *Id.*

210. FDA, Ctr. for Drug Evaluation and Rsch., Guidance for Industry: Environmental Assessment: Questions and Answers Regarding Drugs With Estrogenic, Androgenic, or Thyroid Activity, 2 (March 2016).

211. *Id.* at 5.

212. *See id.* at 1.

213. Pollans & Watson, *supra* note 27, at 26, n.133 (stating, "We found no examples either in the FCN Environmental Decision database or elsewhere [of the use of the extraordinary circumstances exception to categorical exclusions]"). B*ut see* 62 Fed. Reg. 40570, 40573 (noting that FDA indeed "has invoked the extraordinary circumstance exception to categorical exclusions in limited instances").

214. 62 Fed. Reg. 40570, 40573.

215. Pollans & Watson, *supra* note 27, at 5.

IV. The FDA's Duty to More Seriously Implement NEPA and Utilize the Section 7 Consultation Process Due to the Current Mass Extinction Event

The FDA has both the authority to consider the environmental impacts of the approval of new drugs and biologics and an increased imperative to do so because of the current mass extinction event. The current mass extinction event could defensibly fit into the FDA's current NEPA regulations, as a new application of the "extraordinary circumstances" exemption, which already includes a requirement for at least EAs for "actions for which available data establish that, at the expected level of exposure, there is the potential for serious harm to the environment."[216] Additionally, concerns about specific endangered species being harmed by specific kinds of pharmaceutical compounds may also create a legal duty for the FDA under NEPA and the ESA; since both the "extraordinary circumstances" exemption and the ESA are triggered when endangered species are harmed, proof that even one endangered aquatic species is adversely affected may be sufficient to trigger increased environmental scrutiny in the approvals of at least some drugs and biologics.

A. Increased Use of NEPA

This section first describes how NEPA, when combined with the language in the FDCA, permits the FDA to account for environmental factors before analyzing how and why the FDA's current NEPA regulations and their "extraordinary circumstances" exemption to categorical exclusions can be interpreted, in light of the biodiversity crisis, to require the completion of more environmental analyses. While the FDCA contains no explicit requirement to consider the environment in the drug and biologics approval context and instead focuses the FDA's discretion on evaluating safety and efficacy,[217] NEPA broadens the scope of the FDA's authority and permits the FDA to base substantive decisions on environmental considerations, even if they are not directly mentioned in relevant provisions of FDCA.[218]

As a preliminary matter, the language in the FDCA relating to the approval of new drugs may support the inclusion of environmental considerations on its

216. 21 C.F.R. 25.21(a).

217. *See generally* 21 U.S.C. §§ 301–99. *But see* 21 U.S.C. § 350h (requiring rulemaking on produce safety standards to "take into consideration … conservation and environmental practice standards and policies established by Federal … agencies").

218. Env't Def. Fund, Inc. v. Mathews, 410 F. Supp. 336, 338 (D.D.C. 1976) ("This is not to say that NEPA requires FDA's substantive decisions to favor environmental protection over other relevant factors. Rather, it means that NEPA requires FDA to *consider* environmental factors in its decision-making process and supplements its existing authority to permit it to act on those considerations. It permits FDA to base a decision upon environmental factors, when balanced with other relevant considerations.").

own. The FDCA states that the FDA may deny a new drug application for a number of reasons, including (1) if the application does not include "adequate tests by all methods reasonably applicable to show whether or not such drug is safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling thereof," (2) if "results of such tests show that such drug is unsafe for use under such conditions or do not show that such drug is safe for use under such conditions," or (3) if the FDA has "insufficient information to determine whether such drug is safe for use."[219] The references to safety and information adequacy could be read to include environmental safety and thus necessitate, under this broader view of safety, adequate information on the environmental harms of a drug. While the FDA has never refused to approve a new drug application on environmental grounds,[220] the FDA could, on this theory, reject a new drug application because it is environmentally harmful to the point that the drug will harm humans who are chronically exposed to the substance through environmental pollution,[221] therefore making the drug unsafe[222] overall.

Of course, it is unlikely that the FDA could reject a new human drug application *solely* for its environmental impact. The definition of safety, while capacious, is nonetheless linked to a risk-benefit analysis[223] of how the drug will benefit patients and public health.[224] Some factors used in this analysis include "the nature and severity of the condition the drug is intended to treat or prevent, the benefits and risks of other available therapies for the condition, and any risk management tools that might be necessary to ensure that the benefits of the drug outweigh its risks."[225] A denial of a new drug application based on an interpretation of safety that ignores the benefits to humans and focuses only on environmental harms would thus likely be arbitrary and capricious under the Administrative Procedure Act,[226] since at the very least such a decision would entirely fail "to consider an important aspect of the problem."[227]

This is not an argument that the FDA needs to or should interpret "safety" to refer only to environmental harms or that the term "safety" only encompasses

219. 21 U.S.C. § 355(d).

220. Joseph A. Gorman, *Drugs in Our Water: A Legal Proposal for Responsible Nationwide Pharmaceutical Consumption*, 26 J. Land Use & Env't L. 147, 167–68 (2010).

221. Currently, there is little evidence that exposure to trace pharmaceuticals in treated water causes direct harm to humans. Nasser Nassiri Koopaei & Mohammad Abdollahi, *Health risks associated with the pharmaceuticals in wastewater*, 25 DARU J. of Pharm. Sci. 1, 3. However, since there are no "reliable long term toxicological studies" on chronic exposure to pharmaceuticals, *id.*, it is entirely possible that long-term, chronic exposure to pollution poses a risk to human health.

222. *See* 21 U.S.C § 314.125(a)(3).

223. *See* 21 U.S.C. § 355(d).

224. Food & Drug Admin., Benefit-Risk Assessment for New Drug and Biological Products Guidance for Industry 9–11 (Oct. 2023).

225. *Id.* at 4.

226. *See* 5 U.S.C. § 706(a).

227. Motor Veh. Mfrs. Ass'n v. State Farm Ins., 463 U.S. 29, 43 (1983).

environmental factors; it would be morally, and in all likelihood legally, inappropriate for the FDA to deny the approval of an effective, lifesaving drug because of environmental risks. However, just because the FDA cannot ultimately determine whether or not a drug is safe based solely on environmental risks does not mean that environmental considerations are wholly beyond the ambit of the agency's authority, as granted by the FDCA.[228] Rather, the idea here is that the concept of safety in the FDCA is broad enough to encompass some environmental values, potentially on its own; and, this language, when viewed in tandem with NEPA, clearly grants the FDA the authority to account for environmental impact when making decisions.[229]

Federal courts have understood the relationship between the FDCA and NEPA to be as such since at least 1976, when the D.C. Circuit held that the FDA could not, by regulation, ban the consideration of environmental factors in its approval of food additives, new animal drugs, and new drugs, because such a regulation would contravene NEPA.[230] In rejecting the FDA's arguments, the D.C. Circuit stated, "NEPA provides FDA with supplementary authority to base its substantive decisions on all environmental considerations including those not expressly identified in the FDCA and FDA's other statutes. This conclusion finds support in the legislative history, the precise statutory language, the holdings of the courts, and the construction adopted by other Federal agencies."[231] The FDA echoed support for the holding in *Mathews* in its updates to its NEPA procedures in the 1990s, when the agency stated that, "in addition to its other statutory mandates," it must "take environmental considerations into account in its process of decision-making."[232]

This interpretation of safety in the FDCA is also supported by the holding in *Institute for Fisheries Resources v. FDA*, a recent case holding that the FDA must comply with NEPA when approving new animal drugs[233] that are treated substantially the same as new human drugs under the FDCA.[234] Both new animal drug applications and new human drug applications may be denied by the

228. At the very least, the FDA has an immense amount of discretion in making safety determinations when approving new drugs and biologics, as evinced by the fact that a court challenge to a denial of a new drug application has never been successful. HUTT ET. AL., *supra* note 40, at 952.

229. This is one of the core holdings of Env't Def. Fund, Inc. v. Mathews, 410 F. Supp. 336, 338 (D.D.C. 1976).

230. *Id.* at 338–39.

231. *Id.* at 338.

232. National Environmental Policy Act; Revision of Policies and Procedures, 62 Fed. Reg. 40570, 40574.

233. Inst. for Fisheries Res. v. United States Food & Drug Admin., 499 F. Supp. 3d 657, 664–65 (N.D. Cal. 2020).

234. Compare the statutory language on the grounds for refusing an application in 21 U.S.C. § 360b(d)(1), with 21 U.S.C. § 355(d) (illustrating that the same exact reasons may be used for denying applications for new drugs both parts of the statute, with the exception of a specific reason for denying carcinogenic drugs in the new animal drug context).

FDA for largely the same reasons and use substantially similar, if not nearly identical, language.[235] The court based its determination on both the statutory language on safety in the FDCA and the fact that NEPA itself "counsels in favor of a broader understanding of the agency's authority."[236] Otherwise, NEPA's purpose would be entirely undermined if "the FDA were . . . [implicitly] . . . precluded from acting on the concerns that NEPA requires it to consider."[237]

Moreover, there is also room for environmental considerations in the FDA's current NEPA regulations. While the current FDA regulations that delineate the reasons the FDA may *refuse* an application for a new drug do not explicitly enumerate environmental considerations as a valid reason for rejecting a drug and instead focus on safety and efficacy, similar to the text of the FDCA,[238] a separate set of regulations listing FDA requirements for a new drug application to be considered complete *do* include a consideration of the environment. Under these regulations, the FDA "may refuse" to recognize a new drug application as complete unless it either includes an EA or a claim of a categorical exclusion.[239] Not recognizing a new drug application as complete is known as a "refusal to file," and generally speaking, a "refusal to file" designation either significantly delays the approval process or results in an ultimate rejection of the application.[240] Thus, if the FDA wanted to more robustly implement NEPA, leveraging the threat of refusing to file new drug applications if the applications lack EA would likely be sufficient to ensure that the industry will comply and gather the necessary environmental data.

This argument on the FDA's authority to consider the environment when approving new drugs or biologics, if implemented, could be the first step toward effectively addressing the harms of pharmaceutical pollution, even if under this interpretation the FDA does not actually go so far as to reject a drug solely for its environmental consequences. Rather, one of the key issues with the impact of new drugs and biologics on aquatic species is that the impacts on endangered wildlife are largely unknown[241] until they have already entered the environment and have begun to negatively impact the behavior, reproductive capacity, and

235. *Id.*

236. Inst. for Fisheries Res., 499 F. Supp. 3d at 664.

237. *Id.* The court did clarify that the situation would be different if the FDCA had an explicit bar on considering the environment.

238. *See* 21 C.F.R. § 314.125.

239. *See id.* §314.101(d).

240. *See* Harinder Singh Chahal et al., *Contents of US Food and Drug Administration Refuse-to-File Letters for New Drug Applications and Efficacy Supplements and Their Public Disclosure by Applicants*, 181 JAMA Internal Med. 522, 525–27 (2021).

241. *See* Christopher T. Nidel, *Regulating the Fate of Pharmaceutical Drugs: A New Prescription for the Environment*, 58 Food & Drug L.J. 81, 88 (2003); *see also* Karl Fent et al., *Ecotoxicology of human pharmaceuticals*, 76 Aquatic Toxicology 122, 122 (2006) (noting that "targeted ecotoxicological studies [on pharmaceuticals' impact on aquatic environments] are lacking almost entirely and such investigations are needed focusing on subtle environmental effects").

resiliency of aquatic species.[242] If the FDA required more information-gathering up front in the process, then environmental policymakers, states, and the owners of wastewater treatment facilities might be able to make more informed decisions about waste-water management. For example, this information could allow states to set appropriate TMDLs and therefore address non-point sources of pollution, since in the absence of baseline information collected by the FDA it is doubtful that they would venture to set pharmaceutical TMDLs.

Additionally, if the FDA was made aware of the full environmental impacts of a new drug or biologic, such as through an EIS it could require the manufacturer to implement elements of "green" drug design and pharmacokinetics, including higher specificity to modes of actions, environmental biodegradability, minimizing the use of known harmful moieties and functional groups, and better delivery mechanisms that permit ultra-low dose formulations.[243] While this will not mitigate the impacts of drugs and biologics which have already been approved, it can ensure that this problem does not worsen in the future as more drugs are approved and enter the waterways.

The FDA can take all of these actions immediately, without first making any changes to its current NEPA regulations, by recognizing that the current mass-extinction event and anthropogenically-caused decline in aquatic species are "extraordinary circumstances" that warrant, at the very least, the completion of more EAs.[244] It would likely be difficult for a plaintiff to bring a case to force the FDA to apply the "extraordinary circumstances" exemption in such a way, based on the deferential standard of review that other agencies have received in litigation challenging their application of analogous "extraordinary circumstance" provisions,[245] but this very deference, which has resulted in

242. *See e.g.*, Martínez Carrasco Néstor & Cuautle Mariana, *Impact of Pharmaceutical Waste on Biodiversity*, 66 Ecopharmacovigilance 235, 235 (2017).

243. *See* Caroline T. A. Moermond et al., *GREENER Pharmaceuticals for More Sustainable Healthcare*, 9 Env't Sci. Tech. Lett. 699, 700–2 (2022).

244. *See* 21 C.F.R. § 25.21(a) – (b). The connection between pharmaceutical pollution and the risk of serious harm to the environment was seemingly first raised by Shawna Bligh, an environmental attorney, in her article on pharmaceutical pollution. Shawna Bligh, *Pharmaceuticals in Surface Waters: Use of NEPA*, 24 Nat. Res. & Env't 56 56 (2009).

245. *See* Sierra Club v. U.S. Forest Serv., 828 F.3d 402 (6th Cir. 2016); Native Ecosystems Council v. Marten, No. 19-35084, 800 Fed. Appx. 543 (9th Cir. April 7, 2020) (not for publication); Wild Watershed v. Hurlocker, 961 F.3d 1119 (10th Cir. 2020) (relating to the interpretation of a statutory categorical exclusion); Padgett v. Surface Trans. Board, 804 F.3d 103 (1st Cir. 2015) (finding that plaintiffs were not able to demonstrate extraordinary circumstances and that the agency's use of a categorical exclusion was valid). *But see* Rhodes v. Johnson, 153 F.3d 785 (7th Cir. 1998) (holding, in a case where the agency did not dispute that the existence of an endangered species was an extraordinary circumstance, that despite the substantial deference an agency typically receives in its application of its own regulations, "the presence of an extraordinary circumstance requires the Forest Service to prepare an environmental assessment"); City of Phoenix v. Huerta, 869 F.3d 963 (D.C. Cir. 2017).

largely unsuccessful NEPA litigation against agencies,[246] points to the fact that an agency like the FDA has broad discretion to determine the exact scope of what constitutes an "extraordinary circumstance." Therefore, this area is ripe for reinterpretation by the FDA, especially based on the growing scientific evidence linking pharmaceutical pollution and harm to the environment.

As previously discussed, the FDA's extraordinary circumstances exception to categorical exclusions in its current NEPA regulations applies when there is "potential for serious harm to the environment" and when adverse impacts occur to endangered or threatened "species or the critical habitat of that species."[247] According to FDA guidance, such extraordinary circumstances may occur "based on the production, use, or disposal from use of the FDA-regulated" substance.[248]

In the present, there is clear scientific proof that both serious harm to the environment is occurring and that endangered or threatened species are being adversely impacted.[249] Pharmaceutical pollution causes serious problems that jeopardize the survival of aquatic species, including amphibians, fish, and corals, all of which are experiencing a heightened risk of extinction and endangerment at the species level.[250]

Examples of this harm include "histopathological changes to tissues, feminization of male fish, and behavioral changes in both fish and aquatic invertebrates."[251] Amphibians experience decreases in fertility and reproductive capacity when exposed to estrogenic compounds,[252] and, because so many amphibian species are in decline worldwide (more than 70%),[253] a marked change in reproductive capacity and fertility has dire implications for amphibian species' risk of extinction. Additionally, exposure to opioid residues causes aquatic animals such as fish to engage in unhealthy behaviors that increase the risk of predation,[254] make animals more likely to be antisocial, and compromise locomotion or otherwise depress activity levels.[255] Likewise, antidepressants found in surface water impact "the behavior, reproduction, development, and survival

246. John C. Ruple & Kayla M. Race, *Measure the NEPA Litigation Burden: A Review Of 1,499 Federal Court Cases*, 50 Env't L. 479, 511–12 (2020).
247. 21 C.F.R. § 25.21(a)–(b).
248. Food & Drug Admin., Center for Drug Evaluation and Research, Guidance for Industry: Environmental Assessment of Human Drug and Biologics Applications (July 1998) at 6.
249. *See supra* notes 14–22, and accompanying text.
250. *Id.*
251. Moermond et al., *supra* note 242, at 699.
252. Säfholm et al., *supra* note 15, at 1, 2.
253. Hayes, *supra* note 16, at 921.
254. Alexandra A. Taylor, *As more opioids go down the drain, scientists are tracking them in the environment*, Chem. and Eng'g News (Apr. 21, 2019), https://perma.cc/7M4T-ZG2A.
255. Marcus Michelangeli et al., *Predicting the impacts of chemical pollutants on animal groups*, 37 Trends Ecology and Evolution 789, 794 (2022).

of aquatic invertebrates and vertebrates."[256] Currently, there is little evidence linking biologics to direct harm to endangered species, and in fact some biologics, such as therapeutic proteins, may actually be more environmentally sustainable comparatively because of natural metabolic processes.[257] However, biologic products tend to represent the "cutting-edge" of medical technology,[258] and new technologies, such as gene therapies, pose novel risks to the environment, such as the risk of genetic shedding and alterations to wild animals' genomes.[259] These new technologies may therefore be proven one day to cause as much harm as drug exposure has been proven to cause already.

All of the deleterious behavioral changes to aquatic life caused by drug exposure also result in a decreased reproductive capacity for animal species, especially those exposed to opioids and antidepressants, since they alter group dynamics between animals or otherwise make it less likely for an animal to reach the age of reproduction.[260] Some studies have further found that, more generally, pharmaceutical pollution triggers behavioral changes in animal species which leads to changes at the population level and thus "precedes extinction."[261] Finally, exposure to pharmaceutical pollution may also be plainly toxic for certain animal species above certain concentrations; one meta-analysis found that chemical pollution, which includes pharmaceutical pollution, impacts amphibians dramatically and results in "a 14.3% decrease in survival, a 7.5% decrease in mass, and a 535% increase in abnormality frequency."[262]

While these studies generally do not point to an exact or singular endangered species which experiences these harms, since the deleterious impacts of pharmaceutical pollution impact amphibians and fish generally, it still stands to reason that it is reasonably foreseeable for specific endangered amphibian and fish species to be impacted just as much as other animals in their general class. Thus, the FDA could apply the extraordinary circumstances exception much more broadly, especially considering that such a high proportion of amphibian species are endangered and that amphibians are so deeply impacted by the presence of drugs and biologics in the water. At the very least, the already proven risks to amphibians and other aquatic species generally should constitute, under

256. Pavla Sehonova et al., *Effects of waterborne antidepressants on non-target animals living in the aquatic environment: A review*, 631 Sci. Total Env't 789, 789 (2018).

257. *See* Thomas C. Kühler et al., *Do Biological Medicinal Products Pose a Risk to the Environment?*, 32 Drug Safety 995, 995–98 (2009).

258. *What Are "Biologics" Questions and Answers*, Food & Drug Admin. (Feb. 26, 2018), https://perma.cc/3QKR-NZ52.

259. *See* Kühler et al., *supra* note 256, at 997–99.

260. *See id.*; Néstor & Mariana, *supra* note 241, at 325.

261. Néstor & Mariana, *supra* note 241, at 325.

262. Andrés Egea-Serrano et al., *Understanding of the impact of chemicals on amphibians: a meta-analytic review*, 2(7) Ecol. Evolution 1382 (2012). Note that this study included an analysis of literature that studied other chemical pollutants, such as pesticides, and was not exclusively focused on pharmaceutical pollution. *Id.*

the FDA's current NEPA regulations, "available data" on the "potential for serious harm to the environment."[263] This would give the FDA a reason to force the regulated industry to provide information about the environmental consequences of any proposed new drugs or biologics and would permit the FDA to more robustly implement NEPA immediately, since the current regulations authorize requiring at least EAs in light of the undeniable scientific proof of harm to aquatic life, including endangered aquatic life.

Such a change also would not significantly impair the FDA's ability to ensure that drugs with immense benefits are approved for use in a timely manner. While some may argue that increasing the amount of EAs and EIS's will delay the availability of life-saving medication, there is scant evidence that completing EAs slows agency action.[264] The burden of completing EAs is also already placed on the drug applicant,[265] as well, meaning that the FDA would not need to expend its own resources to ensure the production of environmental documents under NEPA.

B. Increased Compliance with ESA Section 7

In addition to more rigorously adhering to NEPA, the FDA must also increase its compliance with the requirements of Section 7 of the ESA. Because of the likelihood that endangered aquatic species are being adversely impacted by drugs and biologics, when the FDA takes actions related to new drugs and biologics it should consult with USFWS or NMFS, especially if the drug at issue is likely to impact the behavior and reproductive capacity of aquatic species. Section 7 duties are triggered when an agency takes a discretionary action that is likely to affect an endangered or threatened species or its critical habitat.[266] FDA approval of new drugs and biologics is certainly an action per Section 7 implementing regulations, which define action as "all activities or programs of any kind authorized, funded, or carried out, in whole or in part, by Federal agencies in the United States or upon the high seas," including, but not limited to "the

263. 21 C.F.R. § 25.21(a).

264. John C. Ruple, Jamie Pleune, & Erik Heiny, *Evidence-Based Recommendations for Improving National Environmental Policy Act Implementation*, 47 Colum. J. Env't L. 237, 237 (2022) ("Contrary to widely held assumptions, we found that a less rigorous level of analysis often fails to deliver faster decisions. Delays, we found, are often caused by factors only tangentially related to [NEPA], like inadequate agency budgets, staff turnover, delays receiving information from permit applicants, and compliance with other laws.").

265. 21 C.F.R. § 25.40(b); 21 C.F.R. § 314.101(d).

266. Theodore Z. Wyman, *Construction and Application of the Consultation Requirement Under Section 7 of the Endangered Species Act, 16 U.S.C.A. § 1536(a) to (d)*, 1 A.L.R. Fed. 3d Art. 4 (2015).

promulgation of regulations . . . the granting of licenses . . . or actions directly or indirectly causing modifications to the land, water, or air."[267]

Approvals of new drugs and biologics by the FDA are also likely discretionary. The Supreme Court has held that discretionary agency actions in the ESA context do not include actions that an agency is "*required* by statute to undertake once certain specified triggering events have occurred."[268] In other words, if an agency does not have any discretion on whether or not to take a certain action, the obligations of the ESA cannot apply since the agency would not be able to prevent jeopardizing any endangered or threatened species, anyway.[269]

Under the FDCA, the approval of a new drug application is not required after some threshold of research or scientific merit has been proven by an applicant, but rather approval is based upon the Secretary's findings and an evaluation of substantial evidence.[270] While there are statutory factors listed that the

267. 50 C.F.R. § 402.02.

268. Nat'l Ass'n of Home Builders v. Defs. of Wildlife, 551 U.S. 644, 646 (2007).

269. *Id.* at 667.

270. *See* 21 U.S.C. § 355(d) ("*If the Secretary finds*, after due notice to the applicant in accordance with subsection (c) and giving him an opportunity for a hearing, in accordance with said subsection, that (1) the investigations, reports of which are required to be submitted to the Secretary pursuant to subsection (b), do not include *adequate* tests by all methods reasonably applicable to show whether or not such drug is safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling thereof; (2) the results of such tests show that such drug is unsafe for use under such conditions or do not show that such drug is *safe* for use under such conditions; (3) the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug are inadequate to preserve its identity, strength, quality, and purity; (4) *upon the basis of the information submitted to him as part of the application, or upon the basis of any other information before him with respect to such drug, he has insufficient information to determine whether such drug is safe for use under such conditions*; or (5) *evaluated on the basis of the information submitted to him as part of the application and any other information before him with respect to such drug, there is a lack of substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the proposed labeling thereof*; or (6) the application failed to contain the patent information prescribed by subsection (b); or (7) based on a fair evaluation of all material facts, such labeling is false or misleading in any particular; he shall issue an order refusing to approve the application. *If, after such notice and opportunity for hearing, the Secretary finds* that clauses (1) through (6) do not apply, he shall issue an order approving the application. As used in this subsection and subsection (e), the term "substantial evidence" means evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and responsibly be concluded by such experts that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof. If the Secretary determines, based on relevant science, that data from one adequate and well-controlled clinical investigation and confirmatory evidence (obtained prior to or after such investigation) are sufficient to establish effectiveness, the Secretary may consider such data and evidence to constitute substantial evidence for purposes of the preceding sentence. *The Secretary shall implement a structured risk-benefit assessment framework in the new drug approval process to facilitate the balanced consideration of benefits*

Secretary must consider in evaluating whether to approve or deny a new drug application, similar to the "specific triggering events" enumerated by statute at issue in *National Association of Home Builders*, approvals or refusals to approve a new drug falls reasonably within the FDA's ultimate discretion, since the agency is not mandated by the statute to make its findings in one way or another.[271] The statutes repeated use of capacious terms, like safety and adequacy, as well as the requirement for the FDA to complete a risk-benefit assessment to determine a drug's safety,[272] all point to a significant enough level of discretion for the purposes of the ESA. Likewise, the regulations implementing biologics license approvals confirm that issuances and denials of licenses for biological products are based upon the Secretary's determinations.[273]

Litigation on EPA's compliance with Section 7(a)(2) in the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) context provides support for the assertion that FDA's approvals of new drugs and biologics are discretionary actions and therefore subject to Section 7(a)(2). FIFRA requires that all pesticides sold in the United States are "registered" by the EPA, similar to the FDA's approval requirements for new drugs. [274] Like in the FDCA, FIFRA states that the EPA "shall" register a pesticide, as long as a pesticide registration application meets a certain number of listed criteria.[275] FIFRA's statutory language on pesticide registration has been found, in a number of cases, to constitute the type of discretionary decision necessary for 7(a)(2) to apply.[276] While FIFRA does more clearly state environmental considerations in its approval criteria, such as a balancing of whether the pesticide "will perform its intended function without

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and risks, a consistent and systematic approach to the discussion and regulatory decisionmaking, and the communication of the benefits and risks of new drugs. Nothing in the preceding sentence shall alter the criteria for evaluating an application for marketing approval of a drug.") (emphases added).

271. *Id.*

272. *Id.* Note also that the leading casebook on food and drug law describes the FDA as having "enormous discretion" in determining what is and is not safe. *See* HUTT ET AL., *supra* note 40, at 932. Additionally, in the context of a different statute, the Federal Torts Claim Act, at least one court has determined the approval of a new drug application to be discretionary. Forsyth v. Eli Lilly & Co., 904 F. Supp. 1153 (D. Haw. 1995).

273. 21 C.F.R. § 601.4(a)–(b) ("(a) A biologics license shall be issued upon a determination by the Director, Center for Biologics Evaluation and Research or the Director, Center for Drug Evaluation and Research that the establishment(s) and the product meet the applicable requirements established in this chapter. A biologics license shall be valid until suspended or revoked. (b) If the Commissioner determines that the establishment or product does not meet the requirements established in this chapter, the biologics license application shall be denied and the applicant shall be informed of the grounds for, and of an opportunity for a hearing on, the decision. If the applicant so requests, the Commissioner shall issue a notice of opportunity for hearing on the matter pursuant to § 12.21(b) of this chapter.").

274. *Compare* 21 U.S.C. § 355(a), *with* 7 U.S.C. § 136a.

275. *Compare* 21 U.S.C. § 355(a), *and* 42 U.S.C. § 262(a)(1)(A), *with* 7 U.S.C. § 136a(c)(5).

276. Migrant Clinicians Network v. U.S. Env't Prot. Agency, 88 F.4th 830, 847 (9th Cir. 2023); Ctr. for Food Safety v. Regan, 56 F.4th 648, 657–58 (9th Cir. 2022).

unreasonable adverse effects on the environment,"[277] (1) the overall structure of the application approval provisions and (2) the requirement to balance the benefits of a product versus its risks in both statutes provides evidence that the FDCA, like FIFRA, involves the requisite discretion necessary for Section 7(a)(2) of the ESA to apply.

Thus, because approval of new drugs and biologics are likely discretionary decisions, and the manufacturing, use, and disposal of human drugs (and potentially the manufacturing, use, and disposal of biologics, though this is unclear as of now)[278] is likely to impact endangered or threatened species, Section 7 of the ESA applies. It does not matter the extent of impacts of an action on protected animal species; any impact, "however small," are sufficient to implicate duties under Section 7,[279] and certainly dramatic behavioral changes and reproductive damage counts as impacts to an endangered species.

There is precedent that supports the argument that the FDA must consult with USFWS or NMFS more often than it currently does. First, the court in *Institute for Fisheries Resources. v. United States Food & Drug Administration* required the FDA to initiate consultation in order to determine whether the new animal drug it had approved would impact protected salmon species.[280] Second, other agencies have been ordered to comply with the ESA in contexts analogous to the actions that FDA takes when it approves new drugs and biologics. For example, as previously mentioned, EPA has been ordered by a court to comply with the ESA in making a decision to have a pesticide retain its status as registered under FIFRA.[281]

Just as the FDA must evaluate the safety and efficacy of new drugs and biologics before they are sold in interstate commerce, EPA must evaluate pesticides for their safety to the environment before they can be sold or distributed.[282] When EPA registers pesticides or allows pesticides to remain registered after their initial approval, it cannot ignore the requirements of the ESA, including presumably Section 7 consultations. Based on this duty to continue to ensure

277. 7 U.S.C. § 136a(5)(c).

278. For example, a study summarizing the potential environmental risk of protein kinases, a type of biological product used as an anti-cancer drug, in surface waters, stated that "nothing is known on their occurrence and biological effects (if any) on aquatic non-target organisms, and only limited data are available for Erlotinib. Nevertheless, considering their universal mode of action and increasing consumption amounts, they should be taken into consideration and assessed for occurrence, and if need be, for ecotoxicity." Jean-Philippe Besse et al., *Anticancer drugs in surface waters: What can we say about the occurrence and environmental significance of cytotoxic, cytostatic and endocrine therapy drugs?*, 39 Env't Int'l 73, 82 (2012), (citations omitted).

279. Inst. for Fisheries Res. v. United States Food & Drug Admin., 499 F. Supp. 3d 657, 668 (N.D. Cal. 2020).; *see also* Karuk Tribe of California v. U.S. Forest Service, 681 F.3d 1006, 1027 (9th Cir. 2012).

280. *Inst. for Fisheries Res.*, 499 F. Supp. 3d at 668.

281. Defenders of Wildlife v. Administrator, E.P.A., 882 F.2d 1294 (8th Cir. 1989).

282. *Compare* 21 U.S.C § 355(a) and 42 U.S.C. § 262(a)(1)(A), *with* 7 U.S.C. §§136–136y.

compliance with the ESA, in *Defenders of Wildlife v. Administrator, E.P.A.*, EPA was held liable for a violation of the ESA when it authorized a pesticide without first receiving certain approvals from USFWS.[283] The same logic may be applied to the FDA; just because the FDA is approving a substance according to a separate statutory scheme does not mean that it can ignore the requirements of the ESA, like EPA wrongfully did in *Defenders of Wildlife*,[284] especially considering the mounting scientific evidence that human drugs cause adverse consequences to endangered or threatened species and may be contributing to their heightened risk of extinction.

However, any party seeking to challenge the FDA's compliance with Section 7(a)(2) is likely to face a number of obstacles in prevailing on their claim, despite the fact that there is an arguably strong case for Section 7(a)(2) applying to the FDA's approvals of new drugs and biologics and scientific evidence illustrating the harms pharmaceutical pollution causes to the environment.

For one, Section 7 claims are generally species-specific or specific to a critical habitat area;[285] arguing that pharmaceutical pollution harms aquatic species generally would thus likely be inadequate to trigger Section 7. Instead, a party would have to allege that the resulting pollution caused by the approval of a specific drug or biologic would have "reasonably certain" consequences to either a specific species or its critical habitat.[286] While this would limit the application of Section 7, there are still plausible allegations that would satisfy this requirement. For example, if a drug that is part of a class of drugs known to have harmful effects on aquatic habitats is likely to be used heavily in regions where wastewater treatment facilities are found within or nearby a species' critical habitat, then such a drug's approval would be a good candidate for a Section 7(a)(2) consultation. There are also listed species which are already known to be harmed by certain types of pharmaceutical pollution, such as the razorback sucker, the desert pupfish, and the Santa Ana sucker.[287] A party could thus allege that, for new drugs and biologics that are (1) similar enough in structure or mode of action to the pharmaceuticals harming these specific species and (2) likely to be used by people in the areas near these species, there is enough of a risk of jeopardizing these species' existence that a Section 7 consultation is necessary.

Second, part of the issue with pharmaceutical pollution is that there is a lot of scientific uncertainty and lack of information on the harms caused by these

283. *See generally* Defenders of Wildlife v. Administrator, E.P.A., 882 F.2d 1294 (8th Cir. 1989). Note that the EPA had consulted with USFWS to some degree, but the EPA's exact failure was that it did not request authorization for incidental takes from USFWS, which is governed by a different section of the ESA. Nonetheless, this case illustrates that approving a substance through an act can trigger responsibilities under the ESA.

284. *See id.*

285. 50 C.F.R. § 402.10(a).

286. 50 C.F.R. § 402.02.

287. Jacki Lopez, *Endocrine-disrupting Chemical Pollution: Why The EPA Should Regulate These Chemicals Under The Clean Water Act*, 10 Sustainable Dev. L. and Pol'y 19, 20–21 (2010).

substances before they are released into the environment. The Section 7 process ultimately relies on an analysis of the "best available scientific and commercial data,"[288] and the scientific uncertainty in this field may mean that there is not enough data to justify either a biological opinion, if consultation is initiated, or the determination needed to initiate even informal conference. In at least some cases, courts have held that USFWS or NMFS can rely on "imperfect, weak, and not necessarily dispositive data,"[289] but nonetheless there still needs to be at least some "sufficiently strong" evidence to support the agency's conclusions.[290] At least under the 9th Circuit's interpretation of the ESA, it is "not enough for [USFWS] to simply invoke 'scientific uncertainty' to justify" its decisions.[291] This means that, in some cases involving pharmaceutical risks, there may not be enough evidence to support a consultation requirement under Section 7(a)(2).

Despite these potential difficulties, the importance of more common Section 7 consultations and the more frequent use of the extraordinary circumstances cannot be overstated, given the context of the current ecological crisis. Biodiversity loss is not just detrimental to ecosystems and animals in and of itself but also to humanity; the loss of aquatic life may contribute to food insecurity, economic distress, and the potential loss of medically important species, especially for vulnerable populations.[292] The current loss of biodiversity and mass extinction event is unprecedented and requires immediate action, or else we risk "eroding the very foundations of our economies, livelihoods, food security, health and quality of life worldwide."[293] The FDA must recognize the novel and dire nature of the biodiversity crisis and should thus take immediate action to gather the necessary information to ensure that the drugs and biologics that it approves are not needlessly exacerbating this crisis. It can do this immediately, without either altering its regulatory framework or waiting for Congress to amend the laws; all the FDA has to do is comply with the laws and regulations which are already in place under NEPA and the ESA.

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288. 50 C.F.R. 402.14(d); 50 C.F.R. 402.34; U.S. Fish & Wildlife Serv., Consultation Handbook: Procedures for Conducting Consultation and Conference Activities Under Section 7 of the Endangered Species Act xxi (Mar. 1998).

289. League of Wilderness Defs./Blue Mountains Biodiversity Project v. Connaughton, 752 F.3d 755, 764 (9th Cir. 2014); Greenpeace Action v. Franklin, 14 F.3d 1324, 1336–37 (9th Cir. 1992).

290. *League of Wilderness*, 752 F.3d at 764.

291. Ctr. for Biological Diversity v. Zinke, 900 F.3d 1053, 1072 (9th Cir. 2018) (discussing uncertainty in a number of cases, particularly those involving the ESA and climate change).

292. Peter Giger, *Biodiversity loss puts our food supplies and medical care at risk. It must be stopped*, World Economic Forum (Jan. 15, 2020), https://perma.cc/7V8Q-UUR5.

293. *UN Report: Nature's Dangerous Decline 'Unprecedented'; Species Extinction Rates 'Accelerating'*, United Nations: Sustainable Development Goals (May 6, 2019), https://perma.cc/GZ2E-3FFN.

Conclusion

As America's most famous frog once said, "it's not easy being green."[294] But, just because a certain course of action may not be easy does not mean it is not worthwhile to pursue. The FDA has an opportunity to pursue a more environmentally protective approach when it takes actions related to new drugs and biological products, and in fact the FDA does not need to undertake rulemaking or a formal change in policy in order to do this. Rather, all it must do is more robustly implement the laws as they are written now, since the FDA can immediately ensure it is not worsening risks to endangered and protected aquatic species by using its current NEPA regulations and Section 7(a)(2) of the ESA. For one, the FDA can require the completion of more EAs and EIS's based on a new interpretation of the extraordinary circumstances exception in its current NEPA regulations.[295] Additionally, more robust environmental analysis may reveal dangers to human health caused by drugs that other testing does not, meaning that this approach is also useful from a human health perspective.

The FDA also can take time to consult with USFWS and NMFS, especially for the approvals of drugs which are likely to harm aquatic life, including drugs with estrogenic, androgenic, and thyroid activities, which impact the reproductive capabilities of aquatic life, and drugs which otherwise impact the behavior and survival of aquatic species, including antidepressants and opioids. That way, the FDA is consulting with the experts on protected species to ensure that it knows the potential risks to those species as well as ways to mitigate those risks. In sum, if the FDA gathers information on the impacts of these drugs before they enter the marketplace, even if it ultimately decides to approve the drug, then at least other agencies, advocates, companies manufacturing the drugs, and governments will have information at hand in order to mitigate harms to aquatic life.

The FDA can also acknowledge the extent and imminence of the biodiversity crisis and ensure that it does not harm the environment through its other policies. For example, it can change its policy on which drugs should be disposed of by flushing them if drug take-back locations are unavailable.[296] The FDA "flush list", which mostly includes opioids, has the potential to result in the discharge of drugs that influence the behavior of possibly endangered or threatened species in ways that impair their likelihood of survival.[297] Since

294. Sesame Street, It's Not Easy Being Green (Kermit's Song), YouTube (Dec. 11, 2008), https://perma.cc/K6JV-TLFG.

295. *See supra* Part IV.

296. *Drug Disposal: FDA's Flush List for Certain Medicines*, U.S. Food & Drug Admin. (Oct. 10, 2020), https://perma.cc/5G9N-EQQZ.

297. *See supra* notes 166–78 and accompanying text. The main study that FDA cites in support for its flush list having negligible environmental impacts acknowledges that limited data was available and that "only limited ecological toxicity data were available for some flush list

this list was published informally, the FDA can change its recommendations on which drugs are permissible to flush, or otherwise can follow through with other alternative drug disposal proposals, such as the use of mail-back envelopes included with drug packaging.[298]

At this point, the frog is out of the pond—FDA has already approved tens of thousands of drugs and biologics.[299] But going forward, the FDA can ensure that it is fulfilling its obligations under federal environmental laws and gathering all of the requisite information in order to minimize harms to the environment. The nature of the biodiversity crisis demands immediate action, because once a species is extinct, it is gone forever. The FDA must take action to ensure that when the next generation goes on to fish in a pond, catch tadpoles in a creek, or snorkel among coral reefs, there are still fish, frogs, and corals left in the wild to find.

APIs. In addition, relatively little is known about behavioral and other more subtle effects of flush list APIs on aquatic biota and, in turn, if such effects could result in population-level consequences." Usman Khan et al., *Risks associated with the environmental release of pharmaceuticals on the U.S. Food and Drug Administration "flush list"*, 609 Sci. Total Env't 1023, 1037.

298. Providing Mail-Back Envelopes and Education on Safe Disposal With Opioid Analgesics Dispensed in an Outpatient Setting; Establishment of a Public Docket; Request for Comments, 87 Fed. Reg. 23869 (2022).

299. *Fact Sheet: FDA at a Glance*, U.S. Food & Drug Admin. (Aug 17, 2022), https://perma.cc/7QLR-5E4M.