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THE UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF CALIFORNIA

INSTITUTE FOR FISHERIES RESOURCES; PACIFIC COAST FEDERATION OF FISHERMEN'S ASSOCIATIONS; GOLDEN GATE SALMON ASSOCIATION; KENNEBEC REBORN; FRIENDS OF MERRYMEETING BAY; CASCADIA WILDLANDS; CENTER FOR BIOLOGICAL DIVERSITY; ECOLOGY ACTION CENTRE; FRIENDS OF THE EARTH; FOOD AND WATER WATCH; THE QUINAULT INDIAN NATION; and CENTER FOR FOOD SAFETY, *Plaintiffs,* v. SYLVIA MATHEWS BURWELL, Secretary of the United States Department of Health and Human Services; DR. ROBERT M. CALIFF, M.D., Commissioner of the United States Food And Drug Administration; the UNITED STATES FOOD AND DRUG ADMINISTRATION; and the UNITED STATES FISH AND WILDLIFE SERVICE, *Defendants.*	Case No. 3:16-cv-01574-VC **AMENDED COMPLAINT FOR DECLARATORY AND INJUNCTIVE RELIEF**

INTRODUCTION

1. This case challenges the United States Food and Drug Administration's approval of a novel genetically engineered salmon for human consumption without considering or fully disclosing the environmental and other risks of this unprecedented decision.

2. Plaintiffs Institute for Fisheries Resources, Pacific Coast Federation of Fishermen's Associations, Golden Gate Salmon Association, Kennebec Reborn, Friends of Merrymeeting Bay, Cascadia Wildlands, Center for Biological Diversity, Ecology Action Centre, Friends of the Earth, Food and Water Watch, the Quinault Indian Nation, and Center for Food Safety (collectively Plaintiffs), on behalf of their adversely affected members, challenge Defendants' November 19, 2015, decision to approve an application by AquaBounty Technologies, Inc. (AquaBounty) to develop, market, and sell for human consumption genetically engineered (GE) salmon.

3. AquaBounty's GE salmon (AquAdvantage salmon) is a novel, man-made animal: an Atlantic salmon genetically engineered with genes from a deep water ocean eelpout and a Pacific Chinook salmon in order to make it grow unnaturally fast.

4. The approval of GE salmon by the United States Food and Drug Administration; Sylvia Mathews Burwell, Secretary of the United States Department of Health and Human Services; and Dr. Robert M. Califf, Commissioner of the United States Food and Drug Administration (collectively FDA or the agency) marks the first occasion in history where any country has authorized the mass production of a GE animal of any variety to be sold as food. Accordingly, this action will serve as a precedent for the assessment and regulation of all potential future GE animals manufactured for human consumption, and for review of their impacts on public health and the environment.

5. Pursuant to the FDA approval, AquaBounty will manufacture its GE salmon at a facility located on Prince Edward Island, Canada, and then transport, by land and air, the resulting eggs to a separate facility located in Panama, where the GE eggs will be grown to maturity, before being processed and shipped back to the United States for sale. Those two operational sites present substantial environmental risks, as discussed below.

6. Importantly, this case concerns more than these two sites; it has much broader implications. In order to gain FDA approval and downplay risks and concerns from the public, AquaBounty sought to limit its application to just these two facilities; yet, since at least 2010, the company has been engaged in efforts to expand the production of GE salmon to facilities around the world, repeatedly telling its investors that it plans to raise GE salmon at other locations, in both other foreign markets and the United States, beginning in 2016, and to sell the salmon in other markets, including Canada, Argentina, Brazil, and China. In fact, AquaBounty has already communicated its intent to import GE salmon eggs into the U.S. to be grown at other sites, and has recently expanded its operations on Prince Edward Island. These expansions are a necessary outgrowth of the AquaBounty business plan, since large-scale aquaculture is not economically viable if it relies solely upon the highly convoluted, 5,000-mile multinational journey that AquaBounty has initially proposed. This constitutes merely the company's effort to open the regulatory door. Yet, despite the company's public statements, FDA approved the AquaBounty application without disclosing or analyzing the significant environmental effects from this foreseeable expansion.

7. The challenged decision is unlawful because FDA has not adequately assessed the full range of potentially significant environmental and ecological effects presented by the AquaBounty application, and/or significant changed circumstances since that application was submitted, in violation of the Federal Food, Drug, and Cosmetics Act, 21 U.S.C. §§ 301-399(f) (FFDCA); the National Environmental Policy Act, 42 U.S.C. §§ 4221-4370h (NEPA); the Endangered Species Act, 16 U.S.C. §§ 1531-1544 (ESA); and the Administrative Procedure Act, 5 U.S.C. §§ 701-706 (APA). FDA has created a GE animal program that is a major federal action, without preparing or engaging in a programmatic or other analysis of the impacts of that program as required by NEPA. FDA also arbitrarily and capriciously denied the 2011 citizen petition filed by several of the Plaintiffs by not preparing a full Environmental Impact Statement (EIS) pursuant to NEPA on the foreseeable impacts of its decision.

8. Instead, FDA completed an extremely limited environmental assessment (EA) and made a finding of no significant impact (FONSI) for the approval of AquaBounty's GE salmon,

which together fail to discuss or adequately evaluate myriad scientific questions regarding the risk of significant and irreversible environmental, ecological, and intertwined socioeconomic harms related to the production, commercialization, and proliferation of AquaBounty's GE fish. These threats include: the risk that GE salmon will escape from the facilities where they are manufactured or grown and interbreed with wild endangered salmon, compete with them for food and space, or pass on infectious diseases; the interrelated impacts to salmon fisheries and the social and economic well-being of those who depend on them; and the risks to ecosystems from the introduction of an invasive species. Expert scientists, including those within other federal agencies charged with the protection of fish and marine ecosystems, repeatedly cited these risks and expressed great concern with FDA's narrow, incomplete, unsubstantiated, and outdated analysis of the potential environmental and ecological threats posed by GE salmon. But, FDA ignored those concerns in its decisionmaking.

9. The inadequate EA, FONSI, and attendant decision not to prepare a comprehensive EIS are the result of FDA's failure to take the legally required "hard look" at these direct, indirect, and cumulative impacts of the agency's decision to allow mass production of AquaBounty's GE salmon, and are arbitrary, capricious, and contrary to NEPA. In addition, the agency's review was improperly segmented from AquaBounty's broader plan; it failed to adequately consider or assess numerous other reasonable alternatives to the proposed action; FDA has not supplemented that analysis based on AquaBounty's expanded Canadian facilities and operations; and it improperly relied on AquaBounty's proposed mitigation.

10. The challenged decision is also unlawful, in violation of the ESA, because FDA failed to consult with the federal fish and wildlife agencies to insure that its approval of AquaBounty's application was not likely to jeopardize endangered and threatened species or adversely modify critical habitat. The expert biologists at the wildlife and fisheries agencies, the National Marine Fisheries Service and U.S. Fish & Wildlife Services (collectively Services), urged FDA to engage in ESA consultation in association with its review of AquaBounty's application. These agencies' scientists described the very real potential that approval of the application may affect endangered Atlantic salmon populations. FDA's determination that its

action would have "no effect" on any endangered or threatened species or critical habitat—and consequently, its refusal to complete ESA consultation with the expert agencies—was based on the faulty assumption that GE salmon could not escape from AquaBounty's facilities, FDA's outdated risk analysis methods, and the agency's unlawfully constricted view of the foreseeable impacts of its approval decision.

11. Even apart from these vital considerations, FDA's decision to approve AquaBounty's GE salmon application should be vacated and set aside because FDA lacks the statutory authority to regulate GE animals as a "new animal drug" under the FFDCA. The FFDCA does not explicitly grant FDA authority to regulate GE animals. Indeed, Congress never intended or provided a means for FDA to regulate twenty-first century GE animals using its 1938 authority over veterinary animal drugs. To the contrary, GE animals present enormously different risks and impacts than drugs, requiring different expertise, analyses, and regulation than were contemplated when Congress enacted the FFDCA. Nevertheless, FDA issued Guidance for Industry 187, *The Regulation of Genetically Engineered Animals Containing Heritable Recombinant DNA Constructs* (GE Animal Guidance or the Guidance), interpreting the definition of "new animal drug" under the FFDCA to include GE animals, asserting exclusive authority over GE animals under the new animal drug provisions of the FFDCA, and purportedly outlining the steps that FDA will follow when considering applications for GE animals. FDA's approval of AquaBounty's application and the issuance of its GE Animal Guidance represent an unlawful effort to extend FDA's regulatory reach far beyond the statutory mandates of the FFDCA. FDA's assertion of jurisdiction under the GE Animal Guidance and its approval of the AquaBounty application are thus *ultra vires* and contrary to law in violation of the APA and the FFDCA.

12. Finally, even if FDA had the authority to issue the GE Animal Guidance, the guidance itself fails to explain how FDA will substantively incorporate important environmental considerations into its assessment of safety and effectiveness as a part of the review and approval of GE animals. As a practical result of the inadequacies of the GE Animal Guidance, FDA failed

to adequately consider environmental risks as part of its statutory "safety" evaluation when reviewing and approving AquaBounty's GE salmon application in this case.

13. Accordingly, Plaintiffs ask this Court to: (1) declare that FDA's decision to approve the AquaBounty application for GE salmon is arbitrary, capricious, and in violation of the APA, NEPA, and the ESA; (2) declare that the FDA GE Animal Guidance is unlawful under the APA and the FFDCA, that FDA has no jurisdiction to regulate GE animals under the new animal drug provisions of the FFDCA, and that FDA's approval of AquaBounty's application is *ultra vires* and contrary to law under the APA and the FFDCA; (3) vacate FDA's November 19, 2015 approval decision; and (4) enjoin FDA to withdraw its assertion of jurisdiction over GE animals and enjoin FDA from taking further action on AquaBounty's GE salmon application or any other application for commercialization of a genetically engineered food animal until Congress provides explicit statutory authority governing regulation of such products and vests clear authority for such regulation in a named agency of the Executive Branch of the United States.

JURISDICTION AND VENUE

14. This Court has jurisdiction over this action pursuant to 28 U.S.C. § 1331 (federal question), 28 U.S.C. § 1346 (United States as a defendant), 28 U.S.C. §§ 2201-02 (declaratory and injunctive relief) and 5 U.S.C. §§ 701-706 (APA). An actual controversy exists between the parties within the meaning of 28 U.S.C. § 2201.

15. The Court has jurisdiction to review FDA's failure to consult with the Services under the citizen-suit provision of the ESA, 16 U.S.C. § 1540 (g)(1), which provides that the "district courts shall have jurisdiction … to enforce any such provision or regulation" of the ESA. As required by the ESA, Plaintiffs provided sixty days' notice of their intent to sue by letter sent to FDA and the Services on December 22, 2015 and January 25, 2016. Copies of those letters are appended as Exhibit 1. FDA has not remedied the violations set out in those sixty-day notices. *See* 16 U.S.C. § 1540(g)(2)(A).

16. Venue is properly vested in this judicial district under 28 U.S.C. § 1391 (e)(1)(C) because no real property is involved in this action, several of the Plaintiffs reside in and/or

maintain places of business in this district, and members of the Plaintiff organizations reside in this district.

PARTIES

Plaintiffs

17. Plaintiff **Institute for Fisheries Resources** (IFR) is a nonprofit public interest marine resources protection and conservation organization. IFR's members, most of whom are commercial salmon fishermen or women, have personal interests in the restoration of salmon fisheries.

18. Plaintiff **Pacific Coast Federation of Fishermen's Associations** (PCFFA) is a nonprofit membership organization composed of trade associations of commercial fisherman on the west coast, from San Diego to Alaska. PCFFA is separate from, but closely related to, IFR. PCFFA is incorporated in and headquartered in California. For over thirty years, PCFFA has advocated to ensure the rights of individual fishermen and to fight for the long-term survival of commercial fishing as a livelihood and way of life. PCFFA's port and member associations and at-large members represent nearly 1,200 commercial fishing families who are small and mid-sized commercial fishing boat owners and operators, most of whom derive all or a portion of their income from the harvesting of Pacific salmon.

19. Plaintiff **Golden Gate Salmon Association** (GGSA) is a coalition of salmon advocates, including commercial and recreational fishermen, businesses, restaurants, tribes, environmentalists, and communities that rely on salmon, from Oregon to the Central Coast, through the Bay-Delta and into the Central Valley. GGSA seeks to protect and restore California's largest salmon producing habitat in the Central Valley for the benefit of the Bay-Delta ecosystem and the diverse communities that rely on salmon as a long-term, sustainable commercial, recreational and cultural resource.

20. Plaintiff **Center for Food Safety** (CFS) is a public interest, nonprofit organization whose mission is to empower people, support farmers, and protect the earth from the adverse impacts of industrial food production. CFS has more than 750,000 members across the country and offices in San Francisco, California; Portland, Oregon; Washington, D.C.; and

Honolulu, Hawaii. CFS is a recognized national leader on the issue of genetically engineered crops and other GE organisms, and has worked to improve their regulation and address their impacts continuously since the organization's inception in 1997.

21. Plaintiff **Friends of the Earth, U.S.** (FoE) is a national, nonprofit environmental advocacy organization founded in 1969 and incorporated in the District of Columbia, with its headquarters in Washington, D.C. and an office in Berkeley, California. FoE's mission is to defend the environment and champion a healthy and just world. To this end, FoE promotes policies and actions that address the climate change crisis, minimize the negative impacts of environmental pollution, keep toxic and risky technologies out of the food we eat and products we use, and protect marine ecosystems and the people who live and work near them. FoE has more than 175,000 members in all fifty states.

22. Plaintiff **Center for Biological Diversity** (the Center) is a nonprofit incorporated in California and headquartered in Tucson, Arizona, with field offices throughout the United States, including Arizona, New Mexico, California, Nevada, Oregon, Washington, Alaska, Minnesota, Vermont, Florida, and Washington, D.C. The Center uses science, law, and media to secure a future for all species, great or small, hovering on the brink of extinction.

23. Plaintiff **Food and Water Watch** (FWW) is a national, nonprofit consumer advocacy organization with its headquarters in Washington, D.C. and several offices throughout the United States, including in Oakland, California. FWW works to ensure safe food and clean water, advocating for safe, wholesome food produced in a humane and sustainable manner, and public, rather than private control of water resources, including oceans, rivers, and groundwater. For more than five years, FWW has advocated for stronger regulation and labeling of genetically engineered organisms, including salmon. FWW has approximately 76,000 members and 900,000 supporters in the United States.

24. Plaintiff **Ecology Action Centre** (EAC), established in 1971, is Nova Scotia's largest and oldest environmental organization, serving Nova Scotia in a variety of capacities for over forty years. EAC has over 3,000 members who reside predominantly in Nova Scotia, with some members residing in the other Atlantic provinces, the rest of Canada and internationally.

Drawing on current science and public policy, staff and members of the organization work to protect and conserve terrestrial and aquatic ecosystems in Nova Scotia and Atlantic Canada. EAC has played a pivotal role in protecting important ecological areas in Nova Scotia including some of the remaining Atlantic salmon rivers and their surrounding habitat. EAC has a strong track record when it comes to marine conservation, with staff participating in a range of provincial, national and international processes and fora to advance sustainable fishing practices and the protection of endangered or threatened species such as Atlantic salmon. In early 2014 EAC, along with Living Oceans Society, challenged the Canadian government's decision to allow AquaBounty Canada Inc. to manufacture and export genetically modified salmon eggs. EAC considers genetically modified salmon and genetic contamination a serious threat to Atlantic salmon in Nova Scotia and throughout its range.

25. Plaintiff **Cascadia Wildlands** (Cascadia) is a nonprofit organization incorporated in Oregon, with a field office in Cordova, Alaska, that focuses on conservation of the wildlife and communities of the Cascadia bioregion (*i.e.*, the Pacific coastal temperate rainforest, stretching from northern California to southeast Alaska). Cascadia has approximately 5,000 members throughout the United States, including subsistence, commercial, and recreational fishermen; and, processors, marketers, and consumers of salmon. Cascadia educates, agitates, and inspires a movement to protect and restore Cascadia's wild ecosystems, including healthy wild salmon populations. Salmon are widely acknowledged as a keystone species in the bioregion, and so Cascadia members, like most residents, have a special relationship with salmon.

26. Plaintiff **Kennebec Reborn** is a 501(c)(3) Maine nonprofit conservation organization founded in 2011 to advocate and promote the restoration of Atlantic salmon and other native sea-run fish to their historic habitat in the rivers of New England. Kennebec Reborn and its board members work closely with allied national, regional, and local conservation groups at various levels of formality to bring native sea-run fish back to their homes by advocating for fish passage and improved habitat conditions within the Kennebec and Maine's other coastal watersheds. Kennebec Reborn members have been involved as plaintiffs and citizen intervenors

since 1996 in successful litigation to protect native Atlantic salmon in Maine under the ESA, including litigation to expand ESA protections to Atlantic salmon in the Kennebec, Androscoggin, and Penobscot Rivers. Kennebec Reborn also is the caretaker of the Atlantic Salmon History Project, an online archive of historic documents and records that describe the former abundance of sea-run fish in New England rivers and their progressive diminution since the late 1700s.

27. Plaintiff **Friends of Merrymeeting Bay** is a nonprofit organization, incorporated in Maine, dedicated to preserving the ecological, aesthetic, biological, and commercial values of Merrymeeting Bay, its watershed, and the Gulf of Maine (the part of the Northwest Atlantic Ocean where Merrymeeting Bay is located). Friends of Merrymeeting Bay and its members work to protect these waters and their fish and wildlife through research, advocacy, education, and land conservation. Friends of Merrymeeting Bay and its members are dedicated to the protection of the last remaining Atlantic salmon populations in Maine and were instrumental in the fight to secure the ESA listing for Atlantic salmon in the Kennebec, Androscoggin, and Penobscot Rivers.

28. Plaintiff **Quinault Indian Nation** is a federally-recognized Indian tribe and sovereign nation consisting of the Quinault and Queets tribes and descendants of five other coastal tribes: Quileute, Hoh, Chehalis, Chinook, and Cowlitz. The Quinault Reservation is located in the southwestern corner of the Olympic Peninsula in Washington State and is comprised of magnificent forests, swift-flowing rivers, gleaming lakes, and twenty-three miles of unspoiled Pacific coastline. The Quinault have been called the Canoe People because of the primacy of the ocean, bays, estuaries, and rivers to every aspect of tribal life. The Quinault Indian Nation is a signatory to the Treaty of Olympia (1856) in which it reserved a right to take fish at its "usual and accustomed fishing grounds and stations" and the privilege of hunting and gathering, among other rights, in exchange for ceding lands it historically roamed freely. Treaties create a special fiduciary duty and trust responsibility upon all agencies of the United States and states to protect treaty rights, including fishing rights. *Seminole Nation v. United States*, 316 U.S. 286, 297 (1942). These rights cannot be abrogated except by explicit

Congressional authorization. In the landmark "Boldt decision," a federal court confirmed that Indian tribes, including the Quinault Nation, have a right to half of the harvestable fish in state waters and established the tribes as co-managers of the fisheries resource with the State of Washington. The Boldt decision also confirmed the Quinault Nation's usual and accustomed fishing areas include Reservation waters, Grays Harbor and the streams emptying into it, and the Pacific Ocean adjacent to its territory. *United States v. Washington*, 384 F. Supp. 312, 374-375 (W.D. Wash. 1974). The Quinault Indian Nation has an obvious and keen interest in protecting the fish and fish habitat that it relies on to exercise its federally-guaranteed treaty fishing rights, as well as the traditional areas used for gathering plants for traditional cultural use. FDA's approval of GE salmon for commercial production and human consumption without adequate consideration for the environmental consequences of that approval threatens these interests and harms the Quinault's commercial, recreational, aesthetic, spiritual, and other interests.

29. Members of the Plaintiff organizations and the Quinault Indian Nation use and enjoy salmon and salmon habitats on both the east and west coasts of the United States and Canada for recreational, scientific, aesthetic, cultural, spiritual, subsistence, and commercial purposes. Plaintiffs' members observe and interact with Atlantic and Pacific salmon and their marine and freshwater habitats through wildlife observation, study and photography, and recreational, commercial, and subsistence fishing. These activities require viable populations of wild Atlantic and Pacific salmon that contribute to healthy, functioning ecosystems. The identity and genetic integrity of wild salmon runs, populations, and fisheries is itself an asset that is used and valued by Plaintiffs' members. Plaintiffs and their members derive or, but for the threatened and endangered status of many Atlantic and Pacific salmon species, would derive recreational, scientific, aesthetic, cultural, spiritual, and commercial benefits from the existence of these species in the wild.

30. FDA's approval of the AquaBounty GE salmon harms Plaintiffs and their members' past, present, and future enjoyment of salmonids and salmonid habitat by allowing production of GE salmon to proceed without adequate regulation and analyses of associated, and potentially irreversible, environmental and ecological impacts. These aesthetic, cultural,

spiritual, conservation, recreational, commercial, subsistence, scientific, and procedural interests of Plaintiffs and their respective members have been, are being, and, unless the relief prayed for herein is granted, will continue to be adversely affected and irreparably injured by FDA's failure to comply with NEPA, the APA, the ESA, and the FFDCA, as described below. Plaintiffs have no adequate remedy at law.

Defendants

31. Defendant Sylvia Mathews Burwell is the Secretary of the United States Department of Health and Human Services, which includes the United States Food and Drug Administration. The Secretary of the U.S. Department of Health and Human Services, "through the Commissioner" of FDA, regulates new animal drugs. 21 U.S.C. § 393(d)(2). Secretary Burwell is named a defendant solely in her official capacity.

32. Defendant Dr. Robert M. Califf, M.D. is the Commissioner of the U.S. Food and Drug Administration. In that capacity, he is directly responsible for overseeing the FDA review process for the AquaBounty application and is tasked with the authority to approve or deny AquaBounty's application upon a finding that applicable legal requirements have or have not been met. Commissioner Califf is named as a defendant solely in his official capacity. Commissioner Califf is responsible for the approval of AquaBounty's application on November 19, 2015, through Bernadette M. Dunham, D.V.M., Ph.D., Director, Center for Veterinary Medicine, who formally signed the agency's approval letter.

33. Defendant United States Food and Drug Administration is a federal agency within the U.S. Department of Health and Human Services. FDA is charged with the regulation of medical products, tobacco, foods, and veterinary medicine. As described by the agency itself, FDA is responsible for protecting public health by assuring that foods (except for meat from livestock, poultry, and some egg products which are regulated by the U.S. Department of Agriculture) are safe, wholesome, sanitary, and properly labeled; ensuring that human and veterinary drugs, vaccines and other biological products, and medical devices intended for human use are safe and effective; protecting the public from electronic product radiation; assuring cosmetics and dietary supplements are safe and properly labeled; regulating tobacco

products; and advancing the public health by helping to speed product innovations. FDA's November 19, 2015, approval of the AquaBounty new animal drug application is the only existing federal agency approval of AquaBounty's GE salmon.

34. Defendant United States Fish and Wildlife Service (FWS) is a federal agency within the Department of the Interior authorized and required by law to protect and manage fish, wildlife, and native plant resources of the United States, including enforcing the ESA. FWS has been delegated authority by the Secretary of the Interior to implement the ESA for many endangered fish species, including shared responsibility for making decisions and promulgating regulations for endangered Atlantic salmon.

STATUTORY AND REGULATORY BACKGROUND

I. Federal Food Drug and Cosmetic Act

35. In enacting the FFDCA in 1938, Congress provided FDA the authority and obligation to protect public health and safety by overseeing certain food products, drugs, and cosmetics. Through the FFDCA, Congress charged FDA to "promote the public health" by ensuring that "human and veterinary drugs are safe and effective." 21 U.S.C. § 393.

36. The FFDCA does not explicitly authorize FDA to assert exclusive jurisdiction over the production and commercialization of GE animals or their food products. *See, e.g.*, 21 U.S.C. § 321 (providing definitions for the FFDCA, and not defining "animals" or making any reference to "genetic engineering"); *id.* §§ 341-350*l* (establishing food safety and testing laws, with no mention of genetic engineering); *id.* §§ 351-360ddd-2. Instead, FDA has asserted such jurisdiction under the "new animal drug" provisions of the FFDCA. *Id.* § 360b.

37. Under the FFDCA, the term "drug" includes, among other things, "articles (other than food) intended to affect the structure or any function of the body of man or other animals…." 21 U.S.C. § 321(g)(1)(C). "New animal drug" is any drug intended for use in animals that has not been used to a material extent or for a material time, and is not recognized by "experts qualified by scientific training and experience" as safe and effective for use under the conditions prescribed. *Id*. § 321(v).

38. Generally, under the FFDCA, a new animal drug is deemed "unsafe" unless FDA has approved a new animal drug application for the drug and its use conforms to its labeling and the conditions of the approved application. 21 U.S.C. § 360b(a)(1).

39. The FFDCA requires an applicant to submit reports to demonstrate whether the drug is "safe and effective for use." 21 U.S.C. § 360b(b)(1)(A); *see also* 21 C.F.R. § 514.1(8) (FDA regulations requiring applicant to submit evidence to establish the "safety and effectiveness" of a new animal drug). The applicant must also submit "other use restrictions . . . in order to assure that the proposed use of such drug will be safe." 21 U.S.C. § 360b(b)(1)(H).

40. A new animal drug application must also contain either an environmental assessment or present an analysis and justification for why the applicant believes that it qualifies for a categorical exemption under NEPA. 21 C.F.R. § 514.1(b)(14). Consideration of this information is integral to FDA's review of the application. *See* 21 C.F.R. § 514.110(b)(10). Indeed, FDA shall disapprove the application if "[t]he applicant fails to submit an adequate environmental assessment under § 25.40 of this chapter or fails to provide sufficient information to establish that the requested action is subject to categorical exclusion under § 25.30 or § 25.33 of this chapter." 21 C.F.R. § 514.111(a)(9).

41. FDA's approval of an application hinges upon the agency's finding that the new animal drug is "safe and effective" for the purposes intended and for use under the prescribed conditions. *See, e.g.*, 21 U.S.C. §§ 360b(d)(1)(A), (B), (D), (E).

42. The FFDCA does not define the phrases "safe and effective," or "safety and effectiveness," or the term "effective." The statute states generally that the term "safe" "has reference to the health of man or animal." 21 U.S.C. § 321(u). In considering whether a drug is "safe," FDA may consider, among other things: (1) "the cumulative effect on man or animal of such drug;" (2) "safety factors" which experts consider appropriate; and (3) whether the conditions in the proposed labeling are reasonably certain to be followed. 21 U.S.C. § 360b(d)(2).

43. When FDA approves a new animal drug application, it must publish in the Federal Register any "conditions and indications of use of the new animal drug … and such other

information, … as the Secretary deems necessary to assure the safe and effective use of such drug." 21 U.S.C. § 360b(i); *see also* 21 C.F.R. § 514.105.

44. FDA's authority to oversee and enforce new animal drug approvals is tied to the continued "safety" of the drug. A drug is considered "unsafe" if the use does not conform to the approved application. 21 U.S.C. § 360b(a)(1)(A). FDA also has authority to withdraw approval of a new animal drug if it finds that its use is "unsafe" even under the approved conditions or if the applicant makes any changes from the standpoint of "safety or effectiveness." 21 U.S.C. § 360b(e)(1).

45. FDA's regulations provide that an applicant may make "minor," "moderate," or "major" changes to the manufacturing process for a previously approved new animal drug. 21 C.F.R. §§ 514.8(b)(2), (3), (4). FDA regulations do not precisely define these terms, but provide a non-exclusive list of examples. *Id*. An applicant can make "minor changes" to the manufacture of a drug without seeking any additional approval from FDA. 21 C.F.R. § 514.8(b)(4). An applicant is only required to inform FDA of these "minor changes" on an annual basis. *Id*. §§ 514.8(a)(iii), (b). FDA is not required to review, evaluate, or approve any such minor changes. *Id*.

46. "Moderate" or "major" manufacturing changes require an applicant to submit a supplemental application. 21 C.F.R. §§ 514.8(b)(2), (3). The agency's regulations leave it to the applicant to determine independently whether its changes are "major" or "moderate" and therefore require submission of a supplemental application. *Id.* The regulations do not require FDA to review or evaluate an applicant's changes in order to determine whether it has correctly classified those changes under the regulations. *See* 21 C.F.R. § 514.8. In addition, an applicant may proceed with making "moderate" changes before receiving approval for a supplemental application submitted to FDA. *Id*. § 514.8(b)(3).

47. Once an applicant submits a supplemental application, FDA determines whether to reevaluate the safety or effectiveness of the drug as part of the approval process. 21 C.F.R. § 514.106(b). The regulations allow FDA to determine what type of environmental analysis to apply when reviewing the application, including whether a new EA or other additional NEPA

analysis is required, or if an applicant can rely on the original EA for the new application. *See* FDA, Guidance for Industry 82, Development of Supplemental Applications for Approved New Animal Drugs (2002), at 8, 10-22.

48. FDA's approval of a new animal drug application is a major federal action subject to the requirements of NEPA. *See* 21 § C.F.R. § 25.20(m).

II. The National Environmental Policy Act

49. NEPA is our "national charter for protection of the environment." 40 C.F.R. § 1500.1(a). Its purpose is to "promote efforts which will prevent or eliminate damage to the environment." 42 U.S.C. § 4321. Regulations promulgated by the Council on Environmental Quality (CEQ) implement NEPA and govern FDA's decisionmaking. *See* 40 C.F.R. §§ 1500-1508; 21 C.F.R. Part 25.

50. When enacting NEPA, Congress expressed great concern for the "profound impact of man's activity on the interrelations of all components of the natural environment, particularly the profound influences of … new and expanding technological advances …." 42 U.S.C. § 4331(a). Congress was specifically wary of "[a] growing technological power which is far outstripping man's capacity to understand and ability to control its impact on the environment." S. Rep. No. 91-296, 91st Cong., 1st Sess., at 6, 1969 U.S. Code Con. & Admin. News 1969.

51. The twin pillars of NEPA are the requirements that agencies (1) carefully evaluate the environmental impacts of proposed actions before undertaking the action; and (2) fully advise the public of the potential impacts of those actions, and of alternatives. NEPA requires federal agencies to fully consider and disclose the environmental consequences of an agency action before proceeding with that action—to take a "hard look." 42 U.S.C. § 4332(2)(C); 40 C.F.R. §§ 1501.2, 1501.4, 1502.5. An agency's evaluation of environmental consequences must be based on "accurate scientific" information of "high quality." 40 C.F.R. § 1500.1(b). If there are not sufficient data available, the agency must follow the requisite procedure for addressing or evaluating the impacts in view of incomplete or unavailable information. *Id*. § 1502.22.

52. NEPA requires federal agencies to prepare an EIS for all "major [f]ederal actions significantly affecting the quality of the human environment." 42 U.S.C. § 4332(2)(C); 40 C.F.R. § 1501.4. Under certain circumstances, the agency can prepare an EA that provides "sufficient evidence and analysis for determining whether to prepare" an EIS and that contributes to the agency's compliance with NEPA. 40 C.F.R. §§ 1508.9, 1501.4.

53. In determining whether an action "significantly" affects the environment, the agency must analyze significance in several contexts "such as society as a whole (human, national), the affected region, the affected interests, and the locality." 40 C.F.R. § 1508.27(a). Determining the significance of an action also requires the agency to consider the intensity of the impact by evaluating factors enumerated at 40 C.F.R. § 1508.27(b).

54. Federal agencies cannot segment or manipulate the scope of their actions in order to avoid a finding of significance and evade the full environmental impact study NEPA demands. 40 C.F.R. § 1508.27(b)(7) ("Significance cannot be avoided by … breaking [an action] down into small component parts."). Rather, when determining the scope of its environmental review under NEPA, an agency must consider "connected, cumulative, and similar actions" together to prevent an agency from "dividing a project into multiple 'actions,' each of which individually has an insignificant environmental impact, but which collectively have a substantial impact." 40 C.F.R. § 1508.25; *see, e.g.*, *Earth Island Inst. v. U.S. Forest Serv.*, 351 F.3d 1291, 1305 (9th Cir. 2003). Actions are connected if they: "(i) Automatically trigger other actions which may require environmental impact statements; (ii) Cannot or will not proceed unless other actions are taken previously or simultaneously; or (iii) Are interdependent parts of a larger action and depend on the larger action for their justification." 40 C.F.R. § 1508.25.

55. In a NEPA analysis, the federal agency must identify the direct, indirect, and cumulative impacts of the proposed action, consider alternative actions and their impacts, and identify all irreversible and irretrievable commitments of resources associated with the proposed action. 42 U.S.C. § 4332(2)(C); 40 C.F.R. §§ 1508.7, 1508.8, 1502.14. Direct effects are those "which are caused by the action and occur at the same time and place." 40 C.F.R. § 1508.8(a). Indirect effects are "caused by the action and are later in time or farther removed in distance, but

are still reasonably foreseeable." *Id*. § 1508.8(b). Cumulative impacts are impacts from "past, present and reasonably foreseeable future actions regardless of what agency (federal or non-federal) or person undertakes such other actions." *Id*. § 1508.7. "Cumulative impacts can result from individually minor but collectively significant actions taking place over a period of time." *Id*. "Effects" or "impacts" (synonymous) include "ecological (such as the effects on natural resources and on the components, structures, and functioning of affected ecosystems), aesthetic, historic, cultural, economic, social, or health, whether direct, indirect, or cumulative." 40 C.F.R. § 1508.8.

56. NEPA also requires agencies to evaluate economic or social and natural or physical environmental effects that are interrelated. 40 C.F.R. § 1508.14.

57. NEPA requires agencies to consider "alternatives to the proposed action." 42 U.S.C. § 4332(2)(C)(iii) & (E); 40 C.F.R. § 1508.25. The analysis of alternatives is the "heart" of the NEPA process and must provide "a clear basis for choice among options by the decisionmaker and the public." 40 C.F.R. § 1502.14.

58. NEPA also requires agencies to disclose and analyze measures to mitigate the impacts of proposed actions. 40 C.F.R. §§ 1502.14(f), 1502.16(h). An agency's analysis of mitigation measures must be reasonably complete in order to properly evaluate the severity of the adverse effects of an agency's proposed action prior to the agency making a final decision.

59. CEQ guidance allows an agency to consider and rely on mitigation when making its significance determination. This includes both mitigation measures proposed by the agency and those included in the action "where the proposal itself so integrates mitigation from the beginning that it is impossible to define the proposal without including the mitigation." 46 Fed. Reg. 18,026, 18,038 (Mar. 23, 1981). Particularly in situations where the agency is relying upon mitigation to support a decision to rely upon an EA and a FONSI—and therefore not to prepare an EIS—the agency must carefully evaluate any proposed mitigation, and engage in on-going monitoring in order to ensure that mitigation measures are being followed. Mitigation measures used to support a FONSI must be enforceable and the agency must have sufficient resources to perform or ensure performance of mitigation measures.

60. CEQ regulations require the preparation of a programmatic EIS "for broad Federal actions such as the adoption of new agency programs or regulations." 40 C.F.R. § 1502.4(b); *see also* 40 C.F.R. § 1508.18(b)(4) (definition of major federal action includes "[a]doption of programs, such as a group of concerted actions to implement a specific policy or plan"). Under the CEQ regulations, a programmatic EIS is appropriate for a program that exists in fact, but is not necessarily declared by the agency. *See id*. § 1508.23 (defining "proposal" to include that a "proposal may exist in fact as well as by agency declaration that one exists.").

61. A programmatic EIS should be "relevant to policy and [] timed to coincide with meaningful points in agency planning and decisionmaking," and "shall be prepared on such programs and shall be available before the program has reached a stage of investment or commitment to implementation likely to determine subsequent development or restrict later alternatives." 40 C.F.R. § 1502.4.

62. Moreover, NEPA and its implementing regulations impose a continuing duty on agencies to prepare a supplemental environmental impact statement whenever "(i) The agency makes substantial changes in the proposed action that are relevant to environmental concerns; or (ii) There are significant new circumstances or information relevant to environmental concerns and bearing on the proposed action or its impacts." 40 C.F.R. §§ 1502.9(c)(1)(i), (ii).

63. NEPA requires that an agency incorporate its environmental analysis into its decision making process. "NEPA's purpose is not to generate paperwork—even excellent paperwork—but to foster excellent action." 40 C.F.R. § 1500.1(c); *see also id*. ("Ultimately … it is not better documents but better decisions that count."); 40 C.F.R. § 1502.1 ("primary purpose" of an EIS is to "serve as an action-forcing device to insure that the policies and goals defined in the Act are infused into the ongoing programs and actions of the Federal Government…. An environmental impact statement is more than a disclosure document. It shall be used by Federal officials in conjunction with other relevant material to plan actions and make decisions.").

III. The Endangered Species Act

64. When a species is listed as threatened or endangered under the ESA, section 7(a)(2) of the Act requires that all federal agencies "insure" that their actions "are not

likely to jeopardize the continued existence of any endangered species or threatened species or result in the destruction or adverse modification of" their critical habitat. 16 U.S.C. § 1536(a)(2). The "institutionalized caution" embodied in the ESA requires federal agencies to give the benefit of the doubt to listed species and places the burden of risk and uncertainty on the proposed action. *See Sierra Club v. Marsh*, 816 F.2d 1376, 1386 (9th Cir. 1987); *Tennessee Valley Auth. v. Hill*, 437 U.S. 153, 180 (1978).

65. The ESA establishes an interagency consultation process to assist federal agencies in complying with their substantive section 7(a)(2) duty to guard against jeopardy to listed species or destruction or adverse modification of critical habitat. Under section 7(a)(2), federal agencies must consult with the appropriate expert fish and wildlife agency to determine whether their actions will jeopardize any listed species' survival or adversely modify designated critical habitat and, if so, to identify ways to modify the action to avoid that result. *See* 50 C.F.R. § 402.14. The National Marine Fisheries Service (NMFS) is the expert fish and wildlife agency with respect to most anadromous and marine species and FWS is the expert agency with respect to many terrestrial and freshwater species.

66. The Services have adopted joint regulations governing the section 7(a)(2) consultation process. Under the joint regulations, a federal agency must initiate a section 7(a)(2) consultation with NMFS or FWS whenever it undertakes an "action" that "may affect" a listed species or critical habitat. 50 C.F.R. § 402.14(a). The threshold for a "may affect" determination and the required ESA section 7(a)(2) consultation is low. *See* 51 Fed. Reg. 19,926, 19,949 (June 3, 1986) ("Any possible effect, whether beneficial, benign, adverse, or of an undetermined character, triggers the formal consultation requirement."). *See also* FWS, *Endangered Species Consultation Handbook* at 3-13, 4-26 (1998). An agency is relieved of the obligation to consult only if the action will have "no effect" on listed species or designated critical habitat.

67. The joint regulations broadly define the scope of agency actions subject to ESA section 7(a)(2) mandates to encompass "all activities or programs of any kind authorized, funded, or carried out, in whole or in part, by [f]ederal agencies," including the promulgation of

regulations and the granting of licenses. 50 C.F.R. § 402.02 (definition of "action"). Courts interpret the term "agency action" broadly under the ESA. *See, e.g., Karuk Tribe of California v. U.S. Forest Service*, 681 F.3d 1006, 1020 (9th Cir. 2012) (en banc).

68. Under the ESA, the "action area" is broadly defined as "all areas to be affected directly or indirectly by the federal action and not merely the immediate area involved in the action." 50 C.F.R. § 402.02. The potential "effects" of an agency action that an agency must consider are similarly broad and include both the "direct" and "indirect" effects of the action and all activities "interrelated or interdependent" with that action. *Id.*

69. In insuring that any action is not likely to jeopardize a listed species or result in the adverse modification of critical habitat, the ESA requires every agency to use only the best scientific and commercial data available at every step of the process. 16 U.S.C. § 1536(a)(2); 50 C.F.R. § 402.14(g)(8).

70. If an agency determines that its action "may affect" but is "not likely to adversely affect" a listed species or its critical habitat, ESA regulations permit "informal consultation," in which there is no requirement for a biological opinion so long as NMFS or FWS concurs in writing with the "not likely to adversely affect" determination. 50 C.F.R. § 402.13. If the Service(s) do not concur in the "not likely to adversely affect" determination or if the action agency determines that the action is "likely to adversely affect" the listed species, the agencies must engage in "formal consultation." 50 C.F.R. §§ 402.12, 402.14(a), (b).

71. Formal consultation "is a process between the Service and the [f]ederal agency that commences with the [f]ederal agency's written request for consultation under section 7(a)(2) of the Act and concludes with the Service's issuance of the biological opinion under section 7(b)(3) of the Act." 50 C.F.R. § 402.02.

72. Compliance with the procedural provisions of the ESA—identifying the likely effects of the action through the consultation process—is integral to compliance with the substantive requirements of the Act. Under the statutory framework, federal actions that "may affect" a listed species or critical habitat may not proceed unless and until the federal agency ensures, through completion of the consultation process, that the action is not likely to cause

jeopardy or adverse modification of critical habitat. 16 U.S.C. § 1536(a); 50 C.F.R. §§ 402.14, 402.13; *see also* 16 U.S.C. § 1536(d).

IV. The Administrative Procedure Act

73. The APA grants a right of judicial review to "[a] person suffering legal wrong because of agency action, or adversely affected or aggrieved by agency action…." 5 U.S.C. § 702.

74. Under the APA, a court must "hold unlawful and set aside agency action … found to be … arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law…." *Id*. § 706(2)(A). An agency action is "arbitrary and capricious if the agency has relied on factors which Congress has not intended it to consider, entirely failed to consider an important aspect of the problem, offered an explanation for its decision that runs counter to the evidence before the agency, or is so implausible that it could not be ascribed to a difference in view or the product of agency expertise." *Motor Vehicle Mfrs. Assoc. v. State Farm Mutual Auto. Ins. Co*., 463 U.S. 29, 43 (1983).

75. Under the APA, a court must also "hold unlawful and set aside" any agency action taken that is "in excess of statutory jurisdiction, authority, or limitations, or short of statutory right." 5 U.S.C. § 706(2)(C).

76. Finally, under the APA, a court shall also "hold unlawful and set aside" any agency action that was promulgated "without observance of procedure required by law." *Id.* § 706(2)(D).

FACTUAL BACKGROUND AND ALLEGATIONS

I. FDA's Highly Controversial and Opaque Review of the AquaBounty GE Salmon

77. AquaBounty's GE salmon is a genetically engineered Atlantic salmon that is manipulated to produce an insulin-like growth factor hormone (IGF-1) year-round, allowing it purportedly to reach full size in less time than most conventional farmed salmon. The engineered genetic construct combines a growth hormone protein from the unrelated Pacific Chinook salmon (*Oncorhynchus tshawytscha*) with regulatory sequences from an antifreeze protein gene derived from an ocean pout (*Macrozoarces americanus*, also known as an eelpout),

which AquaBounty inserts into the genome of Atlantic salmon. The ocean pout promoter acts like a switch, keeping the growth hormone protein from turning off, which allows for continued growth of the fish. According to AquaBounty, its GE salmon grows to commercial size in half the time of conventional Atlantic salmon and is therefore desirable for commercialization.

78. Although AquaBounty began developing its GE salmon in 1989, the public did not learn about the GE salmon or that FDA was evaluating AquaBounty's GE salmon for potential commercial approval until 2001. At that time, FDA reviewed a draft EA prepared by AquaBounty in support of the investigational use of the GE salmon and issued a finding of no significant impact for this investigational use. Plaintiffs and the public were not provided with notice or an opportunity to comment on either of these documents.

79. In 2001, neither FDA, nor any other agency, had or had developed a regulatory framework for GE animals, or formally explained how U.S. federal agencies would regulate GE animals and GE fish or products created from them. Upon learning that the federal government was considering a commercial approval of GE salmon, Plaintiff CFS and a coalition of other groups filed a suite of legal petitions in 2001 with multiple agencies, including FDA, the Department of the Interior, the Department of Commerce, the U.S. Army Corps of Engineers, and the Department of Agriculture. These petitions called on FDA and these other agencies to, *inter alia*, establish new regulations specific to GE fish; establish regulations requiring monitoring, reporting, and inspection procedures for any producers; require labeling of any GE fish; prohibit any approval of GE fish until and unless an EIS and/or programmatic EIS was completed; permanently prohibit such activities should they be shown to harm the environment; and prohibit any approval until and unless FDA or any other agency charged with oversight consulted with the expert wildlife agencies pursuant to the ESA. No agency responded in any fashion to any of these petitions for roughly eight years.

A. Development of FDA's GE Animal Guidance

80. On September 18, 2008, FDA released a draft of its GE Animal Guidance for a sixty-day public comment period. This draft GE Animal Guidance formally announced for the first time that the agency would extend its jurisdiction to cover GE animals, including those

produced for food like AquaBounty's GE salmon, purportedly pursuant to its statutory authority to regulate new animal drugs, 21 U.S.C. § 321, *et seq*. CFS and other public interest groups filed extensive comments related to the GE Animal Guidance, pointing out the flaws in FDA's guidance and the inapposite nature of the animal drug provisions when applied to the risks of genetically engineered animals. These included comments specific to the risks of GE fish filed by a coalition of commercial fishing organizations. FWS also submitted comments urging FDA to consult with its fish experts before taking action on any application involving the production of GE fish.

81. FDA published the GE Animal Guidance on January 16, 2009. Guidance for Industry 187, Regulation of Genetically Engineered Animals Containing Heritable Recombinant DNA Constructs, 74 Fed. Reg. 3,057 (Jan. 16, 2009). In response to comments, FDA provided only generic short statements about the adequacy of the new animal drug process and claimed that the GE Animal Guidance offered only "non-binding recommendations" and did "not establish legally enforceable responsibilities."

82. Relying on the GE Animal Guidance, FDA denied Plaintiff CFS's 2001 legal petition requesting, among other things, that FDA establish a comprehensive regulatory framework under the FFDCA to fully address the environmental impacts caused by GE fish. In the January 15, 2009, denial letter, FDA stated its belief that regulations were not necessary because the GE Animal Guidance details how FDA's existing new animal drug application requirements apply to GE fish.

83. In the GE Animal Guidance, FDA invokes and interprets the FFDCA definitions of "drug" and "new animal drug" to encompass the recombinant DNA (rDNA) construct engineered into a GE animal because it is "intended to affect the structure or function" of the GE animal. GE Animal Guidance at 6.

84. Although the GE animal itself cannot possibly be a drug, FDA also asserted that the new animal drug provisions of the FFDCA allow it to regulate the GE animals carrying the rDNA construct. As asserted by the agency, its interpretation of "drug" covers all GE animals,

regardless of their intended use, even those produced as food for human consumption. The GE Animal Guidance states:

> Each new animal drug approval covers all animals containing the same rDNA construct (the regulated article or new animal drug) derived from the same transformation event, including, for example, animals containing that rDNA construct as a result of breeding between a non-GE animal and a GE animal.

GE Animal Guidance at 7.

85. FDA's GE Animal Guidance also explains how the agency would extrapolate the existing "new animal drug" requirements to apply to applications for approval of GE animals, including AquaBounty's GE salmon, such as the types of data and other information needed to fulfill the new animal drug regulatory requirements in the GE animal context.

86. In the GE Animal Guidance, FDA interprets "safety and effectiveness" to include an evaluation of environmental risks. FDA includes three components of safety to be considered as part of the pre-approval assessment: food safety, feed safety, and environmental safety. GE Animal Guidance at 24.

87. Despite FDA's finding that environmental risks are a part its evaluation of "safety and effectiveness," the guidance does not further detail or address precisely how FDA will evaluate environmental safety or otherwise consider environmental impacts as a factor in its safety and effectiveness evaluation. *See, e.g.*, GE Animal Guidance at 20, 26.

88. Although the Guidance purports to establish FDA authority over all GE animals, FDA also attempts to retain unbridled discretion to determine whether or not to enforce new animal drug application requirements for some GE animals, in some instances, as it sees fit. GE Animal Guidance at 7-8. In exercising this discretion, FDA states that NEPA does not apply to its decision whether to require a new animal drug application for certain GE animals (a decision FDA calls its "enforcement discretion"). GE Animal Guidance at 8. Nevertheless, FDA states that "environmental risks are among the factors we intend to consider in determining whether to exercise enforcement discretion" and outlines some of the factors it will consider in determining whether to require a new animal drug application, including whether the GE animal poses a

"human, animal, or environmental risk." *Id.* (stating that environmental risks are among the "safety questions" FDA considers when exercising its enforcement discretion).

89. FDA revised the GE Animal Guidance in June 2015 in order to change language regarding what transparency measures and public meetings would be conducted for future GE animal determinations. The revised guidance now purports to assign FDA the unfettered discretion to decide whether or not to convene public meetings in advance of decisions on applications.

90. Although the Guidance establishes for the first time a regulatory approval framework for all GE animals, FDA did not prepare a programmatic EIS or any other NEPA review for the expansive framework it describes in the GE Animal Guidance and the establishment of a GE animal approval process under the FFDCA.

B. FDA's Failure to Consider the Environmental Impacts of GE Salmon

91. In August 2010—ten years after the public first learned of AquaBounty's GE salmon—FDA finally released to the public AquaBounty's draft EA for the company's GE salmon new animal drug application. AquaBounty's EA contained limited information about the GE salmon and the application for approval that had been pending with the FDA.

92. AquaBounty's draft EA did, for the first time, describe the far-flung, international, and unusual production processes the company proposed for GE salmon in its application. Specifically, the draft EA revealed that GE salmon was first generated by injecting the genetically engineered rDNA construct into fertilized eggs, which were subsequently bred for at least eight generations to produce the fertile GE salmon adults (broodstock). In the draft EA, AquaBounty proposed to produce eggs using fertile GE salmon broodstock at a facility located on Prince Edward Island, Canada, and then ship the live GE eggs by air to an undisclosed site in Panama for grow-out. In Panama, the GE salmon would be raised to commercial size and slaughtered, then processed and shipped back to the U.S. for sale as a food product.

93. AquaBounty's draft EA asserted that its GE salmon would pose no environmental or ecological risks because the proposed production processes at the Prince Edward Island and Panama sites would be subject to physical, biological, and geographic/geophysical containment

measures designed to prevent the GE salmon from escaping into and establishing in the natural environment. According to FDA, these proposed limitations on the production and grow-out of AquaBounty's GE salmon were designed to "mitigate potential adverse environmental impacts."

94. The draft EA relied on the approach it outlined in FDA's GE Animal Guidance to review AquaBounty's application, including assessment under the new animal drug provisions of the FFDCA and the environmental review required by NEPA and FDA's regulations.

95. Shortly after the release of AquaBounty's draft EA, FDA announced it would convene a public meeting of its Veterinary Medicine Advisory Committee (VMAC) in September 2010, to consider the science, safety, and effectiveness of the AquaBounty application, and hold a separate public hearing regarding the labeling of food derived from AquaBounty's GE salmon. *See* Notice of Public Hearing, 75 Fed. Reg. 52,602 (Aug. 26, 2010) (labeling hearing); Notice of Meeting, 75 Fed. Reg. 52,605 (Aug. 26, 2010) (VMAC meeting).

96. In advance of and during the VMAC meeting, representatives of numerous environmental and public health organizations, including Plaintiffs CFS, FWW, and FoE, and non-FDA scientists voiced serious and specific concerns about both the environmental safety of the GE salmon and FDA's review of AquaBounty's application, in both written comments and oral testimony.

97. The preeminent scientific experts on GE fish, Dr. Anne Kapuscinski and Dr. Frederick Sundström, provided written comments to FDA before the VMAC meeting detailing the various significant deficiencies in the science (and scientific approach) underlying AquaBounty's and FDA's assessment of the potential environmental and ecological risks presented by AquaBounty's GE salmon. In particular, these scientists explained the kinds of failures that FDA should account for in its evaluation of AquaBounty's proposed containment measures, using the best available quantitative failure mode analysis, and recommended that FDA undertake a "failure mode analysis for the full range of facilities that may obtain AquaBounty's GE salmon eggs in the foreseeable future, as part of a full EIS." They also explained that the draft EA did not provide all of the information needed to predict the environmental effects of GE salmon, and the need for an EIS. Their comments were

summarized in oral testimony at the VMAC during the public meeting held on September 19, 2010.

98. Even members of FDA's own VMAC recognized the flaws and gaps in FDA's environmental analysis. The only fish scientist on the VMAC concluded that in light of these concerns, "considering this issue in a comprehensive way, together with other agencies through an environmental impact statement, would be the best way to proceed."

99. Over the next two years, from the end of 2010 to the end of 2012, members of the public, commercial fishermen, environmental and consumer groups, and members of U.S. Congress and state legislatures, continued to raise serious concerns regarding the sufficiency and limited scope of FDA's review and the agency's lack of environmental expertise. These stakeholders specifically called on FDA to halt its consideration of GE salmon, and to prepare a comprehensive EIS assessing the full range of environmental and ecological risks it posed.

100. During this time, scientists with expertise in fish biology and GE fish from FWS and NMFS also expressed serious concerns about the scope of FDA's review and its failure to properly analyze relevant risks associated with AquaBounty's GE salmon, particularly as such risks relate to wild salmon stocks and aquatic ecosystems. One FWS scientist noted, for example, that FDA's 2010 VMAC Briefing Packet for AquaBounty's GE salmon "falls short of providing an actual risk assessment of putative environmental damages in the event of escapement" and that he was troubled by the apparent lack of any policy for monitoring or enforcement with respect to operations and escapement at these facilities.

101. FWS's comments on AquaBounty's 2010 draft EA, stated that "it must be assumed that escape will … occur," and that "any interaction between wild and [GE] salmon must be considered a serious threat." FWS concluded that "we do not feel enough evidence has been provided to conclude the risks to natural populations of Atlantic salmon in Canada and the U.S. are negligible." Dr. Gregory Moyer, a FWS regional geneticist sent FDA a letter in 2010 expressing criticisms and concerns with FDA's risk assessment.

102. In 2010, a body of FWS fish conservation geneticists comprising the Conservation Genetics Community of Practice (COP) also expressed "great concern" with

respect to the risk of escapement and "possible interaction of [AquaBounty's GE] salmon with endangered wild salmon stocks" citing, in particular, historical evidence of massive escapes of commercially reared fish from aquaculture farms. The COP stated further that the EA lacked needed information and that its conclusions are based on limited data that must be supplemented with a number of studies, observing that the EA "is overly simplistic and does not adequately capture the actual risk of environmental damages to wild Atlantic salmon or the ecosystem."

103. A number of other FWS scientists, from numerous regional offices, expressed concerns similar to those presented by the COP, revealing that the concerns were pervasive throughout the agency. On October 29, 2010, it was reported internally at that agency that "all but one Region oppose[] FDA approval" of AquaBounty's GE salmon application.

104. NMFS expressed similar concerns in 2010. NMFS sent a letter to FDA raising serious questions regarding containment of fertile GE salmon broodstock at the Prince Edward Island facility and the future marketing of GE salmon eggs. NMFS also questioned FDA's decision to narrowly limit the analyzed "action area" to Canada and Panama only, noting that "the action area as defined in the ESA (50 C.F.R. § 402.02), should be identified as all areas of potential impacts as a result of this action. The topics of selling commercially and rearing fertile adult males at the Canadian production facility both potentially increase the size of the action area to include the United States."

105. In particular, NMFS pointed out the inconsistency between FDA's statements that (1) its approval would be limited to particular restrictions and locations, as stated in the current application; and (2) the agency's discussion of GE eggs produced for commercial sale. NMFS explained that "[b]ecause the egg production facility and the grow-out facility are owned by AquaBounty Technologies, Inc., there would be no reason to sell the eggs unless another aquaculture facility was involved."

106. NMFS expressed other significant concerns about the potential implications of the AquaBounty application, including that the sterilization process for the GE salmon eggs would not be 100% effective, that the GE salmon could indeed escape containment, and that the escaped GE fish could catastrophically harm native salmon populations.

107. Between 2010 and 2012, FDA held closed-door meetings with various agencies, including the Council on Environmental Quality, FWS, and NMFS about the adequacy of its environmental review. Presumably faced with concerns from sister agencies, FDA characterized its approval decision as confined strictly to the Panama and Prince Edwards Island sites and the conditions presented in AquaBounty's application. FDA emphasized in those meetings that environmental impacts of plans to alter or expand the production of its GE salmon, including requests to produce the GE fish in the United States, could be assessed in later supplemental approvals.

108. On December 26, 2012, FDA released its own draft EA and FONSI for the AquaBounty new animal drug application for public review and comment. Despite the ongoing substantial scientific controversy and the repeated calls for a more comprehensive environmental review, FDA's draft EA varied only slightly from the 2010 EA prepared by AquaBounty; it did not include new or additional data or environmental analyses regarding the environmental risks or other potential impacts that could occur if AquaBounty's GE salmon escaped containment.

109. Many organizations and individuals submitted extensive comments on FDA's draft EA, explaining, among other things, that FDA lacks the legal authority to approve GE salmon for production and commercialization, and that the agency's extremely inadequate draft EA renders FDA's FONSI and decision not to prepare an EIS arbitrary and unlawful. These submissions included comments from yet another independent scientist with expertise in fish biology, ecology, and genetic introgression, who provided detailed concerns regarding FDA's failure to assess the potentially significant and irreparable harm GE salmon could pose to any environment in which they may be released.

110. Comments on FDA's 2012 draft EA from Drs. Kapuscinski and Sundström explained that FDA continued to ignore their 2010 recommendations for conducting an adequate risk assessment that is consistent with current science, a failure that rendered the draft EA "weak and scientifically unacceptable." These comments highlighted that FDA continued its indefensible use of outdated risk methods, which Dr. Kapuscinski herself developed in the

1990s, but which she and others have had since replaced with improved, science-driven, rigorously reviewed methodologies.

111. By the close of the comment period on FDA's draft EA on April 26, 2013, over 1.8 million comments had been submitted to FDA objecting to the proposed approval of AquaBounty's GE salmon application on the basis of environmental and public health risks.

112. Despite these objections, FDA announced its final approval of the AquaBounty new animal drug application to produce and market its GE salmon on November 19, 2015. 80 Fed. Reg. 73,104 (Nov. 24, 2015). FDA did not require labeling of AquaBounty's GE salmon, but instead allowed for voluntary labeling of the product.

113. FDA purported to sufficiently consider environmental safety as part of its approval process, and concluded that the GE animal and conditions presented in the application did not present "safety concerns" to the environment. In the final EA, FDA stated that GE salmon would be considered "unsafe" if AquaBounty did not conform with the "specific set of conditions enumerated and described in the [new animal drug application] and the approval letter." In the final EA, FDA stated that it reviewed environmental safety and effectiveness under these "specified conditions of use" and concluded that they would "serve to mitigate environmental risks."

114. In its approval letter to AquaBounty, FDA also included a detailed set of conditions that the agency placed on the approval—including restrictions on facilities, containment, breeding and production methods, and shipment of eggs—each of which relates to environmental safety. *See also* 21 C.F.R. § 514.105 (also listing several of these conditions and a prohibition on the use of net pens as among those FDA "deems necessary to assure the safe and effective use of the drug."). FDA's approval letter specifies that its approval is predicated upon compliance with each of these conditions and that "[d]eviations from these commitments and requirements will result in the article being considered an unsafe new animal drug" and an adultered animal drug and food under the FFDCA.

115. FDA's limited consideration of environmental risks, however, was based on a final EA and FONSI that, like the draft EA, are improperly limited in scope, devoid of sound

scientific analyses, and replete with unsupported assumptions. Despite receiving significant and substantive comments, the passage of five years since the original AquaBounty 2010 draft EA, and three years since the FDA draft EA, the final EA was substantially similar to, and in many cases virtually indistinguishable from, FDA's 2012 draft EA.

116. FDA's final EA included numerous unsubstantiated, misleading assumptions about environmental risk. For example, neither FDA nor AquaBounty has studied the potential biological fitness of the specific GE salmon that FDA has approved for commercialization; instead the agency relied on—and extrapolated from—studies about the fitness of other types of GE fish, which do not adequately support FDA's conclusions.

117. Similarly, FDA did not provide sufficient evidence or analysis to support the presumed sterility of AquaBounty's GE salmon. In fact, FDA acknowledged that up to five percent of the GE salmon produced at Prince Edward Island may not be sterile, following implementation of AquaBounty's biological containment process (induction of triploidy), and that "there are no specific data demonstrating that triploid [AquaBounty] salmon are indeed sterile, that is incapable of producing viable offspring." FDA also admitted the existence of fertile GE salmon broodstock at the Prince Edward Island facility, noting that approximately one half of them are fertile males. Nonetheless, the agency arbitrarily assumed, for purposes of its EA and FONSI, that *all* GE salmon will be functionally sterile, and therefore did not provide any relevant analysis regarding possible risks presented by fertile GE salmon.

118. Moreover, the final EA lacked analysis of risks associated with Infectious Salmon Anemia Virus (ISAV). ISAV is a viral disease in salmon that causes severe anemia in the fish, and has spread quickly among Atlantic salmon in salmon farms, causing wide-spread losses in many locations. In December 2011, through Canadian proceedings regarding a separate matter, it was discovered for the first time that fish eggs at AquaBounty's Prince Edward Island facility were infected with ISAV in 2009. In the 2012 draft EA, FDA for the first time acknowledged that this outbreak occurred, but it never attempted to explain how the ISAV entered the facility, how to prevent it from happening again, or what might happen if a similar outbreak occurs again and an infected GE salmon were to escape into the natural environment.

C. AquaBounty's Plans for Expansion

119. With FDA's approval in hand, absent judicial intervention, AquaBounty is now able to begin production and commercialization of its GE salmon for sale in the U.S.

120. AquaBounty has publicly and repeatedly confirmed its intent to expand capacity and begin field trials with prospective customers in the U.S. Public statements and financial disclosures from AquaBounty demonstrate that the company will not limit the manufacture of GE salmon to the facilities approved in this application, but rather plans to expand its production operations to other countries. AquaBounty's chief executive officer has stated that the company has been moving forward with field trials in several foreign countries to import and grow its GE salmon eggs.

121. The company's own annual reports further detail and confirm its expansion efforts. For example, in its 2014 Form 10 to the Securities and Exchange Commission, AquaBounty stated "we currently plan to increase our supply of unfertilized Atlantic salmon eggs through either expansion of our existing Canadian hatchery or through the purchase of an existing egg producer." In that Form 10, the company stated, "we currently plan to apply for regulatory approval of a second hatchery that would likely be located in the United States."

122. In a recent February 2016 financial disclosure document, AquaBounty stated that it was "finalizing its proposed commercialization strategy," and "exploring capital raising opportunities to fund expansion."

123. FDA knew about these existing requests for government action, but failed even to mention them in its draft or final EA, and neither document analyzed the impacts from the foreseeable expansion of AquaBounty's production, manufacturing, and sale of GE salmon eggs and fish.

124. Even FWS recognized internally that "[AquaBounty's] Canada-Panama scenario seems far-fetched as a business strategy" and that AquaBounty "may be using it as a means of gaining FDA approval in anticipation of a wider operation."

125. On March 22, 2016, AquaBounty submitted an application to the Prince Edward Island Department of Communities, Land and Environment to acquire and redevelop an existing

aquaculture facility for the purpose of rearing Atlantic salmon broodstock to increase production of GE salmon eggs. In conjunction with its application, AquaBounty hired an outside contractor to complete a Canadian Environmental Impact Statement (Canadian EIS) to evaluate its proposal, in accordance with Canadian law.[1] According to its May 19, 2016 Canadian EIS, AquaBounty plans to use the site to raise conventional (non-GE) broodstock to produce eggs for its GE salmon manufacturing process at the company's nearby existing facility in Fortune. EIS at 1. The proposed redeveloped site will hold close to 13,000 fish and have the capacity of producing upwards of 10 million eggs per year. *Id*. at 17-18. AquaBounty's purchase of the facility was expected to be completed in April 2016. *Id*. at 7. Renovation and construction at the new facility are planned to begin in May and completed in August 2016. *Id*. at 6-7. The Canadian government approved AquaBounty's application on June 10, 2016.[2]

126. The Canadian EIS explains that the purpose of this second facility is to facilitate increased GE salmon production "to enable Aqua Bounty to expand and scale up to commercial production of their operation on [Prince Edward Island]." *Id*. at 4. According to the EIS:

> With the recent USFDA [U.S. Food and Drug Administration] approval, Aqua Bounty must begin to scale up to commercial production. Aqua Bounty's Fortune facility currently houses AquAdvantage salmon broodstock and conventional Atlantic salmon. The number of conventional Atlantic salmon required for commercial production purposes far exceeds the available space at the [existing] Fortune facility. The facility at Rollo Bay presents an opportunity for Aqua Bounty to acquire a site that will house up to four year classes of conventional Atlantic salmon which in turn can be used to produce eggs for their production requirements.

Id. at 5.

127. AquaBounty produces its GE salmon eggs on Prince Edward Island by fertilizing conventional Atlantic salmon eggs with milt from adult GE salmon "neomales." AquaBounty plans to produce these unfertilized eggs from the broodstock conventional salmon at the Rollo

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[1] Environmental Impact Statement, Proposed Acquisition of Snow Island's Atlantic Sea Smolt Ltd. Facility, Report Prepared for Aqua Bounty Canada Inc., May 19, 2016, http://www.gov.pe.ca/photos/original/CLE_2016_AquaBo.pdf.

[2] Letter from Robert Mitchell to Dawn Runinghan (Jun. 10, 2016), http://www.gov.pe.ca/photos/original/CLE_AquaB_App.pdf.

Bay facility and transfer them to the AquaBounty facility in nearby Fortune "where fertilization and incubation would take place." EIS at 17.

128. In its approval for GE salmon, FDA repeatedly referenced only the existing AquaBounty facility in Fortune. Indeed, in its approval letter, FDA specifically stated as one of the "conditions established in the approval" that "only the following facilities will be used for manufacturing, processing, and packing [AquAdvantage salmon] or its components, i.e., producing, raising, and harvesting [AquAdvantage salmon]: (1) [AquaBounty's] land-based, contained broodstock facility on Prince Edward Island, Canada, where triploid eyed-eggs will be produced (PEI facility), as described in the application; and [the Panama facility]." (emphases added). FDA specifically defined "Components of [AquAdvantage salmon]" to "include all materials and precursors that are required to produce the final marketed product (i.e., [AquAdvantage salmon] that meets the product definition). These include, but are not limited to, the various DNA fragments composing the final rDNA construct, as well as the [AquaBounty] and other Atlantic salmon that are precursors of [AquAdvantage salmon]."

129. FDA also repeatedly emphasized in its approval letter that any deviation from these conditions would require a supplemental application from AquaBounty, stating prior to making any changes to the process "described in the approved application, including changes in production, facilities, equipment." In response to comments, FDA similarly emphasized that "changes in manufacturing facilities is also a condition of the AquAdvantage Salmon [new animal drug application] approval. Consequently, establishment of a new facility to produce AquAdvantage salmon either in the U.S., or in a foreign country to produce AquAdvantage salmon for import into the U.S., would require prior FDA approval of a supplemental [new animal drug application], which would trigger NEPA review requirements." FDA stated that any "supplemental application will require its own NEPA analysis of potential environmental impacts of those facilities."

130. Despite the limited nature of FDA's original NEPA analysis and the specific terms of its new animal drug application approval, FDA has not conducted any supplemental NEPA analysis of AquaBounty's expanded facilities on Prince Edward Island. At the very least,

AquaBounty's rapid expansion of its operations (both the new facility and the additional eggs produced as a result of the production changes enabled by that facility) fatally undermines the FDA's assumptions that GE salmon production would be limited to the original facility and highlights the agency's limited analysis of the environmental impacts of the original new animal drug application. Instead, this immediate expansion further illustrates AquaBounty's expansion plans; increased GE salmon egg production will either be used for increased production at existing facilities or for new facilities and markets. Neither of these scenarios were considered in FDA's EA and FONSI. Increased GE salmon production, as facilitated by this new facility, is relevant to environmental concerns because an increase in GE salmon produced will increase the magnitude and likelihood of the risks to the environment as detailed further herein. This significant change in circumstances triggers FDA's duty to prepare a supplemental environmental impact statement or other supplemental NEPA analysis.

D. FDA's Failure to Ensure Approval Would Not Jeopardize Protected Species

131. Beginning at least as early as 2001, both NMFS and FWS urged FDA to engage in ESA consultation in connection with AquaBounty's application to produce and market GE salmon. In a joint October 30, 2001 letter to FDA about AquaBounty's application, FWS and NMFS stated that "[t]here is a large body of scientific evidence that clearly indicates genetic and ecological interactions between wild and aquaculture salmon can adversely affect wild populations…. The introduction and use of genetically modified salmon by the salmon farming industry has the potential to adversely affect endangered wild salmon and thus, is of concern to the Services."

132. As of 2009, FDA had finally asked the Services to consult under Section 7 of the ESA on the impacts of GE salmon on several ESA-listed species. In response to FDA's request to initiate consultation, NMFS stated that it had an interest in the consultation because AquaBounty's proposal "may have effects on endangered species and species that support commercial fisheries."

133. In August 2010, FDA sent both of the Services letters, concluding that approval of AquaBounty's application "may affect" but was "not likely to adversely affect" endangered Atlantic salmon populations.

134. In or around October 2010, FWS suggested that FDA should clarify the approval would have "no effect" on listed salmon. FDA amended its ESA determination a few months later. In subsequent letters to the Services, FDA stated that it now believed that approval of AquaBounty's application under the proposed conditions of use would instead have "no effect" on endangered Atlantic salmon populations. FDA requested that the Services send a written response to FDA's determination.

135. At the end of 2010, FWS sent a letter to FDA accepting its "no effect" determination and stating that concern for endangered Atlantic salmon would exist if there was even a "detectible probability" that the GE salmon could interbreed with or consume Atlantic salmon, but discounted those outcomes as unlikely.

136. In July 2011, after numerous "technical discussions" with FDA, NMFS sent FDA a letter acknowledging only that FDA had terminated the consultation process. Internal NMFS email correspondence indicated that NMFS staff did not agree with FDA's "no effect" determination.

E. Citizen Petition for Comprehensive Analysis

137. On May 25, 2011, Plaintiffs CFS, FoE, and FWW, along with other groups filed a legal petition with FDA requesting that the agency refrain from taking final action on the AquaBounty new animal drug application until the agency completed a comprehensive EIS fully analyzing the potential environmental and ecological impacts associated with GE salmon and until FDA developed regulations that included mandatory consideration of environmental safety when approving GE animals.

138. On November 19, 2015, the same day that it approved the AquaBounty GE salmon, FDA denied Plaintiffs' legal petition. FDA stated that the GE salmon approval would not have a significant impact on the environment, relying entirely on its conclusion that containment would prevent release. FDA refused to consider cumulative impacts, stating that

any future sale of eggs or additional production facilities were not foreseeable because the agency had not received any additional formal proposals or applications from AquaBounty at that time.

II. Risks to Aquatic Ecosystems, Wild Fish Populations, and Fisheries

139. Of particular concern to Plaintiffs are the potential impacts of FDA's approval of AquaBounty's GE salmon application upon already vulnerable wild fish populations, including, but not limited to, members of genera *Salmo* (Atlantic salmon and trout) and *Oncorhynchus* (Pacific salmon and trout). Over time, these species have been decimated by a variety of human-induced pressures.

140. In 2000, NMFS and FWS issued a final rule designating the Gulf of Maine Distinct Population Segment (GOM DPS) of Atlantic salmon as endangered under the ESA. A final rule designating critical habitat for the GOM DPS was published in the Federal Register on June 19, 2009. 74 Fed. Reg. 29,300 (June 19, 2009).

141. According to the National Oceanic and Atmospheric Association's (NOAA's) Office of Protected Resources, "[t]he populations of Atlantic salmon present in the Gulf of Maine DPS represent the last wild populations of U.S. Atlantic salmon." Of the New England rivers in which Atlantic salmon runs were historically found, only sixteen percent currently support salmon. In these rivers, Atlantic salmon are considered to be in "critical condition."

142. As FDA acknowledges, the migratory range of the endangered Gulf of Maine Atlantic salmon includes areas surrounding Prince Edward Island, Canada, where AquaBounty will house GE fertile broodstock fish, including fertile males, and eggs. Indeed, these salmon populations spend "as many as five winters at sea, thousands of miles away." They "leave Maine rivers sometime in April or May, and can be found in the waters off Labrador and Newfoundland by mid-summer. They then migrate to take advantage of available food supplies and generally spend their first winter at sea off the coast of Greenland."

143. Atlantic salmon continue to face many threats that may jeopardize their environment and continued existence. Although salmon fishing is currently prohibited in Maine, illegal harvest, bycatch, habitat destruction and modification, incidental take, and other pressures

still represent significant risks to the recovery of Atlantic salmon in the U.S. NMFS recognizes aquaculture practices as one of the threats facing the Maine DPS Atlantic salmon population as they "pose ecological and genetic risks." In 2003, citing the need for greater protections for the endangered Atlantic salmon population from growing risks, NMFS issued a biological opinion stating, *inter alia*, that production of GE fish species in net-pen aquaculture off the coast of Maine is prohibited.

144. Like Atlantic salmon, Pacific salmon populations on the west coast of the United States have faced significant declines. Many Pacific salmonids are listed as endangered or threatened under the ESA, including certain populations of Chinook salmon (*Oncorhynchus tshawytscha*), chum salmon (*Oncorhynchus keta*), coho salmon (*Oncorhynchus kisutch*), sockeye salmon (*Oncorhynchus nerka*), and steelhead trout (*Oncorhynchus mykiss).* NMFS has listed the following Pacific salmon and steelhead Evolutionarily Significant Units (ESUs) and Distinct Population Segments (DPSs)[3] as threatened or endangered: California coastal Chinook salmon, Central Valley spring-run Chinook salmon, Lower Columbia River Chinook salmon, Puget Sound Chinook salmon, Sacramento River winter-run Chinook salmon, Snake River fall-run Chinook salmon, Snake River spring/summer-run Chinook salmon, Upper Columbia River spring-run Chinook salmon, Upper Willamette River Chinook salmon, Columbia River chum salmon, Hood Canal summer run chum salmon, Central California Coast coho salmon, Southern

[3] In order for an imperiled species to be protected by the ESA, it must first be placed on the Act's "threatened" or "endangered" species lists. 16 U.S.C. § 1533(c). A "species" that may be listed for protection under the ESA includes "any subspecies of fish or wildlife or plants, and any distinct population segment of any species of vertebrate fish or wildlife which interbreeds when mature." 16 U.S.C. § 1532(16). When deciding whether to list populations of Pacific salmon for protection as a "distinct population segment" under this definition, NMFS employs the concept of "evolutionarily significant unit" (ESU). A population of Pacific salmon is an ESU if it is "(1) … reproductively isolated from other population units of the same species, and (2) … an important component in the evolutionary legacy of the biological species." 64 Fed. Reg. 14,308, 14,310 (Mar. 24, 1999). In 2006, NMFS issued revised listings for all west coast steelhead populations applying the joint Distinct Population Segment (DPS) policy developed by NOAA and the U.S. Fish and Wildlife Service in 1996. See 71 Fed. Reg. 834 (Jan. 5, 2006) (revised steelhead listings); 61 Fed. Reg. 4,722 (Feb. 7, 1996). Though the ESU and DPS policies are consistent, there are differences in emphasis between them. The different emphases are not relevant here.

Oregon and Northern Coastal California coho salmon, Lower Columbia River coho, Oregon Coast coho salmon, Snake River sockeye salmon, Central California Coast steelhead, California Central Valley steelhead, Lower Columbia River steelhead, Middle Columbia River steelhead, Northern California steelhead, Snake River Basin steelhead, South-Central California Coast steelhead, Southern California steelhead, Upper Columbia River steelhead, and Upper Willamette River steelhead. The few wild Pacific salmon runs that remain healthy enough support vibrant subsistence, recreational, and commercial fisheries, which in turn support vibrant coastal communities. Pacific salmon fisheries constitute some of the best and most valuable remaining wild fisheries on earth.

145. All five species of wild Pacific salmon live in the western U.S. and Alaska: Chinook (King); Coho (Silver); Pink; Sockeye (Red), and Chum (Dog). While there are variations between species, Pacific salmon generally spend from several months to several years in freshwater before migrating to the ocean for one to five years of feeding in the North Pacific Ocean as juveniles and sub-adults. Generally, little is known about marine behavior of salmon. They are known to travel vast distances, presumably in search of food, with wide variation in the behavior among runs and over time. After reaching maturity in the ocean, Pacific salmon return to their natal freshwater streams to spawn. As is the case with Atlantic salmon, Pacific salmon can cover thousands of miles during their fresh and saltwater migrations.

146. Among different populations and salmon runs, individual Pacific salmon populations have evolved distinctive characteristics, including various physical and physiological characteristics and behavioral differences, such as differences in size, color, shape, life span, and marine feeding patterns. These diverse adaptations can have ecological significance.

147. Salmon are rightly revered for their integral roles in their native ecosystems, as their sacrificial anadromous journeys transfer vast amounts of marine nutrients to freshwater and terrestrial species, including aquatic invertebrates, other fish, marine mammals, birds, and terrestrial mammals. The contribution of salmon to the quality of the environment is substantial and far-reaching. The Pacific Northwest rainforests are to a large extent fed by returning salmon. Studies have found that trees like the Sitka spruce alongside salmon rivers can grow

more than three times faster than counterparts along rivers without salmon. Species such as bear and bald eagle feed on salmon, as do myriad other species.

148. Wild Pacific salmon fisheries constitute an important source of jobs and enjoyment for thousands of U.S. citizens and hundreds of coastal communities, including many members of the Plaintiff organizations that work in the salmon industry as fishers, producers, processors, marketers, and chefs. Recreational salmon fishing is an economic engine along the U.S. west coast and Alaska, in addition to contributing greatly to the quality of life for thousands of enthusiasts. Subsistence salmon fisheries remain an important source of food for many rural residents and tribal members. Families up and down the U.S. west coast still depend on healthy wild fish stocks for their livelihoods, as was once the case for Atlantic salmon fisheries on the east coast.

149. These fisheries rely on the health and diversity of Pacific salmon. The various populations and runs of Pacific salmon have developed distinctive identities, many of which have substantial aesthetic, cultural, social, and economic significance. Connoisseurs and consumers of salmon appreciate the distinctive physical and socio-cultural characteristics of each different run, and so too has the salmon industry profitably capitalized on this aesthetic appreciation. The "Copper River salmon" is one famous, and profitable, example. Copper River salmon have a distinct taste, color, and texture, as well as timing and cultural context, which are prized in the marketplace and by discerning consumers.

150. The environmental risks of GE fish are both very real and potentially disastrous. Studies have found that GE fish may be more competitive, less discriminate in choosing prey, more likely to attack novel prey, and better at using lower quality food when compared to wild salmon. When the GE salmon do escape, the impacts on the environment are significant and irreversible, in the form of, *inter alia,* (1) ecological impacts on native species via predation and/or competition for limited food and space; (2) transfer of exotic pathogens or an increase in the amount of pathogens present in the environment; (3) ecological disturbance through interference competition or the disruption of ecological processes like predator/prey interactions or migration patterns; and (4) genetic impacts via hybridization and genetic introgression.

Additionally, GE salmon's over-production of the growth hormone, IGF-1, may lead to behavioral changes, such as increased aggressiveness and altered breeding and migration patterns.

151. If GE salmon breed with wild fish, these and other traits ultimately impact the fitness of wild salmon. The introduction of GE salmon with any mating success into a wild population would affect the genetic makeup of the population. This can have two consequences. First, successful mating of GE salmon with wild salmon would spread the altered gene throughout the wild population, with each successive generation, until the wild, unaltered population no longer exists. Second, GE salmon reportedly have reduced viability—i.e., they are less fit to survive in the wild than wild salmon—and successful mating with wild salmon could pass along this genetic heritage to the next generation, reducing the overall survival of the salmon population as a whole. It is survival of the "unfittest:" engineered salmon may successfully mate, but because of unexpected physiological havoc caused by the new genes, their offspring might die more often or sooner than wild salmon. While these effects are detrimental to any population of fish, they are especially problematic for smaller, imperiled populations where every individual member makes a difference.

152. Once engineered organisms escape or are released into the environment, it is impossible to recall or eliminate them. Unlike chemical pollution, GE contamination is a living pollution that can propagate itself over space and time via gene flow. As federal courts have found in the context of GE plants, "once the gene transmission occurs and a farmer's seed crop is contaminated with the [engineered] gene, there is no way for the farmer to remove the gene from the crop or control its further spread." *Geertson Seed Farms v. Johanns*, No. 06–01075, 2007 WL 518624, at *5 (N.D. Cal. 2007).

153. As detailed above, scientists with FWS (which, unlike FDA, has expertise in fish biology and ecology) found that FDA's assessment of the risks of escape was "overly simplistic," and failed to "adequately capture the actual risk of environmental damages" to wild salmon in the event of escape. Independent fisheries scientists and those with NMFS echoed these concerns. Because containment measures cannot guarantee that GE salmon will not escape

into the wild, and because survival and reproduction of escaped GE salmon is possible, any escape or release event would be significant and irreparable. The GE salmon, once in rivers or the ocean, are free to reproduce, and mutate to adapt to their environment; in other words, to do what fish in the wild do. Their ability to affect already decimated wild salmon populations will continue, and may even increase, over time.

154. Distinct from effects on the viability of wild salmon populations themselves, escaped engineered fish contaminating salmon populations or salmon fisheries would adversely impact those resources and humans' relationship with them. First, escapes will have secondary adverse economic effects on the commercial fishing industry by further straining already imperiled salmon populations, thus affecting salmon fishermen's livelihoods. Contamination of wild runs could also result in fishing closures. Second, commercial, subsistence, and recreational fisheries that are linked with the identity of particular populations or fisheries would suffer immediate and irreparable harm if an engineered fish found its way into a fishing net or a market. Market and public perceptions of even a small, isolated release of GE salmon—even in the absence of any negative physical effect on wild salmon populations—would disproportionately impact these fisheries. Polls repeatedly conclude that U.S. consumers reject the approval of GE salmon, or at a minimum, demand they be labeled. Many major U.S. grocery chains have already agreed not to sell the GE salmon for this very reason. FDA's approval and the lack of any point-of-sale labeling requirements for GE salmon could reduce consumers' confidence in and purchasing of salmon, causing negative effects on salmon markets and further affecting fishing men and women. FDA refused to consider, let alone analyze, these intertwined economic and environmental effects.

155. Yet, the incalculable worth of the species cannot be measured solely in scientific or monetary terms. Harm to wild salmon runs further degrades or destroys the profound cultural identity and social and aesthetic values supported by salmon as well. The cultural values of salmon are profound. Salmon are a sacred animal in many cultural traditions, including Native American traditions, as well as regional traditions. On the U.S. west coast, salmon have been the centerpiece of cultural and spiritual life for thousands of years. GE contamination of salmon

runs would have significant adverse effects on the cultural identities associated with those wild stocks. FDA did not consider these impacts.

FIRST CLAIM FOR RELIEF
VIOLATION OF THE FFDCA AND APA
ULTRA VIRES ACTIONS OF THE GE SALMON APPROVAL
AND GE ANIMAL PROGRAM

156. Plaintiffs re-allege, as if fully set forth, each and every allegation set forth in paragraphs 1 through 155 of this Complaint.

157. As described above, FDA has asserted exclusive jurisdiction over the approval of GE animals, including GE salmon, under its FFDCA authority to approve new animal drugs. 21 U.S.C. § 360b.

158. Genetically engineered animals are not animal drugs. The FFDCA does not explicitly or implicitly authorize the FDA to approve for production and commercialization GE food animals intended for human consumption. *See* 21 U.S.C. §§ 321(g)(1)(C), 321(v). FDA has erroneously overextended its drug authority to encompass these novel organisms and their concomitant novel significant risks.

159. The FFDCA defines the term "drug," *inter alia*, as "articles (other than food) intended to affect the structure or function of the body of man or other animals…." 21 U.S.C. § 321(g)(1)(C). The FFDCA defines the term "new animal drug" as "any drug intended for use for animals…." 21 U.S.C. § 321(v).

160. In the GE Animal Guidance, and as applied in its approval of AquaBounty's GE salmon, FDA interprets the definition of "new animal drug" to include the "rDNA construct" that genetically engineers the animal as an article that is "intended to affect the structure or function" of the animal. The GE Animal Guidance does not define "rDNA construct," but states that "[t]he rDNA construct at a specific site in the genome is the subject of the [new animal drug application]." FDA is likely referring to the artificially made DNA sequence that exists in a GE animal as an integral part of its genome, or genetic code. Such integral DNA sequences, however, are not items or objects that can be manipulated or regulated separate and apart from the animal itself. The rDNA is not even introduced into the GE animal, but is rather a part of the

animal that is passed along to its progeny which inherit the rDNA along with the animal's other genetic material.

161. An "rDNA construct" is not a "drug" that is separate and apart from the body of an animal or something that is "intended for use for animals," but rather is a part of the animal itself. The "rDNA construct" in a GE animal does not meet the FFDCA definition of "drug" or "new animal drug."

162. In the GE Animal Guidance, FDA also asserted its authority over the entire GE organism containing the "drug," not merely the rDNA construct that exists inside the GE animal. The GE animal itself is not a "new animal drug" either because it is not an article that is intended to affect the structure or function of another animal under the FFDCA's definition.

163. Neither the FFDCA nor the FDA's regulations support FDA's assertion that either the "rDNA construct" or the entire GE animal fits within its statutory authority over "new animal drugs." These provisions were instead intended to regulate the far more familiar scenario where an animal is provided with medication that is temporary in the sense that it can be metabolized and is not passed on to its offspring.

164. The FFDCA definition of "drug" also expressly excludes "food." 21 U.S.C. § 321(g)(1)(C). However, AquaBounty's GE salmon is clearly intended for use as food, and thus, by the statute's own plain language, FDA lacks the authority to regulate GE salmon, or other future GE animals to be produced as food, solely as a "drug." The terms are mutually exclusive in the statutory scheme.

165. FDA's assertion of exclusive authority to regulate GE animals as new animal drugs in its GE Animal Guidance, its application of its GE Animal Guidance, and its approval of GE salmon under its new animal drug authority are *ultra vires* actions "in excess of statutory jurisdiction, authority, or limitations, or short of statutory right," and are "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law" in violation of the FFDCA and the APA, 5 U.S.C. §§ 706(2)(A), (C).

166. The actions and inactions of the Defendants described in this Cause of Action are causing injuries to the Plaintiffs, for which they have no adequate remedy at law.

SECOND CLAIM FOR RELIEF
VIOLATION OF NEPA AND APA:
FAILURE TO TAKE A HARD LOOK AT THE EFFECTS OF THE ACTION

167. Plaintiffs re-allege, as if fully set forth, each and every allegation set forth in paragraphs 1 through 166 of this Complaint.

168. NEPA requires that federal agencies take a "hard look" at the environmental consequences of their actions, before action is taken. *See, e.g.*, *Blue Mountains Biodiversity Project v. Blackwood*, 161 F.3d 1208, 1211 (9th Cir. 1998). NEPA's implementing regulations require FDA to assess the environmental impacts of the proposed action, including direct and indirect effects, which are reasonably foreseeable but removed in time or space. 42 U.S.C. § 4332(C); 40 C.F.R. §§ 1502, 1508.7. NEPA further requires FDA to use high quality, accurate scientific information and to ensure the scientific integrity of this analysis. 40 C.F.R. §§ 1500.1(b), 1502.24.

169. In violation of these mandates, FDA's FONSI is based on an unlawfully narrow, incomplete, and inadequate EA that fails to take a hard look at the potential impacts of AquaBounty's GE salmon on the environment and aquatic ecosystems. The available information—including that provided by the public, independent scientific experts, and other federal agencies in comments on the EA—detail the extensive environmental and ecological threats posed by GE salmon, including the potential that the AquaBounty GE salmon will enter and survive in the natural marine and/or freshwater ecosystems, the potential impacts of escaped or otherwise released GE salmon on wild fish populations (including already imperiled Atlantic salmon and Pacific salmonids and other fish species such as trout) as well as potential socioeconomic impacts on commercial fisheries and subsistence fishing communities intertwined with and stemming from those environmental harms. The agency's EA and FONSI entirely failed to consider and/or to adequately analyze these substantial impacts associated with AquaBounty's application.

170. FDA's refusal to analyze or even consider the further effects of its approval was based on the agency's erroneous assumption and determination that any impacts would be insignificant because the proposed AquaBounty production processes at the Prince Edward

Island and Panama facilities would be subject to physical, biological, and geographic/geophysical containment measures that would prevent any risk of the GE salmon escaping into and establishing in the natural environment. Based on this assumption, FDA acted contrary to basic principles of risk assessment and erroneously stopped its analysis, refusing to consider the reasonably foreseeable indirect effects of its approval if and when these containment measures fail.

171. FDA also made unsubstantiated assumptions about the biological fitness of AquaBounty's GE salmon and the sterility of the salmon, failing to investigate the risks of fertile GE salmon if they escaped into the environment, including the risk that GE salmon could be carrying infectious disease. As a consequence, FDA's risk assessment falls far short of providing a scientifically defensible analysis of possible consequences should AquaBounty's GE salmon be released into any natural environment, including waters outside the Prince Edward Island and Panama facilities, or areas the GE salmon could enter upon proliferation.

172. FDA entirely failed to consider high quality, accurate scientific information as NEPA requires, including the standard practice of conducting a quantitative failure mode risk analysis, and instead relied on outdated risk analysis methods in analyzing the direct and indirect environmental effects of AquaBounty's GE salmon. Independent, expert scientists have made clear that the kind and extent of harm escaped or released GE salmon may impose on natural environments and ecosystems are unique and extremely uncertain. These scientists have warned, repeatedly, that FDA must utilize additional, more comprehensive studies and up-to-date scientific methods to assess risks.

173. NEPA also requires FDA to take a hard look at the potential aesthetic, historic, cultural, economic, social, and health impacts, including harm to commercial fisheries, recreational fishing, and fishery-dependent communities of its GE salmon approval. 40 C.F.R. § 1508.8. Genetic contamination of native salmon populations by released GE salmon could have devastating impacts on salmon fisheries and markets. Similarly, GE contamination of native salmon could cause irreparable damage to biodiversity and native and cultural traditions

so venerating salmon. The agency refused to consider, let alone adequately analyze, these intertwined socioeconomic and environmental impacts of its approval decision.

174. For the above reasons, FDA violated NEPA, and the EA and FONSI are invalid because they fail to take a hard look at the direct and indirect effects arising from the potential for AquaBounty's GE salmon to enter the environment and adversely affect threatened and endangered fish species or marine ecosystems in either the U.S. or in any foreign jurisdiction.

175. By issuing an EA and FONSI that fail to meet the standards laid out in NEPA, its implementing regulations, and governing precedent, FDA has acted in a manner that is arbitrary, capricious, an abuse of discretion, and not in accordance with law, and without observance of procedures required by law, in violation of NEPA, 42 U.S.C. § 4332, its implementing regulations, and the APA, 5 U.S.C. §§ 701-706.

176. The actions and inactions of the Defendants described in this Cause of Action are causing injuries to the Plaintiffs, for which they have no adequate remedy at law.

THIRD CLAIM FOR RELIEF
VIOLATION OF NEPA AND APA:
IMPROPER SEGMENTATION, FAILURE TO CONSIDER CONNECTED, CUMULATIVE, AND INTERDEPENDENT ACTIONS

177. Plaintiffs re-allege, as if fully set forth, each and every allegation set forth in paragraphs 1 through 176 of this Complaint.

178. NEPA and its implementing regulations require the scope of FDA's analysis to include "connected actions" that "automatically trigger other actions," "cannot or will not proceed unless other actions are taken previously," or "are interdependent parts of a larger action and depend on the larger action for their justification." 40 C.F.R. § 1508.25. FDA must also consider "cumulative actions," which include those that "when viewed with other proposed actions have cumulatively significant impacts," and "similar actions" that "when viewed with other reasonably foreseeable or proposed agency actions have similarities that provide a basis for evaluating their environmental consequences together." *Id.*

179. By contrast, NEPA prohibits an agency from doing what FDA did here: dividing a project into multiple actions, or "breaking it down into small component parts," in order to avoid

a determination that "the action is related to other actions with individually insignificant but cumulatively significant impacts." 40 C.F.R. § 1508.27(b)(7).

180. FDA impermissibly segmented its review of the effects of AquaBounty's GE salmon by considering production only at the Panama and Canada sites, when this approval is only the first step in the company's public plans to commercially develop their GE salmon. This cabined scope of review prevented FDA from properly considering the potentially significant environmental and ecological impacts associated with known and reasonably foreseeable connected, similar, and cumulative actions to expand production of AquaBounty's GE salmon in other areas and at other sites, including the U.S., Canada, Argentina, Chile, China, and other parts of the world, as previously and repeatedly announced by the company.

181. FDA claims that changes to the approved process for producing AquaBounty's GE salmon, including expansions, will be subject to the agency's supplemental application process; however the FDA's own regulations do not support the agency's position. In fact, pursuant to the existing regulations, the agency cannot assure that such changes will be subject to additional environmental analysis and public review, even if they have the potential to cause significant impacts. *See* 21 C.F.R. § 514.8. FDA's overly constrained review risks that the broader impacts of the AquaBounty approval may never be analyzed, and violates NEPA's fundamental requirement that such impacts be analyzed at the earliest possible time, and before the agency makes a decision with far-reaching environmental impacts.

182. For the reasons described above, FDA has violated NEPA and the EA and FONSI are invalid because they fail to adequately assess connected, cumulative, and similar actions.

183. By issuing an EA and FONSI that fail to meet the standards laid out in NEPA, its implementing regulations, and governing precedent, FDA has acted in a manner that is arbitrary, capricious, an abuse of discretion, and not in accordance with law, and without observance of procedures required by law, in violation of NEPA, 42 U.S.C. § 4332, its implementing regulations, and the APA, 5 U.S.C. §§ 701-706.

184. The actions and inactions of the Defendants described in this Cause of Action are causing injuries to the Plaintiffs, for which they have no adequate remedy at law.

FOURTH CLAIM FOR RELIEF
VIOLATION OF NEPA AND APA:
FAILURE TO ADEQUATELY EVALUATE CUMULATIVE EFFECTS

185. Plaintiffs re-allege, as if fully set forth, each and every allegation set forth in paragraphs 1 through 184 of this Complaint.

186. NEPA and its implementing regulations require the FDA to analyze the cumulative effects of its actions. 40 C.F.R. §§ 1508.25 (a)(2), (c); 1508.7, 1508.8. A cumulative impact is the "incremental impact of the action when added to other past, present, and reasonably foreseeable future actions regardless of what agency (federal or non-federal) or person undertakes such other actions. Cumulative impacts can result from individually minor but collectively significant actions taking place over a period of time." 40 C.F.R. § 1508.7. The duty to comprehensively evaluate cumulative impacts is distinct from FDA's duty to evaluate connected, cumulative, and interdependent actions in a single NEPA analysis. *Earth Island Inst. v. Forest Service*, 351 F.3d at 1306 ("Even if a single, comprehensive EIS is not required, the agency must still adequately analyze the cumulative effects of the projects within each individual EIS.").

187. To satisfy NEPA's cumulative impacts mandates, FDA was required to consider the cumulative impacts of its approval of this single new animal drug application in combination with other actions, including but not limited to, AquaBounty's reasonably foreseeable plans to expand production of GE salmon; other GE fish in development; and any other actions that could affect the marine and freshwater environments impacted by FDA's approval, regardless of what agency or entity is responsible for those actions. This should also have included an analysis of other current threats to Atlantic and Pacific salmon stocks; and other socioeconomic threats to fishing communities and those dependent on healthy ocean ecosystems, such as impacts from existing industrial aquaculture, or habitat changes due to climate change and how these impacts accumulate with the impacts of the company's existing and/or reasonably foreseeable plans to expand production beyond the sites proposed in its application.

188. Instead of casting the wide net NEPA requires, FDA took an extremely narrow and unlawful view of what potential cumulative impacts it had to consider and analyze, concluding that because there are no other pending or reasonably foreseeable new animal drug

applications for GE salmon, there is thus no need for a cumulative impacts analysis. By focusing solely on formal, similar, new animal drug applications, FDA has unlawfully refused to analyze or provide any information concerning the cumulative impacts of its decision to approve AquaBounty's application, as required by 40 C.F.R. § 1508.7.

189. For the reasons described above, FDA has violated NEPA and the EA and FONSI are invalid because they entirely fail to consider and/or to adequately assess the cumulative effects of FDA's actions in conjunction with past, present, and reasonably foreseeable future actions.

190. By issuing an EA and FONSI that fail to meet the standards laid out in NEPA, its implementing regulations, and governing precedent, FDA has acted in a manner that is arbitrary, capricious, an abuse of discretion, not in accordance with law, and without observance of procedures required by law, in violation of NEPA, 42 U.S.C. § 4332, its implementing regulations, and the APA, 5 U.S.C. §§ 701-706.

191. The actions and inactions of the Defendants described in this Cause of Action are causing injuries to the Plaintiffs, for which they have no adequate remedy at law.

FIFTH CLAIM FOR RELIEF
VIOLATION OF NEPA AND APA:
ALTERNATIVES ANALYSIS VIOLATIONS AND IMPROPER PURPOSE AND NEED

192. Plaintiffs re-allege, as if fully set forth, each and every allegation set forth in paragraphs 1 through 191 of this Complaint.

193. NEPA and its implementing regulations require an agency to "[r]igorously explore and objectively evaluate all reasonable alternatives." 40 C.F.R. § 1502.14(a). *See also* 42 U.S.C. § 4332(C), (E); 40 C.F.R. § 1508.25. Indeed, the alternatives analysis to the proposed action is "the heart" of the NEPA process, and is intended to provide a "clear basis for choice among options by the decision-maker and the public." 40 C.F.R. § 1502.14. *See also* 42 U.S.C. § 4332(C)(iii), (E); 40 C.F.R. § 1508.25.

194. The scope of a NEPA alternatives analysis is a function of the "purpose and need" for the agency action under review. 40 C.F.R. § 1502.13. The purpose and need statement in the EA is unclear. On the one hand, FDA states that the purpose and need is limited to whether to

approve AquaBounty's new animal drug application. On the other hand, FDA describes the purported need for this GE fish to help address the world-wide overfishing crisis, and the attendant decline in wild stocks, including Atlantic salmon populations, as well as address increasing demand for fish protein. FDA has either erroneously defined its purpose and need, failed to consider an adequate range of alternatives for its stated justifications, or both.

195. To the extent that FDA's purpose and need is limited to whether to approve AquaBounty's application, FDA either too narrowly defined the purpose and need to be limited to its statutory obligations to review and approve a new animal drug application, or failed to consider any alternatives that would condition its approval to better protect the environment. The only alternative FDA considered was denial of AquaBounty's application. FDA explained that it dismissed this "no action" alternative based on its belief that the FFDCA required approval of the GE salmon application so long as there are no specific grounds under the FFDCA to deny approval.

196. However, even under this restrictive iteration of the purpose and need, numerous alternatives to FDA's approval of AquaBounty's application were available, but FDA failed to adequately evaluate any of them. For example, FDA failed to adequately consider the inclusion of additional regulatory conditions on the approval to protect the environment and sensitive marine and freshwater areas affected by AquaBounty's application including temporal, process, facilities, and transport restrictions; limiting the volume of GE fish that could be grown at once; imposing more stringent monitoring, recordkeeping, or reporting requirements; requiring additional training or qualifications for workers; refusing to permit facilities beyond FDA's jurisdiction; or granting only a limited, pilot project. FDA also failed to consider any alternatives that would require concurrent review and approval/restrictions by other agencies with relevant expertise in fisheries biology, such as NMFS or FWS. 40 C.F.R. § 1502.14(c) (alternatives discussion shall "include reasonable alternatives not within the jurisdiction of the lead agency").

197. To the extent that the purpose and need for this action includes addressing the world-wide overfishing crisis, the agency arbitrarily considered the proposed GE salmon

approval as the only potential solution. FDA failed to consider any other options that could feasibly, effectively, and safely improve the world's overstressed fisheries and meet the demand for fish protein without the environmental risks of GE salmon. Such alternatives were presented to the agency by commenters, including development of new projects and policies designed to support and expand sustainable commercial fishing or aquaculture practices; actions to protect and restore native Atlantic salmon populations; and non-GE alternatives to developing "faster growing" salmon, such as that developed by SalmoBreed in Norway. FDA ignored all of these reasonable alternatives that would have satisfied its purpose and need.

198. NEPA requires agencies to consider "a range of reasonable actions which might meet goals of the agency by using different approaches that might reduce the environmental impacts of the agency's action." *See, e.g.*, *Soda Mountain Wilderness Council v. Norton*, 424 F. Supp. 2d 1241, 1265 (E.D. Cal. 2006). *See also* 40 C.F.R. § 1508.25(b) (requiring agency to consider other reasonable courses of action and that include mitigation measures not in proposed action). By considering only one alternative—approval of AquaBounty's application as presented—the agency failed to adequately consider other reasonable alternatives to the proposed action that could fulfill either articulation of the agency's purpose and need for the action.

199. FDA has violated NEPA and its EA and FONSI are invalid because they fail to rigorously explore and evaluate a full range of reasonable alternatives. FDA has acted in a manner that is arbitrary, capricious, an abuse of discretion, and not in accordance with law, and without observance of procedures required by law in violation of NEPA, 42 U.S.C. § 4322, its implementing regulations, and the APA, 5 U.S.C. §§ 701-706.

200. The actions and inactions of the Defendants described in this Cause of Action are causing injuries to the Plaintiffs, for which they have no adequate remedy at law.

SIXTH CLAIM FOR RELIEF
VIOLATION OF NEPA AND APA:
FAILURE TO PREPARE AN ENVIRONMENTAL IMPACT STATEMENT

201. Plaintiffs re-allege, as if fully set forth, each and every allegation set forth in paragraphs 1 through 200 of this Complaint.

202. NEPA requires federal agencies to prepare an EIS for all "major [f]ederal actions significantly affecting the quality of the human environment." 42 U.S.C. § 4332(2)(C); 40 C.F.R. § 1501.4. Under certain circumstances, the agency can prepare an EA that provides "sufficient evidence and analysis for determining whether to prepare" an EIS and that contributes to the agency's compliance with NEPA. 40 C.F.R. §§ 1508.9, 1501.4.

203. Determining the significance of an action in an EA or elsewhere requires the agency to consider the intensity of the impact by evaluating factors enumerated at 40 C.F.R. § 1508.27(b), including, *inter alia*, the degree to which the action affects public health or safety; the degree to which the effects are likely to be highly controversial; the degree to which effects are highly uncertain or involve unique or unknown risks; whether the action establishes a precedent for future actions or represents a decision in principle about a future consideration; the degree to which the action may affect endangered or threatened species; and whether the action is related to actions with individually insignificant but cumulatively significant impacts.

204. As detailed above and in the preceding claims for relief, FDA's decision to approve the AquaBounty application to manufacture GE salmon and sell it in the U.S. is highly controversial; it involves uncertain, unique, and unknown risks; it is precedent-setting, as the first-ever GE animal for human consumption and first GE fish; it involves significant cumulative impacts; it involves unanalyzed connected, cumulative, and similar action; it poses risks to ecologically critical areas and to species protected under the ESA; and it could adversely affect significant cultural and native resources, in the form of protected salmon stocks and traditional fisheries.

205. For these reasons, the plain language of NEPA, the CEQ regulations implementing NEPA, the FDA regulations implementing NEPA, and well-established precedent all require FDA to prepare an EIS before deciding whether to approve the AquaBounty application. 42 U.S.C. § 4332(2)(C); 40 C.F.R. §§ 1508.27, 1502.3; 21 C.F.R. § 25.42(b).

206. In 2011, Plaintiffs CFS, FoE, and FWW formally petitioned FDA to refrain from taking any final action on the AquaBounty application until FDA had completed an EIS. FDA denied the petition on the same day it issued the GE salmon approval.

207. By issuing an inadequate EA and FONSI instead of preparing an EIS and by denying several of the Plaintiffs' petition seeking an EIS, FDA has acted in a manner that is arbitrary, capricious, an abuse of discretion, not in accordance with law, and without observance of procedures required by law, in violation of NEPA, 42 U.S.C. § 4332, and the APA, 5 U.S.C. §§ 701-706.

208. The actions and inactions of the Defendants described in this Cause of Action are causing injuries to the Plaintiffs, for which they have no adequate remedy at law.

SEVENTH CLAIM FOR RELIEF
VIOLATION OF NEPA AND APA:
IMPROPER RELIANCE ON MITIGATION

209. Plaintiffs re-allege, as if fully set forth, each and every allegation set forth in paragraphs 1 through 208 of this Complaint.

210. NEPA requires agencies to disclose and analyze measures to mitigate the impacts of proposed actions. 40 C.F.R. §§ 1502.14(f), 1502.16(h). Here, FDA relies on AquaBounty's containment plan for the Prince Edward Island and Panama facilities to mitigate environmental risks associated with the escape of AquaBounty's GE salmon, but the agency has not actually established that these mitigation measures will effectively mitigate all potential significant risks, nor has it ensured compliance with the described mitigation measures through monitoring or other means.

211. Reliance on AquaBounty's purportedly sufficient mitigation measures is not a substitute for FDA compliance with NEPA's mandate to examine potential significant environmental impacts. An agency cannot rely on mitigation measures to avoid performing a detailed analysis of the environmental impacts of an action. *See, e.g., Northern Plains Resource Council v. Surface Transp. Bd.*, 668 F.3d 1067, 1085-86 (9th Cir. 2001). Here, FDA has improperly relied on AquaBounty's containment measures, and failed to analyze the potential impacts should/when any or all of those measures fail. Although it is standard scientific practice, FDA has not conducted a quantitative failure mode analysis to test the reliability of AquaBounty's various biological, geographical, and physical measures. Nor did FDA consider or analyze any alternative mitigation measures.

212. Mitigation must also be enforceable, including the on-going duty of the agency to monitor and ensure compliance. Yet FDA's FONSI depends in part on its reliance on containment and other mitigation measures developed by, and solely under the control of, AquaBounty. FDA has not explained how it will monitor continued compliance with the containment measures at either facility described in AquaBounty's application, or any other facility that may foreseeably produce AquaBounty's GE salmon. This is particularly vital given AquaBounty's plans to expand production to various other sites around the world.

213. Courts examine mitigation measures to see whether such measures keep impacts below the EIS threshold, which sets a "low standard" for whether a project "may have a significant effect." *See, e.g., Klamath Siskiyou Wildlands Center v. Boody*, 468 F.3d 549, 562 (9th Cir. 2006). FDA cannot use uncertain, unanalyzed, and unenforced mitigation to evade meeting the low EIS threshold and preparing an EIS.

214. FDA's reliance on mitigation provided by, and subject to the sole control of, AquaBounty was arbitrary, capricious, an abuse of discretion, not in accordance with law, and without observance of procedures required by law, in violation of NEPA, 42 U.S.C. § 4332, its implementing regulations, and the APA, 5 U.S.C. §§ 701-706.

215. The actions and inactions of the Defendants described in this Cause of Action are causing injuries to the Plaintiffs, for which they have no adequate remedy at law.

EIGHTH CLAIM FOR RELIEF
VIOLATION OF NEPA AND APA:
FAILURE TO COMPLY WITH NEPA FOR ITS GE ANIMAL PROGRAM

216. Plaintiffs re-allege, as if fully set forth, each and every allegation set forth in paragraphs 1 through 215 of this Complaint.

217. Under NEPA, all federal agencies must prepare an EIS on "every recommendation and report on proposals for legislation and other major federal actions significantly affecting the quality of the human environment." 42 U.S.C. § 4332(2)(C).

218. The definition of "major federal action" includes "adoption of programs, such as a group of concerted action to implement a specific policy or plan." 40 C.F.R. § 1508.18(b)(3). Agency polices are also "major federal action[s]." *Id.* §§ 1508.18, 1508.18(a) ("'Major federal

action' includes … new or revised … policies."); 46 Fed. Reg. 18,026, 18,038 (Mar. 23, 1981) ("When are EISs required on policies, plans or programs? An EIS must be prepared if an agency proposes to implement a specific policy.").

219. NEPA regulations require agencies to prepare a programmatic EIS "for broad Federal actions such as the adoption of new agency programs or regulations." 40 C.F.R. § 1502.4(b). An agency "program" or "proposal" that exists in fact but is not necessarily declared by the agency still requires a programmatic EIS. *Id.* § 1508.23 (defining "proposal" to include that a "proposal may exist in fact as well as by agency declaration that one exists."). Such programmatic EISs should be undertaken "before the program has reached a stage of investment or commitment to implementation likely to determine subsequent development or restrict later alternatives." *Id.* § 1502.4(c)(3).

220. FDA has purported to create the regulatory framework for GE animal approvals under the FFDCA's new animal drug provisions in its 2009 GE Animal Guidance. FDA recently revised and reissued the GE Animal Guidance in June 2015. The GE Animal Guidance is a major federal action significantly affecting the human environment. FDA has not completed any NEPA analysis on the effects of the GE Animal Guidance framework.

221. FDA approved the first GE animal for human consumption pursuant to the GE Animal Guidance, the AquaBounty GE salmon, in November 2015. FDA's approval of the AquaBounty application marks the first GE animal commercially approved for human consumption commercial approval within this new, highly significant, and unprecedented program.

222. An EIS is particularly crucial here, when FDA is acting and purporting to establish and apply a new framework regarding novel GE organisms. FDA's continuing failure to prepare a programmatic EIS (or any other NEPA analysis) for its GE animal approval program, as purportedly established by its GE Animal Guidance, and as now concretely applied in its GE salmon approval, violates NEPA.

223. FDA's decision to create the GE animal program and then begin specific approvals without analyzing any of the impacts of its unprecedented program was arbitrary,

capricious, an abuse of discretion, not in accordance with law, and without observance of procedures required by law, in violation of NEPA, 42 U.S.C. § 4332, its implementing regulations, and the APA, 5 U.S.C. §§ 701-706.

224. The actions and inactions of the Defendants described in this Cause of Action are causing injuries to the Plaintiffs, for which they have no adequate remedy at law.

NINTH CLAIM FOR RELIEF
VIOLATION OF NEPA 42 U.S.C § 4332 AND APA:
FAILURE TO PREPARE A SUPPLEMENTAL NEPA ANALYSIS

225. Plaintiffs re-allege, as if fully set forth, each and every allegation set forth in paragraphs 1 through 224 of this Complaint.

226. NEPA and its implementing regulations impose a continuing duty on agencies to prepare a supplemental environmental impact statement ("SEIS") whenever "(i) The agency makes substantial changes in the proposed action that are relevant to environmental concerns; or (ii) There are significant new circumstances or information relevant to environmental concerns and bearing on the proposed action or its impacts." 40 C.F.R. §§ 1502.9(c)(1)(i), (ii). AquaBounty's expansion of GE salmon production on Prince Edward Island triggers this duty.

227. For the reasons described above, FDA has violated NEPA, and the EA and FONSI are invalid because FDA has failed to prepare a an SEIS, or any other supplemental NEPA analysis, in light of the changes that are being made to the action through the establishment of an additional facility to support increased GE salmon production on Prince Edward Island. These chnages are relevant to environmental concerns and present significant new information and changed circumstances that trigger the need for supplemental NEPA analysis.

228. The APA authorizes reviewing courts to compel agency action unlawfully withheld and to set aside federal agency action that is arbitrary, capricious, an abuse of discretion, and not in accordance with law. 5 U.S.C. § 701-706.

229. By issuing and EA and FONSI that fail to meet the standards laid out in NEPA, its implementing regulations, and governing case law, and by failing to supplement this analysis in light of substantial changes, significant new information, and changed circumstances, FDA

has unlawfully withheld action that is legally required and/or has acted in a manner that is arbitrary, capricious, an abuse of discretion, and not in accordance with law, in violation of NEPA, 42 U.S.C. § 4332, and the APA, 5 U.S.C. § 701-706.

230. The actions and inactions of the Defendants described in this Cause of Action are causing injuries to the Plaintiffs, for which they have no adequate remedy at law.

TENTH CLAIM FOR RELIEF
VIOLATION OF ESA:
FAILURE TO CONSULT REGARDING APPROVAL OF NEW ANIMAL DRUG APPLICATION FOR GE SALMON

231. Plaintiffs re-allege, as if fully set forth, each and every allegation set forth in paragraphs 1 through 230 of this Complaint.

232. Section 7(a)(2) of the ESA prohibits agency actions that jeopardize the survival of listed species or that destroy or adversely modify their critical habitat. 16 U.S.C. § 1536(a)(2). To assist in complying with this duty, federal agencies, like FDA, must consult with NMFS and FWS whenever they take an action that "may affect" a listed species or the species' critical habitat. *Id.*; 50 C.F.R. § 402.14(a).

233. The ESA and its implementing regulations broadly define agency action. 50 C.F.R. §§ 402.02, 402.03. FDA's approval of AquaBounty's new animal drug application constitutes "agency action" under ESA section 7(a)(2). *Id.*

234. Under the ESA, agency actions that "may affect" a listed species or critical habitat may not proceed unless and until the federal agency first ensures, through completion of the consultation process, that the action is not likely to cause jeopardy or adverse modification of critical habitat. 16 U.S.C. § 1536(a), (d); 50 C.F.R. §§ 402.14, 402.13. The threshold for a "may affect" determination and the required ESA section 7(a)(2) consultation is low. *See* 51 Fed. Reg. 19,926, 19,949 (June 3, 1986) ("Any possible effect, whether beneficial, benign, adverse or of an undetermined character, triggers the formal consultation requirement.").

235. As detailed above and as highlighted by fisheries biologists at both FWS and NMFS, the activities permitted by FDA's approval of the new animal drug application—including the breeding, transportation, and husbandry of GE salmon at the Prince Edward Island

and Panama facilities and the reasonably foreseeable production of GE salmon production at other facilities—"may affect" listed species and their critical habitat by, *inter alia*, risking release of GE salmon that may: compete with listed wild salmon populations that inhabit or migrate in areas near the facilities for food, space, and mates; cause genetic introgression and reduction in fitness by breeding with listed wild salmon; and spread disease to wild populations. These impacts satisfy the low threshold that the ESA, its implementing regulations, and the Services' Consultation Handbook set for a "may affect" determination.

236. FDA's determination that its action has "no effect" on listed salmon species fails to consider these impacts, improperly assumes that untested and unproven mitigation measures can address these impacts, and is not based on the best scientific and commercial data available about the risks posed by commercial production of GE salmon. FDA also based its determination on a limited definition of the scope of its action to include only effects directly associated with the production of GE salmon on Prince Edward Island and in Panama, ignoring AquaBounty's stated plans to expand its operations to additional facilities, both domestically and abroad. FDA likewise limited its analysis because it did not consider impacts to other threatened or endangered species aside from Atlantic salmon, including effects on listed Pacific salmon and other salmonids, like steelhead and trout.

237. FDA has violated the ESA by approving the new animal drug application for GE salmon without first completing consultation with NMFS and FWS regarding an action that "may affect" listed species and/or their critical habitat. FDA's failure to consult with the Services to insure that its action is not likely to jeopardize endangered or threatened species or adversely modify critical habitat violates the ESA, 16 U.S.C. § 1536(a)(2), its implementing regulations; and the APA, 5 U.S.C. §§ 701-706.

238. The actions and inactions of the Defendants described in this Cause of Action are causing injuries to the Plaintiffs, for which they have no adequate remedy at law.

ELEVENTH CLAIM FOR RELIEF
VIOLATION OF ESA AND APA:
FWS'S DETERMINATION THAT CONSULATION WAS NOT REQUIRED IS ARBITRARY AND CONTRARY TO LAW

239. Plaintiffs re-allege, as if fully set forth, each and every allegation set forth in paragraphs 1 through 238 of this Complaint.

240. The ESA's implementing regulations allow an agency to pursue an optional informal consultation process for actions that "may affect" listed species. 50 C.F.R. § 402.13. If during that process the Services concur in writing with the agency's conclusion that an action is "not likely to adversely affect" listed species, the consultation process is complete. *Id.* § 402.14(b)(1). If an agency concludes that its action has "no effect" on listed species—and thus that it need not engage in any consultation with the Services—it may not seek a written concurrence from the Services. The action agency is solely responsible for its compliance with the mandates of Section 7. 16 U.S.C. § 1536(a)(2).

241. By at least 2009, FDA initiated consultation with the Services regarding AquaBounty's new animal drug application. In August 2010, FDA sent the Services letters concluding that its approval of AquaBounty's application "may affect" but was "not likely to adversely affect" endangered Atlantic salmon populations.

242. In October 2010, based on input from FWS, FDA changed its previous conclusions. FDA informed FWS and NMFS that it had determined its approval of AquaBounty's new animal drug application would instead have "no effect" on listed species.

243. On December 16, 2010, FWS sent a letter to FDA purporting to concur in the agency's "no effect" determination because it adopted FDA's limited analysis and characterization of the new animal drug application. FWS's purported concurrence with FDA's "no effect" determination is the consummation of informal consultation between FWS and FDA.

244. As with FDA's narrow analysis, FWS's purported concurrence was reached without considering all of the relevant factors and contrary to the best scientific and commercial data available, in violation of the ESA, 16 U.S.C. § 1536(a)(2), and the APA, 5 U.S.C. §§ 701-706.

245. FWS's concurrence in FDA's "no effect" determination for an action that "may affect" listed species is a final agency action that violates the ESA, 16 U.S.C. § 1536(a)(2), its implementing regulations, and the APA, 5 U.S.C. §§ 701-706.

246. The actions and inactions of the Defendants described in this Cause of Action are causing injuries to the Plaintiffs, for which they have no adequate remedy at law.

TWELFTH CLAIM FOR RELIEF
VIOLATION OF THE FFDCA AND APA:
FAILURE TO ENSURE ENVIRONMENTAL SAFETY OF GE ANIMALS AND GE SALMON

247. Plaintiffs re-allege, as if fully set forth, each and every allegation set forth in paragraphs 1 through 246 of this Complaint.

248. FDA's new animal drug authority is directly tied to whether the drug is "safe and effective" for its intended use. 21 U.S.C. § 360b(b)(1). Under the FFDCA and FDA regulations, the review and approval of new animal drug applications is focused on the "safety and effectiveness" of the new animal drug. *See, e.g.*, 21 U.S.C. §§ 360b(a)(1), (b)(1)(H), (d)(1)-(2), (i); 21 C.F.R. §§ 514.1(b)(8), 514.105. FDA can only approve a new animal drug application for a drug that is "safe" under the prescribed or recommended conditions of the application. 21 U.S.C. § 360b(d). FDA's approval of GE salmon violated the FFDCA and was arbitrary and capricious because it failed to rationally consider all the factors relevant to ensuring that the GE salmon drug approval was safe for, *inter alia*, the environment.

249. The FFDCA does not limit the factors that FDA considers when evaluating whether a drug is safe and effective during review and approval of a new animal drug application and when exercising its ongoing enforcement authority over those applications. *See, e.g.*, 21 U.S.C. § 360b(d)(2). In its GE Animal Guidance and, as applied in its GE salmon approval, FDA has expressly interpreted the FFDCA to include environmental risks as a relevant factor when evaluating the safety and effectiveness of a drug.

250. Despite FDA's acknowledgment that it must consider environmental safety as part of its "safety and effectiveness" evaluation, the GE Animal Guidance fails to rationally explain what factors FDA will consider relevant to this determination and how FDA will weigh

or consider such factors when it evaluates whether an application is "safe and effective" in its approvals and decisionmaking.

251. FDA does not detail or explain, for example, how it will assess and determine the environmental or ecological risks posed by GE animals, how or whether it will require adoption of measures or methods necessary to ensure that GE animals will not escape confinement, introduce or spread diseases, or otherwise contaminate wild populations or ecosystems. FDA does not detail or explain what requirements, measures, or methods are necessary to mitigate or remediate any accidental release of GE animals into the environment or how it will require and enforce the adoption of such measures to ensure the continued safety of approved GE animals. Nor does FDA detail how it will weigh and combine these or other relevant factors in its decision that a new animal drug is "safe" for the environment. FDA's GE Animal Guidance was developed without full consideration of these and other factors relevant to environmental risk and fails to rationally explain how FDA will substantively consider environmental risk as part of its review and approval of new animal drug applications.

252. When purportedly applying this guidance to its review and approval of AquaBounty's GE salmon new animal drug application, FDA failed to ensure that AquaBounty's GE salmon was "safe and effective" under the FFDCA because it failed to adequately consider or evaluate all of the factors and evidence relevant to environmental safety. As described above, FDA's environmental safety evaluation of AquaBounty's GE salmon was legally flawed and scientifically inadequate, for at least the following reasons: (1) it failed to adequately assess the risks of escape or release of AquaBounty's GE salmon, and failed to encompass or meaningfully review the environmental and interrelated risks associated with such escape or release and; (2) it failed to consider the best scientific evidence available regarding the environmental risks of AquaBounty's GE salmon. As a result, FDA's conclusion that AquaBounty's GE salmon was "safe" was arbitrary and not based on a rational assessment of the factors relevant to environmental risks.

253. FDA's failure to consider and rationally explain how it will consider the factors relevant to environmental safety in its GE Animal Guidance is arbitrary and capricious, an abuse

of discretion, and not in accordance with law, in violation of the APA, 5 U.S.C. §§ 701-706, and the FFDCA, 21 U.S.C. §§ 301-399(f).

254. In purportedly applying the GE Animal Guidance in its approval of the new animal drug application for GE salmon, FDA similarly failed to consider the factors relevant to the environmental safety of GE salmon and/or to rationally explain its conclusion that GE salmon is safe for the environment. FDA's conclusion that AquaBounty's GE salmon is "safe" is arbitrary, capricious, an abuse of discretion, and not in accordance with law, in violation of the APA, 5 U.S.C. §§ 701-706, and the FFDCA, 21 U.S.C. §§ 301-399(f).

255. The actions and inactions of the Defendants described in this Cause of Action are causing injuries to the Plaintiffs, for which they have no adequate remedy at law.

THIRTEENTH CLAIM FOR RELIEF
VIOLATION OF APA, FDA MODERNIZATION ACT OF 1997:
THE 2009 AND 2015 GE ANIMAL GUIDANCE

256. Plaintiffs re-allege, as if fully set forth, each and every allegation set forth in paragraphs 1 through 255 of this Complaint.

257. Through the adoption of the GE Animal Guidance, and through the agency's subsequent revisions to that document, FDA has created a new program and regulatory framework for review and approval of GE animals under its new animal drug authority.

258. Under the APA, a "rule" is "the whole or a part of an agency statement of general or particular applicability and future effect designed to implement, interpret, or prescribe law or policy." 5 U.S.C. § 551(4). Rules generally must be promulgated with public notice, an opportunity for comment, consideration of and response to those comments, and must be codified in the Code of Federal Regulations. *Id.* § 553; 44 U.S.C. § 1510.

259. Under the Food and Drug Administration Modernization Act of 1997 (Modernization Act), FDA may issue guidance documents in certain limited circumstances, but must ensure that such guidance documents "shall not create or confer any rights for or on any person" and are not binding. 21 U.S.C. § 371(h)(1)(A)-(B).

260. FDA announced its decision to regulate GE animals under the new animal drug provisions of the FFCDA in its GE Animal Guidance, purportedly in accordance with the

procedures in the Modernization Act. FDA did not publically notice its decision to apply the new animal drug provisions to GE Animals or the framework it developed for doing so as a regulation, the public did not comment on this decision as a binding regulation, and it is not codified in the Code of Federal Regulations.

261. The GE Animal Guidance is a de facto amendment to FDA's existing regulations for new animal drugs, which do not specifically extend or provide a framework for the approval of GE animals, to include the review and approval of GE animals. 21 U.S.C. § 321(g)(1) (definition of "drug") and § 321(v) ("new animal drug"). The GE Animal Guidance does not qualify as "guidance" under the Modernization Act, and should have been promulgated as a rule, because it confers legal rights to entities seeking approval of GE animals and binds FDA to accept and review those applications.

262. According to FDA's practice and statements, development and adoption of the GE Animal Guidance was necessary before the agency could review and approve new animal drug applications for GE animals, including GE salmon. Prior to its promulgation, FDA could reject an application for approval of a GE animal (and its lineage) under the new animal drug provisions because GE animals were not considered "drugs." No regulatory pathway for GE animals existed and no GE animals were approved. After the Guidance, FDA now must accept and process such new animal drug applications, as evidenced by its approval, after the issuance of the Guidance, of new animal drug applications for GE Salmon, GE goats, GE chickens, and GE rabbits.[4]

263. While FDA did offer notice and comment on the GE Animal Guidance, its failure to offer such notice and comment in the APA formal rulemaking context deprived stakeholders, including Plaintiffs, of the formality and finality in FDA's determination and interpretation of its authority.

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[4] FDA, *Genetically Engineered Animals*, http://www.fda.gov/AnimalVeterinary/DevelopmentApprovalProcess/GeneticEngineering/GeneticallyEngineeredAnimals/default.htm; FDA, *FDA approves first drug to treat a rare enzyme disorder in pediatric and adult patients*, http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm476013.htm; FDA, *FDA approves new product to treat rare genetic disease*, http://www.fda.gov/newsevents/newsroom/pressannouncements/ucm405526.htm.

264. FDA's failure to promulgate its framework for regulating GE animals under the new animal drug provisions of the FFDCA as a rulemaking violates the Modernization Act and its implementing regulations, 21 U.S.C. § 371(h); 21 C.F.R. § 10.115; the APA, 5 U.S.C. §§ 553; 706(2)(A), (D); and the Federal Register Act, 44 U.S.C. § 1510.

265. The actions and inactions of the Defendants described in this Cause of Action are causing injuries to the Plaintiffs, for which they have no adequate remedy at law.

PRAYERS FOR RELIEF

WHEREFORE, the Plaintiffs respectfully request that the Court:

1. Adjudge and declare that the FDA decision to approve the AquaBounty GE salmon and the GE Animal Guidance are not authorized by the FFDCA, and are instead *ultra vires* agency action, in violation of the FFDCA and the APA;

2. Issue an injunction requiring FDA to withdraw its assertion of jurisdiction over GE animals, and prohibiting FDA from asserting jurisdiction over, or initiating any rulemaking or enforcement proceedings based on any illegal assertion of jurisdiction over the manufacture, labeling, or marketing of GE animals;

3. Adjudge and declare that the FDA decision to approve the AquaBounty application, as well as the EA and FONSI issued by the FDA in connection with that approval, are in violation of the FFDCA, NEPA, the ESA and the APA;

4. Adjudge and declare that FDA violated NEPA by failing to prepare a programmatic EIS or any other NEPA analysis for its development and adoption of the GE Animal Guidance, which establishes a policy and a de facto program for GE animal regulation by FDA that requires NEPA compliance;

5. Adjudge and declare that FDA violated NEPA by failing to prepare a supplemental NEPA analysis in light of the changes that made to the proposed action that are relevant to environmental concerns and significant new information and changed circumstances;

6. Adjudge and declare that the FDA GE Animal Guidance, on its face and as applied to GE salmon, is arbitrary and capricious in violation of the FFDCA, and the APA;

7. Declare that FDA is in violation of section 7(a)(2) of the ESA, 16 U.S.C. § 1536(a)(2), by failing to complete consultation necessary to ensure that its GE salmon approval is not likely to jeopardize the continued existence of listed species or destroy or adversely modify their critical habitat;

8. Declare that FWS is in violation of the ESA and the APA by purporting to concur in FDA's conclusion that its approval of GE salmon would have "no effect" on listed species in violation of section 7(a)(2) of the ESA, 16 U.S.C. § 1536(a)(2) and the APA;

9. Vacate the FDA decision to approve the AquaBounty application, enjoin the agency from taking any action pursuant to that decision, and order that the FDA comply with all requirements of NEPA, the ESA, and the APA, including preparing an EIS and engaging in consultation with the Services, in the event that the agency conducts a new review of that application;

10. Vacate FWS's purported concurrence with FDA's "no effect" determination for listed species;

11. Vacate the GE Animal Guidance and order FDA to undertake formal rulemaking procedures if the agency is to attempt to apply the FFDCA to GE animals, and order the FDA to first undertake an EIS on that program;

12. Award the Plaintiffs their fees, costs, expenses, and disbursements, including reasonable attorneys' fees, associated with this litigation under the Equal Access to Justice Act, 28 U.S.C. § 2412 and the Endangered Species Act, 16 U.S.C.§ 1540; and

13. Grant such further and additional relief as this Court deems just and proper.

Respectfully submitted this 15th day of July, 2016 in San Francisco, California.

/s/ Adam Keats

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Counsel for Plaintiffs

Exhibit 1

December 22, 2015

VIA CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Sylvia Mathews Burwell, Secretary
Department of Health & Human Services
200 Independence Avenue S.W.
Washington, D.C. 20201

Dr. Stephen Ostroff, M.D., Acting Commissioner
Food and Drug Administration
10903 New Hampshire Ave
Silver Spring, MD 20993

Penny Pritzker, Secretary
Department of Commerce
1401 Constitution Ave., N.W.
Washington D.C. 20230

Eileen Sobeck, Assistant Administrator for NOAA
NOAA Fisheries Service
1315 East West Highway, SSMC3
Silver Spring, MD 20910

Sally Jewell, Secretary
Department of the Interior
1849 C Street N.W.
Washington D.C. 20240

Daniel Ashe, Director
Fish and Wildlife Service
1849 C. Street N.W.
Washington DC 20240

NATIONAL HEADQUARTERS
660 Pennsylvania Avenue, SE, Suite 302
Washington, D.C. 20003
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CALIFORNIA OFFICE
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Honolulu, Hawaii 96813
T: 808-681-7688

office@centerforfoodsafety.org centerforfoodsafety.org

Sixty-Day Notice of Intent to Sue FDA Pursuant to the Endangered Species Act
Re: Approval of Genetically Engineered "AquAdvantage" Salmon

Acting Commissioner Ostroff:

The Food and Drug Administration is hereby notified, unless the violations described herein are remedied within sixty days, that the organizations listed below intend to sue the Food and Drug Administration and its Acting Commissioner Dr. Ostroff (collectively FDA), for violations of the Endangered Species Act (ESA), 16 U.S.C. § 1531, *et seq.*, associated with FDA's approval of the genetically engineered (GE or transgenic), "AquAdvantage" salmon (GE salmon). *See* New Animal Drugs in Genetically Engineered Animals; opAFP–GHc2 Recombinant Deoxyribonucleic Acid Construct, 80 Fed. Reg. 73,104 (Nov. 24, 2015). FDA has violated and remains in violation of Section 7 of the ESA by, *inter alia*, failing to insure, through consultation with the National Marine Fisheries Service (NOAA Fisheries) and the U.S. Fish and Wildlife Service (FWS) (collectively, the Services), that its approval of the GE salmon is not likely to jeopardize the continued existence of any threatened or endangered species and/or result in the destruction or adverse modification of the critical habitat of any listed species. Center for Food Safety and Earthjustice provide this letter pursuant to Section 11(g) of the ESA, 16 U.S.C. § 1540(g), on behalf of Cascadia Wildlands, Center for Biological Diversity, Center for Food Safety, Ecology Action Centre, Food & Water Watch, Friends of the Earth, Golden Gate Salmon Association, Institute for Fisheries Resources, and Pacific Coast Federation of Fishermen's Associations.

I. IDENTITY OF THE ORGANIZATIONS GIVING NOTICE: The names, addresses, and phone numbers of the organizations giving notice of intent to sue under the ESA are:

Cascadia Wildlands
PO Box 10455
Eugene, OR 97440
541-434-1463

Center for Biological Diversity
1212 Broadway, St. #800
Oakland, CA 94612
510-844-7100

Center for Food Safety
917 S.W. Oak St.
Portland, OR 97205
971-271-7372

Ecology Action Centre
2705 Fern Lane
Halifax, NS B3K 4L3
902-429-2202

Food & Water Watch
1616 P Street NW
Washington, DC 20036
202-683-2500

Friends of the Earth
1101 15th Street NW, 11th Floor
Washington, DC 20005
202-783-7400

Golden Gate Salmon Association
1370 Auto Center Drive
Petaluma, CA 94952
855-251-4472

Institute for Fisheries Resources
PO Box 29370
San Francisco, CA 94129-0370
415-561-5080

Pacific Coast Federation of Fishermen's
Associations
PO Box 29370
San Francisco, CA 94129-0370
415-561-5080

II. REQUIREMENTS OF THE ESA

Section 7 of the ESA requires federal agencies such as FDA, in consultation with the expert wildlife agencies, to insure that any action authorized, funded, or carried out by the agency is not likely to jeopardize the continued existence of any threatened or endangered (T&E) species, or result in the destruction or adverse modification of the critical habitat of such species. 16 U.S.C. § 1536(a)(2). An action is considered to result in jeopardy where it would reasonably be expected, directly or indirectly, to reduce appreciably the likelihood of both the survival and recovery of a listed species in the wild by reducing the reproduction, numbers, or distribution of that species. 50 C.F.R. § 402.02. "Action" is broadly defined to include all activities or programs of any kind authorized, funded, or carried out by federal agencies, including actions directly or indirectly causing modifications to the land, water, or air. 50 C.F.R. § 402.02.

To carry out this substantive mandate, the ESA and its implementing regulations require federal agencies to consult with the wildlife agencies on the effects of their proposed actions. 16 U.S.C § 1536(a)(2); 50 C.F.R. §§ 402.12-402.16. This process begins with the requirement that the "action" agency, such as FDA here, ask the expert agencies whether any listed or proposed species may be present in the area of the agency action. 16 U.S.C. § 1536(c)(1); 50 C.F.R. § 402.12. If listed or proposed species may be present, the action agency must prepare a "biological assessment" to determine whether the listed species is likely to be affected by the proposed action. *Id*. The biological assessment generally must be completed within 180 days. 16 U.S.C. § 1536(c)(1); 50 C.F.R. § 402.12(i).

If the action agency determines the action "may affect" a listed species or critical habitat, the action agency must formally consult with NOAA Fisheries and/or FWS to "insure" that the action is "not likely to jeopardize the continued existence" of that species, or "result in the destruction or adverse modification of habitat … determined … to be critical…." 16 U.S.C. § 1536(a)(2); 50 C.F.R. § 402.14(a); *see Citizens for Better Forestry v. United States Dep't of Agric.*, 481 F. Supp. 2d 1059, 1092 (N.D. Cal. 2007).[1] The threshold for a finding of "may affect" is extremely low. A triggering effect need not be significant; rather "any possible effect, whether beneficial, benign, adverse, or of an undetermined character, triggers the formal consultation requirement…." Interagency Cooperation—Endangered Species Act of 1973, as Amended; Final Rule, 51 Fed. Reg. 19,926, 19,949 (June 3, 1986); Final ESA Section 7 Consultation Handbook at xvi (Mar. 1998) (defining "may affect" as "the appropriate conclusion when a proposed action may pose *any* effects on listed species….").

If a proposed action "may affect" a listed species or designated critical habitat, formal consultation is required unless the Service(s) concur in writing with an action agency's finding that the proposed action "is not likely to adversely affect" listed species or designated critical

habitat. 50 C.F.R. §§ 402.02, 402.13(a), 402.14 (a). This "informal consultation" process consists of discussions and correspondence between the Services and the action agency and is designed to assist the action agency in determining whether formal consultation is required. 50 C.F.R. § 402.13(a). *See also Pac. Rivers Council v. Thomas*, 30 F.3d 1050, 1054 n.8 (9th Cir. 1994). An action is "likely to adversely affect" protected species, and formal consultation is required, if: "any adverse effect to listed species may occur as a direct or indirect result of the proposed action or its interrelated or interdependent actions, and the effect is not discountable, insignificant, or beneficial." *Endangered Species Consultation Handbook*, March 1998, p. xv.

To complete formal consultation, NOAA Fisheries and/or FWS must provide FDA with a "biological opinion" explaining how the proposed action will affect the listed species or habitat. 16 U.S.C. § 1536(b); 50 C.F.R. § 402.14. In fulfilling Section 7 consultation duties, agencies are required to use the best scientific and commercial data available. 16 U.S.C. § 1536(a)(2); *Heartwood, Inc. v. United States Forest Serv.*, 380 F.3d 428, 434 (8th Cir. 2004). Until the consulting agency issues a comprehensive biological opinion, the action agency may not commence the action. *Pac. Rivers Council*, 30 F.3d at 1056-57; *and see* 16 U.S.C. § 1536(d). Further, during consultation, FDA is prohibited from making any irreversible or irretrievable commitment of resources with respect to the agency action which may foreclose the formulation or implementation of any reasonable and prudent alternative measures. 16 U.S.C. § 1536(d).

If NOAA Fisheries and/or FWS concludes that the proposed action "will jeopardize the continued existence" of a listed species, the biological opinion must outline "reasonable and prudent alternatives." 16 U.S.C. § 1536(b)(3)(A). If the biological opinion concludes that the action is not likely to jeopardize the continued existence of a listed species, and will not result in the destruction or adverse modification of critical habitat, NOAA Fisheries and/or FWS must provide an "incidental take statement," specifying the amount or extent of such incidental taking on the listed species, any "reasonable and prudent measures" that they consider necessary or appropriate to minimize such impact, and setting forth the "terms and conditions" that must be complied with by FDA to implement those measures. 16 U.S.C. § 1536(b)(4); 50 C.F.R. § 402.14(i). In order to monitor the impacts of incidental take, FDA must monitor and report the impact of its action on the listed species to the Services as specified in the incidental take statement. 16 U.S.C. § 1536(b)(4); 50 C.F.R. §§ 402.14(i)(1)(iv), 402.14(i)(3). If during the course of the action the amount or extent of incidental taking is exceeded, FDA must reinitiate consultation with the Services immediately. 50 C.F.R. § 402.14(i)(4).

Federal agencies have an independent and substantive obligation to insure that their actions are not likely to jeopardize the continued existence of endangered or threatened species or adversely modify critical habitat. *See Pyramid Lake Paiute Tribe of Indians v. United States Dep't of the Navy*, 898 F.2d 1410, 1415 (9th Cir. 1990). Indeed, a "no jeopardy" biological opinion from NOAA Fisheries or FWS does not absolve the action agency of its independent duty to insure that its actions comply with the ESA. *Res. Ltd., Inc. v. Robertson*, 35 F.3d 1300, 1304 (9th Cir. 1994). Federal agencies also have a continuing duty under Section 7 of the ESA to re-initiate consultation whenever "new information reveals effects of the action that may affect listed species or critical habitat in a manner or to an extent not previously considered," where the action in question is "subsequently modified in a manner that causes an effect to the listed species or critical habitat that was not considered in the biological opinion," or where "a

new species is listed or critical habitat designated that may be affected by the identified action." 50 C.F.R. § 402.16(b)-(d).[2]

Finally, Section 9(a) of the ESA, 16 U.S.C. § 1538(a), prohibits the "take" of an endangered species by any person. This prohibition has generally been applied to many species listed as "threatened" through the issuance of regulations under Section 4(d) of the ESA, 16 U.S.C. § 1533(d); 50 C.F.R. § 17.31(a).[3] "Take" includes actions that kill, harass, or harm a protected species. 16 U.S.C. § 1532(19). "Harass" is defined to include acts that create the likelihood of injury to wildlife by annoying it to such an extent as to significantly disrupt normal behavioral patterns. 50 C.F.R. § 17.3. "Harm" includes significant habitat modification or degradation that actually kills or injures wildlife by significantly impairing essential behavioral patterns. *Id.*; 50 C.F.R. § 222.102.

III. FACTUAL BACKGROUND

FDA has now approved GE salmon pursuant to authority it asserts under a unique and unlawful interpretation of its Federal Food Drug and Cosmetic Act (FFDCA) duty to regulate "new animal drugs." 80 Fed. Reg. 73,104 (Nov. 24, 2015). The GE salmon is the first GE fish (and the first GE animal for human consumption) that FDA has approved. In doing so, FDA has made an erroneous determination that its approval action will have "no effect" on threatened or protected species or their critical habitat. *See* FDA, Finding of No Significant Impact at 6-7 (Nov. 12, 2015). Endangered species such as imperiled Atlantic salmon (*Salmo salar*) (and in the predictable future, Pacific salmon), may be affected by the approval. FDA was therefore required to consult with the expert wildlife agencies under the ESA before reaching any decision.

A. Affected Species and Critical Habitat

The protected species and critical habitat that may be affected by FDA's approval action include, but are not limited to, the Gulf of Maine Distinct Population Segment of Atlantic salmon (*Salmo salar*) and Pacific salmonids, including certain populations of Chinook salmon (*Oncorhynchus tshawytscha*), chum salmon (*Oncorhynchus keta*), coho salmon (*Oncorhynchus kisutch*), sockeye salmon (*Oncorhynchus nerka*), and steelhead trout (*Oncorhynchus mykiss*).[4]

Wild Atlantic salmon populations have experienced steep declines due to a variety of human-induced pressures including overexploitation, degradation of water quality, and damming of rivers.[5] In 2000, NOAA Fisheries and FWS issued a final rule designating the Gulf of Maine Distinct Population Segment (GOM DPS) as endangered under the ESA.[6] The Services subsequently published a final rule in 2009 listing the expanded GOM DPS, updating the geographic boundaries of the freshwater range of the Atlantic salmon population to include the Androscoggin, Kennebec, and Penobscot River basins.[7] A final rule designating critical habitat for the GOM DPS was published in the Federal Register on June 19, 2009.[8]

According to NOAA's Office of Protected Resources, "[t]he populations of Atlantic salmon present in the Gulf of Maine DPS represent the last wild populations of U.S. Atlantic salmon."[9] NOAA recognizes aquaculture practices as one of the threats facing the remaining Atlantic salmon population as they "pose ecological and genetic risks."[10] The same is true for transgenic salmon, which have been banned off the coast of Maine since 2003.[11]

Pacific salmonid populations have also faced significant declines on the west coast of the United States.[12] Pacific salmonid species are vulnerable to a number of significant natural and human threats, among them: aquaculture,[13] hydropower, agriculture, flood control, natural resource extraction, and fishing.[14]

According to NOAA's Office of Protected Resources, the majority of all fish listed as endangered or threatened under the Endangered Species Act are Pacific salmonids, including certain populations of Chinook salmon (*Oncorhynchus tshawytscha*), chum salmon (*Oncorhynchus keta*), coho salmon (*Oncorhynchus kisutch*), sockeye salmon (*Oncorhynchus nerka*), and steelhead trout (*Oncorhynchus mykiss*).[15] NOAA Fisheries has issued a final rules designating critical habitat for 25 species of West Coast salmon and steelhead under the ESA.[16]

B. FDA Has Taken Action that "May Affect" Listed Species and Their Designated Critical Habitat Without Consulting with the Services.

Pursuant to the FDA approval, AquaBounty would manufacture its GE salmon at a facility located on Prince Edward Island, Canada, and transport, by land and air, the resulting eggs to a separate facility located in Panama, where they would be grown to maturity before being processed for sale in the United States. Like its approval decision, FDA's conclusion concerning endangered or threatened species rests on an extremely limited inquiry that failed to adequately consider the significant risks of harm to listed species related to the production and proliferation of AquaBounty's GE fish at the Prince Edward Island and Panama facilities, as well as from AquaBounty's ongoing efforts to expand these operations and produce GE salmon at numerous additional facilities around the world.

Both the Prince Edward Island (PEI) and Panama facilities where GE salmon will be engineered, grown, and housed create risks of escape, and potential harm to endangered and threatened species. The ESA requires FDA to consult on these potential impacts, even under FDA's unlawfully narrow scope of review. These threats, and the risks of escape from these sites, are detailed in numerous comments to FDA, including those from NOAA Fisheries and FWS[17] and many independent scientists.[18] This evidence also demonstrates that transgenic salmon are capable of surviving outside either facility. The PEI facility, for example, is near water bodies that historically have held salmonid species and is within the current range of the species' marine habitat. *See* Final EA at 75-6. The GE salmon's transgenic nature makes it more likely to survive because of its more aggressive nature and enhanced growth rate.[19] Studies have found that GE fish may be more competitive (Devlin et al., 1999), less discriminate in choosing prey (Sundström et al., 2004), more likely to attack novel prey (Sundström et al., 2004), and better at using lower quality food (Raven et al., 2006) when compared to wild relatives. The great weight of evidence of past experiences with invasive species and escapes further supports this conclusion.[20] When the GE salmon do escape, the impacts on the environment may be significant and irreversible, in the form of, *inter alia*, (1) ecological impacts on native species via predation and/or competition; and (2) genetic impacts via hybridization and genetic introgression.[21]

Scientists at FWS expressed these very concerns. Commenting on the FDA's 2010 EA and Briefing Packet, FWS's Northeast Region explained:

- Transgenic fish, regardless of where they are, pose a clear and present danger to wild fish populations. Given the extremely low populations of wild Atlantic salmon in the Maine DPS, any interaction between wild and transgenic salmon must be considered a serious threat, which can disrupt runs of wild fish, compete with wild fish for available food and habitat, interbreed with wild fish, transfer disease and/or parasites, and degrade benthic habitat. The scientific literature is full of actions indicating that interactions of wild fish and aquaculture escapees (read transgenic escapees) may lead to decreased numbers of wild fish and in the worst scenario, lead to extirpation of the remaining stocks in the U.S.

- History dictates it is reasonable to assume that fish held in aquaculture facilities, either land- or water-based, will escape unless strict quarantine/water treatment/screening/ bioengineering modifications are in place and aggressively monitored. And even then, it must be assumed that escape will still occur, and protocols must be in place to deal with such a non-native organism released into the environment, and its subsequent effect on native species, habitat, and aquatic communities. Transgenic fish, whether reproductively viable or sterile, must be maintained only in biosecure (zero discharge) land-based facilities ideally positioned outside of any wild fish watersheds until appropriate laboratory and field research has been undertaken to ensure that the risk of adverse effects on wild fish has been minimized.

- [AquaBounty Technologies (ABT)] appears to have established several physical and biological containment mechanisms to prevent the escape of AquAdvantage salmon. However, there is still risk of escapement and we think this risk is most prevalent at the PEl facility. If the brood stock from the PEI facility were released either accidentally or with malicious intent, we do not feel enough evidence has been provided to conclude the risks to natural populations of Atlantic salmon in Canada and the U.S. are negligible. Additional experimentation needs to be conducted to verify that any escapees from the PEI facility will not be able to tolerate the brackish water in the vicinity of the facility. Also, the lack of information on the transport procedures from PEI to Panama is troublesome. It is during this stage of the operation that malicious activities could result in these fish being lost from the direct control of ABT.

- If there is an escape event, competition from the GMO salmon would negatively impact the wild stocks. Research has shown that aquaculture-raised salmon can outcompete wild salmon, and given the already endangered status of the wild stocks, any additional threat is amplified in their impacts. References are available.

- Aside from the potential spread of the GMO growth gene if they escape and successfully reproduce, the genetic origin of the broodstock that has been developed is likely genetically distinct from Maine salmon. The concern is if escape and reproduction occurs, this could lead to a disruption of the locally adapted gene complexes of the endangered populations. In the FDA report-petition, we didn't see reference to the origin of the broodstock.[22]

FWS's Conservation Genetics Community of Practice[23] sent FDA a letter in October 2010 noting these same risks and the need for FDA to conduct more thorough analyses:

> [T]he biological containment at either the PEI or Panama facilities along with the possible interaction of AquAdvantage salmon with endangered wild salmon stocks is of great concern to the COP. To this regard, AquaBounty Technologies has established several physical and biological containment mechanisms to prevent the escape of AquAdvantage salmon and the [EA] indicated escapement risk and establishment risks were low. However, history dictates that fish held in aquaculture facilities, either land- or water-based—escape. In addition, the information provided by AquaBounty Technologies for the likelihood of establishment relies on the assumption that farmed Atlantic salmon have not established themselves in North America. This assumption is clearly violated because Atlantic salmon juveniles have been found in several streams in the state of Washington as well as British Columbia. While interactions of these fish with native salmon are unknown[,] any interaction between wild and transgenic salmon must be considered a serious threat. Numerous scientific publications have documented that interactions of wild and introduced fish have led to decreased numbers of wild fish (for ESA listed Atlantic stocks this is of great concern).[24]

Dr. Gregory Moyer, a FWS Regional Geneticist also sent FDA a letter in October 2010 outlining "several criticisms and concerns" regarding the Briefing Packet, specifically the environmental risk analysis.[25] Dr. Moyer noted that the Briefing Packet "falls short of providing an actual risk assessment of putative environmental damages in the event of escapement."[26] He explained that the "environmental analysis should provide an overview of the general risks associated with escapement or hybridization of GE and wild type individuals" which "would provide readers with an understanding of the potential harm and the degree of harm posed by GE organisms even when the risk of escapement is low."[27] He urged FDA to "more accurately quantif[y]" both the risk of escapement and degree of harm if escaped. Dr. Moyer added that he was concerned with phrases like "are unlikely to survive if exposed to high salinity and low temperature" "when no data have been collected on AquAdvantage salmon to evaluate the likelihood of these scenarios," and that although AquaBounty currently has "in place various standard operating procedures to minimize escapement and test for durability of the gene construct," he "fail[s] to see any policy in place for monitoring or enforcement of these SOPs by the [FDA]."[28]

Likewise, NOAA Fisheries recognized that "[p]reventing escapes is essential to minimizing the risks to genetic deterioration of wild fish populations, especially endangered and threatened salmonids whose effective populations are particularly vulnerable to the effects of interbreeding."[29] A memo from NOAA Fisheries notes that while it may not be likely, it is possible that AquAdvantage salmon will escape from the PEI and Panama facilities, and when they do, "they will likely [] reproduce in the wild because hatchery released fish and hatchery sterilized fish continue to behave similar to wild fish (Trested et al., 2002)."[30] This memo also warns that "successfully sterilized salmon would be attractive mates for wild fish and may reduce wild population fitness." It goes on to explain that, *inter alia*:

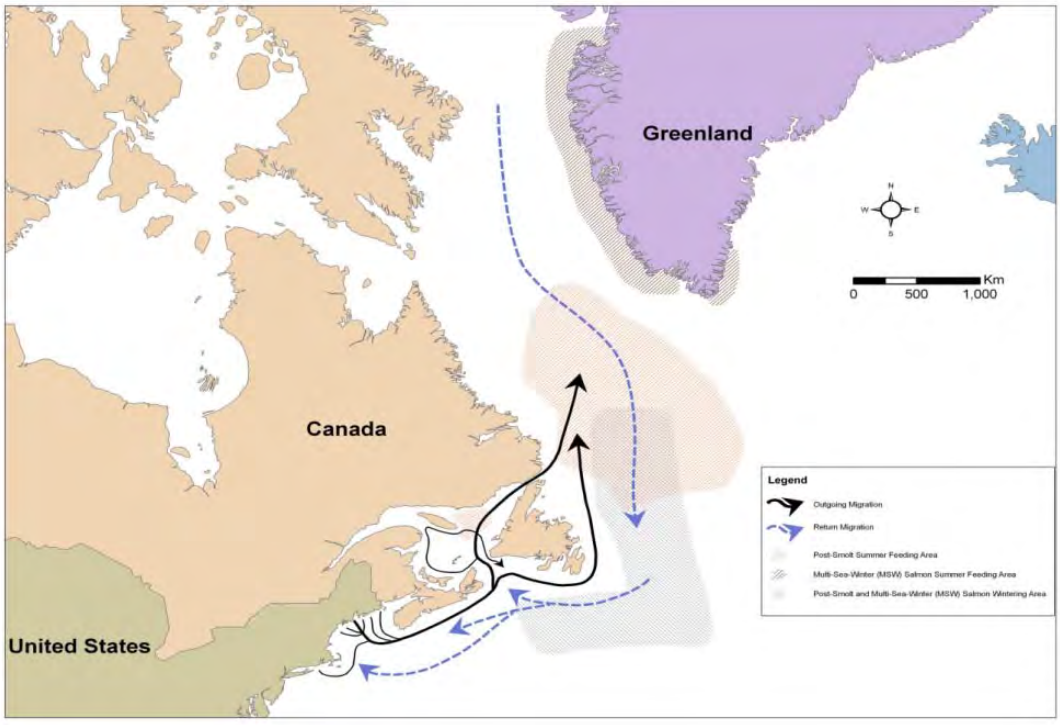
- An introduction of genetically engineered Atlantic salmon could pose catastrophic threats to wild listed species.

- The egg production facility may pose a threat to wild Atlantic salmon, including Gulf of Maine DPS Atlantic salmon.

- Any fish introduced along the Pacific Coast would have the potential to affect Pacific salmonids through hybridization.[31]

NOAA Fisheries has long recognized the potential harms associated with transgenic fish. In 2003, it issued an ESA Section 7 Biological Opinion (BiOp) for the Army Corps of Engineers regarding aquaculture fish pens within the state of Maine, banning transgenic salmonids in aquaculture sites off the coast of Maine due to the risks they could pose to wild, endangered Atlantic salmon populations.[32] There, NOAA Fisheries expressly referenced the potential risks associated with FDA's consideration of the AquaBounty NADA, and relied on studies by Dr. Kapuscinski to call for more research "to identify the impacts [] escaped transgenic salmon would have on natural populations and their habitat before use for commercial aquaculture is considered."[33]

FDA claims that it is "highly unlikely that [GE salmon] or diploid ABT salmon would affect" endangered Atlantic salmon from the Gulf of Maine or from Maine rivers because the "environmental conditions [surrounding the Prince Edward Island facility] are hostile to survival [of salmon], as evidenced by the lack of self-sustaining salmon populations in an environment that used to possess plentiful salmon runs." Final EA at 115. But, as shown by the following map from NOAA, endangered Atlantic salmon from Maine rivers and the Gulf of Maine migrate in and around the waters surrounding Prince Edward Island:[34]



Because containment measures cannot guarantee that GE salmon will not escape into the wild,[35] and because survival and reproduction of escaped GE salmon is possible, such an escape or release event would be significant and irreparable.[36] Indeed, FDA itself recognized the seriousness of these potential risks when it previously acknowledged that it would formally consult with the Services if these fish were grown in net pens.[37] These likely impacts far exceed the low threshold for actions that "may affect" listed Atlantic and Pacific species and trigger FDA's duty to consult with FWS and NOAA Fisheries regarding its approval of AquaBounty's application. As explained above, for an action that *may* affect any species or its critical habitat—"whether beneficial, benign, adverse, or of an undetermined character"—FDA *must*, at a minimum, seek the Services' expertise through consultation. *Western Watersheds Project v. Kraayenbrink*, 632 F.3d 472, 496 (9th Cir. 2010). "[A]ctions that have *any chance of affecting* listed species or critical habitat—even if it is later determined that the actions are 'not likely' to do so—require at least some consultation under the ESA." *Karuk Tribe of California v. U.S. Forest Service*, 681 F.3d 1006, 1027 (9th Cir. 2012) (en banc) (emphasis added). FDA's failure to complete consultation with the expert fish and wildlife Services violates the ESA.

For the same reasons, FDA also violated its independent duty to consult on the potential effects to any habitat designated as "critical" pursuant to ESA § 4(a)(3)(A), 16 U.S.C. § 1533(a)(3)(A). The legal standard for triggering FDA's duty to consult where its approval "may affect" a listed species' designated critical habitat is identical to the requirement to consult where the action "may affect" the species itself. *Karuk Tribe*, 681 F.3d at 1027 ("[A]ctions that have *any chance of affecting* listed species or *critical habitat*—even if it is later determined that the actions are 'not likely' to do so—require at least some consultation under the ESA.") (emphases added); *id*. ("Any possible effect, whether beneficial, benign, adverse or of an undetermined character" triggers the requirement) (citations omitted).

C. FDA's "No Effect" Determination Is Arbitrary and Did Not Use the Best Available Scientific and Commercial Data Available.

Rather than consult with the Services after a may affect determination, FDA instead relied entirely on its own internal assessments of the risks to conclude that its approval of GE salmon will have "no effect" on any listed species or designated critical habitat. FDA's "no effect" conclusion—and the process by which it reached that conclusion—violates the ESA.

As a threshold matter, FDA carries a heavy burden to demonstrate that its "no effect" determination is justified. Indeed, the ESA requires FDA to prove its approval will not jeopardize any listed species, nor adversely affect any critical habitat, and it has not met that burden. *See, e.g.*, *Wash. Toxics Coalition v. Envtl. Prot. Agency*, 413 F.3d 1024, 1035 (9th Cir. 2005) ("Placing the burden on the acting agency to prove the action is non-jeopardizing is consistent with the purpose of the ESA and what we have termed its 'institutionalized caution mandate[].'"). Consistent with these requirements, FDA may decline to undergo consultation with the expert agencies *only* if it legitimately determines that its action will have no chance of affecting any listed species or critical habitat. This means *none*; any effect, however minor, compels consultation. *See supra.*

FDA, however, based its conclusions on its own inexpert—and fatally flawed—assumptions regarding the risk that GE salmon may escape into the environment and unilaterally concluded that the affected species have absolutely no chance of possibly being harmed.

First, as detailed above and extensively in the comments FDA received from Dr. Kapuscinski and other independent experts, the agency's assumption that GE salmon will not escape from AquaBounty's facilities is not based on the best available scientific and commercial data, including the standard practice of conducting a quantitative failure mode risk analysis. Instead, FDA relied on outdated risk analysis methods when considering risk of escapes and the direct and indirect environmental effects of AquaBounty's GE salmon on listed species. FDA cannot rely on outdated and inaccurate information to determine the potential effects on listed species. 16 U.S.C. § 1536(a)(2) (requiring agencies to use only the best available scientific and commercial data available).

Second, FDA arbitrarily limited the geographic scope of its inquiry to just the immediate vicinity of PEI and Panama sites. However, under the ESA, the "action area" is expressly defined as "all areas to be affected directly or indirectly by the federal action and not merely the immediate area involved in the action." 50 C.F.R. § 402.02 (emphasis added). The agency's approval will affect substantially more than just areas in Panama and PEI, due to the highly mobile and migratory nature of the species, its presence throughout the Gulf of Maine and in rivers in New England and throughout Atlantic Canadian provinces, and because of the likely proliferation of GE salmon in other locations, including within the United States, as reflected by pending requests for importation of AquaBounty's GE salmon eggs and AquaBounty's stated plans for expansion following this initial approval decision.

In addition, the area affected by any GE salmon that may be released or that may escape is far greater than just the immediate area around the facility—these fish could enter any number of marine environments that are home to endangered or threatened aquatic species.[38] FDA's "no effect" determination is based on its unlawfully restricted view of the action area as limited to just the areas immediately around the facilities.

Third, FDA similarly arbitrarily limited the scope of the "action" and the "effects" it considered. Under the ESA, "'agency action' is to be construed broadly." *See Karuk Tribe*, 681 F.3d at 1020. "[T]he scope of the agency action is crucial because the ESA requires the biological opinion to analyze the effect of the entire agency action." *Conner v. Burford*, 848 F.2d 1441, 1453 (9th Cir. 1988). Courts "interpret the term 'agency action' broadly," because "caution can only be exercised if the agency takes a look at all the possible ramifications of the agency action." *Id.*

Moreover, the "effects" of the broad action that must be considered under the ESA include not just direct, but also "indirect effects of an action on the species or critical habitat, together with the effects of other activities that are interrelated or interdependent with that action…." *Wild Fish Conserv. v. Salazar*, 628 F.3d 513, 525 (9th Cir. 2010) (quoting 50 C.F.R. § 402.02). "Indirect effects are those that are caused by the proposed action and are later in time, but still are reasonably certain to occur. Interrelated actions are those that are part of a larger action and depend on the larger action for their justification. Interdependent actions are those

that have no independent utility apart from the action under consideration." *Id*. *See, e.g.*, *National Wildlife Federation v. Federal Emergency Management Agency*, 345 F. Supp. 2d 1151 (W.D. Wash. 2004) (rejecting agency argument that it could limit its scope to just the issuance of floodplain insurance and holding that the agency must also assess the impacts of later housing construction that the insurance would facilitate). FDA's duties under the ESA thus require it also consider its action's indirect effects, and the effects of all activities "interrelated or interdependent" with that action. 50 C.F.R. § 402.02.

Yet, FDA has defined the action and its effects to include only those effects it believes are directly associated with the production of the GE salmon in PEI and Panama. FDA unlawfully ignored the reasonably foreseeable direct, indirect, and cumulative impacts of its decision. Evidence in the record shows that petitions are already being submitted to grow these transgenic salmon elsewhere. Indeed, AquaBounty's own public statements admit that they plan to grow them elsewhere. And as commenters have observed, it is not economically feasible to grow these fish at just these two small facilities. AquaBounty's current application is thus just a foot in the door; AquaBounty is clearly dependent on future growth to justify its operation.[39]

Fourth, FDA's "no effect" determination is arbitrary and contrary to law because FDA did not consider impacts to threatened or endangered aquatic species and their habitats other than Atlantic salmon. As expert scientists have noted, the introduction of GE fish like AquaBounty's GE salmon could affect entire ecosystems.[40] Given, in particular, the foreseeable proliferation of GE salmon and the risks of escape inherent in the current application, FDA was required to consider possible effects on Pacific salmon and other salmonids, such as steelhead and trout.[41]

Indeed, just a short time after the close of the comment period on FDA's draft EA, a new study was published on June 3, 2013 in the Proceedings of the Royal Society, further belying the agency's assumptions and concluding that the AquaBounty GE salmon can successfully cross-breed with brown trout.[42] The scientists who authored the study "…suggest that interspecific hybridization be explicitly considered when assessing the environmental consequences should transgenic animals escape to nature." The study also concluded that the GE hybrid offspring could outgrow wild salmon, non-GE hybrid offspring, and even GE salmon.[43] The GE hybrids also outcompeted wild salmon in simulated stream environments. Although acknowledging this study in its Final EA, FDA dismissed the possibility of cross-breeding between brown trout and escaped GE salmon, and failed to discuss the potential of any effects from such cross-breeding on threatened and endangered species, including the GOM DPS Atlantic salmon. Final EA at 40-41 and 100, 104.

Finally, FDA violated its "rigorous" duty to "insure" against jeopardy by relying entirely on AquaBounty's third-party, uncertain measures to mitigate any harm. *See, e.g.*, *Ctr. for Biological Diversity v. Rumsfeld*, 198 F. Supp. 2d 1139, 1152 (D. Ariz. 2002) (holding that mitigation measures must be "certain to occur," "subject to deadlines or otherwise-enforceable obligation," and "must address the threats to the species in a way that satisfies the jeopardy and adverse modification standards"). Rather than being included as enforceable mitigation measures, the containment measures are merely described as "conditions of production and use," not even "conditions of approval." FDA fails to describe, and apparently has failed to consider, how it would enforce or monitor AquaBounty's purported protective measures to prevent

escapes or otherwise prevent environmental harm.[44] FDA cannot avoid consultation by relying on mitigation measures not within its control. *See Nat'l Wildlife Fed'n v. Nat'l Marine Fisheries Serv.*, 254 F. Supp. 2d 1196, 1213-14 (D. Or. 2003) (Biological Opinion inadequate where it relied on non-federal mitigation actions not reasonably certain to occur); *Sierra Club v. Marsh*, 816 F.2d 1376, 1385 (9th Cir. 1987) ("This reliance on the proposed actions of [others] does not satisfy [FDA]'s burden of insuring that its actions will not jeopardize the continued existence of the [endangered species]."). Without any provision for enforcement, these "mitigation measures" must be considered as being outside FDA's control and unlawfully uncertain.

IV. CONCLUSION

In sum, FDA's "no effect" finding and failure to consult is arbitrary and capricious and violates the ESA, because it fails to follow the ESA's mandated procedures, fails to use the best scientific and commercial data available, fails to consider significant aspects of the issue, and offers an explanation that runs counter to the evidence before the agency. As more fully detailed above, FDA is hereby notified that it has violated Section 7 of the ESA, 16 U.S.C. § 1536(a)(2), in at least the following ways:

Prior to approving the GE salmon, FDA failed to request from the expert agencies whether any threatened or endangered species, or designated critical habitat, may be present within or near the areas of the proposed actions. 16 U.S.C. § 1536(c)(1); 50 C.F.R. § 402.12.

Prior to approving the GE salmon, FDA failed to prepare a "biological assessment" to determine whether any threatened and endangered species that may be present within or near the areas of the proposed actions may be affected. 16 U.S.C. § 1536(c)(1); 50 C.F.R. § 402.12.

Prior to approving the GE salmon, FDA failed to consult with the expert fish and wildlife Services regarding the potential adverse effects of the GE salmon on threatened and endangered species, and/or their critical habitat. 16 U.S.C. § 1536(a); 50 C.F.R. §§ 402.13-14.

FDA has failed to insure, in consultation with the expert agencies, that its action is not likely to jeopardize the continued existence of any threatened or endangered species or result in the destruction or adverse modification of the critical habitat of such species. 16 U.S.C. § 1536(a)(2).

FDA has failed to insure that the agency or AquaBounty will not make any irreversible or irretrievable commitment of resources with respect to the GE salmon prior to initiating and completing consultation with NOAA Fisheries. 16 U.S.C. § 1536(d).

FDA has failed, in consultation with the expert agencies, to utilize its authorities in furtherance of the purposes of the ESA by carrying out programs for the conservation of endangered and threatened species, in violation of the ESA. 16 U.S.C. § 1536(a)(1). More specifically, FDA has failed to utilize its authorities to carry out programs for the conservation of the threatened and endangered species located in areas where GE salmon will be foreseeably farmed, in violation of the ESA. 16 U.S.C. § 1536(a)(1).

FDA's determination that its approval of AquaBounty's GE salmon NADA will have "no effect" on listed species is arbitrary and fails to use the best available science.

For the above stated reasons, FDA has violated and remains in ongoing violation of Section 7 of the ESA. If these violations of law are not cured within sixty days, the listed organizations intend to file suit against the responsible agency/agencies and officials to enforce the ESA, seeking declaratory and injunctive relief, as well as attorney and expert witness fees and costs. 16 U.S.C. § 1540(g)(4). This notice letter was prepared based on good faith information and belief after reasonably diligent investigation. If you believe that any of the foregoing is factually erroneous or inaccurate, please notify us promptly. Further, during the notice period we are available to discuss effective remedies and actions that will assure future compliance with the ESA.

Sincerely,

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Center for Food Safety
918 SW Oak St.
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917-271-7372

Steve Roady
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[1] "Jeopardize" means taking action that "reasonably would be expected, directly or indirectly, to reduce appreciably the likelihood of both the survival and recovery of a listed species in the wild by reducing the reproduction, numbers, or distribution of that species." 50 C.F.R. § 402.02. A species' "critical habitat" includes those areas identified as "essential to the conservation of the species" and "which may require special management considerations or protection." 16 U.S.C. § 1532(5)(A).

[2] Section 7(a)(1) of the ESA requires FDA, in consultation with and with the assistance of the Services, to utilize its authorities in furtherance of the purposes of the ESA by carrying out programs for the conservation of endangered and threatened species. 16 U.S.C. § 1536(a)(1).

[3] NOAA has adopted rules pursuant to ESA § 4(d) that extend the take prohibition to Pacific salmon and steelhead species that are listed as "threatened." 16 U.S.C. § 1533(d); Endangered

and Threatened Species: Final Listing Determinations for 16 ESUs of West Coast Salmon, and Final 4(d) Protective Regulations for Threatened Salmonid ESUs, 70 Fed. Reg. 37,160 (June 28, 2005) (updating 4(d) rules for Pacific salmon species); Endangered and Threatened Species: Final Listing Determinations for 10 Distinct Population Segments of West Coast Steelhead, 71 Fed. Reg. 834 (Jan. 5, 2006) (incorporating updated 4(d) rules for steelhead).

[4] The specific listed species include: California coastal chinook salmon, Central Valley spring-run chinook salmon, Lower Columbia River chinook salmon, Puget Sound chinook salmon, Sacramento River winter-run chinook salmon, Snake River fall-run chinook salmon, Snake River spring/summer-run chinook salmon, Upper Columbia River spring-run chinook salmon, Upper Willamette River chinook salmon, Columbia River chum salmon, Hood Canal summer run chum salmon, Central California Coast coho salmon, Southern Oregon and Northern Coastal California coho salmon, Lower Columbia River coho salmon, Oregon Coast coho salmon, Snake River sockeye salmon, Central California Coast steelhead, California Central Valley steelhead, Lower Columbia River steelhead, Middle Columbia River steelhead, Northern California steelhead, Snake River Basin steelhead, South-Central California Coast steelhead, Southern California steelhead, Upper Columbia River steelhead, and Upper Willamette River steelhead. 70 Fed. Reg. 37,160 (June 28, 2005) (listing salmon); 71 Fed. Reg. 834 (Jan. 5, 2006) (listing steelhead).

[5] Office of Protected Resources, NOAA Fisheries, Atlantic salmon (*Salmo salar*), http://www.nmfs.noaa.gov/pr/species/fish/atlanticsalmon.htm (last visited Dec. 21, 2015).

[6] Endangered and Threatened Species; Final Endangered Status for a Distinct Population Segment of Anadromous Atlantic Salmon (*Salmo salar*) in the Gulf of Maine, Final Rule, 65 Fed. Reg. 69,459 (Nov. 17, 2000).

[7] Endangered and Threated Species; Designation of Critical Habitat for Atlantic Salmon (*Salmon salar*) Gulf of Maine Distinct Population Segment: Final Rule, 74 Fed. Reg. 29,300 (June 19, 2009).

[8] *Id.*

[9] Office of Protected Resources, NOAA Fisheries, Atlantic salmon (*Salmo salar*), *supra* n.5.

[10] *Id.*

[11] Endangered Species Act Section 7 Consultation, Biological Opinion, Proposed modification of existing ACOE permits authorizing the installation and maintenance of aquaculture fish pens within the State of Maine (November 19, 2003), attached to this letter as Attachment 1.

[12] *See generally* Endangered and Threatened Species: Listing of Several Evolutionary Significant Units (ESUs) of West Coast Steelhead, 62 Fed. Reg. 43,937 (Aug. 18, 1997); Endangered and Threatened Species: Threatened Status for Two ESUs of Steelhead in Washington, Oregon, and California, 63 Fed. Reg. 13,347 (Mar. 19, 1998); Endangered and Threatened Species: Threatened Status for Two ESUs of Steelhead in Washington and Oregon, 64 Fed. Reg. 14,517

(Mar. 25, 1999); Endangered and Threatened Species; Threatened Status for Three Chinook Salmon Evolutionarily Significant Units (ESUs) in Washington and Oregon, and Endangered Status for One Chinook Salmon ESU in Washington, 64 Fed. Reg. 14,308 (Mar. 24, 1999); Endangered and Threatened Species: Threatened Status for Ozette Lake Sockeye Salmon in Washington, 64 Fed. Reg. 14,528 (Mar. 25, 1999).

[13] *See, e.g.,* R. L. Naylor, *et al., Salmon aquaculture in the Pacific Northwest a global industry with local impacts,* Environment: Science and Policy for Sustainable Development 45(8) (2003) 18-39.

[14] *Id.*

[15] Office of Protected Resources, NOAA Fisheries, Endangered and Threatened Marine Species under NMFS' Jurisdiction, http://www.fisheries.noaa.gov/pr/species/esa/listed.htm#fish (last visited Dec. 21, 2015).

[16] Endangered and Threatened Species; Designation of Critical Habitat for 12 Evolutionarily Significant Units of West Coast Salmon and Steelhead in Washington, Oregon, and Idaho, Final Rule, 70 Fed. Reg. 52,630 (Sept. 2, 2005); Endangered and Threatened Species; Designation of Critical Habitat for Seven Evolutionarily Significant Units of Pacific Salmon and Steelhead in California, 70 Fed. Reg. 52,488 (Sept. 2, 2005) (designation of Critical Habitat for California Coastal Chinook salmon, Northern California Steelhead, Central California Coast Steelhead; South Central Coast Steelhead; Southern California Steelhead; Central Valley spring run Chinook salmon; and Central Valley Steelhead); Designated Critical Habitat; Snake River Sockeye Salmon, Snake River Spring/Summer Chinook Salmon, and Snake River Fall Chinook Salmon, 58 Fed. Reg. 68,543 (Dec. 28, 1993); Designated Critical Habitat; Central California Coast and Southern Oregon/Northern California Coasts Coho Salmon, 64 Fed. Reg. 24,049 (May 5, 1999); Endangered and Threatened Species: Final Threatened Listing Determination, Final Protective Regulations, and Final Designation of Critical Habitat for the Oregon Coast Evolutionarily Significant Unit of Coho Salmon, 73 Fed. Reg. 7,816 (Feb. 11, 2008).

[17] After FDA changed course and found that its approval would have "no effect" on listed species, FWS and NOAA sent separate letters to FDA in which the agencies did not object to FDA's determination. *See* Final EA, Appendix D. Neither of these letters discusses any of these agencies' previous findings and comments, or the scientific evidence concerning risks posed by the release of GE salmon from the PEI, Panama, or any other facilities. To the extent that FDA interprets these letters to support its "no effect" determination, the letters have no legal significance in the ESA's consultation process, and to the extent that FDA believes they represent any conclusions by the Services, the positions articulated in those letters are not based on the best available science and are themselves arbitrary and capricious.

[18] *See* Dr. Jon Rosenfield Comments, attached to this letter as Attachment 2.

[19] *Id.*

[20] *Id.*

[21] *Id.*

[22] FWS Region 5 Fisheries Program Comments on FDA approval process for Aqua Bounty Technologies, Inc. (ABT)/AquAdvantage GMO salmon (emphases added), attached to this letter as Attachment 3.

[23] This is FWS's coalition of fish conservation genetics experts. *See* http://www.fws.gov/ConservationGeneticsCOP/index.html.

[24] FWS Conservation Genetics Community of Practice Letter to FDA (Oct. 6, 2010) (emphases added), attached to this letter as Attachment 4.

[25] Dr. Gregory Moyer Letter to FDA (Sept. 30 2010), attached to this letter as Attachment 5.

[26] *Id*.

[27] *Id*.

[28] *Id*.

[29] NMFS, Talking Points for Senate Commerce Committee Staff Briefing on S. 1717 "Prevention of Escapement of Genetically Altered Salmon in the United States Act" (Dec. 5, 2011), attached to this letter as Attachment 6.

[30] NMFS Concerns Memo and Letter from Therese Conant, NMFS Acting Division Chief, Endangered Species Division, to Larissa Rudenko (Nov. 30, 2011), attached to this letter as Attachment 7.

[31] *Id*.

[32] 2003 BiOp, *supra* n.11.

[33] *Id*. at 74-75.

[34] http://www.nefsc.noaa.gov/press_release/2008/MediaAdv/MA0807/2Saunders_MigrationRoute.jpg.

[35] Anne Kapuscinski and Fredrik Sundstöm, *Comments on Environmental Assessment for AquAdvantage Salmon and Briefing Packet on AquAdvantage Salmon for the Veterinary Medicine Advisory Committee* at 4 (2010) ("As scientists, we cannot agree with this approach because it assumes 100% achievement of multiple confinement without presenting the failure mode analysis that is standard practice in technology risk assessment. Even if actual exposure is

very close to zero, it is still necessary to assess ecological consequences…."), attached to this letter as Attachment 8.

[36] See, Dr. Jonathan Rosenfeld Comments, *supra* n.18; *see also* FWS Region 5 Comments, *supra* n.22, FWS COP letter, *supra* n.24, NFMS Concerns Memo and Letter, *supra* n.30.

[37] 2009 FDA denial of 2001 CFS petition, attached to this letter as Attachment 9.

[38] As NOAA Fisheries previously indicated, because FDA's action contemplates the selling of eyed eggs commercially and rearing fertile adult males at the PEI facility, the action area must include the United States. *See* NOAA Fisheries Concern Memo, *supra* n.30 and Letter to FDA from Therese Conant, *supra* n.29.

[39] FDA may not rely on the potential to consult later to addresses these fatal flaws in its "no effect" conclusion. The precautionary approach embodied in Section 7(a)(2) requires consultation before an action begins, not to conduct a post mortem years later. *See, e.g., Wild Fish Conservancy v. Salazar*, 628 F.3d 513, 524 (9th Cir. 2010) (intent to consult later does not cure failure to complete consultation at the outset concerning action's full extent).

[40] Dr. Jonathan Rosenfeld Comments, *supra* n.18. *See also* NMFS Concerns Memo, *supra* n.30 ("Any fish introduced along the Pacific Coast would have unknown potential for affecting Pacific salmonids through hybridization.").

[41] *Id.* Accidental or other release of fish from aquaculture facilities is plainly "reasonably certain to occur;" indeed, it is already in progress in many parts of the United States and elsewhere in the world. *See, e.g.*, Fischer, et al., *Occupancy dynamics of escaped farmed Atlantic salmon in Canadian Pacific Coastal Salmon Streams: Implications for Sustained Invasions*, Biological Invasions, Vol. 16, Issue 10, pp 2137-2146 (October 2014), *available at* https://goo.gl/QpRWsD; Morris, et al., *Prevalence and Recurrence of Escaped Farmed Atlantic Salmon in Eastern North American Rivers*, Can. J. Fish. Aquat. Sci. Vol. 65 (2008), *available at* http://0101.nccdn.net/1_5/165/1c4/1be/morrisetal2008.pdf.

[42] K. B. Oke, *et al. Hybridization between genetically modified Atlantic salmon and wild bran trout reveals novel ecological interactions*, The Royal Society (May 2013), *available at* http://rspb.royalsocietypublishing.org/content/280/1763/20131047.

[43] Rebecca Morelle, *GM salmon can breed with wild fish and pass on genes*, BBC News (May 29, 2013), http://www.bbc.co.uk/news/science-environment-22694239.

[44] *See 2010* Kapuscinski and Sundström VMAC Comments at 2, *supra* n.35 (questioning how FDA will oversee the facilities; "How will FDA assure and audit the company's implementation of this 'integrated confinement system'"?).

Attachment 1

Sixty-Day Notice of Intent to Sue FDA Pursuant to the Endangered Species Act
Re: Approval of Genetically Engineered "AquAdvantage" Salmon

UNITED STATES DEPARTMENT OF COMMERCE
National Oceanic and Atmospheric Administration
NATIONAL MARINE FISHERIES SERVICE
NORTHEAST REGION
One Blackburn Drive
Gloucester, MA 01930-2298

NOV 19 2003

Christine Godfrey
Chief, Regulatory Branch
Construction/ Operations Division
New England District, Corps of Engineers
696 Virginia Road
Concord, Massachusetts 01742-2751

Ref: Transmittal of Final Biological Opinion and Response to Comments on Draft F/NER/2002/00936

Dear Ms. Godfrey:

Enclosed is a biological opinion (Opinion) issued by the National Marine Fisheries Service (NOAA Fisheries) on the U.S. Army Corps of Engineers (ACOE) proposed continuation and modification of existing permits authorizing the installation and maintenance of net pens to raise finfish off the coast of Maine. The NOAA Fisheries national Section 7 tracking number is F/NER/2002/00936.

The Opinion is submitted in accordance with section 7 of the Endangered Species Act (ESA) of 1973, as amended (16 U.S.C. 1531 *et seq.*). This Opinion concludes that the proposed continuation and modification of existing permits authorizing the installation and maintenance of fish pens in the state of Maine (including incorporation of the special conditions to protect the Gulf of Maine Distinct Population Segment (DPS) of Atlantic salmon) may adversely affect but is not likely to jeopardize the continued existence of the endangered Atlantic salmon within the DPS. Please note that any changes to the proposed action, including any changes to the special conditions proposed to protect wild Atlantic salmon, may change the conclusion in this Opinion and would warrant further Section 7 consultation. No other federally-listed species is likely to be affected by the proposed action.

While the ACOE's proposed permit modifications do contain conditions for the protection of wild Atlantic salmon, the incorporation of these conditions does not eliminate the potential for the permitted activities to result in "take" of Atlantic salmon within the DPS; therefore, an Incidental Take Statement (ITS) has been issued with this Opinion. The anticipated incidental take from the existing aquaculture industry's marine sites that were the subject of this consultation (42 sites) is the detection at weirs or traps of up to 21 escaped fish per year, based on a three year rolling average. If the ITS is exceeded, consultation must be reinitiated. To validate the ITS, the ACOE must implement the non-discretionary Reasonable and Prudent Measures contained therein. Discretionary Conservation Recommendations are also included with this Opinion.

Reinitiation of this consultation is required if: (1) the amount or extent of taking specified in the ITS is exceeded; (2) new information reveals effects of these actions may affect listed species or critical habitat in a manner or to an extent not previously considered; (3) project activities are subsequently modified in a manner that causes an effect to the listed species that was not considered in this Opinion; (4) significant changes to the proposed action are made that may change the conclusion in this Opinion; or (5) a new species is listed or critical habitat designated that may be affected by the identified actions. If any one of the conditions requiring reinitiation of consultation is triggered, the ACOE should contact NOAA Fisheries. Alternatively, NOAA Fisheries may provide written advice to the ACOE relative to the need to reinitiate consultation. Requests for reinitiation must be in writing and must contain sufficient information to record the nature of the change in the action or its effects and the rationale for any modifications.

Conclusion

NOAA Fisheries greatly appreciate your cooperation during this Section 7 consultation. If you have any questions concerning this Opinion, please contact Jessica Anthony of my staff at (978) 281-9328 ext 6532. We look forward to working with you in the future to ensure compliance with permit conditions and protection of the Atlantic salmon DPS.

Sincerely,

Patricia A. Kurkul
Regional Administrator

cc:
Jessica Anthony - NOAA Fisheries
Rick Bennett - USFWS
Wende Mahaney - USFWS

ENDANGERED SPECIES ACT SECTION 7 CONSULTATION

BIOLOGICAL OPINION

Agency:	Department of the Army, New England District, Corps of Engineers
Activity:	Proposed modification of existing ACOE permits authorizing the installation and maintenance of aquaculture fish pens within the State of Maine
Conducted by:	National Marine Fisheries Service, Protected Resources Division, Northeast Region (F/NER/2002/00936) and the U.S. Fish and Wildlife Service, New England Field Office [MEFO 02-001(F)]

Date Issued: Nov. 19, 2003

Approved by:

Patricia A. Kurkul
Regional Administrator
Northeast Region
National Marine Fisheries Service

INTRODUCTION

This constitutes the biological opinion (opinion) of the National Marine Fisheries Service (NOAA Fisheries) and the U.S. Fish and Wildlife Service (USFWS) (collectively referred to as the Services) on the continuation and proposed modification of existing U.S. Army Corps of Engineers (ACOE) permits previously issued under Section 10 of the Rivers and Harbors Act of 1899 (RHA Section 10) (33 U.S.C. §403), following the Services' listing of the Gulf of Maine (GOM) Distinct Population Segment (DPS) of Atlantic salmon (*Salmo salar*) as an endangered species on November 17, 2000. These existing ACOE permits have authorized the installation and maintenance of fish pens within the State of Maine. While the Services agree that the proposed modifications to the existing permits will reduce the impact of the aquaculture industry on the listed Atlantic salmon, these modifications do not eliminate the impacts to listed salmon. Since adverse effects to the listed salmon are still anticipated after implementation of the proposed permit amendments, the Endangered Species Act (ESA) requires formal consultation to: 1) ensure that the action is not likely to jeopardize the continued existence of the listed salmon in the wild; and 2) provide exemptions to the take prohibitions of Section 9 for take that may occur incidentally. This opinion is based on the following: (1) information provided in the ACOE's August 9, 2001 initiation letter and attachments in support of formal consultation under the ESA; (2) previous consultations among the Services and the Environmental Protection

e. All reproductively-viable non-North American Atlantic salmon must be removed from net pens prior to March 1, 2006. Within 30 days after removal of fish, the facility shall provide the ACOE with written confirmation regarding compliance with this condition.

2. Transgenic salmonids are prohibited at these facilities. Transgenic salmonids are defined as species of the genera *Salmo*, *Oncorhynchus* and *Salvelinus* of the family Salmonidae and bearing, within their DNA, copies of novel genetic constructs introduced through recombinant DNA technology using genetic material derived from a species different from the recipient, and including descendants of individuals so transfected. This prohibition does not apply to vaccines.

3. Prior to stocking salmonid species other than Atlantic salmon at these facilities, certification from the Maine Fish Health Technical Committee and DMR of compliance with disease management standards permitting the culture of alternative salmonid species shall be provided to the ACOE. No alternative salmonid species shall be stocked without prior written approval from the ACOE.

4. The facility shall employ a fully functional marine containment management system (CMS) designed, constructed, and operated so as to prevent the accidental or consequential escape of fish to open water. Each CMS plan shall include a site plan or schematic with specifications of that particular system. Each facility shall develop and utilize a CMS consisting of management and auditing methods to describe or address the following: inventory control procedures, predator control procedures, escape response procedures, unusual event management, severe weather procedures, and training. The CMS shall contain a facility-specific list of critical control points (CCP) where escapes have been determined to potentially occur. Each CCP must include the following: the specific location, control mechanisms, critical limits, monitoring procedures, appropriate corrective actions, verification procedures that define adequate CCP monitoring, and a defined recordkeeping system.

a. The CMS will be audited at least once per year and within 30 days of a reportable escape (more than 50 fish two kg or larger) by a party other than the facility operator or owner who is qualified to conduct such audits and is approved by the ACOE and the Services. The first annual audit shall be conducted prior to March 1, 2004. The ACOE, with the approval of the Services, may exempt a facility from an escape-triggered audit when circumstances preclude the possibility that it was the source of the escaped fish. A written report of these audits shall be provided to the facility, the ACOE, and the Services within 30 days of the audit being conducted. If deficiencies are identified during the audit, the report shall contain a corrective action plan, including a timetable for implementation and re-auditing to verify that deficiencies are addressed in accordance with the corrective action plan. Additional third party audits to verify correction of deficiencies shall be conducted in accordance with the corrective action plan or upon request of the ACOE. The facility shall notify the ACOE and the Services upon completion of corrective actions.

b. At each facility, personnel responsible for routine operation shall be properly trained and qualified to implement the CMS.

disease affecting most species of fish, including farmed Atlantic salmon. Therefore, vibriosis is also thought to affect wild salmon populations (Baum 1997).

The retrovirus salmon swimbladder sarcoma virus (SSSV) appears to exist at some level in wild populations of salmon in Maine, although symptoms have not been observed in wild salmon (AASBRT 1999). In 1998, SSSV was detected in Pleasant River broodstock held by the USFWS, resulting in the decision to destroy all captive broodstock for this river. SSSV has been identified at very low levels in captive broodstock populations from three other GOM DPS rivers.

Coldwater disease is caused by the bacterium *Flavobacterium psychrophilum* and has recently been found to be a serious problem for Atlantic salmon in New England waters. The pathogen causes mortality in juvenile salmon. The pathogen is transmitted vertically from carrier sea-run adults to offspring via eggs [U.S. Atlantic Salmon Assessment Committee (USASAC) 2000; 65 FR 69476, Nov. 17, 2000)].

The infectious salmon anemia virus (ISAV) appeared on the North American continent in 1996 in Canadian aquaculture pens, within the known infective range of U.S. sea pens. ISAV was first detected at a Maine salmon farm in Cobscook Bay in January 2001, with subsequent outbreaks at several other salmon farms in Cobscook Bay. The ISAV virus is extremely destructive to maturing salmon, and there is no known cure (USASAC 2000; 65 FR 69476, Nov. 17, 2000).

Known predators of Atlantic salmon include marine mammals (e.g., seals, porpoises, and dolphins), terrestrial mammals (e.g., otters, minks), birds, fish and sharks. Atlantic salmon post-smolts are preyed upon by cod, whiting, cormorants, ducks, terns, gulls, and many other opportunistic predators (Hvidsten and Møkkelgjerd 1987; Gunnerød *et al.* 1988; Hvidsten and Lund 1988; Montevecchi *et al.* 1988; Hislop and Shelton 1993). Cormorants and striped bass are transitory predators that impact migrant juveniles in the lower river and estuarine areas. Seals have reached high population levels not reported before, and salmon remain vulnerable to seal predation throughout much of their range.

Competitive interactions of Atlantic salmon with non-salmonine fish, especially introduced species, are not well understood (AASBRT 1999). Interactions between wild Atlantic salmon and other salmonids are mostly limited to brook trout, and occasionally brown trout. Competition appears to play an important regulatory role shortly after fry emerge from redds, when fry densities are at their highest (Hearn 1987). These interactions may cause Atlantic salmon and brook and brown trout populations to fluctuate from year to year. Since brook trout and Atlantic salmon co-evolved, however, wild populations should be able to co-exist with minimal long-term effects (Hearn 1987; Fausch 1988). Where resources are limited, interspecific competition can exist between brown trout and Atlantic salmon and may cause interactive segregation, or affect the growth and survival of these species. Several other fish species occur in the GOM DPS rivers, including smallmouth and largemouth bass, pickerel, and landlocked salmon. In general, conclusions cannot be drawn regarding the competitive effects of these species on salmon, as no data are currently available (AASBRT 1999). Atlantic salmon and rainbow trout produced by the aquaculture industry (including non-North American strains

and potentially transgenics) that escape from hatcheries or net pens also compete with wild Atlantic salmon. (This topic is discussed further later in this section of the opinion, as well as in the Effects of the Action section.)

C. Population Dynamics

1. *Historical Abundance*

Anadromous Atlantic salmon were native to nearly every major coastal river north of the Hudson River in New York (Atkins 1874; Kendall 1935). The annual historic Atlantic salmon adult population returning to U.S. rivers has been estimated to be between 300,000 (Stolte 1981) and 500,000 (Beland 1984). The largest historical salmon runs in New England were likely in the Connecticut, Merrimack, Androscoggin, Kennebec, and Penobscot Rivers.

By the early 1800s, Atlantic salmon runs in New England had been severely depleted due to the construction of dams, over fishing, and water pollution, all of which greatly reduced the species' distribution in the southern half of its range. Restoration efforts were initiated in the mid-1800s, but there was little success due to the presence of dams and the inefficiency of early fishways (Stolte 1981). There was a brief period in the late nineteenth century when limited runs were reestablished in the Merrimack and Connecticut Rivers by artificial propagation, but these runs were extirpated by the end of the century (USFWS 1989). By the end of the nineteenth century, three of the five largest salmon populations in New England (in the Connecticut, Merrimack, and Androscoggin Rivers) had been eliminated.

2. *Current Abundance*

As with most anadromous species, Atlantic salmon can exhibit temporal changes in abundance. Angler catch and trapping data from 1970 to 1998 provide the best available composite index of recent adult Atlantic salmon population trends within the GOM DPS rivers. These indices indicate that there was a dramatic decline in the mid-1980s, and that populations have remained at low levels ever since. Figure 6 demonstrates this trend (AASBRT 1999).

Total documented (rod and trap caught fish) natural (wild and stocked fry) GOM DPS spawner returns for 1995 through 2001 are: 1995 (85); 1996 (82); 1997 (38); 1998 (23); 1999 (32); 2000 (28); and 2001 (60) (USASAC Annual Report 2002/14). These counts (as well as the counts shown in Figure 6) represent minimal estimates of the wild adult returns, because not all GOM DPS rivers have trapping facilities (e.g., weirs) to document spawner returns in all years. The counts of redds conducted annually by the Maine Atlantic Salmon Commission (ASC) demonstrate that salmon do return to those rivers for which no adult counts are possible. Since 2001, scientists have made an estimate of the total number of returning salmon to the GOM DPS. This estimate is calculated using capture data on GOM DPS rivers with trapping facilities (Dennys, Pleasant, and Narraguagus Rivers), combined with redd count data from the other five GOM DPS rivers. Documented returns based on these redd counts and trap data estimate a total of 91 adult returns in 2000 and 98 adults in 2001, at 95% probability. The 90% probability

site-specific marks will enable facility operators to work with the ACOE and the Services to quickly identify the cause of escapement and to correct problems leading to the escape. The ability to reduce, and ideally eliminate, the presence of escapees in rivers is dependent on the ability to identify and control the losses at the net pens.

Special Condition No. 5 will also minimize effects by requiring reporting of known or suspected escapes of more than 50 fish with an average weight of 2 kg each or more within 24 hours. Fifty fish was identified by the aquaculture industry as a minimum number of escapees that they could reasonably detect; a 2 kg fish was identified by the Services and the ASC as a minimum weight at which an Atlantic salmon could be sexually mature. This reporting requirement will enhance the ability to retrieve escaped fish when possible and alert field scientists operating weirs on GOM DPS rivers to the fact that an escape has occurred. The reporting requirement will also contribute to a database that, in combination with information on detection of escapees in rivers, will allow for a clearer understanding of the chain of events that starts with salmon escaping from a net pen and ends with escapees entering rivers. This system will help determine, over time, what specific factors (e.g., season, age/size class, proximity to GOM DPS rivers, etc.) are more or less likely to result in escapees entering the GOM DPS rivers.

Proper containment (Special Condition No. 4), fish husbandry practices, and disease management (Special Condition No. 3) for other salmonid species reared in marine cages will collectively reduce the risks that disease transfer and competition pose to wild Atlantic salmon.

D. Transgenics

The potential use of transgenic salmonids in the aquaculture industry has recently been identified as a possible threat to wild Atlantic salmon populations. Transgenic salmonids include fish species of the genera *Salmo, Oncorhynchus*, or *Salvelinus* in the family Salmonidae that bear, within their DNA, copies of novel genetic constructs introduced through recombinant DNA technology using genetic material derived from a species different from the recipient, and descendants of any individuals so transfected. Escaped, reproductively-viable transgenic salmon could interbreed with wild fish. Research to develop transgenic fish for aquaculture increased through the 1980s and had advanced to the extent that, by 1989, production of 14 species of transgenic fish, including Atlantic salmon, had been reported (Kapuscinski and Hallerman 1990).

Transgenic fish produced for culture in marine net pens must be selected to survive under nearly natural physical and chemical environmental conditions. If they escape, therefore, it is likely that a portion of them will survive. In a study by Sheela *et al.* (1999), transgenes were inherited in many progeny from transformed fish, as determined through DNA analyses and through expression of the reporter gene. If an introduced construct can find its way onto or into a chromosome before the first cell division of a newly-fertilized egg, all the cells in the developing organism, including future germ cells, will contain copies (Lutz 2000). The transmission of novel genes to wild fish could lead to physiological and behavioral changes, and traits other than those targeted by the insert gene are likely to be affected. Ecological effects are expected to be greatest where transgenic fish exhibit substantial altered performance. Such fish could destabilize or change aquatic ecosystems (Kapuscinski and Hallerman 1990).

In a study by Cook *et al.* (2000), growth-enhanced transgenic Atlantic salmon exhibited a 2.62- to 2.85-fold greater rate of growth relative to non-transgenic salmon, over the body weight interval examined. This study found that the transgenic experimental subjects possessed the physiological plasticity necessary to accommodate acceleration in growth well beyond the normal range for this species, with few effects other than a greater appetite and a leaner body (Cook *et al.* 2000). Because aquatic ecosystems function through complex interactions involving transfers of energy, organisms, nutrients, and information, it is difficult to predict the community-level impacts of releasing transgenic fishes that exhibit one or more types of phenotypic change (Kapuscinski and Hallerman 1990). At this time, more research is needed to identify the impacts that escaped transgenic salmon would have on natural populations and their habitat before use for commercial aquaculture is considered.

Research and development efforts on transgenic forms of Atlantic salmon and rainbow trout are currently being directed toward their potential use for sea pen aquaculture. Emphasis has been placed on enhancement of growth and low water temperature tolerance through the transfer of genetic material from other cold-tolerant species, such as flounder. In 2002, the Food and Drug Administration received an application for approval to sell and possibly grow transgenic salmon in the United States for use by the aquaculture industry.

The prohibition on the use of transgenic salmonids at existing marine sites off the coast of Maine (Special Condition No. 2) will eliminate the potentially adverse disease and ecological risks posed by the use of transgenic salmonids in aquaculture. The risk posed by a transgenic salmonid to wild salmon would be greatly affected by the specific gene manipulation conducted. Anyone proposing the use of transgenic salmonids in aquaculture would need to provide information on the methods used and the potential for genetic, fish health and ecological impacts on wild stocks. This information would have to be evaluated to determine the level of risk posed to wild Atlantic salmon stocks and a decision would have to be made as to whether that level of risk was acceptable or not. The use of transgenic salmonids will be prohibited under Condition No. 2 until such time as these risks can be evaluated.

Summary of Effects

In summary, the proposed action is most likely to adversely affect individual Atlantic salmon by causing take through harm or harassment in the GOM DPS rivers without weirs or traps (i.e., Sheepscot, Ducktrap, Machias, and East Machias Rivers, and Cove Brook). Some take may also occur in rivers with weirs, for example where there is spawning habitat located downstream of the weir or if a fish enters when the weir is not in place. The harm or harassment is reasonably certain to result from one or more factors discussed above, including redd superimposition, competition, and genetic introgression. The scientific studies, escape reports from the aquaculture industry, and the detection of aquaculture fish in Maine rivers all discussed in this opinion establish that the anticipated impacts are reasonably certain to occur.

In view of this, the Services have evaluated these impacts at a very detailed level of analysis and evaluated several factors influencing the impact these effects will have on the GOM DPS. This

analysis helps to distinguish the important difference between the impacts to individual GOM DPS salmon and effects to the population of salmon defined by the GOM DPS. The demonstrated influx of aquaculture fish into at least one GOM DPS river, repeatedly, over the last several years makes these impacts to wild salmon reasonably certain to occur. The greater the number of escapees that enter the GOM DPS rivers and the greater the period of time over which these events occur, the greater is the likelihood that the entire GOM DPS salmon population would be impacted versus occasional impacts to individual salmon within the GOM DPS.

Although the Services are reasonably certain that one or more of these impacts (e.g., introgression) will occur as a result of the action, the Services do not believe that every incidence of an aquaculture fish entering a GOM DPS river will result in such take of GOM DPS salmon. The Services do not anticipate that each aquaculture escapee that enters a GOM DPS river will cause introgression or redd superimposition. For example, an escapee may not find a wild fish to spawn with.

While a certain level of impact is still anticipated, including some take, there are a number of factors mitigating these impacts at the GOM DPS population level. First, the new permit conditions will both reduce the number of escapees entering GOM DPS rivers and eliminate the greatest long-term threat to wild salmon by phasing out the use of non-North American strains. Furthermore, there are multiple rivers in the GOM DPS and multiple-year classes present at any given time for each river (both within the river and at sea); consequently, each time an aquaculture escapee enters a GOM DPS river and causes an impact to wild salmon, the effect of that impact (e.g., redd superimposition or hybridization) is limited to only a subset of the entire river's population. The operation of a weir or trap on three of the GOM DPS rivers also substantially reduces the opportunities for interactions between aquaculture escapees and wild salmon. Finally, the USFWS's river-specific stocking program currently helps to maintain populations for six of the eight GOM DPS rivers, helping to offset the extremely low number of adult returns in recent years.

Therefore, while the probability of impacts to some individuals will remain high, the magnitude of these impacts to the population is anticipated to decrease over time due to the new special conditions. The potential for impacts to individuals will decrease as a result of the expected 25% decrease in escapees associated with implementation of the CMS. A decrease in the frequency of impacts to individuals will further reduce the potential for impacts to a year class and a river population. The severity of impact that any individual aquaculture escapee poses will also be decreased as the use of non-North American Atlantic salmon is eliminated.

IV. CUMULATIVE EFFECTS

Cumulative effects include the effects of future state, tribal, local or private actions that are reasonably certain to occur in the action area considered in this opinion. Future federal actions that are unrelated to the proposed action are not considered in this section, because they require separate consultation pursuant to Section 7 of the ESA.

Attachment 2

Sixty-Day Notice of Intent to Sue FDA Pursuant to the Endangered Species Act
Re: Approval of Genetically Engineered "AquAdvantage" Salmon

3101 Deakin St.
Berkeley, CA 94705

Division of Dockets Management (HFA–305)
Food and Drug Administration,
5630 Fishers Lane, rm. 1061,
Rockville, MD 20852

April 25, 2013

[Docket No. FDA–2011–N–0899]

Submitted electronically to: http://www.regulations.gov

Introduction and Background

My name is Jonathan Rosenfield. I have Doctoral and Master's of Science degrees in the evolution, ecology, behavior, and conservation of vertebrates with a particular emphasis in the mechanisms and consequences of inter-specific genetic exchange among fish species. I have authored or co-authored several published, peer-reviewed manuscripts on hybridization and genetic introgression (the gene exchange that accompanies successful reproduction by hybrid organisms) among fishes, including species in the family salmonidae. Attached for reference is my current Curriculum Vitae.

I am writing to express grave concerns with the FDA's proposed approval of AquAdvantage transgenic salmon produced by AquaBounty Technologies (AquaBounty). FDA approval would allow mass production of genetically engineered (GE) Atlantic salmon at two locations, Panama and Prince Edwards Island (PEI), and will likely lead to expanded production of the fish in other locations around the world, including within the United States. My concerns are that AquAdvantage salmon are likely to escape captivity (including either from the facilities described in the draft EA, from other facilities that Aquabounty may developed to produce these fish in the future, or from facilities operated by other entities, to which AquaBounty may sell their eggs) and that when these genetically engineered salmon escape their hatchery or rearing environments, they are likely to wreak havoc on natural ecosystems, endangered species, and/or commercially valuable fisheries.

These concerns are based on my background and expertise in production and rearing of fish in captivity, the ecology and behavior of salmonids and fishes in general, and, in particular, my experience with non-native invasive fish species and genetic introgression (transfer of genetic material among distinct populations) that often accompanies introduction of organisms into a novel evolutionary environment. I urge the FDA to reconsider its proposed acceptance of the application to permit production of GE salmon until project proponents can demonstrate that there is zero risk of escape now or in the future and that the fish cannot survive outside of their hatchery environment under any circumstances. I am aware that this request sets a high standard for certainty; these assurances are appropriate for a situation such as this, where escape of a GE organism could cause significant and potentially irreversible environmental and economic damage. I recommend that FDA conduct a much more thorough review than is contained in the current Draft Environmental Assessment (EA) and Finding of No Significant Impact (FONSI)

and produce a full and rigorous environmental impact statement that accounts for the wide range of risks AquAdvantage Salmon could pose to any environment in which they may be released. Because it is clear that FDA's approval of the production of GE Atlantic salmon may affect the status of threatened and endangered organisms in the wild, I also call on the FDA to refrain from permitting their production until it has engaged in formal Endangered Species Act consultation with the United States Fish & Wildlife Service (USFWS) and National Marine Fisheries Service (NMFS) to assess the risks AquAdvantage salmon may pose to endangered fish populations, including, but not limited to, members of the genera *Salmo* (Atlantic salmon and trout) and *Oncorhynchus* (Pacific salmon and trout).

I. Genetically engineered salmon are likely to escape captivity.

I have reviewed the FDA's Draft EA and related information regarding AquaBounty Technology's plans for confining the egg, larval, and juvenile salmon they will rear. It appears to me that the project's proponents have taken seriously the possibility of escape (as well they should); they describe a number of systems that seem as though they could impede many avenues of fish escape from their facilities.

Given the opportunities for escaped salmon to cause damage and the irreparable consequences of some of those impacts (described below), evaluation of the risk posed by these organisms must assume that these fish will escape either: (a) the containment systems described in the EA; (b) during transport between facilities; or (c) some other facility into which these fish may be introduced in the future. One only has to look to other examples where seemingly well-designed (on paper), redundant, and expensive security systems failed in order to understand that, even when project proponents dedicate great effort, engineering, and considerable resources to preventing foreseeable accidents, accidents still happen, often repeatedly.

The prospects for fish escape and survival in the wild are far from theoretical. A great deal of the modern scientific literature on the ecology and conservation of fishes has to do with the consequences of non-native fish species invasions. There are far too many examples of intentional and unintentional fish introductions that resulted in harm or even extirpation of native fishes and/or irreversible alteration of ecosystem function to document all of them here[1]. In his paper describing the potential and known impacts of Atlantic salmon escaped from aquacultural facilities, Gross (1998:133) reports:

[1] To name just two dozen examples: Wagner and Stauffer 1982; Campton 1987; Allendorf and Leary 1988; Hindar et al. 1991; Waples 1991; Dowling and Childs 1992; Mills et al. 1994; Smith et al. 1995; Moyle and Light 1996; Echelle et al. 1997; McGinnity et al. 1997; Clifford et al. 1998; Ricciardi and MacIsaac 2000; USFWS 2000; Scott and Helfman 2001; Perry et al. 2002; McGinnity et al. 2003; Ruzycki et al. 2003; Clavero et al. 2004; Streelman et al. 2004; Campton and Kaeding 2005; Hanfling 2007; Light and Marchetti 2007; and Hoagstrom et al. 2010. Many more such events are described in books that are wholly or partially dedicated to this topic, including: Courtenay and Stauffer 1984; Mooney and Drake 1986; Minckley and Deacon 1991; Avise 1994; Lockwood and McKinney 2001; Moyle 2002; and Sax et al. 2005, etc. Finally, entire scientific periodicals are dedicated, in whole or in part, to studying the consequences of biological invasions (e.g. Biological Invasions, Aquatic Invasions, Conservation Biology, Biological Conservation, etc.).

> *At a global level, exotic introductions have shown many significant negative impacts and invading aliens are considered second only to habitat loss as the major threat to native biodiversity and the integrity of natural communities (IUCN 1997).*

The EA considers only two possible avenues of fish escape from either AquaBounty facility: vandalism or failure of all containment systems due to a physical disaster. As a result, the EA ignores the potential for the containment systems to fail under "sunny day" conditions. This faith in human infallibility appears to underlie the project proponents' choice to employ a flow-through systems rather than a land-based recirculation systems; this choice of system design creates a hydrological connection between the fish rearing facility and exterior environments and assumes that barriers to fish movement (screens, sumps, chlorine, etc) will work 100% of the time. This is a poor assumption indeed. Whereas the containment measures described in the EA may appear to be efficacious, each requires perfectly reliable and well-trained employees who do not make mistakes (such as failing to notice a clogged or broken stem-pipe filter, failing to replace a chlorine puck at the appropriate time, etc.). It is completely unreasonable to expect that the containment protocols described by the project proponent will be perfectly implemented *in perpetuity* or that organizations to which AquaBounty may sell its product to in the future will maintain the same set of protocols and the same commitment to implementing them.

As for the potential mechanisms of GE fish escape that the EA does consider (vandalism and natural disaster), I find its analysis and dismissal of these phenomena completely unconvincing. With regard to vandalism, we are all aware that intruders break into guarded facilities upon occasion. In my own experience, two separate areas of my doctoral research facility were vandalized, in different events, in the four years I maintained live animals, despite the fact that both areas were behind locked doors and the fish I was studying at the time were of no commercial, recreational, or culinary value. I can offer no estimate of the likelihood that vandals will disrupt either the PEI or Panama facilities, or transit between these facilities, or other facilities that may house GE fish in the future, but it is simply naïve to assume that, just because facilities are guarded, vandalism that leads to release of GE salmon is not possible.

The potential for catastrophic events to disrupt activities at either the PEI or Panama facility (or on transit routes between the facilities) seems substantial, yet the EA dismisses them as unlikely. On page 57, the EA states that PEI:

- *"… is frequently affected by outcomes such as power outages, rain and snow storms from December until April…"*
- *"…in September 2003, high winds (~90 mph) associated with Hurricane Juan devastated central Nova Scotia[2], killing eight people and causing an estimated C$200 million in losses that extended into Prince Edward Island"*

[2] More recently, although Hurricane Sandy (2012) did not track towards PEI, it caused torrential rains and high winds well into Canada and generated tremendous destruction and transportation problems along all the routes (air, ground, and sea) connecting AquaBounty's PEI and Panama facilities. There is obviously no certainty that the next large hurricane on the East Coast of North America will not follow a track that leads to PEI.

- *" …in February 2004, a blizzard nicknamed "White Juan" brought a record one-day snowfall of ~40 inches that briefly crippled the area."*
- *"Flooding and severe storm surges … occur with regularity in the vicinity of Charlottetown on the south side of PEI (the ABT egg production facility is located on the northeast side)."*
- *"Two tsunamis have been reported east of Nova Scotia in the vicinity of southern Newfoundland and the Grand Banks, and one tornado has been reported in coastal New Brunswick northwest of Moncton …"*

The EA's own list seems to contradict its claim that weather events that could disrupt GE salmon containment at the PEI facility are "*rare or extremely rare*". [p. 68] Rather, they indicate that the PEI facility may be subjected to extended power outages and/or significant physical damage and/or isolation from trained personnel as a result of powerful storms and that these events can be expected to occur with some frequency.

Regarding the Panama facility, the EA [p. 71] states:

> *The grow-out facility in Panama is potentially subject to flooding conditions from a nearby river. The area receives a significant amount of annual rainfall, approximately 570 cm or 224 inches per year (Table 5), with much of it coming in the wet summer months. There was a significant flood of the river in the recent past that caused extensive damage at locations downstream of the grow-out facility. The facility itself, however, was not directly affected by flood waters and sustained no serious damage. …Considering that this flooding was among the worst to ever occur in the area, it seems improbable that the grow-out facility would be impacted by future events of this type in a manner that could cause accidental release of GE fish. In addition, all tanks in the facility have appropriately sized top netting to prevent fish escape in the unlikely event that flooding would occur on the grounds of the facility.*

Again, this revelation does not demonstrate to me that catastrophic power outages or barriers to key personnel performing essential protocols will be "rare or extremely rare". Moreover, the fact that the Panama site is so wet only increases the likelihood that escaped fish will survive long enough to find their way to the adjacent river or coastal areas.

The fact is domesticated Atlantic salmon escape from their rearing facilities frequently, sometimes in large numbers, and from a diversity of facilities despite efforts to prevent such escapes. Gross (1998:136) summarizes:

> *The movement of domestic* [Atlantic salmon] *... into the wild is not uncommon. Recent estimates from the salmon farming in- dustry in British Columbia suggest that up to 2% may enter the wild each year (Alverson and Ruggerone 1997). Losses can occur in large pulses or through small leakages. For example, in 1988 a single winter storm along the middle coastal region of Norway released about 700,000 individuals into the Atlantic Ocean (Gausen and Moen 1991). In the Pacific, 101,000 Atlantic salmon were released into Puget Sound, Washington*

> *State, on 2 July 1996 and over 360,000 on 18 July 1997 from mishaps at single farms (Thomson and McKinnell 1997; personal communication from A. Thomson, Atlantic Salmon Watch B.C.). Escapement into the wild is known to occur at all life stages from yolk-sac fry up to and including adults (e.g., Lough et al. 1997).* [Emphasis added]

Gross (1998) and others also report catches of escaped, domesticated Atlantic salmon *in the Pacific Ocean* (i.e. well-beyond their rearing facility) averaging almost 1500 fish per year from 1987-1997. I believe it is highly likely that each of the salmon farm facilities that has lost domesticated salmon to the wild had protocols and facilities intended to prevent such escapes – these are, after all, commercial ventures that lose revenues with each fish that escape. The point is that fish escape containment facilities (sometimes in large numbers and frequently) despite practices, protocols, and hardware designed to prevent such escapes. Whereas the proposed containment of AquAdvantage fish might conceivably reduce the number or frequency of escape, I see nothing in the description that guarantees that fish will not escape, survive escape, or cause harm if they do escape. Again, given the potential consequences, the FDA should require an exceptionally high level of certainty that the production of these transgenic fish will not cause harm to the environment, the sport angling economy, or commercial fishing operations. That standard has not been met by the current proposal or its review in the EA.

II. AquAdvantage salmon that escape are capable of surviving outside either the Prince Edward Island or Panama facilities.

After AquAdvantage fish escape captivity, the main factor that regulates the harm they can cause is their ability to survive and mature in the environments outside of the facilities. In short, I find no reason to believe that AquAdvantage salmon would not survive in many of the aquatic environments outside of the breeding and rearing facilities – indeed, related fish species with similar ecological requirements already survive and reproduce in close proximity to these facilities (e.g. USFWS 2000; EA at pp. 59 and 62). The FDA be aware that, once these GE salmon have escaped, they will be very difficult (or perhaps impossible) to eradicate and can potentially migrate to other environments where conditions will be even more conducive to survival and reproduction.

The EA correctly states:

> *Any consideration of the fitness of Atlantic salmon, regardless of its status with respect to genetic engineering, requires understanding that in general, Atlantic salmon display a high degree of phenotypic plasticity and complex life history that enable them to adapt to variable conditions and rigorous environments. In addition, genotype-by-environment interactions will produce different phenotypes when animals with the same genetic background are exposed to different environmental conditions. Given the high degree of phenotypic plasticity of Atlantic salmon, and the impact of genotype-by-environment interactions, it is not surprising that the wide spectrum of traits observed in wild-type Atlantic salmon generally encompasses that of AquAdvantage Salmon.* (FDA pp. 26-27).

In other words: Atlantic salmon (including GE AquAdvantage salmon) are adept at surviving in a wide range of environments and they are highly variable and plastic (reducing the relevance of findings based on small sample sizes). Despite this, the FDA relies on a small number of studies and/or a large number of assumptions that are contradicted by plain fact and/or voluminous research that suggest that escaped GE salmon are quite likely to be able to survive in environments near to the incubation and rearing facilities described in the EA (to say nothing of environments along the transport route between these two facilities or environments where these fish may be reared in the future).

In general, the EA finds that AquAdvantage fish are similar to the Atlantic salmon (both wild and domesticated) in their environmental tolerances. The EA notes only minor differences in gross anatomy, histopathology, and clinical chemistry in its very small sample of GE salmon, concluding that "*these findings were generally of low magnitude, limited distribution, and non-debilitating nature*" (EA p.27). Similarly, the EA reports no differences in susceptibility to disease among AquAdvantage relatives and other Atlantic salmon. Furthermore, the EA emphasizes similarities between GE AquaAdvantage salmon and high-growth rate, non-GE salmon bred for the hatchery environment. This is ironic because the latter are well-known to escape confinement, survive in the habitats into which they escape, and have deleterious environmental effects when they escape from containment (e.g. Utter et al. 1993; Einum and Fleming 1997; McGinnity et al. 1997; Gross 1998; Clifford et al. 1998, McGinnity et al. 2003; Bourret et al. 2011).

I am unimpressed by the EA's suggestion that some differences between AquAdvantage salmon and wild counterparts make the former incapable of surviving in and emigrating to new habitats following an escape from their breeding or rearing facilities. For example, the EA's evidence that escaped AquAdvantage salmon *might* be impeded by low dissolved oxygen levels in the wild is feeble. The EA states: *"Although these AquAdvantage relatives have demonstrated an ability to reduce their metabolic rate in response to starvation, their enhanced metabolic profile and lower initial energy reserves would greatly reduce the likelihood of their growing rapidly, or even surviving, outside of the highly supportive conditions provided by commercial farming*" (EA p. 30, Emphasis Added). Thus, the EA concedes that any greater metabolic demand for oxygen exhibited by AquAdvantage salmon compared to wild Atlantic salmon is facultative (i.e. can be "switched off" in a low food environment). More importantly, the EA reveals that dissolved oxygen conditions in the river adjacent to the Panama facility are suitable for salmon (and that rainbow trout currently live outside of this facility). Because temperature and dissolved oxygen concentrations are inversely related (low temperatures produce high levels of dissolved oxygen), temperatures common outside the PEI facility (Table 4, p. 56) make it highly unlikely that escaped salmon would ever encounter low dissolved oxygen conditions in the waterways on PEI. Thus, it is hard to imagine that (a) dissolved oxygen conditions in the waterways adjacent to either facility would kill escaped AquAdavantage salmon; (b) such conditions are so extreme or persistent that escaped GE salmon could not swim to more suitable environments; or (c) even when/if such conditions did exist, they would represent a competitive advantage to wild salmonids in competition with GE salmonids (because, as noted, the GE salmon can reduce their demand for dissolved oxygen).

In assessing whether AquAdvantage salmon would survive if (when) they escaped their breeding or rearing facilities, the EA repeatedly immerses the reader in great detail about the physical characteristics of AquAdvantage salmon and their environmental tolerances while ignoring the clear fact that AquAdvantage salmon tolerate conditions like those outside of both the proposed spawning and rearing facilities; in other words, the FDA missed the forest for the trees. For example, it is clear that AquAdvantage fish can survive out of captivity because Atlantic salmon and/or other species of the genus *Salmo* and other salmonid genera have historically survived and reproduced in the waters outside both the breeding facility on Prince Edwards Island (PEI facility) and the rearing facility in Panama. Regarding the PEI facility, the EA states:

> *The local environment near the ABT facility has numerous shallow bays, broad estuaries, and short rivers that contain an abundance of favorable habitat for diadromous fishes, those species that use both marine and freshwater habitats. Fish common to the area include the following: mackerel; herring; eel; gaspereau (e.g., alewife & blueback herring); silverside; smelt; and, salmonids. The salmonid group comprises the following: Atlantic salmon (Salmo salar); brook trout (Salvelinus fontinalis), which is native to the region; and, rainbow trout (Oncorhynchus mykiss), which was introduced into the region in 1925.* (EA p. 59; Emphasis Added).

The fact that Atlantic salmon have been extirpated from the particular drainage on PEI where the spawning facility is located does not, in any way, demonstrate that fish or eggs that escape from the PEI facility will not survive (EA pp.88-89). Thus, there is no reason to believe that escaped AquAdvantage Salmon would be limited by environmental conditions outside of the PEI facility.

Regarding the waterway nearest to the Panama facility, the EA states:

> *The upper part of the local river has favorable conditions for establishing salmonid populations: temperature, DO, and turbidity are all within their tolerances. These conditions change in the mid- and lower-parts of the river where water temperatures exceed the upper lethal limit (~23ºC) that has been identified for Atlantic salmon (see Appendix A.3 and Section 7.3.1.2 for additional information on their temperature tolerance).* (EA p.62).

and

> *There are few natural predatory fish in the area. Freshwater tarpon (Tarpon prochilodus) occur in the warmer waters of the lower basin, and a population of rainbow trout that were introduced in the upper basin could prey on salmon. These rainbow trout were intentionally stocked beginning in 1925, and are reported to constitute an established, naturally reproducing population (Welcomme, 1988); however, their abundance has not been well documented.* (EA p.63, Emphasis Added).

The fact that rainbow trout have survived in the watershed adjacent to the Panama facility for almost 90 years is very strong evidence that escaped AquAdvantage salmon could survive in these waters. The EA incorrectly implies that, though the upper watershed is capable of

supporting self-sustaining populations of salmonids (and does so now), these fish cannot escape to marine environments because temperatures in the lower river exceed 23℃ and this water temperature is too high to support salmon. This assertion is deceptive because (a) the EA's appendix suggests that 23℃ is a temperature at which Atlantic salmon stop feeding, but it also reveals that Atlantic salmon can survive (until starvation) in water with temperatures much higher (>27℃) and (b) the EA reports average temperatures in the lower river, which are, of course, higher than minimum water temperatures escaped fish might encounter. Thus, there is no support for relying on water temperatures in the lower river to block the migration of escaped AquAdvantage salmon out of the Panamanian freshwater environment.

In general, the EA focuses only on the potential for AquAdvantage to escape and establish self-sustaining populations of AquaAdvantage offspring in the waterways into which they escape; little or no attention is paid to the more likely scenario that escaped fish or their progeny will swim or be transported to new environments. For example, the EA ignores the very real possibility that, having escaped containment, a small population of AquAdvantage salmon could serve as a source population for introduction to other areas. In other words, once AquAdvantage salmon escape and survive in the wild, there is nothing to stop people from intentionally moving them to other environments. This kind of intentional introduction is quite common, especially when the target species is a sought-after, edible sportfish (for example, rainbow trout have been introduced *into* the environments outside of both AquaBounty facilities). Furthermore, if escaped AquAdvantage salmon can survive in the site of their initial introduction, they may colonize other environments opportunistically, when conditions permit. Even if the environments immediately outside the production and rearing facilities are sometimes inhospitable to some life stages of escaped AquAdvantage fish, this does not mean that (a) they are always inhospitable or (b) a different life stage of these fish could not tolerate the new environment long enough to find its way into other habitats that would support survival and reproduction. Because AquAdvantage fish are not bred to die prematurely and are similar to their wild relatives in many respects (except where they are superior, *see below*), there is every reason to be concerned that escaped AquAdvantage salmon can survive long enough after escaping captivity to move (or be moved) to distant environments. None of AquaBounty's redundant containment systems will be of any use once these fish have established themselves in watersheds outside of the rearing facility.

In addition, numerous water bodies between these two facilities do now or have historically supported populations of Atlantic salmon or other species in its genus or related genera of the family salmonidae; thus, the AquAdvantage fish could survive if they escaped during transport (e.g. as a result of transport plane or truck crash during operations described in the EA at page 54). Even if AquAdvantage fish escaped or were introduced into an environment where Atlantic salmon have never existed in the past, this would not indicate that they are not capable of surviving in the novel environment. Indeed the modern history of fisheries in North America and across the globe is overflowing with examples of fish introduced into habitats where they did not exist before (*see sample citations throughout this letter*).

In many ways, the EA finds that AquAdvantage fish may be superior to their wild counterparts; for example, the EA states: "*The main difference between AquAdvantage Salmon and non-GE Atlantic salmon, and the basis for the value of the product, is the significant increase in growth rate of the former*." (EA p.28). The EA notes that AquaAdvantage salmon exhibit increased

aggressiveness and reduced anti-predator responses compared to wild Atlantic salmon. Increased growth rate clearly corresponds to increased viability among fishes as, within species, size is correlated positively with swimming ability and negatively with predation rates (Brett 1964; Beamish 1978); increased aggression can confer fitness in particular environments, especially when the risk of predation (and therefore the need to remain hidden) is low — this is the case in the environment immediately outside the Panama facility (EA p.63).

In addition, although the EA strains to explain why the behavior of escaped hatchery fish behavior would inhibit their survival in the wild (EA pp.31-32), the suggestion is contrary to both the abundant scientific evidence that domesticated salmon from other types of rearing facilities escape and survive quite frequently and the EA's own statements about other GE salmon with transgenic growth hormone constructs. With respect to GE coho salmon, the EA states:

> *Under laboratory conditions, GH-transgenic coho salmon (Oncorhynchus kisutch) bearing the OnMTGH1 growth hormone construct have been observed to be more competitive (Devlin et al., 1999), less discriminate in choosing prey (Sundström et al., 2004), more likely to attack novel prey (Sundström et al., 2004), and better at using lower quality food (Raven et al., 2006) when compared to wild relatives. Although these effects would have the potential to influence wild relatives both directly and indirectly, such observations were demonstrably muted when the GE fish were reared under simulated natural conditions (Sundström et al., 2007), indicating the complexity of gene-environment interactions. The extent to which this information on GE coho salmon can predict the behavior of GE Atlantic salmon is also unknown*. [EA p.32]

The citation to Sundström et al. (2007) is curious because, while that study did find that the advantages enjoyed by GE coho salmon over wild salmon were "muted" under simulated natural conditions, these authors still found that GE salmon were significantly superior competitors to wild Coho salmon. They state:

> *"…when fish were reared under naturalized stream conditions, transgenic fish were <u>only 20% longer than the wild fish</u>, and the magnitude of difference in relative predation effects was much reduced. These data show that genotype-by-environment interactions can influence the relative phenotype of transgenic and wild-type organisms and that extrapolations of ecological consequences from phenotypes developed in the unnatural laboratory environment may lead to an <u>overestimation or underestimation</u> of ecological risk. Thus, for transgenic organisms that may not be released to nature, the establishment of a range of highly naturalized environments will be critical for acquiring reliable experimental data to be used in risk assessments."* [Sundström et al., 2007:3889, Emphasis Added]

The main point of Sundström et al. (2007) is to demonstrate "the complexity of gene-environment interactions" and speak to the importance of these interactions in understanding the likely impact of non-native fish introductions (or, in this case, escape of a GE salmon). Other

studies of the impacts of fish interactions (e.g. Smith et al. 1995; Hatfield and Schluter 1999; Rosenfield et al. 2000; Kodric-Brown and Rosenfield 2004) make the same point: the outcomes of any given fish introduction depend on environmental conditions experienced by the escaped fish and the genotype of the introduced group of fish. Sundström et al (2007) also make clear that these interactions can work both ways, i.e., in another simulated (or actual) natural environment, GE salmon might enjoy even greater fitness advantages over wild fish. In fact, the authors explicitly state:

> *"... our results cannot be taken as evidence that growth-enhanced transgenic salmonids reared in nature will not influence prey population survival and growth differently than wild salmonids. Although development in a simulated natural environment reduced the difference in predation effects between transgenic and wild predators, the small number of replicates (n = 4 per predator type as the result of logistic reasons) reduced the likelihood of detecting small, but significant, differences (i.e., low power of test). In addition, the present experiments have only mimicked one type of "natural" environment during both rearing and experimental monitoring (e.g., for only the fresh-water phase of the salmon's life history). Because environment appears to have a strong influence on phenotype, other rearing conditions not tested in this experiment (e.g., prey density) may still affect phenotypic development of a transgenic animal and subsequent ecological consequences."* [Emphasis Added]

and

> "*For risk assessments of transgenic animals that cannot be released to nature, it is important to examine the animals under a range of contained naturalized environments that yield the full breadth of phenotypes and ecological scenarios that transgenic animals would experience in the wild. Further, determining whether rearing conditions cause permanent or reversible phenotypic changes is critical, because this determination will influence the potential of animals from a rearing facility to become more "wild-like" which, in turn, will influence their long-term fitness and ecological impact in nature.*" [Emphasis Added]

The FDA's failure, to heed this extremely salient message, is a significant inadequacy of the EA. That the EA takes this study out of context and, as it does elsewhere, grasps at a small number of small studies to support (weakly) its preferred alternative is unpardonable.

Similarly, the EA's discussion of ocean return rates among domesticated triploid salmon (similar, but not identical, to AquAdvantage salmon) demonstrates that the possibility of escape, survival (through fresh and salt water environments), and return to "home" streams is not at all theoretical. But, contrary to their plain import, the EA treats the ominous findings of a few studies on GE salmon as though they were proof of the efficacy of induced triploidy in preventing harm to natural ecosystems or populations of wild fish. The EA states:

> *Ocean migration studies in Ireland revealed that male triploids returned to their natal area in nearly the same proportions as diploids, whereas female triploids mostly did not (Wilkins et al., 2001). In another Irish study, the return rates of female triploid Atlantic salmon, both to the coast and to fresh water, were*

> *substantially reduced (four- to six-fold lower) compared to those for their diploid counterparts (Cotter et al., 2000a).* [EA p. 32, Emphasis Added]
>
> These findings do not square with the EA's interpretation that:
>
> *".. triploidy could be used as a means both for eliminating genetic interactions between cultured and wild populations and for reducing the ecological impact of escaped farmed fish."* [EA p. 32, Emphasis Added]

The fact that, in some studies, gender-differences have been documented in adult return rate among domesticated triploid fishes actually demonstrates the potential risks of releasing these fish more than it quells such fears – some triploid salmon of both sexes home to their river of origin. In addition, the reduced detection of triploid salmon females in the wild does not mean that these fish did not (a) compete with other salmon in the ocean environment and/or (b) return to other, non-natal potential spawning streams (a process known as "straying" in the literature on Pacific salmon; Quinn 2005) where they have interacted with native fish populations. Furthermore, the Irish study referenced by the EA was conducted in 1 year with only three release groups; thus, it represents little more than an anecdotal observation of the efficacy of induced triploidy. As elsewhere in the EA, the analysis and conclusions presented here are not based on the study of AquAdvantage salmon nor were they conducted in environments close to the AquaBounty facilities where these fish are more likely to escape. Thus, the EA's hand waving at the importance of environment*genotype interactions to the contrary, the FDA ignores the potential for AquAdvantage salmon to behave quite differently from fish in the small sample studies it relies upon.

In sum, the FDA fails to make the case that escaped AquAdvantage salmon would not survive in the wild long enough to cause environmental impacts in waterways surrounding their incubation and rearing facilities or to escape (or be transported) to other habitats where they may cause lasting environmental impacts. In part, this is because escaped, domesticated Atlantic salmon quite frequently survive in natural environments, where they cause significant damage, and because native and/or introduced salmonid populations (with environmental tolerances similar to those described for AquAdvantage salmon) already exist outside the PEI and Panama facilities. In part, the FDA's case that escaped GE Atlantic salmon will not survive in the wild is unconvincing because the EA itself describes several fitness advantages of these fish relative to their wild counterparts. Finally, the EA relies on very limited studies its case and these reports for the most part did not involve actual AquaAdvantage salmon and were not conducted in a range of environments that escaped AquAdvantage salmon might encounter; thus, the potential for environment*genotype interactions to foster undesirable results among escaped AquAdvantage salmon remains almost completely unevaluated.

III. **If and when AquAdvantage salmon escape, their impact on environment of the US could be significant and irreversible**.

The record of negative impacts to native aquatic ecosystems and fish species resulting from both intentional and unintentional introductions of non-native fish species (or divergent genotypes within a species) is long and abundant. The potential pathways by which escaped GE salmon may impact aquatic ecosystems, species, and/or fisheries of the U.S. can be segregated into two major categories: (1) ecological impacts on native, wild-type fishes (via predation and/or competition for resources such as food or mating opportunities) and (2) genetic impacts on native wild salmonids via hybridization and genetic introgression (which may, in turn, affect the outcome of the ecological interactions). Gross (1998) illustrated and reviewed the taxonomy of ecological and evolutionary concerns associated with farmed, domestic Atlantic salmon escaping into the wild (Figure 1); this taxonomy is relevant regardless of the genetic background of the domesticated stock.

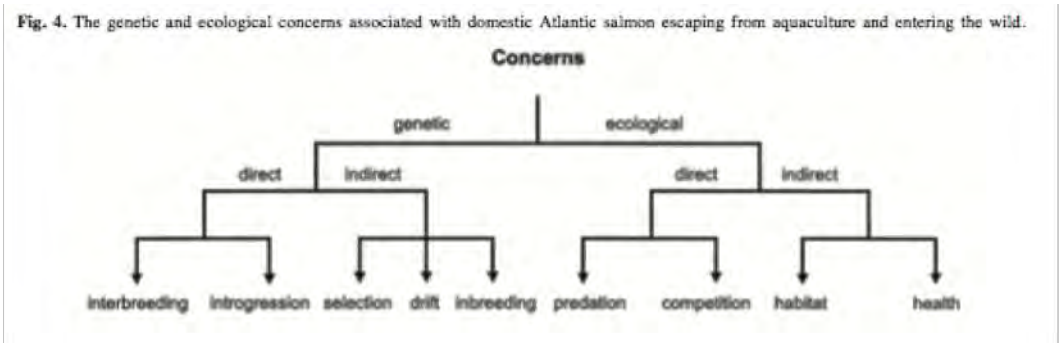

Figure 1: The relationships among various mechanisms of negative impacts associated with the escape of farmed Atlantic salmon into natural ecosystems. Copied from Gross (1998; Figure 4, p. 134)

Gross (1998:137-138) outlined general categories of impact that escaped domesticated Atlantic salmon may have in native environments:

- Ecological impacts (these impacts may occur whether or not escaped GE salmon are reproductively viable)
    - Gross cites Ferguson et al. (1997) to illustrate that farmed Atlantic salmon behaviorally displaced wild Atlantic salmon into less productive habitats – the wild salmon grew more slowly than domesticated salmon or wild *x* domestic hybrids.
    - Gross (1998) cites Webb et al. (1991) to demonstrate the "*common reproductive habitat perturbation*" that occurs because escaped farmed fish typically arrive on the spawning grounds after wild fish spawn; the farmed fish then dig up nests of wild females.
    - Disease and parasite transfer may be facilitated by escaped domesticated fish. Although the EA presents no evidence that GE salmon are more susceptible to disease than other salmon, it is also extremely difficult to

know how these fish will respond to pathogens in the range of natural environments into which they might escape.

- Direct genetic impacts through inter-specific or inter-population hybridization.
    - Gross (1998) cites Sægrov (1993); Youngson et al. (1993); Hindar and Balstad (1994) as indicating that farmed female Atlantic salmon have increased hybridization rates with salmonids in the wild;
    - Gross (1998) refers to personal communication with R. Devlin (Department of Fisheries and Oceans, Vancouver, B.C., Canada) indicating that survival of F1 progeny occurred in 10 of 14 possible crosses between Atlantic salmon, and seven species of Pacific salmon;
    - Gross does not mention the very real possibility that successful inter-specific or intra-population genetic exchange could disqualify imperiled populations (e.g. of wild Atlantic salmon) from protection under the federal Endangered Species Act (e.g., O'Brien and Mayr 1991; Smith et al. 1995) or extinguish them entirely (e.g. Rhymer and Simberloff 1996 *and sources cited therein*; Epifanio and Philipp 2001 *and sources cited therein*; Garrett et al. 2002);
    - Similarly, Gross does not mention the potential for hybrids and their offspring to show hybrid vigor (improved fitness over parental types; e.g. Arnold and Hodges 1995; Rosenfield and Kodric-Brown 2003; Rosenfield et al. 2004) that could allow them to increase their geographic range (e.g. Echelle et al. 1997) and/or increase competition with other native species in the invaded environment.
- Indirect genetic impact of Atlantic salmon attempting to hybridize in populations of native salmonids that are locally endangered and close to extinction. Rosenfield et al. (2000) expressed similar concerns about the long-term effect of Chinook salmon hybridization with pink salmon in the Great Lakes (*see below*) and others have noted the possibility of a "Trojan Gene Effect" wherein escaped, domesticated fish might enjoy an initial mating advantage, but produce offspring that are less fit than wild types, resulting in reduced viability of the wild population in the long-term (e.g. Howard et al. 2004)[3].
- Competition with native salmonid species for food and space.

[3] I am aware that one researcher credited with developing the "Trojan Gene Hypothesis" has distanced himself from the suggestion that this particular outcome might arise as a result of GE salmon interbreeding with wild salmon (e.g. EA p.91). I believe that this phenomenon could be a problem (though only one of many potential problems) that arise from escape of AquAdvantage salmon into the wild. Indeed, it is the expectation of traditional biological concepts of "species" that hybrids between two species will be less viable than the parent species – whereas I present examples in which this has not been the case (*see below*), it is still quite possible that escaped GE salmon might be preferred mating partners by some wild fish (a fitness advantage) and that their offspring might experience reduced fitness in some other aspect of their life cycle. The phenomenon were single genes produce different fitness results throughout the life cycle of an organism is known as plieotropy and its study has a long history in the evolutionary ecology literature. I do not believe anyone is qualified to comment on the likelihood that particular DNA codes will be "purged" following interbreeding of AquAdvantage fish and wild fish; the outcome of such an interaction is simply unknown because it depends, in part, on environment*genotype interactions which have not been adequately studied here.

  - Because of increased growth rate, size, and aggression of domesticated Atlantic salmon, these fish may outcompete native salmonids for food and territorial resources (Gross 1998 *citing* Fausch 1998; Gibson 1981; Beall et al. 1989).
- Perturbation of the habitat resulting from different utilization of habitat by Atlantic salmon.

Gross (1998:136-137) concludes:

> *Although it is difficult to quantify or partition the impacts on wild Atlantic salmon by escapement from the aquaculture niche (e.g., Fig. 4), it can no longer be reasonably questioned that major impacts do occur. Over the last decade, the primary ecological impact on wild fish health is through the transfer of diseases and parasites. While new diseases and parasites will surely appear, the current problems are now better controlled in the aquaculture niche (e.g., Aarflot 1995; Bruno and Poppe 1996; except perhaps for sea lice; also, recent outbreaks of ISA infectious salmon anemia). I suspect that the impact of most concern for wild fish in the future will be genetic, through interbreeding and introgression of aquaculture genes and through increasing drift and inbreeding due to reduced wild population size (due in part to increasing competition and further habitat perturbation). The resulting loss of the wild gene pool may give rise to yet less fit individuals for future evolutionary change and survival in the wild. There is a strong possibility that the magnitude of escapement combined with the biological divergence between the two niches will result in the disappearance of all wild Atlantic salmon populations within areas of aquaculture.* [Emphasis Added].

Below, I briefly expand upon the mechanisms outlined above.

Ecological Impacts of Escaped GE salmon -- The EA clearly identifies attributes of AquAdvantage salmon that would benefit these fish in competition with other salmonid species. For example, these GE fish grow faster and are more aggressive than typical Atlantic salmon. Studies of fast growing and aggressive domesticated strains of farmed salmon demonstrate that they may jeopardize wild populations; for example, Einum and Fleming (1997:634) concluded that farmed salmon were more aggressive and had higher growth rates than native fish and:

> *"In the wild, observations of habitat use and diet suggested that the populations compete for territory and food, and both farmed fish and hybrids expressed higher growth rates than native fish. Our results suggest that these innate differences in behaviour and growth, that probably are linked closely to fitness, will threaten native populations through competition and disruption of local adaptations."*

McGinnity et al. (2003:2449) studied this very question and concluded:

> *"..offspring of escaped farm fishes may also reduce the size of the wild population due to competition. Although overall survival of farm and 'hybrid' fish was lower in the experiment, due to their larger size, surviving fish resulted in competitive displacement of wild parr. Given the selection for increased growth in the farm*

> *strain, this larger size is not surprising. Fleming et al. (2002) have shown that farm salmon show increased aggression, which may further favour such fishes in competitive encounters."*

These authors raised particular concerns about the effect of escaped farm salmon on small, imperiled wild populations of Atlantic salmon, such as those located near the PEI facility.

In a recent review of the ecology of farmed Atlantic salmon and their interaction with wild fish in natural environments,[4] Jonsson and Jonsson (2006:1171) indicate that farmed salmon may have many negative ecological effects on wild salmon populations including "*increasing their emigration and mortality, decreasing their growth rate, biomass, and production, and altering their life history traits*". They conclude:

- *Cultured salmon compete for food, space, and breeding partners with wild conspecifics in nature.*
- *Their performance and reproductive success in nature are variable, but can be much poorer than those of wild conspecifics of similar size.*
  .... [and]
- *Through density-dependent mechanisms, cultured fish in nature may displace wild fish to some extent, increase their mortality, and reduce their growth rates with effects on the associated life history traits, biomass, and production.* (Jonsson and Jonsson 2006:1174).

Given that Atlantic salmon populations across the east coast have been decimated (e.g. USFWS 2000), the addition of a superior competitor to any of their remaining habitat would be an unwelcome development. In fact, populations of Atlantic salmon located just over the U.S./Canada Border from the PEI facility are listed under the US Endangered Species Act (ESA) as threatened, in part, because concern over the impacts on wild populations of escaped farmed salmon. The USFWS found:

> *Atlantic salmon that either escaped or were released from aquaculture facilities have been found in the St. Croix, Penobscot, Dennys, East Machias, and Narraguagus Rivers in the United States (Baum, 1991; USASAC, 1996; 1997). In 1994 and 1997, escaped farmed fish represented 89 percent and 100 percent, respectively, of the documented run for the Dennys River, and in 1995, 22 percent of the documented run for the Narraguagus River. Escaped farmed salmon have also been documented as an incidental capture in the recreational fishery, and observed in the Boyden, Hobart, and Pennamaquan Rivers. The first aquaculture escapee in the State of Maine was documented in 1990, and the first sexually mature escapee was documented in 1996. Escaped farmed fish are of great concern in Maine because even at low numbers they can represent a substantial portion of fish in some rivers. Also, populations at low levels are particularly*

[4] It is worth noting that the escape of domesticated Atlantic salmon is so common and their real and potential impacts on wild Atlantic salmon populations is of such concern that at least four separate *reviews* of literature on the topic were published between 1997 and 2006.

> *vulnerable to genetic intrusion or other disturbance caused by escapees (DFO, 1999; Hutchings, 1991*. (USFWS 2000:6947; Emphasis Added)

Thus, impacts to native, imperiled Atlantic salmon and their historic riverine ecosystems from escaped farmed salmon are already occurring; in light of this, the placement of a new aquaculture facility, especially one with through-flow connection to wild environments, that rears fish which are a potentially grave threat to wild Atlantic salmon populations and their ecosystems, seems unwise, at best. At the very least, approval of a GE salmon production facility on PEI would seem to require a consultation by FDA with USFWS and NMFS under Section 7 of the Endangered Species Act. Similarly, if AquAdvantage fish escaped from the Panamanian rearing facility and/or were transported to the Pacific coast, they could compete with wild Pacific salmon and trout (genus: *Oncorhynchus*), many of which are also imperiled (Allendorf et al. 1997).

Genetic Impacts of Escaped GE salmon –The potential for escaped GE salmon to cause genetic impacts to wild populations of salmon and/or trout is higher than the EA acknowledges. The EA's analysis of the risks posed by introduced GE salmon is premised on the assumption that the level of impacts is directly correlated with the number and frequency of fish introductions. For example, the EA states:

> *The scale and frequency of introductions of GE fish into a particular environment will have a large influence on potential ecological risks and their magnitude. Any introductions would have to involve a critical mass (sufficient number) that could offset natural mortality, and be of sufficient frequency in proper season to allow for long-term survival and establishment. If the scale and frequency of the escapes (i.e., introductions to the environment) are small, the chances of becoming established in the natural setting are extremely low (Kapuscinski and Hallerman, 1991).* (EA p.20).

This assumption is wrong: Although ecological impacts are related to the frequency or number of introduced GE salmon, the potential genetic impacts of escaped GE salmon on wild populations of salmonids (Atlantic salmon and others) does **not** necessarily depend on the number of escaping individuals or their persistence in the environment; in fact, there are many examples of a small number of introduced fishes having irreversible genetic impacts on other unique populations (*see* Case Studies *below*). As a result, the EA severely underestimates the risk of escaped GE salmon on wild populations of salmon and trout (i.e. members of the family Salmonidae).

Genetic impacts of escaped GE salmon can arise even if the escaped fish are not fertile (Hindar et al. 1991; Gross 1998). For example, if escaped, sterile GE salmon compete successfully with wild salmon for mates, breeding opportunities, and/or limited spawning territories, the wild population will suffer decreased productivity as a result of false matings. The release of sterile members of one sex to reduce the growth rate of an entire population is, in fact, the principle behind some efforts at pest control (see myriad examples cited in Dyck et al. 2005). Because GE salmon females are likely to be larger and more aggressive than native salmon and size is positively correlated with reproductive success among salmon (Gross 1985; van den Berghe and Gross 1989; Healy 1991), it is very likely that they would attract and stimulate mating activity

from wild male salmon. Because many salmon populations are small (to the point of being at peril of extinction) and because males and females die after spawning, wasted spawning opportunities may have a severe impact on population growth rates. Similarly, the mere act of creating a nest (redd) by escaped GE salmon may lead to destruction of viable eggs from the pairing of wild males and females (nest superimposition; Gross 1998).

Successful reproduction between escaped AquAdvantage salmon and wild Atlantic salmon (or salmonids) is a clear danger, the consequences of which would likely be irreversible. As discussed below, hybridization and gene flow (introgression) among fish species is common and gene flow in the wild ("natural" hybridization and introgression) has long been known and studied among the salmon genera *Salmo* and *Oncorhynchus*. Interestingly, these impacts may be *more* likely to occur if (a) the number of GE salmon on the breeding grounds is small and (b) if the GE salmon are all of one sex – the observation that hybridization is more common when abundances of the two inter-breeding populations and sex ratios are asymmetrical has been well documented for over 50 years (e.g. Hubbs 1955, 1961). Further, the potential consequences of gene flow from AquAdvantage salmon to wild salmonids are uniquely troubling because the former carry genetic material from a third species (a transgene); once that novel genetic material is transferred to viable offspring in the wild, the potential negative impacts to wild populations (and even entire species) of salmon are numerous and severe.

Hybridization and genetic introgression (meaning here: successful gene flow between species) are well-known among plants and animals and particularly among fish species[5] (e.g. Hubbs 1955, 1961; Campton 1987; Minckley and Deacon 1991; Smith 1992; Avise 1994; Smith et al. 1995; Arnold 1997; Echelle et al. 1997; Hatfield and Schluter 1999; Rosenfield and Kodric-Brown 2003, etc.). The potential for and occurrence of genetic exchange in the wild among salmonids is exceptionally common and well-documented (Foerster 1935; Hunter 1949; Simon and Noble 1968; Smirnov 1972; Chevassus 1979; Allendorf and Leary 1988; Bartley et. al. 1990; Waples 1991; Dowling and Childs 1992; McGowan and Davidson 1992; Rosenfield 1998; Rosenfield et al. 2000; Kirkpatrick et al. 2007). And, hybridization, genetic introgression, and other genetic effects between escaped domesticated salmon and wild populations of Atlantic salmon (and other salmonids) are already widely reported and studied mechanistically (e.g., Hindar et al. 1991; Einum and Fleming 1997; McGinnity et al. 1997, 2003; Clifford et al. 1998; Gross 1998; USFWS 2000; Bourret et al. 2011).

AquaBounty hopes to reduce the risk of gene flow between escaped AquAdvantage fish and wild Atlantic salmon (or other salmonids) by producing all-female, triploid GE salmon; the EA states:

> *The proposed conditions of use specify that a minimum of 95% of the AquAdvantage Salmon eggs sold for commercial production use would be triploid and 100% are expected to be female. Based on the method validation study, the actual average percentage of triploidy is expected to be 99.8%. The fertility of triploid females is negligible compared to normal diploid females. The combination of triploidy and an all-female population is expected to render*

[5] I have restricted my review to hybridization and introgression among fishes. The FDA should also consider the long record of these phenomena among plants, and even GE plants when contemplating the risks posed by GE salmon.

AquAdvantage Salmon effectively and functionally sterile resulting in complete reproductive containment. [EA at p. 86].

The EA is improperly comfortable with the genetic risks presented by escaped GE salmon. As noted above, interspecific gene flow in the wild between species does not require the presence or viability of both sexes – in fact, asymmetric or unidirectional hybridization and introgression are well known among fishes (e.g. Foerster 1935; Hubbs 1955; Campton 1987; McGowan and Davidson 1992; Kirkpatrick et al. 2007). Thus, the production of all-female lines of AquAdvantage salmon provides less than complete barriers to hybridization and introgression. Also, the induction of triploidy (infertility) is said to be 99.8% effective on average (EA p.37 footnote 18); but the terms of operation allows for retainment and use of egg batches with triploidy as low as 95%. Although this may seem impressive, the EA also describes the very large number of eggs that will be produced (e.g.~10,000 eggs/tray x 12-16 trays or up to 200,000 eggs per upwelling jars). Simple math indicates that 20-500 fish in every tray of AquAdvantage fish produced will be fertile. Thus, the prospect that some transgene fish will be fertile is very real and cannot be ignored.

Several indisputable lessons of the past century of fish biology suggest that FDA should not be sanguine about the potential damage that could be caused by even a few escaped AquAdvantage salmon, especially if they are even partially fertile:

1. people move fish into novel environments, intentionally and unintentionally;
2. these introductions frequently succeed (sometimes, against all odds) and non-native fish establish themselves in novel environments; and,
3. when this occurs, the results for native species and ecosystems are often devastating and irreversible
4. The mechanisms by which non-native fish impact the ecosystems they colonize include:
    a. predation on/competition with native species for food and other habitat resources
    b. competition for mates, mating territories, and reproductive opportunities that do not generate viable offspring, and thus waste the reproductive potential of the native population
    c. competition for mates, mating territories, and reproductive opportunities that generate viable offspring, which may then lead to introgression and permanent loss of a population (or species') unique genetic identity and genetic architecture

The effect of each of these mechanisms is amplified when non-native fish invade populations of of native species that are already imperiled – this would be the case for many, if not most, populations of Atlantic or Pacific salmon and trout (genus: *Salmo* and *Oncorhynchus* respectively; Slaney et al. 1996; Allendorf et al. 1997). The latter of these mechanisms (hybridization and genetic introgression) is of particular concern in this case because the AquAdvantage salmon carry novel genetic material (transplanted from a completely different species in a different family of fish) that would be transferred into economically, culturally, and ecologically important species if hybridization and introgression were successful.

Below, I summarize some general principles of hybridization and introgression and how they are relevant to the potential for escaped GE salmon to impact wild salmonids through genetic introgression (Table 1).

Table 1: Principles arising from decades of research into animal hybridization and genetic introgression (with a small sample of citations for each) that are relevant to the potential of escaped GE salmon to impact wild salmonids through direct genetic interactions.

Principle	**Selected Citations**	**Relevance to GE salmon**
Hybridization and introgression may be facilitated by asymmetry in the abundance of the interacting species or the sex ratio of either species	Hubbs 1955; Arnold 1997	The magnitude of potential impacts due to genetic introgression are not necessarily related to the number of GE fish that escape captivity, the sex ratio of escapees, or the frequency of such escapes
Gene flow may be facilitated by asymmetry in size or male aggressive behavior between species or between one species and their hybrids	Hubbs 1955; Arnold 1997; Rosenfield et al. 2000; Kodric Brown and Rosenfield 2003; Rosenfield et al. 2004	AquAdvantage GE salmon are expected to be larger and more aggressive than wild salmonids they may encounter; this may increase their mating success under some conditions)
Hybridization (formation of the 1st generation of organisms with interspecific heritage) is often the biggest barrier to gene flow, backcrosses and introgression are often less challenging to produce in the lab or in the wild	Arnold 1997; Rosenfield & Kodric-Brown 2003; Rosenfield et al. 2004	Difficulty in forming F1 hybrids of with GE Atlantic salmon may be much greater than that of producing genetic introgression after F1 individuals have been produced. The risk of transgenes escaping into wild populations is greater than may implied by any difficulty in producing F1 hybrids
Hybridization and genetic introgression are well-documented among salmonids in the laboratory and in the wild	Foerster 1935; Hunter 1949; Simon & Noble 1968; Smirnov 1972; Chevassus 1975; Campton 1987; Bartley et al. 1990; McGowan & Davidson 1992; Smith 1992; Dowling & Childs 1992; Smith et al. 1995; Gross 1998 (citing *pers. comm.* of A. Devlin); Rosenfield et al. 2000; Donald & Alger 2003	FDA should not doubt that the potential for hybridization and genetic introgression between Atlantic salmon and other salmonid species is very real. Obviously, there is also potential for "intraspecific introgression" from GE Atlantic salmon to non-GE Atlantic salmon.
Hybrids and backcrossed individuals may be as/more successful than one/both of their parental species and may lead to extirpation/loss of protection for native populations	O'Brien & Mayr 1991; Minckley & Deacon 1991; Dowling & Childs 1992; Epifanio & Philipp 2001; Arnold & Hodges 1995; Arnold 1997; Perry et al. 2002; Rosenfield et al. 2004; Campton & Kaeding 2005	Hybrid individuals are generally not protected by laws designed to protect the environment. More likely, these laws would prompt attempts to exterminate hybrids.
Hybrid formation and backcross viability/fertility are context dependent (as it is for parental species)	Smith et al. 1995; Arnold 1997; Hatfield & Schluter 1999; Kodric-Brown & Rosenfield 2004; Sundström et al. 2007	It is difficult/impossible to predict outcomes of ecological/genetic interactions based on a small number of test environment* genotype combinations

To the reader who is unfamiliar with the history of fish ecology, introductions, and invasions, the potential for AquAdvantage GE salmon to escape captivity, survive, and cause significant environmental damage may seem distant because this outcome would rely on the contemporaneous occurrence of several unpredictable events. However, those who have made a study of non-native species invasions and, in particular, genetic introgression following such invasions, know that unpredicted events frequently align to produce just devastating outcomes. In fact, approximately 40% of North America's threatened, endangered, and recently extinct fish species gained that status, at least in part, through hybridization and/or genetic introgression (Miller et al. 1989; Williams et al. 1989; Rosenfield et al. 2004) When species invasions occur, the results are often devastating on at least one species and they are almost always irreversible.

Below, I present two case studies from my own research that illustrate the potential for, and negative consequences of, AquAdvantage salmon escape with special reference to the principles described in Table 1. I want to stress that these two examples are far from unique in the fish biology literature or in the literature of genetically modified organisms[6].

Case Study #1 – Chinook salmon and pink salmon hybrids in the Laurentian Great Lakes.

My Master's thesis research described genetic hybridization (Rosenfield 1998) and genetic introgression (Rosenfield et al. 2000) between Chinook salmon (*Oncorhynchus tshwaytscha*) and pink salmon (*Oncorynchus gorbuscha*) after both of these species were introduced to the Great Lakes. Chinook salmon (the largest of the Pacific salmon) were introduced intentionally and repeatedly as a sport fish; this is quite a common phenomenon as Chinook salmon, like Atlantic salmon are a prized sport and commercial fish (Healy 1991; Quinn 2005). Pink salmon (the smallest species of Pacific salmon) were introduced into Lake Superior accidentally and only once after a plan to introduce them elsewhere in Canada was abandoned (Kwain and Lawrie 1981). Both species introductions were successful, despite the fact that these anadromous fish have no access to marine environments from the Great Lakes and other major differences between the Great Lakes ecosystem and the Pacific coast environments where both of these species originated. In fact, offspring of the single introduced population of pink salmon eventually colonized all of the remaining four Great Lakes (Kwain and Lawrie 1981; Wagner and Stauffer 1982).

My research demonstrated that these fish hybridized in the wild and my detection of backcross individuals (offspring between F1 hybrids and Chinook salmon) demonstrated that hybrids survived and were reproductively viable. In addition, genetic analysis of my small sample of hybrids revealed that each had been produced by Chinook salmon females mating with pink salmon males; in other words, the hybridization was unidirectional and did not require female

[6] Although neither of these case studies deals directly with Atlantic salmon hybridization and introgression, their ability to hybridize and introgress in the wild with brown trout (*Salmo trutta*) is exceptionally well-documented (e.g. McGowan and Davidson (1992 *and sources cited therein*) as well as multiple studies references in this letter and several laboratory studies have detected at least some viability among crosses with species in the salmonid genera *Salvelinus* (e.g. Foerster 1935; Chevassus 1977) and *Oncorhynchus* (Gray et al. 1993).

pink salmon or male Chinook salmon to proceed. This hybridization and introgression continues and the number of hybrids and hybrid generations continues to increase (Kirkpatrick et al. 2007).

Because these hybrid and backcross pink x Chinook salmon are isolated from natural, native populations of either parental species and because the Great Lakes environment is already so heavily engineered and modified, it is difficult to say what their long-term impact may be (Rosenfield et al. 2000). However, if any of these Great Lakes salmonids were transported to either coast, the ecological implications and those for Pacific salmon systematics, conservation, and biogeography, could be severe.

The relevance of this case study for the potential of AquAdvantage to escape, survive, and cause harm is clear:

- Small numbers of hatchery-spawned and reared fish, released accidentally and only once can, nevertheless, colonize vast areas (e.g. the Laurentian Great Lakes);
- Introduced fish can be reproductively successful despite the fact that their new environment prohibits them from completing their life cycle in typical fashion (e.g. neither species can migrate to marine environments though, in the wild, both species are almost always obligately anadromous; Quinn 2005);
- Different fish species can hybridize with each other and produce fertile offspring despite large physical differences and extremely long evolutionary separation (e.g. Smith et al. 1995);
- Asymmetrical hybridization (involving only one parent of each species) can occur (and is, in fact, common) and may proceed despite (or perhaps because) of asymmetries in the abundance and sex ratios of each species involved (i.e. production of all-female AquAdvantage salmon provides little protection against genetic interactions with other species or Atlantic salmon populations);
- Hybridization and genetic introgression are extremely context dependent (e.g. Smith et al. 1995; Arnold 1997; Seehausen et al. 1997; Hatfield and Schluter 1999). One would have thought that their side-by-side coexistence in numerous Pacific Coast habitats for millions of years would guarantee that pink salmon and Chinook salmon could not and would not interbreed; however, when the environmental context changed, hybridization and genetic introgression occurred.

<u>Case Study #2 – The sudden and near complete replacement of Pecos pupfish by its hybrid with sheepshead minnow</u>.

My doctoral research was conducted in the North American desert southwest. Here, several species in the genus *Cyprinodon* (pupfishes) are jeopardized by genetic introgression and/or competition with a distant relative, the sheepshead minnow (*Cyprinodon variegatus*; Echelle and Echelle 1992, 1994, 1997). The introductions of sheepshead minnow are believed to have occurred as a result of "bait-bucket" transfers by sportfishermen who, having finished fishing, dumped their remaining bait (sheepshead minnow) into waterways where native *Cyprinodon* species existed. In each of these cases, the sheepshead minnow was introduced well-outside of its native marine coastal environment into hot, freshwater, saline, or, sometimes hyper-saline inland lakes, rivers, and springs (Echelle and Echelle 1992). There is evidence that (a) the initial introductions involved only a few individuals and (b) that sequential transfers (from one fishing

spot to another) were required to transport the sheepshead minnow from their source population (probably on the Gulf Coast of Texas) to the waterways that were inhabited by native members of the pupfish genus (Echelle and Echelle 1992; Childs et al. 1997).

In the case I studied, a small population of sheepshead minnow introduced into the Pecos River in western Texas quickly hybridized with the rare endemic, Pecos pupfish (*Cyprinodon pecosensis*; Echelle and Connor 1989; Childs et al. 1996). The fertile hybrids of this initial cross replaced the native Pecos pupfish throughout most of its range in less than 5 years (Echelle and Connor 1989) vastly increasing this species' likelihood of extinction (Garrett et al. 2002; Rosenfield et al. 2004). The hybrids have been so successful that they have actually expanded beyond the former geographic range of Pecos pupfish to occupy new habitats (Echelle et al. 1997); the consequences of this range expansion on the Pecos River ecosystem or its fish fauna is currently unknown.

My research demonstrated that the explosive expansion of this hybrid swarm was due to a combination of sexual selection and hybrid vigor that favored the introduced species over the native species and that favored F1 hybrids over either parental species (Rosenfield and Kodric Brown 2003; Rosenfield et al. 2004). We also found that the degree to which hybrids were favored in competition with Pecos pupfish varied depending on the source of the native population – in other words, the rate and pattern of genetic introgression were resulted from environment*genotype interactions (Kodric-Brown and Rosenfield 2004).

Again, this case study demonstrates several salient points when considering the potential of AquAdvantage to escape, survive, and cause harm.

- An exceedingly small numbers of introduced fish, released unintentionally and only once can completely exterminate the entire population of a different species;
- Introduced fish can reproduce successfully (and even exceed the reproductive performance of a native species) despite the novelty of their new environment;
- Different fish species can hybridize with each other and produce fertile offspring that are even more fit than either of their parent species;
- People (and anglers and aquarists, in particular) tend to move fish from one water body to another, often repeatedly; when a fish population exists in the wild, there is some likelihood that it will be transported to new habitats by people (especially if it is a desirable food, bait, or aquarium species) or swim beyond its normal range when environmental conditions permit;
- When fish introductions occur, they are extremely difficult if not impossible to reverse. Clearly, the introgression of genetic material is irreversible, and, in an interesting sidenote to this case study, the Texas Department of Fish and Wildlife attempted to eradicate invasive sheepshead minnow from the small lake that served as the source population for introductions into the habitats of three rare, endemic, *Cyprinodon* species. Despite draining the lake, treating it with copious amounts of a potent fish toxin (rotenone), and introducing non-native predators to the pond, sheepshead minnow were still present in the lake (Garrett 2002).

Conclusion: My experience studying fish species behavior and ecology, invasive species dynamics, and salmonids, leads me to conclude that, despite AquaBounty's assurances, there is

nothing exceptional about the GE AquAdvantage fish or the controls that are described for their breeding or rearing facility that is likely to prevent their escape from captivity at some point in the future, perhaps more than once. This is particularly true because I understand that AquBounty intends to expand production in the future to other facilities not described in the current EA and to sell AquAdvantage eggs and juveniles to other entities – this raises the likelihood that GE salmon will escape into wild habitats. Also, the constraints placed on production of GE salmon by AquaBounty's existing protocols are clearly expensive and it is easy to believe that there will be pressure in the future to reduce the cost and complexity of these operations to increase profits from AquBounty fish production. Once FDA approves GE salmon production, there will be little public oversight of AquaBounty's fish containment protocols.

If and when AquAdvantage fish escape into the wild, there is a considerable chance that they will persist and interact with resident fish populations and ecosystems to produce negative consequences. Furthermore, there is a real likelihood that, once they have escaped, these fish will find their way or be transported to other environments where they can do even more harm – very simply, there is no way to put this genie back in its bottle. The consequences of GE salmon escape into the environment are potentially catastrophic, especially for small and imperiled populations of Atlantic or Pacific salmon with which they may interbreed and/or compete. Whereas aquaculture of Atlantic salmon has already caused great harm to wild salmon populations, the potential for additional harm caused by GE salmon is unknown (and potentially far worse) because they will carry novel genetic material (the transgene) into novel environments (both genetic and ecological). Thus, FDA's approval of GE salmon may affect the conservation status of ESA-listed populations of Atlantic salmon and warrants a formal ESA consultation with both USFWS and NMFS.

Finally, I am aware that FDA's approval of GE salmon (as proposed here) could serve as a precedent for approval of other GE animals; given the potentially extreme environmental consequences of GE salmon and/or other GE animals on natural organisms and ecosystems, I believe the FDA should set a very high standard here for preventing such unintended consequences in the future. Thus, I strongly recommend that the FDA prepare a full Environmental Impact Statement that covers all of the potential impacts I have highlighted here and that FDA initiate formal consultation with the US Fish and Wildlife Service and National Marine Fisheries Service under the federal Endangered Species Act regarding the potential effects of GE salmon production on endangered fish and wildlife species.

Sincerely

Jonathan Rosenfield, Ph.D.

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EDUCATION

UNIVERSITY OF NEW MEXICO PHD, BIOLOGY *2001*

Dissertation: Conservation of North American freshwater fish species: the micro and macro of speciation and extinction.

UNIVERSITY OF MICHIGAN MS, CONSERVATION BIOLOGY *1996*

CORNELL UNIVERSITY BS, NATURAL RESOURCES *1991*

PEER-REVIEWED PUBLICATIONS

Nobriga, M. and J.A. Rosenfield. *Submitted*. Toward a freshwater flow recommendation for an estuarine fish: putting stock in San Francisco Estuary longfin smelt. Submitted to Estuaries and Coasts 4/4/2013.

Rosenfield, J.A. *2010*. Conceptual life-history model for longfin smelt (*Spirinchus thaleichthys*) in the San Francisco Estuary. *CBDA Delta Regional Ecosystem Restoration Implementation Plan*, Sacramento, CA.

Rosenfield, J.A. and R. Baxter. 2007. Population dynamics and distribution patterns of longfin smelt in the San Francisco Estuary. *Transactions of the American Fisheries Society* 136:1577-1592.

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Smith, G.R., J.A. Rosenfield, and J. Porterfield. 1995. Processes of origin and criteria for preservation of fish species. Pages 44-57 *in* J.L. Nielsen, P. Brouha, and D. Powers, eds. *Evolution and the aquatic ecosystem: Defining unique units in population conservation.* American Fisheries Society special publication #17. Bethesda, MD.

Rosenfield, J.A. 1991. *Municipal Compost Management: Study Guide.* Cornell University Home Study Program, Cornell University, College of Agriculture and Life Sciences. Ithaca, NY. 50 pp.

Cobb, K. and J.A. Rosenfield, eds. 1991. *Municipal Compost Management*. Cornell University Home Study Program, Cornell Univ., College of Agriculture and Life Sciences. Ithaca, NY. 250 pp.

PROFESSIONAL EXPERIENCE

CONSERVATION BIOLOGIST THE BAY INSTITUTE 2008-PRESENT

Represent a regional environmental non-profit in efforts to protect and restore the native biological diversity and ecosystem services of the San Francisco Estuary. Advocate in policy forums, including testimony before state and federal regulators and legislative committees, for integration of best available science into management plans for the Estuary and its watershed in order to protect imperiled and economically valuable species. Analyze datasets to uncover ecosystem dynamics and recommend management of vital aquatic resources. Collaborate with technical experts and managers from the public, NGO, academic, and private sectors.

SOLE PROPRIETOR AQUATIC RESTORATION CONSULTING 2005-PRESENT

Initiate and manage consulting projects focusing on fish, wildlife, and habitat restoration in and around the San Francisco Estuary and its tributaries.

CALIFORNIA COORDINATOR SAVE OUR WILD SALMON 2005-2008

Lead California campaign to generate support for restoration of endangered salmon species on the Columbia/Snake Rivers. Activities include: develop and implement media strategy, meet with Congressional staff, recruit potential California NGO partners, grassroots organizing, and coordination of coalition members (sport and commercial fishers and environmental NGO's) in these activities.

DIRECTOR, SCIENTIFIC PEER-REVIEW CALFED ERP 2004-05

Manage peer-review of proposals for a multi-million dollar ecosystem restoration grant program. Collaborate on design of web-based proposal and reviewer management databases. Recruit and assign scientists to review technical proposals for both, CalFED's ERP and Science programs. Plan, host, and manage review panels.

POST-DOCTORAL RESEARCHER UC DAVIS 2002-04

Explore long-term datasets to uncover causes of longfin smelt (*Spirinchus thaleichthys*) population decline in the San Francisco Estuary. Products of this research form the basis of an Endangered Species Act petition to list the San Francisco Estuary.

STAR FELLOW US EPA 1998-00

Investigate ecology, behavior, and evolution of a rare desert fish species under the US EPA's graduate fellowship program. Manage 5 student employees and multi-year budgets for 3 government grants totaling >$85,000/yr.

RESEARCH ASSOCIATE SIERRA CLUB LEGAL DEFENSE FUND 1991-93

Analyze technical issues for lawyers in a public-interest, non-profit, environmental law firm.

PROFESSIONAL SERVICE

Manuscript/Grant Referee San Francisco Estuary and Watershed Science, North American Journal of Fisheries Management, Journal of Heredity, Conservation Biology, Behaviour, Behavioral Ecology, Biological Invasions, Global Ecology & Biogeography, Transactions of the American Fisheries Society, Reviews in Fish Biology & Fisheries, CalFed, California Fish & Game

Member Research and Science Committee, California Board of Forestry and Fire Protection

Doctoral Committee Member Dr. Andy Fields, University of the Pacific

ADDITIONAL TRAINING

SCUBA	PADI	*2011*
Non-profit Board Service	Pursue/Upstart	*2010*
Wilderness First Responder	Wilderness Medical Institute	*2008*
National Outdoor Leadership School	Alaska Outdoor Educator	*2004*
Legislative Lobbying	Save Our Wild Salmon	*2004*
Meeting Facilitation	The Western Network	*1997*

AFFILIATIONS

American Fisheries Society; Society for Conservation Biology; California Estuarine Research Society

Attachment 3

Sixty-Day Notice of Intent to Sue FDA Pursuant to the Endangered Species Act
Re: Approval of Genetically Engineered "AquAdvantage" Salmon

Region 5 Fisheries Program Comments on FDA approval process for
Aqua Bounty Technologies, Inc. (ABT)/AquAdvantage GMO salmon

Issue: FDA has released an EA and briefing packet which state the application for commercial approval is limited to raising the AquaAdvantage salmon outside the USA and then importing the processed fish for sale as food in the USA.

The transgenic broodstock would be mated and eggs incubated to eyed stage in a multiple-confinement hatchery on Prince Edward Island, Canada. Eyed stage eggs would be shipped to Panama for growout in a multiple-confinement high-elevation, undisclosed location next to a river. At 18 months of age, fish would be harvested and processed in Panama for shipment to USA for sale.

The 'multiple-confinement' includes biological confinement (eyed eggs that are all-female triploids), 3-5 forms of mechanical and physico-chemical confinement, and geographical confinement (if any eyed eggs or fry escaped from PEI hatchery, presume fry would end up in surrounding seawater and die there; if any grow-out fish escaped the Panama grow-out facility fish would enter the river that has lethal water temperatures downstream plus many dams.

Preferred FWS position: Given all the unknowns and uncertainties regarding the possible ecologic and environmental effects of these fish, combined with the awkward situation where an agency (FDA) whose jurisdiction is not focused on natural resources is entrusted with the authority to approve an act which poses such threat to the country's natural resources, we believe it is premature to approve this request for commercial rearing of transgenic salmon.

Comments related to Regulatory Authority/Oversight.

- If the two locations in Canada and Panama are truly the only places these transgenic fish will ever be raised, then perhaps the EA Section 7 endangered species consultations by NOAA and USFWS are unnecessary or of little importance. However, recent statements by AquaAdvantage indicate if their application is approved they intend to sell eyed-eggs to additional confined grow-out operations in other locations. It is my understanding that current regulations would not require the FDA to publicly release these future EAs before approval. It is also unclear what the USFWS or NOAA roles would be if these facilities are in foreign locations. The current EA under review was released publicly because it sets a crucial precedent regarding human consumption of a transgenic vertebrate (fish). This is why the scientific quality of this first EA sets such a crucial precedent. However, our review and those of other scientists found numerous issues with the scientific quality and completeness of the EA. If the FDA approves the sale of processed AquaAdvantage salmon in the USA and the company plans to submit additional EAs to grow fish at other facilities then the current EA is too narrow. The FDA should consider a full EIS that takes into account the full scale at which the company intends to sell eyed-eggs over say the next 10 years.

- How will the FDA assure, monitor, and verify that multiple confinement is continually achieved at the two facilities and in future facilities as farming of these fish proliferates?
    - Failure analysis of triploid induction should quantify the frequency of triploid failure.
    - Do exceptional diploids occur among treated transgenic fish, and if so, are they fertile?

- Failure analysis of geographical confinement should include data on how AquaAdvantage salmon respond to changes in temperature and season.

- The Service seems to have no regulatory authority outside of ESA where applicable.

- This may be something that would need international regulations or agreements in writing through NASCO, etc. to address worldwide trade in these fish.

- After checking with the Maine FO, and based on the Army Corps Section 10 permit (of the Rivers and Harbors Act) for the aquaculture companies, for existing aquaculture sites, the aquaculture companies are not allowed to use transgenic salmon in their net pen sites. For new sites, a new permit would need to be developed.

- Ultimate regulatory authority should be placed with the agencies charged with responsibilities to manage wild stocks and their habitats. Once "the genie is out of the bottle", and into the environment, the consequences affect the general public and the common good. Looking at invasive species as examples of "genies", none to my knowledge have been recaptured into their respective "bottles".

- Consider escaped Atlantic salmon on the west coast and their impact on endangered and threatened Pacific salmonids. These fish are evidently surviving, reproducing, and producing fry and parr. We must assume that smolts will result and that the life cycle completed at some point in time. Were the present regulations sufficient to prevent this situation? Do we know the ultimate ecological consequences? How does this impact the numerous listed aquatic species under the ESA?

- In the case of Atlantic salmon, management responsibility is shared between the FWS and NOAA. Keys to this argument are the authorities for regulation and management of anadromous fish, and the time spent by such fish in either freshwater or saltwater. Regulatory authority must be viewed from the "worst-case" scenario, and not partitioned into a variety of regulatory agencies with disparate turf, but, ultimately, injury to wild fish populations and their habitats and the associated aquatic communities must take priority over economics and development.

- A cascading regulatory framework, where such activities are reviewed, evaluated, and if approved, move to the next level or cascade for review would be optimal. The ultimate or final review would lie with the authorities who manage the potentially impacted species. This would promote a "first do no harm" strategy to the target species and its habitat.

- The current regulatory process is not adequate. Prime examples are NDPES permits with EPA, Corps permits regarding placement of aquaculture netpen facilities, and importation/exportation of non-native species or viable gametes, eggs, etc, into/out of the country. Considering the numerous failures of the above and subsequent impacts to wild fish and their habitats should be enough to determine that we do not yet deal with evolving genetic issues in a reasoned, rational, and risk-adverse manner. The federal agencies must speak with one voice. Again, a tiered mechanism where accountability is ultimately fixed and the final decision point is reached is recommended; that fixed point should rest where the ultimate harm may be inflicted upon the public resources. In the case of

Atlantic salmon, those public resources are also far beyond just the U.S., but also into Canada, the European Union, Russia, and all other NASCO convention countries.

Comments related to Environmental/Ecological Impacts.

- Transgenic fish, regardless of where they are, pose a clear and present danger to wild fish populations. Given the extremely low populations of wild Atlantic salmon in the Maine DPS, any interaction between wild and transgenic salmon must be considered a serious threat, which can disrupt redds of wild fish, compete with wild fish for available food and habitat, interbreed with wild fish, transfer disease and/or parasites, and degrade benthic habitat. The scientific literature is full of actions indicating that interactions of wild fish and aquaculture escapees (read transgenic escapees) may lead to decreased numbers of wild fish and in the worst scenario, lead to extirpation of the remaining stocks in the U.S.
- History dictates it is reasonable to assume that fish held in aquaculture facilities, either land- or water-based, will escape unless strict quarantine /water treatment/screening/ bioengineering modifications are in place and aggressively monitored. And even then, it must be assumed that escape will still occur, and protocols must be in place to deal with such a non-native organism released into the environment, and its subsequent effect on native species, habitat, and aquatic communities. Transgenic fish, whether reproductively viable or sterile, must be maintained only in biosecure (zero discharge) land-based facilities ideally positioned outside of any wild fish watersheds until appropriate laboratory and field research has been undertaken to ensure that the risk of adverse effects on wild fish has been minimized.
- ABT appears to have established several physical and biological containment mechanisms to prevent the escape of AquAdvantage salmon. However, there is still risk of escapement and we think this risk is most prevalent at the PEI facility. If the brood stock from the PEI facility were released either accidentally or with malicious intent, we do not feel enough evidence has been provided to conclude the risks to natural populations of Atlantic salmon in Canada and the U.S. are negligible. Additional experimentation needs to be conducted to verify that any escapees from the PEI facility will not be able to tolerate the brackish water in the vicinity of the facility. Also, the lack of information on the transport procedures from PEI to Panama is troublesome. It is during this stage of the operation that malicious activities could result in these fish being lost from the direct control of ABT.
- The Panama grow-out facility appears to minimize environmental risks of these fish. If fish were to escape the Panama facility, we agree there may be little chance that they would outmigrate from the river and survive due to the warm temperatures in that locale. However, additional experimentation on these fish is needed to determine the upper incipient lethal temperature limit to ensure that these fish could not survive the warmer temperatures in the lower river. Because rainbow trout are established in the river at the Panama facility, it is very likely that escaped AquAdvantage salmon would survive in this portion of the river and potential effects on native fish populations remain.
- The diploid GMO salmon that are produced in this process are fertile, and the modified gene is passed from one generation to the next. The triploids are supposed to be sterile. The concern is twofold: escape by the diploids or their reproductive products and successful reproduction in the wild, and incomplete induction of triploidy allowing reproduction of individuals thought to be non-

reproductive and therefore potentially kept under less secure conditions which could allow an escape event.

- If there is an escape event, competition from the GMO salmon would negatively impact the wild stocks. Research has shown that aquaculture-raised salmon can outcompete wild salmon, and given the already endangered status of the wild stocks, any additional threat is amplified in their impacts. References are available.

- The EA does not give the full information needed to predict environmental effects of AquaAdvantage salmon.
    - Different environmental conditions can alter the differences in overall fitness between transgenic and non-transgenic fish (e.g., Sundstrom et al 2007).
    - GH transgenesis in AquaAdvantage salmon and other salmon enhances appetite and alters behavior. Hence, they are likely to explore novel prey and novel areas (Sundstrom et al 2003).
    - Lower fitness of transgenic fish when they first escape does not necessarily translate into permanently lower environmental risk (Kapuscinski 2007 and Ahrens and Devlin in press)

The key point here is it could be very misleading to base environmental risk assessment on data for only a few traits that do not span the whole life-cycle and are measured under the limited range of environmental conditions and time frames. In short, the EA could be overly simplistic concerning statements of poor fitness of AquaAdvantage salmon without the scientific evidence required to support such a claim.

- Aside from the potential spread of the GMO growth gene if they escape and successfully reproduce, the genetic origin of the broodstock that has been developed is likely genetically distinct from Maine salmon. The concern is if escape and reproduction occurs, this could lead to a disruption of the locally adapted gene complexes of the endangered populations. In the FDA report-petition, we didn't see reference to the origin of the broodstock.

- Where the EA and briefing document give quantitative data related to environmental risk, they omit statistical analyses needed to scientifically verify conclusions.
    - Missing from many tables are: sample size, standard errors, statistical power, or description of statistical tests used.

- The EA and briefing document only compare AquaAdvantage salmon to farmed salmon but environmental risk assessment requires also comparing transgenic fish to wild fish in a similar ecological niche.
    - Genetic consequences of transgenic fish interbreeding with wild relatives are anticipated to be very different from those of domesticated salmon.

- The list of adverse effects which could be caused by transgenic fish throughout its lifecycle include:
    - Escape, with impacts on interbreeding with wild salmon, gene introgression into wild salmon stocks, hybridization with brown trout.

- Disturbance of habitat or displacement of wild stocks as a result of competition for resources, predation, or even cross-mating resulting in population impact.
- Spread of bacteria, viruses, parasites to wild salmon and other aquatic/estuarine species
- Introduction of chemicals used to treat fish diseases.
- Transgenic fish may also exhibit ecological impacts associated with their degree of fitness, interaction with other organisms, role in ecological processes, and potential for dispersal and persistence.

➢ The FDA document rationalizes weaknesses in the proponent's testing/experimental design, e.g., uncertainty, lack of historic records, lack of information.
- Pg 21 – "The primary area of uncertainty is determining the actual rate of adverse outcomes in grow-out facilities, as the relatively heavy culling rate that occurred in the space-limited broodstock facility described in these data sets may have influenced the apparent rate of abnormalities.";
- Pg 26 – "According to the information ABT provided to us, ad hoc culling was historically effected in association with inventory management activities (i.e., removing excess inventory, biomass reduction, separation of fast-growing individuals from slow-growing individuals, and broodstock selection) and often no data were collected on fish culled as excess inventory, particularly early life stages (i.e., eggs, yolk-sac fry and first-feeding fry). Although not specifically described in the report of this study, one would reasonably expect that the culling was done in a manner that selected for improving the broodstock, thus retaining the healthiest and fastest growing individuals in the facility. We have no reason to believe that ABT's culling practices were inconsistent with the approaches used in broodstock operations in the commercial salmon industry; these may differ from commercial grow-out facilities";
- Pg 42 – "Information on smoltification for triploid GE salmon is currently lacking."
- Pg 43 notes that "In addition, Stevens et al. (1998) caution that future growers of growth enhanced salmon should be prepared to either deliver more water or more oxygen in the water per unit of biomass of GE fish compared to that required by non-GE salmon." Although more pertinent to Canada and Panama, we note that delivering more water may affect ground and surface water availability, as well as water treatment facilities.

➢ Pg 121-122 describe the potential for accidental releases of AquAdvantage Salmon due to natural disasters, but the briefing package doesn't address the potential for more frequent extreme events due to climate change.

➢ We would prefer the production of these fish for the entire operation was conducted at the Panama facility. This would keep broodstock geographically isolated from natural populations of Atlantic salmon, eliminate risks associated with transporting these fish from Canada to Panama, and the Panama facility represents a location where the likelihood of establishment of an introduced migratory population is highly unlikely in the event fish escape the facility.

➢ We are pleased to see that the ABT product label warns "fish must be reared in land-based, highly contained systems that prevent their release into the environment" and that the "fish cannot be reared in conventional cages or net pens deployed in open bodies of water." However, if AquAdvantage salmon are approved for commercial production, these fish may eventually find their

way into commercial net pens either through illegal means or through approving future applications. This is a slippery slope and the only real way to be risk adverse is to not approve the current application by ABT.

- Now that there is a developed product, and if it is approved by the FDA for use, considerations about the potential implications to the listed Atlantic salmon stocks in Maine would need to be addressed, including the genetic issues, such as threats such as introgression if escapes occurred.

- We are concerned about the possible sale and transfer of the eggs to other countries where escapement could occur and triploids are not a 100 percent defense.

Note: Many of these comments also cover the Environmental Assessment (EA) for AquAdvanatage salmon dated August 25, 2010. Region 5 personnel have consulted with Dr. Anne Kapuscinski, Professor of Sustainable Science, Dartmouth College, NH. We agree with many of Dr. Kapuscinski's comments on these documents; many comments come directly from her written comments submitted to FDA as part of the public review process. Dr. Kapuscinski is a leader in the field of environmental risk assessment of transgenic fish. The USFWS has benefited from her knowledge on this issue by having her as a keynote speaker at the Future Challenges Workshop at NCTC - August 10-13, 2004 where she spoke about transgenic fish and the need to develop effective ecological risk assessment approaches and regulatory processes (http://www.fws.gov/science/FCWorkshopNCTC0804.html). In addition, Dr. Kapuscinski led a conference this summer which focused on Genetic Biocontrol of Invasive Fish. FHC Asst. Director Bryan Arroyo was a speaker at this conference along with FDA and NOAA administrators to discuss the regulatory process involved with approval of transgenic fish in the USA (http://www.seagrant.umn.edu/ais/biocontrol). Folks assembling any briefing products for Bryan Arroyo should review chapters 5 and 6 in Dr. Kapuscinski's 2007 book titled, "Environmental Risk Assessment of Genetically Modified Organisms, Vol 3: Methodologies for Transgenic Fish", CABI Publishing, UK. 304pp. Craig Martin or Bryan Arroyo should have a copy of this book that was distributed at the Genetic Biocontrol of Invasive Fish conference.

SPECIFIC COMMENTS

Page 21: "...escapees from containment would be less capable of surviving."
There needs to be more information here as to what the decrease in survivorship is. What is the mortality rate and exactly how was this evaluated.
Page 32: 48 fish distributed over four groups does not seem like much of a sample size. How were these fish selected from the 400 - 800 candidates (100 - 200 for each group)?
Page 26: There should be a better description of what these ranks in the Table are. What is slight, moderate and severe?
Page 26: Is there any information on the proportion of fish that are culled and how this compares to other commercial hatcheries?
Page 43: Although the critical oxygen concentration may be higher for GE fish, it is likely that in most natural aquatic systems DO levels will be greater than the critical oxygen concentration and thus not affect survival in natural systems.
Page 52: What is an acceptable rate of triploid induction?
Page 57: So is 2% too much risk in the case of escapees?
Page 58: Don't understand the reasoning why p2 is less than p1?
2- 5% of the fish may not be sterile.

Page 115: It is good to see that ABT has issued this warning statement. However, this does not preclude the illegal rearing of these fish in open bodies of water.
Page 116: What is magic about 3 - 5? Some justification for this number should be presented here.
Page 120: If rainbow trout persist to any degree, survival of Atlantic salmon in this waterbody is also likely. High gradient with abundant rock and boulder substrate would be suitable habitat for juvenile salmon.
Page 123: Not sure about the idea that older fish could not survive the sudden transition from freshwater to brackish water. Natural Atlantic salmon often move back and forth from fresh to brackish water while on spawning runs and kelts can quickly move into brackish waters following spawning. Not convinced that older fish would not survive if they escaped the PEI facility.
Page 123: Agree that fish would likely not be able to survive migration to the marine environment, but this does not preclude establishment within the river near the grow-out facility. This could result in competition with native fishes.
Page 124: Experiments to determine the upper incipient lethal temperature limit are easy to conduct. ABT should do these experiments to verify the assumption that the upper incipient lethal temperature limit of AquAdvantage salmon is the same as for natural Atlantic salmon.
Page 124: Food availability must not be too limiting - rainbow trout are persisting.
Page 127: Quantitative evaluation of the effectiveness in creating an all-female population needs to be done.
Page 128: But male Atlantic salmon are present in the environment (at least in Canadian waters) should AquAdvantage salmon escape the PEI facility.
Page 128: So according to NASCO the procedures used for AquAdvantage salmon would be OK?
Page 129: De-smolitification should be empirically tested for older AquAdvantage salmon.
Page 131: Although populations of Atlantic salmon in PEI and other rivers in North America are dependent on hatchery input, there are still some naturally reproducing fish. Escape from the PEI facility has the potential to compromise the genetic integrity of remaining natural populations.

Attachment 4

Sixty-Day Notice of Intent to Sue FDA Pursuant to the Endangered Species Act
Re: Approval of Genetically Engineered "AquAdvantage" Salmon

United States Department of the Interior

FISH AND WILDLIFE SERVICE

06 October 2010,

This letter briefly outlines several concerns that the Conservation Genetics Community of Practice (COP) has raised regarding the Veterinary Medicine Advisory Committee (VMAC) Briefing Packet for AquAdvantage Salmon.

The AquAdvantage Atlantic salmon (*Salmo salar*) is a genetically engineered (GE) salmon that grows at a rapid rate due to the alteration of their growth hormone gene. Specifically, a gene construct is synthesized using a growth hormone gene (GH; derived from the Chinook salmon, *Oncorhynchus tshawytscha*, pituitary gland) that is linked to an anti-freeze protein regulator sequence (opAFP) found in Ocean pout (*Zoarces americanus*). The anti-freeze regulator acts like a switch keeping the GH protein from turning off and allowing for continued growth of the fish. This gene construct (opAFP-GH) is then injected into Atlantic salmon eggs to form an all female broodstock that will produce future product.

The Briefing Packet provided by VMAC is a detailed synopsis regarding the safety and effectiveness of genetically engineered (GE) Atlantic salmon produced by Aqua Bounty Technologies. The packet provides relevant data to assess the following five critical issues or risks associated with genetically engineered organisms:

1) molecular consequences of the insertion of a gene construct into a lineage of Atlantic salmon,
2) phenotypic effects of the insertion of a gene construct in a lineage of triploid mono-sex Atlantic salmon,
3) genotypic and phenotypic durability of such gene construct,
4) analysis of food feed and safety, and
5) environmental consequences.

COP comments are based on concerns that deal with the environmental risk analysis provided by VMAC and the regulatory oversight of such a program. While this document has been reviewed by the COP, we strongly recommend that other genetic communities such as the American Fisheries Society and National Academy of Sciences review this and other supporting documents as unbiased third party reviewers.

Environmental/Ecological Impacts

The Briefing Packet provides compelling evidence that the risk of escapement by GE AquAdvantage salmon is minimal; however, *it falls short of providing an actual risk assessment of putative environmental damages in the event of escapement.*

First, the environmental analysis should provide an historical overview of the general risks associated with escapement or hybridization of GE and wild type individuals. Has escapement of a GE organism ever occurred? What were the environmental consequences of such an escapement? An overview would provide readers with an understanding of the potential harm (and the degree of harm) posed by GE organisms even when the risks of escapement is low. Both of these risks (risk of escapement and degree of harm if escaped) should be more accurately quantified prior to any Environmental Assessment ruling.

Second, the biological containment at either the PEI or Panama facilities along with the possible interaction of AquAdvantage salmon with endangered wild salmon stocks is of great concern to the COP. To this regard, Aqua Bounty Technologies has established several physical and biological containment mechanisms to prevent the escape of AquAdvantage salmon and the Environmental Assessment indicated escapement risk and establishment risks were low. However, history dictates that fish held in aquaculture facilities, either land- or water-based, escape. In addition, the information provided by Aqua Bounty Technologies for the likelihood of establishment relies on the assumption that farmed Atlantic salmon have not established themselves in North America. This assumption is clearly violated because Atlantic salmon juveniles have been found in several streams in the state of Washington as well as British Columbia. While interactions of these fish with native salmon are unknown, any interaction between wild and transgenic salmon must be considered a serious threat. Numerous scientific publications have documented that interactions of wild and introduced fish have led to decreased numbers of wild fish (for ESA listed Atlantic stocks this is of great concern).

As highlighted in the previous paragraph, the Environmental Assessment does not give the full information needed to predict the environmental effects of AquAdvantage salmon. The interpretation of findings could be very misleading because conclusions are based on data for only a few traits that do not span the life-cycle of the organism and are measured under a limited range of environmental conditions and time frames. The COP recommends incorporating the following scientific data in future environmental risk assessments:

- differences in overall fitness between transgenic and non-transgenic fish (e.g., Sundstrom et al 2007);
- shifts in primary prey and utilization of habitat for AquAdvantage salmon (Sundstrom et al 2003).
- assessing how fitness of transgenic fish, when they first escape, translates into environmental risk (Kapuscinski 2007 and Ahrens and Devlin in press)

It is the view of the COP that the Environmental Analysis is overly simplistic and does not adequately capture the actual risk of environmental damages to wild Atlantic salmon or the ecosystem. Additional studies will be necessary to assess this risk and include (but not limited to)

- interbreeding with wild salmon, gene introgression into wild salmon stocks, hybridization with brown trout,
- disturbance of habitat or displacement of wild stocks as a result of competition for resources, predation, or even cross-mating resulting in population impact,

- spread of bacteria, viruses, parasites to wild salmon and other aquatic/estuarine species,
- ecological impacts associated with their degree of fitness, interaction with other organisms, role in ecological processes, and potential for dispersal and persistence.

Regulatory Authority/Oversight comments

Aqua Bounty Technologies currently has various standard operating procedures to minimize escapement and test for durability of the gene construct; however, the COP fails to see any oversight policy in place for assessment, monitoring, and enforcement of these procedures. The current regulatory process is ineffective in handling such a situation. Economics and development take priority over the potential impact to the species or ecosystem. Instead, agencies (FDA, NOAA, USFWS) might benefit from a tiered approach to regulatory authority where such activities are reviewed, evaluated, and if approved, move to the next level for review. The ultimate or final review should lie with the authorities who manage the potentially impacted species (in the case of Atlantic salmon, those public resources are also far beyond just U.S. jurisdiction and include Panama, Canada, the European Union, and Russia). This approach would promote a "first do no harm" strategy designed to protect public resources (i.e., the target species or ecosystem of concern).

Concluding remarks

There are several unknowns and uncertainties regarding possible genetic, ecological, and environmental effects of AquAdvantage salmon that must be elucidated before an environmental risk assessment can be thoroughly evaluated and approved. This, along with a situation where regulatory oversight is adequate at best, suggests that approval of Aqua Bounty Technologies' request for commercial rearing of AquAdvantage salmon is premature.

Sincerely,

Meredith Bartron, PhD
Denise Hawkins, PhD
Greg Moyer, PhD
John Wenburg, PhD
Wade Wilson, PhD

Attachment 5

Sixty-Day Notice of Intent to Sue FDA Pursuant to the Endangered Species Act
Re: Approval of Genetically Engineered "AquAdvantage" Salmon

United States Department of the Interior

FISH AND WILDLIFE SERVICE
Warm Springs Fish Technology Center
Conservation Genetics Laboratory
5308 Spring Street
Warm Springs, Georgia 31830
Phone: (706) 655-3382 FAX: (706) 655-3389

30 September 2010

This letter briefly outlines several criticisms and concerns regarding the Veterinary Medicine Advisory Committee (VMAC) Briefing Packet for AquAdvantage Salmon. While I feel I can provide a general overview and constructive criticism of this briefing document, more time would allow for a detailed review.

The Briefing Packet provided by VMAC is a detailed synopsis regarding the safety and effectiveness of genetically engineered (GE) Atlantic salmon produced by Aqua Bounty Technologies. The packet provides relevant data to assess the following five critical issues or risks associated with genetically engineered organisms:

1) molecular consequences of the insertion of a gene construct into a lineage of Atlantic salmon;
2) phenotypic effects of the insertion of a gene construct in a lineage of triploid mono-sex Atlantic salmon;
3) genotypic and phenotypic durability of such gene construct;
4) analysis of food feed and safety;
5) environmental consequences

Much of my major concerns are with the environmental risk analysis provided by VMAC and are addressed below. I do not feel comfortable commenting on the analyses of food feed and safety because they are not my areas of expertise. I would also recommend that the American Fisheries Society and National Academy of Sciences review this and other supporting documents as unbiased third party reviewers.

Major criticisms:

The Briefing Packet provides compelling evidence that the risk of escapement by GE AquAdvantage salmon is minimal; however, it falls short of providing an actual risk assessment of putative environmental damages in the event of escapement. The environmental analysis should provide an overview of the general risks associated with escapement or hybridization of GE and wild type individuals. An overview would provide readers with an understanding of the potential harm (and the degree of harm) posed by GE organisms even when the risks of escapement is low. Both of these risks (risk of escapement and degree of harm if escaped) should be more accurately quantified prior to any Environmental Assessment ruling.

I am also concerned with phrases like "are unlikely to survive if exposed to high salinity and low temperature" when no data have been collected on AquAdvantage salmon to evaluate the likelihood of these scenarios. Survival under geographical and geophysical conditions should be evaluated at all life stages in an effort to quantify the likelihood of such escapement scenarios.

Finally, while Aqua Bounty Technologies currently have in place various standard operating procedures to minimize escapement and test for durability of the gene construct, I fail to see any policy in place for monitoring and enforcement of these SOPs by the Food and Drug Administration. The environmental impact of escaped GE salmon is of great concern; therefore, the FDA should carefully monitor each facility and establish/enforce a zero tolerance policy for failure to meet specified containment guidelines.

Minor criticism:

1) Who were the reviewers (including their backgrounds) for this document? I have concerns over whether salmon ecologists and biologist have critiqued the environmental analysis of this document.
2) Scientific names of ocean pout, Chinook, and Atlantic salmon should be reported.
3) page 13 section B.5. A reference should be provided.
4) page 13 section C indicates that supporting data was provided – please reference these data in an appendix.
5) page 14 section A. Again, "data submitted support the Molecular Characterization of . . . ." please reference these data.
6) page 16. section i. "Repeat regions like this are quite variable and nonessential". This needs a citation. While they do not code for anything, repeat regions are probably not non-essential; rather, they serve some purpose.
7) page 43 "AquAdvantage salmon may have reduced tolerance for low DO" – there is much uncertainty in this statement as there is no data to support or reject this. Either a citation is warranted or consider eliminating this statement.
8) page 110 section A the working definition of AquAdvantage salmon. So what are the ones called that are <100 g body weight but are genetically engineered?
9) page111. "The VMAC meeting will be held to solicit comments from the appropriated outside experts (VMAC members)". Do VMAC members really have the expertise to rule on the environmental assessment? I would argue that outside experts such as salmon biologists be considered as a part of this panel.
10) page 123 section a. Again, the conclusion is based on limited data. More studies are necessary to determine containment risks (see major criticisms).
11) page 126. I would argue that a more stringent 98-99% probability of being triploid be invoked. The risk of escapement is too great to be relying on a 95% probability.

Please feel free to contact me regarding further questions or concerns.

Sincerely,

Gregory R. Moyer, PhD

Regional Geneticist

Email: Greg_Moyer@fws.gov

EXHIBIT SIX

(U.S. FWS Conservation Genetics Community of Practice (CoP) letter to U.S. FDA, October 6, 2010)

Attachment 6

Sixty-Day Notice of Intent to Sue FDA Pursuant to the Endangered Species Act
Re: Approval of Genetically Engineered "AquAdvantage" Salmon

For Internal Use Only December 5, 2011

Talking Points for Senate Commerce Committee Staff Briefing on S. 1717
"Prevention of Escapement of Genetically Altered Salmon in the United States Act"

1. Comments on the bill

- S. 1717 does not directly address the issue of escapes and its title is misleading. This bill makes it illegal to "ship, transport, offer for sale, sell, or purchase genetically altered salmon or other marine fish, or a product containing genetically altered salmon or other marine fish, in interstate or foreign commerce; or have custody, control, or possession of, with the intent to ship, transport, offer for sale, sell, or purchase genetically altered salmon or other marine fish, or a product containing genetically altered salmon or other marine fish, in interstate or foreign commerce."

- NOAA's Aquaculture Policy (June 2011) is to support both aquaculture innovation and the protection of wild species and ecosystems. The policy's guidance for aquaculture in federal waters (Appendix 1) establishes an "ecosystem compatibility" goal whereby NOAA will:
  - develop, implement, and enforce conservation and management measures for aquaculture designed to maintain the health, genetics, habitats, and populations of wild species; maintain water quality; prevent escapes and accidental discharges into the environment; and avoid harmful interactions with wild fish stock, marine mammals, birds, and protected species
  - support the use of only native or naturalized species in Federal waters unless best available science demonstrates use of non-native or other species in Federal waters would not cause undue harm to wild species, habitats, or ecosystems in the event of an escape.

- If Congress is interested in working on a bill to prevent escapes of live GE salmon or live GE marine fish, NOAA Fisheries can offer technical assistance on appropriate requirements based upon risk analysis and sound science. Preventing escapes is essential to minimizing the risks to genetic deterioration of wild fish populations, especially endangered and threatened salomids whose effective population sizes are particularly vulnerable to the effects of interbreeding. NOAA Fisheries feels this risk management is best addressed by current regulations and good management practices (which may address, for example, handling and containment of fish, sterilization, and location of facilities).

- It is the opinion of NOAA Fisheries Service that this bill S. 1717, as written, would set an unacceptable precedent by altogether closing a door on future research and innovation for sustainable seafood production in the United States and possibly resulting in an unintentional ban on valuable technologies, such as the use of DNA based vaccines that could aid in disease control in hatchery raised fish, such as Alaskan salmon; the use of GE technologies to halt the spread of invasive species, novel biologics from recombinant DNA technology, and others.

- NOAA Fisheries recognizes that the use of genetically altered organisms is common within traditional agriculture and this bill would set a precedent by effectively banning transgenic marine fish, and may be seen as inconsistent with laws covering other terrestrial animals, plants, marine organisms, or freshwater fish. In addition, the Administration has expressed support for the export of genetically-modified plants. The bill's prohibition on export of genetically-modified salmon or other marine fish would be inconsistent with this provision.

- Including products of GE fish in the prohibition is inconsistent with the stated purpose of preventing escapes.

- The bill could have implications for the domestic oyster industry on the East Coast, as 90% of oysters are triploid oysters and would be considered a "marine fish" under the bill. As such, oyster producers that ship interstate would be in violation of the bill.

- While the bill defines "allotransgenic" and "autotransgenic", it does not include a definition of "transgenic". According to NOAA Fisheries understanding of this term, "transgenic" could include techniques that sterilize fish, as well as DNA-based vaccines for that aid in disease control in hatchery raised fish.

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Comment [BMS1]: Can you please fill in which segment of the oyster industry would be affected.

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Comment [BMS2]: Can you please provide a bit more as to why that is not ideal?

2. Update on work with FDA on GE salmon application

- NOAA has provided technical assistance to the FDA in preparation of the Environmental Assessment for AquaBounty's genetically engineered organism (AquAdvantage salmon). As per the EA, NOAA understands that AquAdvantage salmon is meant to be grown in contained culture (in land-based facilities or other means of containment not deployed in open water), and is produced as a sterile, single-sex fish. The EA describes the potential environmental risks of AquAdvantage salmon under the specific conditions of use; namely the production of eggs in Canada and the grow-out and processing of fish in Panama.

- According to the Executive Summary of the EA, "the likelihood of escape, establishment, and spread of AquAdvantage Salmon is extremely small due to the multiple layers of containment measures, including physical, physio-chemical, geographic/geophysical, and biological measures implemented at the sites of manufacture, use and disposal." According to the EA, even if escapes occur the fish would most likely not survive, due to the high salinity in the case of Canada (lethal to eggs and hatchlings) and to the high temperature in the case of Panama (lethal to adult fish).

- A NOAA Fisheries Aquatic Animal Health Expert, along with FDA staff, visited AquaBounty's grow-out facility in Panama, which is designed for rearing AquAdvantage Salmon® from the eyed-egg stage to market-size, on November 10-12, 2009. This site visit was conducted primarily to verify that the conditions of rearing and containment at the grow-out facility were as described in the draft EA, and to evaluate any other factors which would influence the potential for escape.

- NOAA Fisheries is waiting on the issuance of a final Environmental Assessment by FDA. We do not have any information as to the timeline for this, or FDA's final decision on the AquaBounty salmon application.

3. Status of ESA consultations on GE salmon

- The FDA submitted to NOAA Fisheries an Environmental Assessment, supporting documents, and their determination that the approval of the application for AquAdvantage Salmon® will have no effect on the Gulf of Maine distinct population segment of Atlantic salmon listed under the Endangered Species Act of 1973 (ESA). Because NOAA Fisheries does not review no effect determinations, that letter fulfilled FDA's obligation under section 7 of the ESA.

4. Enforcement implications

Overview

- Senate Bill 1717 the "Prevention of Escapement of Genetically Altered Salmon in the United States Act" has significant enforcement implications. To be specific, it poses many challenges to effective enforcement in light of the provisions and current capabilities of NMFS, OLE and OGC Enforcement Section related to traceability of genetically engineered salmon, forensic testing needs for effective enforcement and prosecution and general enforceability concerns.

- In order to provide effective enforcement, fish must be accountable and traceable throughout the market process. This facilitates traceability of fish and fish products wherever they are found. It also enables enforcement to intercept unlawful seafood at various funnel points such as interstate highways, airports and secondary dealers. Required documentation and labeling protects markets, prevents downward price trends, enhances enforcement and protects the consumer.

    1- Inspection – To include at-sea and shore side facilities constituting the aquaculture operation as well as processing, point of sale, and storage facilities. Inspections should also occur upon import, export and re-export to and from the United States.
    2- Auditing – Forensic auditing of product at all points in the stream of commerce. This auditing will include inspection and sampling of the product, inspection of documents, and biological testing.
    3- Investigation - To include simple to complex investigations, both civil and criminal. These investigations will be in the interest of industry and the general public.

- The bill's enforcement provisions (Sec. 3) are not clear with regard to whether violation of the prohibition on the shipment, transport, sale or purchase of genetically-altered salmon or other marine fish would be subject to criminal or civil penalties under the Magnuson-Stevens Act. The Magnuson-Stevens Act is explicit about criminalizing certain violations. In this case, merely including a prohibition does not determine whether the penalty will be civil or criminal.

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Enforcement Recommendations

- The NOAA Office of Law Enforcement can provide Technical Drafting Assistance upon request.

- Section 3. Enforcement and Penalties in S.B. 1717 describes enforcement powers of the Secretary of Commerce to reside under sections "308, 309, 310, and 311".

- NOAA OLE recommends inclusion of Section 307 "Prohibitions" under the Magnuson-Stevens Act, as well as broader, inclusive language as proposed in the "International Fisheries Stewardship and Enforcement Act (IFSEA)." IFSEA states: "to enforce the provisions of any Act to which this section applies, the Secretary may, with the same jurisdiction, powers, and duties as through section 311 of the Magnuson – Stevens Fishery Conservation and Management Act. . . .

- NOAA OLE seeks specific inclusion of the following enforcement powers as contained within IFSEA, to wit:
    1. Search or inspect any facility or conveyance use or employed in, or which reasonably appears to be used or employed in, the storage, processing, transport, or trade of fish or fish products;
    2. Inspect records pertaining to the storage, transport, or trade of fish or fish products;
    3. Detain for a period of up to 5 days, any shipment of fish or fish product imported into, landed on, introduced into, exported from, or transported within the jurisdiction of the United States; and
    4. Make an arrest, in accordance with any guidelines which may be issued by the Attorney General, for any offense under the laws of the United States committed in the person's presence, or for the commission of any felony under the laws of the United States, if the person has reasonable grounds to believe that the person to be arrested has committed or is committing a felony; may search and seize, in accordance with any guidelines which may be issued by the Attorney General and may be executed and serve any subpoena, arrest warrant, search warrant issued in accordance with rule 41 of the Federal Rules of Criminal Procedure, or other warrant or civil or criminal process issued by any officer or court of competent jurisdiction.
    5. Subpoenas – in addition to any subpoena authority pursuant to subsection (b), the Secretary may, for the purposes of conducting any investigation under this section, or any other statute administered by the Secretary, issue subpoenas for the production of relevant papers, photographs, records, books and documents in any form, including those in electronic, electrical or magnetic form.

Attachment 7

Sixty-Day Notice of Intent to Sue FDA Pursuant to the Endangered Species Act
Re: Approval of Genetically Engineered "AquAdvantage" Salmon

FDA Salmon

Concerns:

Monitoring

- Two facilities – egg production in Canada, grow out in Panama
- On-site self-reporting required

Risk of reproductive adults escaping

- To produce eggs, transgenic females and neomales are used to produce eggs.
- These fish can reproduce in the wild and produce genetically engineered Atlantic salmon alevins.
- It is possible, though not likely, these fish escape.
- If they escape, they would be likely they reproduce in the wild because hatchery released fish and hatchery sterilized fish continue to behave similar to wild fish (Trested *et al.* 2002).

Risk of juveniles escaping

- Sterilization measures are not 100% successful (approximately 95% success).
- Diploid genetically engineered fish would be fully capable of spawning.
- All juvenile fish would be females.
- Successfully sterilized salmon would be attractive mates for wild fish and may reduce wild population fitness.

Barrier concerns

- Described as 3-4 levels of protections, but that is the maximum. In some cases, there is only one screen between the tank and the wild.
- The facility is an old Atlantic salmon production facility and has the appropriate precautions for raising native salmon.
- The EA claims discharges go directly to saltwater, creating a chemical barrier, but in fact discharges enter a several hundred yard long creek that then flows into saltwater. This creek could provide habitat to sustain juveniles.
- The barriers reduce the probability of an escape, but do not insure no escapes could ever happen.

Commercial sale of eggs

- Because the EA didn't address this subject, it is still unclear what risk this poses. Likely, if there is high demand for eggs, that would require more fertile adults to produce those progeny.

Endangered Species Act

- While unlikely, an introduction of genetically engineered Atlantic salmon could pose catastrophic threats to wild listed species.
- The grow-out facility in Panama poses no threat to wild Atlantic salmon because of the location.
- The egg production facility may pose a threat to wild Atlantic salmon, including Gulf of Maine DPS Atlantic salmon.
- Dead transgenic salmon are not likely to pose a threat to ESA listed species.
- Any fish introduced along the Pacific Coast would have unknown potential for affecting Pacific salmonids through hybridization.

Larisa Rudenko
Center for Veterinary Medicine
Food and Drug Administration
Parklawn Building (HFE-88) 5600 Fishers Lane
Rockville, Maryland 20857

Dear Dr. Rudenko:

NOAA's National Marine Fisheries Service (NMFS) received your determination that the Food and Drug Administration (FDA) Center for Veterinary Medicine's approval of an application for AquAdvantage Salmon may effect, but is not likely to adversely affect the endangered Gulf of Maine (GOM) distinct population segment (DPS) of Atlantic salmon in accordance with section 7(a)(2) of the Endangered Species Act (ESA) of 1973, as amended (16 USC 1536(a)(2)). The September 13, 2010, letter included an Environmental Science Review, Briefing Packet, and Environmental Assessment (EA).

The FDA provided all materials that are required to initiate consultation in the EA and supporting documents, however, we would appreciate clarification on three topics prior to initiating consultation on this action. First, under the EA section 2.1 'Limitations of Use,' the FDA stated that the eyed eggs can only be used in "the FDA-approved, physically contained freshwater culture facility." However, those limitations are made less clear by the discussion of eyed eggs for commercial sale (see sections 3.1.1.2 on page 41 and 3.3.1 on page 46). Because the egg production facility and the grow-out facility are owned by Aqua Bounty Technologies, Inc., there would be no reason to sell the eggs unless another aquaculture facility was involved. NMFS requests clarification as to whether commercial resale of eyed eggs should be considered as a part of this action. If eggs will not be sold commercially, the FDA should state definitively that these eggs will not be sold commercially nor would they be used in the United States.

Second, NMFS is unclear about the entire process Aqua Bounty Technologies, Inc. proposes to use to produce eyed eggs. The EA lacks a discussion on how fertile, genetically modified, adult males are maintained on Prince Edward Island and what measures are in place to prevent those fertile and genetically modified fish from escaping and ultimately reproducing. NMFS requests more information about the containment and mitigation measures for the genetically modified adult males in captivity.

Finally, the EA describes an action area limited to Canada and Panama. However, the action area as defined in the ESA (50 CFR 402.02), should be identified as all areas of potential impacts as a result of this action. The topics of selling eyed eggs commercially and rearing fertile adult males at the Canadian production facility both potentially increase the size of the action area to

include the United States. If the action area in the EA is described accurately, NMFS does not anticipate any listed species will occur in the action area, and believes there should be no effect to any listed species under NMFS' jurisdiction.

Thank you for the opportunity to comment on this proposed action. If you have any questions, please contact Jason Kahn, 301-713-1401.

Sincerely,

Therese Conant
Acting Division Chief
Endangered Species Division

Dec. 3 meet to discuss AquAdvantage

Inbox x

Therese Conant <Therese.Conant@noaa.gov> 11/30/10

to Larisa, Joseph, Barry, Eric, Susan, me, Brian, Susan, Craig

Larisa,
Attached is our draft letter with the points of clarification. As you can see, we have questions regarding containment of broodstock and marketing of eggs. If you a feel an in-person meeting is unnecessary to address our questions, please let me know soon. Otherwise, we look forward to your visit on Friday.
Therese

Rudenko, Larisa wrote:

> Yes, it would indeed. We're really looking forward to meeting with you, answering your questions, and perhaps looking towards working together in the future on other applications.
>
> Happy Thanksgiving!

From: Therese Conant [mailto:Therese.Conant@noaa.gov]
Sent: Wednesday, November 24, 2010 12:02 PM
To: Rudenko, Larisa
Cc: Cormier, Joseph; Hooberman, Barry; Silberhorn, Eric
Subject: Re: Follow up

Would Tuesday November 30 provide enough time? We don't have that many questions, so should be rather simple. And yes we are meeting on the 3rd in Building 3 (hand sculpture out-front). Go up elevator to Security. You will need your government ID or other photo ID. When you arrive, have Security call me at 301-713-1401 ext 126. I look forward to meeting you.

Rudenko, Larisa wrote:

> Hi Therese,
>
> First, best wishes for a good Thanksgiving holiday.
>
> I'm just confirming our meeting for Friday the 3rd at 11 at the Silver Spring offices. Do you have any idea of when you'll be able to share your questions with us? No rush, but it might be nice to have a day or so to take a look at them.
>
> Looking forward to meeting with you in person,
> Larisa

From: Therese Conant [mailto:Therese.Conant@noaa.gov]
Sent: Wednesday, November 17, 2010 3:54 PM

Attachment 8

Sixty-Day Notice of Intent to Sue FDA Pursuant to the Endangered Species Act
Re: Approval of Genetically Engineered "AquAdvantage" Salmon

Comments on
Environmental Assessment for AquAdvantage Salmon
and
Briefing Packet on AquAdvantage Salmon for the Veterinary Medicine Advisory Committee

By

Anne Kapuscinski, Professor of Sustainability Science, Dartmouth College, Hanover, NH
and
Fredrik Sundström, Assistant Professor, Department of Ecology and Genetics, Uppsala University, Uppsala, Sweden

Thank you for the opportunity to comment on the application from AquaBounty Technologies to the FDA for commercial approval of AquAdvantage Salmon (AAS). Our comments below focus on environmental risk assessment of these transgenic fish, our major area of expertise with respect to this application.

I. If this application is approved, farming of transgenic AquAdvantage salmon will proliferate in the foreseeable future and other species are likely to follow. Farmed Atlantic salmon is a global commodity, with approximately 1.5 million metric tonnes farmed in 2008 (FAO 2010, Kontali 2009) and typical salmon farms raise 500,000 to 1 million fish in poorly confined growout areas, each as large as four football fields. The applicant will likely want to sell AAS eggs to many growers to be profitable in this global industry. Thus, this is a historic application whose approval could lead to transgenic salmon becoming the first genetically engineered animal farmed on a large scale for human food.

II. We urge the FDA to extend the public comment period on the scientific issues in this historic application before making a final decision. The time between the release of nearly 260 pages of technical documents on Sept 3 (the day before a national holiday weekend) and the September 16 deadline for written comments was much too short for adequate examination by the community of scientific experts on the genetics and ecology of transgenic fish and on methodologies for environmental risk assessment of transgenic fish. The limited review period did not give us enough time to prepare a more complete set of comments on all relevant scientific issues in the documents. And scientists are only one group among diverse stakeholders in this decision. A rushed process does not build public confidence in a decision that requires weighing complex matters in environmental and food safety risk assessment. A rushed process with extremely limited opportunity for comment only when the agency is finally "nearing a decision" (FDA 2010) contradicts research findings on how to gain public trust in risk decision-making. Best practices involve structured deliberation with relevant stakeholders at a few key points in the risk assessment, especially at the early steps that frame the entire process--problem formulation and identification and prioritization of hazards to address in the rest of the risk assessment (NRC 1996 and 2009, Hayes et al. 2007, Nelson et al. 2007, Nelson et al. 2009, Renn 2008). Even the National Research Council report on biological confinement of genetically engineered organisms advised public participation earlier in the process (NRC 2004:189-190)

III. Multiple confinement of these transgenic salmon is crucial to prevent environmental harm especially because of scientific uncertainty regarding their environmental risks

(Kapuscinski et al. 2007, Devlin et al 2006). If the physical or geographical confinement measures fail and there are regular escapes of sterile transgenic fish into environments where they can thrive, they could still alter the environment "in permanent ways, especially if transgenic fish overexploit key resources" such as wild fish prey (Devlin et al. 2007:152). Yet virtually no research has been done on how transgenic fish, including AAS, might affect other fish species in environments where they might end up. Biological confinement, alone, is not sufficient to prevent environmental harm. This is why assurance of multiple confinement is crucial. **Thus, we commend the applicant for proposing multiple confinement of the AAS strain at two relatively small facilities**, a hatchery on Prince Edward Island, Canada and a grow-out facility at an undisclosed location near a river in the highlands of Panama.

IV. However, we have two major concerns:

A. How will the FDA assure and verify that multiple confinement is continually achieved at the two facilities and in many future facilities as farming of these fish proliferates? How will the FDA assure that all sales of processed AAS in the USA come from fish grown under successful multiple confinement? How will the FDA assure and audit the company's implementation of an "integrated confinement system" (Table 10 in the Environmental Assessment)? This is a good idea on paper but the actual achievement of multiple confinement depends on many human actions, and the rigor of audit and regulatory oversight. An even greater challenge is how to assure multiple confinement at many, larger facilities in different environments and nations as commercial production of these fish proliferates. Does the FDA have the staff, financial resources and sufficient overseas jurisdiction for adequate surveillance of diverse domestic and foreign hatcheries and grow-out facilities?

B. The scope of the Environmental Assessment is too narrow and its methods inadequate for the issues at hand. We urge the FDA to now require a complete environmental risk assessment, as a fully transparent Environmental Impact Statement (EIS). The current Environmental Assessment only assesses the likelihood of transgenic salmon escaping from multiple confinement at the two facilities but the proposed multiple confinement does not absolve the need for a complete environmental risk assessment, given the likely proliferation of sales of AAS eggs for growout beyond one facility in Panama. The Environmental Assessment does not provide the full information needed to predict environmental effects of AAS, some of which we describe below. It focuses on an outdated list of issues (from Kapuscinski and Hallerman 1991) and ignores the major advances in methodologies for assessing environmental risks of transgenic fish (Kapuscinski et al. 2007). These advanced methods systematically integrate information about the environment and the transgenic fish's genotype and phenotype to identify and prioritize hazards upon which to focus the environmental risk assessment (Devlin et al. 2007, Kapuscinski et al. 2007a, Hayes et al. 2007).

All parties will benefit from a full assessment of potential environmental harm and benefit presented in a thorough and transparent EIS. All future regulated growers will benefit from more complete information to guide their investments in grow-out facilities that are more likely to be approved. The public interest will be better served by a more complete and transparent process.

We urge that the FDA not make a final decision on this application until our two major concerns are fully addressed. Below, we further describe these concerns and suggestions to address them.

V. Strengthen the assessment and assurance of multiple confinement

The FDA should require a quantitative failure mode analysis for each form of biological, mechanical, chemical, and geographical confinement and for the overall combination of confinement methods (Burgman 2005). Although the limited scope of the Environmental Assessment is justified by arguing that the AAS will be raised only in the two mentioned facilities, the proposed wording for the product label (Environmental Assessment page 48) and limitations for use (Briefing Packet, page 8) leave open the door for possible production in other FDA-approved facilities. Therefore, we urge doing failure mode analysis for the range of facilities that may obtain AAS eggs in the foreseeable future, as part of a full EIS.

A. Biological confinement

Production of 100% all-female populations of salmon is well established, which should make this part of a quantitative failure mode analysis relatively easy. It is not as easy to achieve 100% sterility through pressure-shock induction of triploidy. Failure analysis of triploid induction in AAS should quantify the variability in percent triploids across treated batches of eggs and the frequency of "exceptional diploids". Devlin et al. (2010) obtained 97% to 99.8% successful triploidy when they treated batches of 10,000 to 19,000 transgenic coho salmon eggs. They also detected 1.1% exceptional diploids overall among all pressure-treated groups (54,787 fish). Exceptional "diploid" individuals can contain the transgene but their fertility and ability to transmit the transgene to offspring is not yet known. Do exceptional diploids occur among treated AAS? If yes, it is necessary to determine their fertility or devise a proven way to eliminate them from eggs destined for growout.

B. Physical and chemical confinement

Physical and chemical confinement measures are especially prone to equipment failures, power failures, operational wear, and human error (Mair et al. 2007). Failure mode analysis of these confinement measures is critical. We commend the applicant's proposed "integrated confinement system" plan that aims to reduce these sources of failure. But this does not remove the need for a quantitative failure assessment.

C. Geographical confinement

Failure analysis of geographical confinement should include data on how AAS respond to changes in temperature and season. The Environmental Assessment suggests water temperatures in lower reaches of the Panamanian River and Pacific Ocean will be lethal to AAS but has the thermal tolerance of AAS been measured? In coho salmon, the optimal growth temperature, and presumably other physiological traits relevant for thermal tolerance, at the freshwater stage changed with growth-hormone transgenesis. Growth-enhanced transgenic coho salmon grew faster at 18ºC than at 12 ºC (and the upper thermal limit for their fast growth is unknown because they were not tested above 18 ºC) whereas wild-type coho salmon did not grow significantly faster at 18ºC than at 12 ºC (Lõhmus et al. 2010). How has growth-hormone transgenesis affected thermal tolerance and optimal growth temperature in AAS? Water temperatures given

for the high-elevation portions of the Panamanian river (near the growout facility) range from 15º to 19ºC (Environmental Assessment, Table 3). Are there data on whether the transgenic Atlantic salmon continue to grow fast, are able to survive or perish at these temperatures, in fresh as well as saltwater?

Overall, the Environmental Assessment does not give sufficient data on seasonal variation and habitat complexity in the receiving environments around the Canadian hatchery and Panamanian grow-out facility to identify if AAS escapes could thrive in certain locations and seasons and to estimate the likelihood of this hazard. In Panama, this needs to be examined for the watershed, with full consideration of seasonal variation and habitat complexity. Oceanographic conditions are also very complex in the Gulf of Panama and Pacific coast of Panama. During the dry season, for instance, upwelling of colder and food-rich waters could be hospitable to adult salmon if they make it downriver. Finally, a full EIS should consider seasonal and spatial variation and complexity in environments surrounding the range of possible grow-out facilities.

VI. Require a Scientifically Rigorous Environmental Impact Statement before making a decision on the AAS application

A. The Environmental Assessment does not give the full information needed to predict environmental effects of AAS. It focuses on completing only the "exposure" step of risk assessment, and concludes there is "extremely small" likelihood of exposure due to multiple confinement at the two facilities, thus no consequence and no need to assess consequences. As scientists, we cannot agree with this approach because it assumes 100% achievement of multiple confinement without having presented the failure mode analysis that is standard practice in technology risk assessment. Even if actual exposure is very close to zero, it is still necessary to assess ecological consequences, from low to high severity consequences, and then estimate the overall risk. We also disagree with this approach because of the likely proliferation of farming AAS in numerous grow-out facilities where multiple confinement will be harder to implement and assure (Mair et al. 2007).

B. Where the Environmental Assessment and Briefing Packet do present some quantitative data related to environmental risk, they omit information required to scientifically verify the stated conclusions. Frequently missing information includes: sample sizes (or the given sample sizes seem too small to reliably assess the scientific value of the experimental outcome), standard errors, statistical power, or description of statistical tests used to reach the stated conclusion. Although we focused on sections dealing with environmental risks, we noticed similar omissions in the Briefing Packet's presentation of data for other scientific issues. Such incomplete analysis and presentation of data does not meet commonly accepted scientific standards.

C. The Environmental Assessment does not adequately consider the growing body of research on genetic and ecological risks of transgenic fish. This research shows there will be high scientific uncertainty in predicting the overall fitness and ecological effects of AAS if they enter nature because it is extremely challenging to extrapolate from experiments using semi-natural conditions (reviewed in Devlin et al 2007, Devlin et al. 2006, Kapuscinski et al. 2007). This is due to key biological complexities including gene-environment interactions, background

genetic effects, pleiotropic effects, tradeoffs between traits expressed across different life stages, persistent effects of the environment experienced early in life, evolution of fertile transgenic fish after escape, ecological variability, and poorly understood ecological processes (Devlin et al. 2004b, 2007, Kapuscinski et al. 2007, Neregard et al. 2008, Pennington and Kapuscinski in press, Sundström et al 2007b, 2009).

Overall, this research indicates it could be very misleading to base an environmental risk assessment on data for only a few traits that do not span the whole life-cycle and measured under a limited range of environmental conditions. We are therefore concerned about overly simplistic statements of "poor fitness" of AAS without the kinds of scientific evidence required to support such a claim (e.g. Environmental Assessment, Table 11 on p. 71; Briefing Packet, p. 43 possible implication that higher critical oxygen level of AAS leads to overall poor fitness). Also, the Environmental Assessment gave an unacceptably cursory mention of uncertainty (two paragraphs on page 73) with no application of scientific methods of uncertainty analysis (Hayes et al.2007a).

D. The environmental analysis of AAS presented to the public largely avoids facing the complexity and uncertainty inherent to environmental risk assessment of transgenic fish. We strongly urge the FDA to require a science-driven environmental risk assessment that treats the complexity and uncertainty directly and honestly, using the most current methodologies (Kapuscinski et al. 2007, Burgman 2004). Such an environmental risk assessment in an EIS should follow standard ecological risk assessment steps:

1. Conduct a problem formulation and options assessment that integrates scientific analysis and stakeholder deliberation (Nelson et al. 2007) and define conceptual models of the human and environmental system at issue (Landis 2003).

2. Identify all possible hazards and prioritize which hazards to fully assess (Gong et al. 2007, Kapuscinski et al 2007a, Devlin et al. 2007)

3. Identify and agree upon measurable assessment endpoints--based on identifying possible environmental consequences--for each prioritized hazard (Kapuscinski et al. 2007b);

4. Estimate exposure, i.e., the likelihood of transgenic salmon escaping into and living in natural environments – quantify as much as possible.

5. Estimate likelihood and severity of environmental consequences identified for each prioritized hazard – quantify as much as possible;

6. Identify and appropriately treat uncertainties throughout the exposure and consequence assessment, using contemporary methods (Hayes et al. 2007a); and

7. Characterize the overall risk (exposure x consequences), with explicit presentation of uncertainties that affect exposure and consequence assessment.

The most comprehensive peer-reviewed literature on the biology and ecology of any transgenic fish is for a line of transgenic coho salmon bearing a different salmon growth-hormone construct. Conclusions from this body of research point to the key issues that should be investigated for AAS (Table 1 below). These issues must be pursued for AAS, even though the outcomes may differ between AAS and the transgenic coho salmon due to strain-specific differences in altered traits. The environmental analysis in both the Environmental Assessment and Briefing Packet did not adequately incorporate insights from this body of research. For instance, do gene-environment interactions occur in AAS? If yes, how will this be incorporated into the environmental risk assessment, especially as sales of AAS eggs proliferate to many grow-out facilities?

The peer-reviewed literature, to date, suggests that, at a minimum, a scientifically reliable environmental risk assessment of AAS should address the following issues:

a. Environmental conditions can lead to very different phenotypes and behavior of hatchery-reared versus stream-reared fish which affects the relationship between transgenic and non-transgenic fish (genotype by environment interactions) (e.g. Bessey et al. 2004; Devlin et al. 2004b; Sundström et al. 2007b). Whereas this specific research was done on coho salmon, Atlantic salmon show even more plasticity in terms of life-history and behavior. Hence, the age at which AAS might escape from confinement could have dramatically different effects on their phenotype and on how they function in a natural environment. Further, if AAS are reared in different locations, specific conditions in each location are likely to affect the phenotype in a specific way.

The documents released by FDA lack data on how the environmental conditions affects the phenotypes of AAS at different life stages. These data are crucial for assessing how AAS might behave after escape and, thus, what possible impacts they may have on the ecosystem.

b. Enhanced appetite alters behavior in transgenic salmon (Devlin et al. 1999; Raven et al. 2006). Hence, they are likely to explore novel prey and novel areas (Sundström et al. 2003, 2004b, 2007a). And they also may expose themselves to predation risk (Sundström et al. 2004a).

Hence, using the behavior and habitat selection of wild-type salmon may only partly reveal the extent of impact by transgenic fish as they may venture into areas where wild-type fish do not exist. This should be assessed in conjunction with effects of transgenesis on environmental tolerance (e.g. thermal tolerance pointed out above). It will be very difficult to quantify the tradeoff between possible expansion of prey species versus heightened exposure to predation. What will be the overall effect of this tradeoff on fitness of transgenic salmon in nature? What will be the impact on predators from consuming AAS? How will the trophic role of AAS in the food chain affect the overall ecosystem? These questions can be addressed by conducting ecologically appropriate experiments, applying state-of-the-art methods of uncertainty analysis or a combination of both approaches (Hayes et al. 2007a).

c. Transgenic salmon may have different responses to temperature and season, compared to wild salmon and to domesticated farmed salmon. For instance, growth-enhanced transgenic

coho salmon will likely remain active during winter and thrive at higher temperatures (Devlin et al. 1994 and 2004a; Lõhmus et al. 2008 and 2010). Thus, ecological traits of AAS should be tested under a range of seasonal conditions, including temperature changes.

d. Reduced prey availability will not necessarily be a disadvantage to transgenic salmon. The flexible development of transgenic salmon (point 1) means that these fish are not dependent upon high amounts of food to survive. Studies on coho salmon also show that under most food limited conditions they do as well or better than wild-type salmon, and the transgenic individuals can survive for at least 5 months without showing much growth (Sundström and Devlin 2010). In the extreme, the stronger competitive ability of transgenic individuals may eventually result in cannibalism on outcompeted wild-type (Devlin et al. 2004b). Hence, the statement in the Ecological Assessment document (4.2.2) that "these macroinvertebrates, however, are not abundant." does not exclude persistence of AAS. Thus, AAS should be tested under different food availability conditions to determine potential survival and spread throughout possible receiving environments.

e. Lower fitness of transgenic fish when they first escape does not translate into permanently lower environmental risk. One successfully breeding individual transmitting the transgene is likely to result in a very different phenotype (see point 1 above) with a different fitness potential relative to its parents (Kapuscinski et al. 2007a). Over the long term, evolutionary processes will exert selection on background genetics to compensate for reductions in fitness caused by the transgene (Ahrens and Devlin in press).

E. The Environmental Assessment and Briefing Packet compare traits of AAS to traits of farmed salmon but this is not an adequate comparator for understanding environmental effects. It is necessary to assess ecological differences between AAS and wild fish populations that fill a similar ecological niche in the accessible ecosystems. Following this fundamental ecological principle, **appropriate comparator specimens** for the environmental risk assessment of these transgenic Atlantic salmon are:

1. wild Atlantic salmon, including Atlantic salmon populations in possible escape zones and accessible ecosystems,

2. other salmon and trout species in the accessible ecosystems, which may fill a similar ecological niche and, thus, with which the transgenic salmon could compete, and

3. other fish species in the accessible ecosystems filling a similar niche and, thus, with which the transgenic salmon could compete.

The environmental risk assessment should include all three categories of comparators unless AAS will be farmed only near ecosystems that clearly lack a particular category, for example, in an area where there are no wild Atlantic salmon.

4. In places where there is farming of Atlantic salmon, the environmental risk assessment should assess if transgenic salmon pose additional ecological risks beyond those already

posed by farmed salmon escapees. Risks that the transgenic salmon pose to the salmon farms themselves should also be examined.

Domesticated salmon are currently grown in commercial aquaculture and their environmental effects, as escapees from salmon farms into nature, are currently under significant scientific debate. Published research on this concern is growing. In spite of many similarities between domesticated and growth-enhanced transgenic salmon, the AAS are unlikely to pose the same environmental risks as domesticated salmon. This is because the genetic consequences of transgenic fish interbreeding with wild relatives are very different from those of domesticated salmon interbreeding with wild relatives: any individual inheriting the transgene maintains its phenotypic expression across generations, whereas the effect of integration of domesticated genotypes into wild populations are halved at each generation. To use farmed fish as comparators for the risk-assessment of transgenic fish may therefore not be valid. At a minimum, relevant comparative experimental evidence of phenotypic traits and their consequences should be provided for both farmed and transgenic lines.

VII. Conclusion

Any failure of a multiple confinement system means that, once AquAdvantage salmon escape, the release cannot be undone because these fish are mobile organisms with very low but not zero likelihood of having some fertile escapees. Thus, we conclude it is crucial to conduct a full EIS that assesses the potential genetic and ecological impacts that AquAdvantage salmon could have on wild fish and other aspects of the environment. This is even more crucial because of the scientific uncertainty surrounding how these transgenic salmon will function in different environments, the importance of Atlantic salmon as a major global commodity, and the existing commitment of US society to restore threatened and endangered salmon populations and conserve aquatic biodiversity.

Table 1. Research findings relevant for an EIS of AAS, drawn from peer-reviewed literature on growth-hormone transgenic coho salmon

Key Insights from Research on Growth-Hormone Transgenic Coho Salmon	**Scientific Literature Reference**
Background genetics can strongly modify the effects of a transgene. Need to understand the evolution of transgenic fish in nature to accurately predict risk in the long term. Modeling shows that effects may occur on non-transgenic fish in populations due to the presence of the transgene.	Ahrens and Devlin 2010, Devlin et al. 2001, Neregard et al. 2008
Transgenic fish can show many changes in behaviors and phenotypes (feeding motivation, migration, dispersal, predation, spawning ability). Fish reared in naturalized stream conditions can show very different phenotypes from those reared in hatchery tanks (gene-environment interactions). Thus, data from the latter may only apply for first generation escapes and the former may require separate risk-assessment.	Bessey et al. 2004, Devlin et al 1999, Devlin et al. 2004b, Sundström et al. 2004b, Sundström et al. 2007a, Sundström et al. 2007b, Sundström et al. 2009, Sundström et al. 2010, Sundström and Devlin 2010
Transgenics showed altered swimming ability, respiration rate, oxygen demand, and antioxidant activity	Farrell et al. 1997, Huang et al. 2004, Lee et al. 2003, Leggatt et al. 2003, Leggatt et al. 2007, Stevens and Devlin 2000b, Sundt-Hansen et al. 2007
Environmental conditions affect the phenotypic difference between wild type and transgenic fish.	Lõhmus et al. 2009, Lõhmus et al. 2010, Sundström et al. 2007b, Sundt-Hansen et al. 2007
Growth-hormone transgenesis can affect fitness arising from predation effects, but effects are stage and environment dependent.	Sundström et al. 2003, Sundström et al. 2004a, Sundström et al. 2005, Tymchuk et al. 2005
Seasonal regulation of feeding is disrupted in transgenics (i.e. they do not slow down in winter as do wild types). Transgenics also show stronger growth response to increasing temperatures and food availability.	Devlin et al 2004b, Lõhmus et al. 2008, Lõhmus et al. 2010
Transgenics have altered use of dietary energy (i.e. carbohydrates), and preferentially use lipid as an energy source, sparing protein. Given all the food they want, behavioral effects of GH cause fish to deposit large amounts of fat, whereas under ration limiting conditions, the fish have lower lipid levels. Gut surface area, feed conversion, and digestive capacity enhanced. Starvation endurance is not greatly affected.	Blier et al. 2002, Higgs et al. 2009, Leggatt et al. 2009, Oakes et al. 2007, Raven et al. 2006, Stevens and Devlin 2000a, Stevens et al. 2005, Sundström and Devlin 2010
Disease resistance is lower in the growth-hormone transgenic coho strain	Jhingan et al. 2003
Growth-hormone transgenesis strongly affects expression of many genes. Growth-hormone transgenesis and domestication affect gene expression in similar, but not identical, ways.	Devlin et al. 2009, Mori et al. 2007, Mori and Devlin 2009, Rise et al. 2006, Roberts et al. 2004
GH and IGF-I elevated, the latter being strongly affected by growth rate (i.e. transgenics kept to a wild-type growth rate have normal IGF-I levels). Thyroid hormone systems strongly affected in growth-hormone transgenics.	Devlin et al. 2000, Eales et al. 2004, Kang and Devlin 2004, Raven et al. 2008
Abnormalities in cellular structure and organism morphology can occur in some strains of transgenic salmon.	Devlin et al. 1995b, Hill et al. 2000, Ostenfeld et al. 1998
Transgene structure is complex, and DNA integrates near integrated horizontally transmitted DNA (i.e. from infectious agents (parasites).	Uh et al. 2006
Detection of transgenic by molecular methods can be reliable	Masri et al. 2002, Rehbein et al. 2002
Triploidy induction does not produce 100% triploids in transgenics. Exceptions are gynogens and aneuploid individuals arising from incomplete retention of paternal chromosomes. These exceptions can contain the transgene, but their ability to transmit it to progeny is not yet known.	Devlin et al. 2010
The traits of every growth-enhanced strain are unique and triploidy impairs growth.	Devlin et al. 1994, Devlin et al. 1995a, Devlin et al. 2004a

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Attachment 9

Sixty-Day Notice of Intent to Sue FDA Pursuant to the Endangered Species Act
Re: Approval of Genetically Engineered "AquAdvantage" Salmon

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

JAN 15 2009

Andrew Kimbrell
Executive Director
Center for Food Safety
660 Pennsylvania Avenue, S.E., Suite 302
Washington, D.C. 20003

Re: Docket No. O1P-0230

Dear Mr. Kimbrell:

This letter responds to the citizen petition that was submitted to the Food and Drug Administration (FDA, Agency, we) on May 11, 2001 on behalf of the Center for Food Safety and a coalition of over 60 associated petitioners primarily representing consumer and environmental protection organizations.[1] We recognize that it has taken us a long time to respond, but as you are aware, some of the legal, regulatory and policy issues raised in your petition have been the subject of extensive discussion within FDA and between FDA and other agencies.

The Citizen Petition requests that FDA "impose a moratorium on the domestic marketing, importation, and exportation of transgenic fish" until FDA (1) "establishes a comprehensive regulatory framework under the mandate of the Federal Food, Drug, and Cosmetic Act (FFDCA [or Act]) to evaluate and fully address the human health and environmental impacts caused by the commercialization of transgenic fish"; (2) "completes a comprehensive environmental impact review"; (3) "reviews the impacts of such activities on endangered species and completes the consultation requirement with the Department of the Interior and Department of Commerce as required under the Endangered Species Act, 15 U.S.C. § 1536"; and (4) "all other federal agencies comply with the statutory provisions under such agencies' jurisdiction that are triggered by the introduction of transgenic fish into the environment and/or interstate commerce." For the reasons explained below, FDA is denying your requests.

Since submission of your petition, FDA released a final guidance, Regulation of Genetically Engineered Animals Containing Heritable recombinant DNA Constructs (GE animal guidance), describing how the new animal drug provisions of the FFDCA and its implementing regulations apply to transgenic animals (which the guidance refers to as genetically engineered or GE animals), including transgenic fish (http://www.fda.gov/cvm/Guidance/guide187.pdf).

In brief the guidance notes that a recombinant DNA (rDNA) construct that is intended to affect the structure or function of the body of an animal meets the FFDCA definition of a

[1] Petition Seeking a Moratorium on the Domestic Marketing and Importation of Transgenic Fish, Center for Food Safety et al., May 11, 2001 (GE animal CP).

new animal drug. 21 U.S.C. § 321(v). Thus, GE animals contain a new animal drug that is subject to the new animal drug application (NADA) requirements of the Act, 21 U.S.C. § 360b, and of our implementing regulations.[2] For example, Atlantic salmon genetically engineered to grow faster and use feed more efficiently, such as the AquaBounty (previously, A/F Protein) GE fish referred to in your petition, contain a new animal drug and therefore are regulated under FDA's statutory and regulatory provisions. Such fish[3] must meet the safety and effectiveness requirements of the Act, including the agency's determination that food from such animals is safe.[4] 21 U.S.C. §§ 331, 342, 351, 360b. Imported food from GE fish also must be safe under these provisions. Additionally, FDA will comply with the requirements of the National Environmental Policy Act (NEPA), 42 U.S.C. § 4332, and will prepare an environmental assessment and, if necessary, an environmental impact statement, prior to completing an approval of an NADA for such fish. Thus, FDA believes that it already has "a comprehensive regulatory framework" in place that addresses potential impacts to human health and the environment of GE fish and, because GE fish must comply with the requirements of this regulatory framework we do not believe there is a need for a "moratorium" on the domestic marketing and importation of GE fish and we are denying that request.

Below we list each of the principal arguments in the citizen petition and our responses, followed by FDA's response to the specific requests of the citizen petition.

I. Petitioners' Principal Arguments

A. FDA is required under the Federal Food, Drug, and Cosmetic Act (FFDCA or the Act) to review the human health impacts from consuming transgenic fish.

FDA response: As noted above, and consistent with the GE animal guidance, as part of the NADA process, FDA will review the food safety of GE fish. FDA's review of the food safety of GE fish will, as you request, encompass an evaluation of potential toxicity, unintended effects, and allergenicity. You also request that FDA's evaluation include a determination of "whether the use of antibiotics to control aquaculture diseases in transgenic fish may impact human health." FDA evaluates the safety of antibiotics used to treat aquaculture diseases, including potential impacts on human health, when reviewing the NADAs for those antibiotics. Additionally, the food safety and animal safety components of the GE fish NADA review are complementary and, for example, encompass whether the conditions under which GE fish are raised may lead to food safety concerns such as might occur with increased use of antibiotics to treat or prevent an increased incidence of disease in aquacultured GE fish.

[2] Certain new animal drugs may qualify for either conditional approval or indexing under the minor use and minor species sections of the Act; a GE animal and its products, however, are specifically excluded from these provisions. 21 USC § 360ccc(a)(3)(A) and 21 USC § 360ccc-1(a)(2).

[3] As noted in the guidance document, as a shorthand, we sometimes refer to regulation of the article in GE animals as regulation of the GE animal. GE animal guidance at 6.

[4] The guidance explains that in certain circumstances FDA intends to exercise enforcement discretion with respect to statutory and regulatory requirements for GE animals of non-food species. GE animal guidance at 6-8.

B. FDA must establish full transparency and public involvement in any established regulatory approval process for transgenic fish.

FDA response: While the NADA provisions do not provide for a notice and comment process for NADA approval decisions, FDA is taking steps to increase the transparency of its deliberations and actions. For example, FDA intends to hold public advisory committee meetings prior to completion of GE animal approvals. We may revisit this policy in the future as we gain more experience with reviews of GE animals. For example, on January 9, 2008, CVM participated in a public meeting of the FDA Blood Products Advisory Committee on the Biologics License Application (BLA) for recombinant human antithrombin III produced in the milk of GE goats. At this meeting, with the sponsor's agreement, CVM provided a summary of its review of the NADA pertaining to the GE goats, as well as a summary of the environmental assessment (EA) submitted in support of the NADA. For GE animals intended for food or other non-biopharm use, we intend to hold advisory committee meetings dedicated to consideration of the GE animal NADAs and environmental reviews.

We have also developed a number of consumer-appropriate publications to help inform consumers and other stakeholders about the technology and the agency's regulations of these animals. These are available on the FDA website.

Additionally, FDA's new animal drug approvals (including for GE animals) are published in the Federal Register, codified in the Code of Federal Regulations, and posted on its website in its "FDA Approved Animal Drug Products (the "Green Book") at www.fda.gov/cvm/greenbook. FDA also provides electronic access to a summary of all information (other than confidential business or trade secret information) used in FDA's decisions as part of the freedom of information summary routinely published after approval. These summaries can be found at http://www.fda.gov/cvm/FOI/efoi.html.

Finally, if we intend to exercise enforcement discretion with respect to specific GE animal lineages, we plan to post a statement describing that intent on our website.

C. FDA is required under the National Environmental Policy Act (NEPA) to review the impacts to human health and the environment.

FDA response: FDA is aware of its responsibilities under NEPA and complies with those requirements.

D. FDA is required under the Endangered Species Act (ESA) to consult with DOI and DOC before approving an activity that may affect an endangered or threatened species.

FDA response: FDA is aware of its responsibilities under the ESA and complies with those requirements.

E. FDA is required under the FFDCA to mandate the labeling of all transgenic fish.

FDA response: There are two components of your request: (1) that GE fish be labeled under the FFDCA drug provisions, and (2) that they be labeled under the FFDCA food provisions.

With respect to the drug provisions, NADs must bear accurate labeling. 21 U.S.C. §§ 352, 360b. In the context of GE animals, the guidance explains that labeling should include a summary description of the article, the animal into which the article is introduced (e.g., common name/breed/line; genus and species), the name of the resulting GE animal line, and the intended use of the GE animal containing the article. Where the labeling for a GE animal contains animal care or safety information (e.g., husbandry or containment), the guidance states that the labeling should accompany the animal throughout all stages of its lifecycle. GE animal guidance at 14.

With respect to labeling of food, the guidance notes that labeling of food from GE animals would be subject to the same requirements as food from non-GE animals, and food from GE plants[5]. The fact that the animal from which food was obtained was genetically engineered would not itself be material information with respect to labeling. However, if food from a GE animal is different from that of its non-engineered counterpart, for example if it has a different nutritional profile, in general, that difference would be material information that would have to be revealed in labeling. Id.[6]

F. Before transgenic fish are marketed, FDA must enact monitoring, reporting, and inspecting procedures that adequately address human food safety concerns.

FDA response: We believe that our existing NADA requirements as applied to GE animals adequately address human food safety concerns. While the petition states that there are "unique food safety concerns that may develop during the production and processing of " GE fish, most of the issues the petition identified could also exist with other foods from fish or other animals treated with conventional new animal drugs and containing drug residues, nor did the petition identify any inadequacies in those NADA requirements with respect to human food safety concerns. The only "unique" concern the petition identifies is potential "physical abnormalities" due to the "juggling of genes." We note that the cited abnormality, jaw malformations, would be part of the NADA assessment that the agency would perform in determining whether the introduced rDNA construct is safe to the animal. We therefore believe that the agency has sufficient authority under the new animal drug provisions of the Act to address such concerns. We further note that the assessment would also explicitly evaluate the overall health of the animal with respect to implications for food safety, so that other potential adverse outcomes resulting from "juggling of genes" or insertional mutagenesis, would be

[5] See, for example, FDA's 1992 "Statement of Policy: Foods Derived from New Plant Varieties" (57 FR 22984), and FDA's 2001 draft guidance "Voluntary Labeling Indicating Whether Foods Have or Have Not Been Developed Using Bioengineering" (http://www.cfsan.fda.gov/~dms/biolabgu.html).

[6] FDA's response to the Center for Food Safety's March 21, 2000 citizen petition regarding GE foods (Docket No. 2000-1211/CPI) (CFS 2000 CP) explains why only "material" information must be revealed on labeling. See CFS 2000 CP at 7.

assessed as both posing a risk to the health of animals and as posing potential food consumption risks.

II. Petitioners' Requests

A. FDA should impose a moratorium on the domestic marketing, importation and exportation of GE fish, fish eggs, and food products containing any ingredient or material derived from GE fish until it establishes a comprehensive regulatory framework under the FFDCA to evaluate and fully address the human health and environmental impacts caused by the commercialization of GE fish. The framework should include:

(1) establishment of regulations addressing the safety and efficacy of GE fish by requiring all GE fish producers to complete a review of a GE fish as a new animal drug under 21 USC 360(b) and implementing regulations.

FDA response: As noted above, FDA has published a final guidance detailing how FDA's existing NADA regulations apply to GE animals, including GE fish. FDA has determined that new regulations to address GE fish are not necessary at this time. As a result, FDA is denying petitioners' request to issue new regulations. However, for the reasons explained above, see supra at 2, FDA believes it is accomplishing what petitioners request since the application of the new animal drug statutory and regulatory provisions will address the safety and efficacy of GE fish and the human food safety of food animal fish. Therefore, the necessary regulatory framework is in place and no new regulations are necessary.

(2)establishment of regulations requiring all GE fish to undergo food additive review under 21 U.S.C. § 321(s) and implementing regulations.

FDA response: New animal drugs are excluded from the definition of food additives and so cannot be regulated as food additives. 21 U.S.C. § 321(s)(5). FDA, therefore, must deny this request. However, like food additives, new animal drugs must be found safe for use in food for the drug to be approved for use in food animals.[7] Thus, for example, the food safety of GE salmon will have to be established for FDA to approve an NADA for such a fish.

(3) establishment of regulations providing for premarket monitoring, reporting and inspecting procedures pursuant to FFDCA and accompanying regulations.

[7] The same legal standard for safety applies to both food additives and the human food safety component of a new animal drug review. Food and Drug Administration, Final Decision of the Commissioner: Withdrawal of Approval of the New Animal Drug Application for Enrofloxacin in Poultry, Docket No. 2000N-1571 (July 27, 2005) at 93.

FDA response: We believe that our existing investigational new animal drug (INAD) and NADA regulations as applied to GE animals provide appropriate regulatory oversight. The INAD regulations specify labeling and record-keeping requirements, animal disposition, and conditions under which food from animals used for clinical investigations can be introduced into the food supply. The regulations also require that prior to shipping a new animal drug for clinical tests, a sponsor must submit a Notice of Claimed Investigational Exemption for a New Animal Drug containing specified information. 21 CFR 511.1. In addition, FDA can inspect facilities where GE animals are developed and raised and intends to do so as part of its approval process. We, therefore, are denying this request.

(4) establishment of regulations requiring mandatory labeling of GE fish and food products containing ingredients or material from such fish.

FDA response: As noted above, labeling is required under the new animal drug provisions of the Act. We, therefore, find it is unnecessary to establish new regulations and are denying this request as it concerns new animal drug labeling. As also explained above, labeling of food from GE animals is subject to the same requirements as food from non-GE animals. The fact that the animal from which food was obtained was genetically engineered, itself, would not be material information with respect to labeling. If food from a GE animal is different from that of its non-engineered counterpart, that difference would be material information that would have to be revealed in labeling. We are therefore denying this request as it concerns labeling under the food provisions of the Act.

(5) establishment of regulations providing for post-market monitoring, reporting, and inspecting procedures pursuant to FFDCA and accompanying regulations.

FDA response: We believe that our existing NADA regulations as applied to GE fish provide appropriate regulatory oversight. They mandate premarket approval and post market reporting. In addition, FDA routinely inspects manufacturing facilities prior to approving new animal drugs. We, therefore, are denying this request. We note, however, that the GE animal guidance states FDA's intent to issue further guidance on the application of good manufacturing practices to GE animals. GE animal guidance at 16.

(6) establishment of regulations providing that importers must follow the same statutory and regulatory requirements for GE fish as domestic producers;

FDA response: Under the FFDCA, in order to import food from GE animals, there must either be an approved NADA for the GE animal, 21 U.S.C. §§ 342(a)(2)(C)(ii), 360b, or an FDA-established import tolerance 21 U.S.C. § 360b(a)(6). By law, import tolerances do not require approval of the new animal drug in the United States. Therefore, the requirements for importers of food derived from GE fish and domestic producers of GE fish are not the same and we deny this request. We note, however, that establishment of an import tolerance requires that food safety be established based on "data sufficient to

demonstrate that a proposed tolerance is safe based on similar food safety criteria" used for approval of an NADA.

(7)establishment of regulations providing for permanent prohibition of domestic marketing, importation and exportation of GE fish should such products fail to be proven safe and efficacious or generally recognized as safe, or should such products be otherwise unfit for human consumption.

FDA response: With respect to domestic marketing, as noted above, GE fish containing an rDNA construct intended to affect the structure or function of the body of the fish, and food from such fish, are subject to FDA's NADA regulations, including the requirement that they are safe and that the rDNA construct is effective. Imported food from GE fish also must be safe. Because FDA already has regulations imposing such requirements, we are denying petitioners' request for new regulations. However, we believe our current regulations accomplish what petitioners request. With respect to exports, FDA is denying petitioner's request because the FFDCA, 21 U.S.C. § 381(e), allows the export of products that would be adulterated or misbranded if marketed domestically, unless the product is a new animal drug that FDA has banned. Petitioners have not provided facts demonstrating reasonable grounds to justify banning GE fish. For the reasons explained above, FDA is denying petitioners' request to impose a "moratorium" on the domestic marketing, importation and exportation of GE fish, fish eggs, and food derived from GE fish until the agency establishes a regulatory framework that includes establishment of new regulations addressing the issues set forth above.

B. FDA should impose a moratorium on the domestic marketing, importation and export of all GE fish until it completes a comprehensive environmental impact review as required by NEPA to evaluate and address the human health and environmental impacts caused by GE fish commercialization, including

- an environmental assessment and environmental impact statement as required by NEPA addressing the effects of the domestic marketing, importation and exportation for each and every transgenic fish application,

- a programmatic environmental impact statement as required under NEPA, and

- providing for the permanent prohibition should such activities harm the quality of the environment.

FDA response: As noted above, FDA approvals of new animal drugs are subject to the requirements of NEPA, and FDA complies with those requirements.

An NADA must include either an environmental assessment (EA) or a claim for categorical exclusion (which excuses certain categories of actions from the preparation of an EA where the agency has determined that that category of action does not individually or cumulatively have a significant effect on the human environment, 40 CFR § 1508.4). 21 CFR § 514.3(b)(14). By definition, an EA focuses on "relevant environmental issues relating to the use and disposal from use of FDA-regulated articles" and discusses the environmental impacts of the proposed action and alternatives (such as those presenting less environmental risk). 21 CFR § 25.40. An EA thus conforms to the requirements of

NEPA, which requires a comprehensive environmental review of all "major federal actions significantly affecting the quality of the human environment," such as the granting of an INAD file or approval of an NADA. If, the Agency determines from the EA or information otherwise available that the proposed action may significantly affect the quality of the human environment, it will prepare the more detailed environmental impact statement (EIS). 21 CFR § 25.22(b). However, if FDA determines that the proposed action is not expected to significantly affect the human environment and therefore does not merit the preparation of an EIS, then FDA will make a finding of no significant impact (FONSI) for the action. Thus, consistent with the Council on Environmental Quality's NEPA regulations, 40 CFR § 1508.9(a), not every action that requires preparation of an EA will also require completion of an EIS. FDA makes decisions on whether an EIS is required on a case-by-case basis based on the facts of each, individual action. FDA must therefore deny petitioners' request that both an EA and EIS be prepared for every GE fish NADA.

Regarding the fast-growing GE Atlantic salmon described in the petition, FDA's NEPA evaluation, as with other NADAs, would be conducted primarily by its in-house experts, including aquatic and microbial ecologists, veterinarians specializing in the treatment of aquatic organisms, fish pathologists and aquaculturists. If warranted by the specifics of the NADA, FDA also will make use of the expertise of other federal agencies that regulate environmental resources that may be affected by an approval (e.g., the Fish and Wildlife Service and the National Marine Fisheries Service). For example, FDA recognizes that the commercial use of GE fish in ocean net pens located in public waters would trigger environmental review by several federal and state agencies to ensure compliance with NEPA and related statutes, such as the Endangered Species Act.

FDA, USDA, and other federal agencies are well aware of the potential environmental risks regarding escape associated with raising GE fish in open net pens. These agencies, along with industry and universities, have supported research and extensive educational programs for the development and use of alternative methods of raising fish, such as closed recirculating systems for aquaculture production in the United States. Such emerging technologies could be adopted for the culture of GE Atlantic salmon, and other fish to reduce the risk of an accidental release into the environment. Optimal containment will need to take into account biosecurity systems, incluing physical, geographical, and biological containment. They will, of necessity, be species- and use-specific taking into account application-specific production goals established by the producer, and approved by the agency as part of the NADA approval process. We do not believe that these developing containment strategies lend themselves to standardization of design or operational criteria; in fact, a variety of technologies could be developed for any particular application that would provide adequate confinement.

FDA will thus evaluate the technology each NADA sponsor proposes to use on a case-by-case basis to determine the potential for environmental impacts as well as the facts specific to the nature of GE fish the sponsor proposes to develop. Since FDA is not issuing new regulations concerning GE animals, FDA, therefore, is denying petitioners' request that it prepare a programmatic EIS. GE animal CP at 36 ("If FDA decides to

adopt regulations concerning the commercialization of transgenic fish, the . . . FDA is required to conduct a . . .programmatic environmental impact statement.").

Finally, with regard to petitioners' request that FDA "provide for permanent prohibition" if GE fish "harm the quality of the environment," we note that although NEPA is a procedural requirement and does not give us new authority, such as to prohibit an activity solely because it would harm the quality of the environment, it has been our experience that developers of new animal drugs much prefer to mitigate potential environmental impacts so that FDA can come to a finding of no significant impact on the environment for an NADA approval, rather than have to wait for FDA to complete an environmental impact statement for a product whose approval will have a significant environmental impact. Thus although we are denying petitioners' request, we believe that in practice, any potential environmental impacts will be mitigated in the course of approving an NADA for any GE fish.

C. FDA should impose a moratorium on the domestic marketing, importation and export of all transgenic fish until:

(1) it reviews the impact of such activities on endangered species, in consultation with the Department of the Interior (DOI) and Department of Commerce (DOC) as required by the Endangered Species Act (ESA).

FDA response: FDA is aware of its responsibilities under the ESA and complies with these requirements. Because the agency already complies with these requirements, we do not believe a "moratorium" is necessary and we are denying this request.

(2) "all other federal agencies comply with the statutory provisions under such agencies' jurisdiction that are triggered by the introduction of transgenic fish into the environment and/or interstate commerce."

FDA response: This request is outside the scope of FDA's authority and, as a result, FDA is denying the request. However, FDA has been working with other agencies on oversight of GE animals, including fish. FDA is not aware of any agencies not complying with their statutory provisions triggered by introduction of GE fish into the environment and/or interstate commerce.

Conclusion

For the reasons discussed above, FDA is denying the requests in petitioner's citizen petition.

Sincerely.

Jeffrey E. Shuren, M.D., J.D.
Associate Commissioner for Policy
and Planning

January 25, 2016

VIA CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Sylvia Mathews Burwell, Secretary
Department of Health & Human Services
200 Independence Avenue S.W.
Washington, D.C. 20201

Dr. Stephen Ostroff, M.D., Acting Commissioner
Food and Drug Administration
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Penny Pritzker, Secretary
Department of Commerce
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Washington D.C. 20230

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NOAA Fisheries Service
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Sally Jewell, Secretary
Department of the Interior
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Daniel Ashe, Director
Fish and Wildlife Service
1849 C. Street N.W.
Washington DC 20240

Sixty-Day Notice of Intent to Sue FDA Pursuant to the Endangered Species Act
Re: Approval of Genetically Engineered "AquAdvantage" Salmon

Acting Commissioner Ostroff:

The Food and Drug Administration is hereby notified, unless the violations described herein are remedied within sixty days, that the organizations listed below intend to sue the Food

and Drug Administration and its Acting Commissioner Dr. Ostroff (collectively FDA), for violations of the Endangered Species Act (ESA), 16 U.S.C. § 1531, *et seq.*, associated with FDA's approval of the genetically engineered (GE or transgenic), "AquAdvantage" salmon (GE salmon). *See* New Animal Drugs in Genetically Engineered Animals; opAFP–GHc2 Recombinant Deoxyribonucleic Acid Construct, 80 Fed. Reg. 73,104 (Nov. 24, 2015). FDA has violated and remains in violation of Section 7 of the ESA by, *inter alia*, failing to insure, through consultation with the National Marine Fisheries Service (NOAA Fisheries) and the U.S. Fish and Wildlife Service (FWS) (collectively, the Services), that its approval of the GE salmon is not likely to jeopardize the continued existence of any threatened or endangered species and/or result in the destruction or adverse modification of the critical habitat of any listed species. Center for Food Safety and Earthjustice provide this letter pursuant to Section 11(g) of the ESA, 16 U.S.C. § 1540(g), on behalf of Friends of Merrymeeting Bay and Kennebec Reborn.[1]

I. IDENTITY OF THE ORGANIZATIONS GIVING NOTICE:

The names, addresses, and phone numbers of the organizations giving notice of intent to sue under the ESA are:

Friends of Merrymeeting Bay
P.O. Box 233
Richmond, ME 04357
207-666-1118

Kennebec Reborn
131 Cony Street
Augusta, Maine 04330
207-622-1003

II. REQUIREMENTS OF THE ESA

Section 7 of the ESA requires federal agencies such as FDA, in consultation with the expert wildlife agencies, to insure that any action authorized, funded, or carried out by the agency is not likely to jeopardize the continued existence of any threatened or endangered (T&E) species, or result in the destruction or adverse modification of the critical habitat of such species. 16 U.S.C. § 1536(a)(2). An action is considered to result in jeopardy where it would reasonably be expected, directly or indirectly, to reduce appreciably the likelihood of both the survival and recovery of a listed species in the wild by reducing the reproduction, numbers, or distribution of that species. 50 C.F.R. § 402.02. "Action" is broadly defined to include all activities or programs of any kind authorized, funded, or carried out by federal agencies, including actions directly or indirectly causing modifications to the land, water, or air. 50 C.F.R. § 402.02.

To carry out this substantive mandate, the ESA and its implementing regulations require federal agencies to consult with the wildlife agencies on the effects of their proposed actions. 16 U.S.C § 1536(a)(2); 50 C.F.R. §§ 402.12-402.16. This process begins with the requirement that the "action" agency, such as FDA here, ask the expert agencies whether any listed or proposed species may be present in the area of the agency action. 16 U.S.C. § 1536(c)(1); 50 C.F.R.

§ 402.12. If listed or proposed species may be present, the action agency must prepare a "biological assessment" to determine whether the listed species is likely to be affected by the proposed action. *Id*. The biological assessment generally must be completed within 180 days. 16 U.S.C. § 1536(c)(1); 50 C.F.R. § 402.12(i).

If the action agency determines the action "may affect" a listed species or critical habitat, the action agency must formally consult with NOAA Fisheries and/or FWS to "insure" that the action is "not likely to jeopardize the continued existence" of that species, or "result in the destruction or adverse modification of habitat … determined … to be critical…." 16 U.S.C. § 1536(a)(2); 50 C.F.R. § 402.14(a); *see Citizens for Better Forestry v. United States Dep't of Agric.*, 481 F. Supp. 2d 1059, 1092 (N.D. Cal. 2007).[2] The threshold for a finding of "may affect" is extremely low. A triggering effect need not be significant; rather "any possible effect, whether beneficial, benign, adverse, or of an undetermined character, triggers the formal consultation requirement…." Interagency Cooperation—Endangered Species Act of 1973, as Amended; Final Rule, 51 Fed. Reg. 19,926, 19,949 (June 3, 1986); Final ESA Section 7 Consultation Handbook at xvi (Mar. 1998) (defining "may affect" as "the appropriate conclusion when a proposed action may pose *any* effects on listed species….").

If a proposed action "may affect" a listed species or designated critical habitat, formal consultation is required unless the Service(s) concur in writing with an action agency's finding that the proposed action "is not likely to adversely affect" listed species or designated critical habitat. 50 C.F.R. §§ 402.02, 402.13(a), 402.14 (a). This "informal consultation" process consists of discussions and correspondence between the Services and the action agency and is designed to assist the action agency in determining whether formal consultation is required. 50 C.F.R. § 402.13(a). *See also Pac. Rivers Council v. Thomas*, 30 F.3d 1050, 1054 n.8 (9th Cir. 1994). An action is "likely to adversely affect" protected species, and formal consultation is required, if: "any adverse effect to listed species may occur as a direct or indirect result of the proposed action or its interrelated or interdependent actions, and the effect is not discountable, insignificant, or beneficial." *Endangered Species Consultation Handbook*, March 1998, p. xv.

To complete formal consultation, NOAA Fisheries and/or FWS must provide FDA with a "biological opinion" explaining how the proposed action will affect the listed species or habitat. 16 U.S.C. § 1536(b); 50 C.F.R. § 402.14. In fulfilling Section 7 consultation duties, agencies are required to use the best scientific and commercial data available. 16 U.S.C. § 1536(a)(2); *Heartwood, Inc. v. United States Forest Serv.*, 380 F.3d 428, 434 (8th Cir. 2004). Until the consulting agency issues a comprehensive biological opinion, the action agency may not commence the action. *Pac. Rivers Council*, 30 F.3d at 1056-57; *and see* 16 U.S.C. § 1536(d). Further, during consultation, FDA is prohibited from making any irreversible or irretrievable commitment of resources with respect to the agency action which may foreclose the formulation or implementation of any reasonable and prudent alternative measures. 16 U.S.C. § 1536(d).

If NOAA Fisheries and/or FWS concludes that the proposed action "will jeopardize the continued existence" of a listed species, the biological opinion must outline "reasonable and prudent alternatives." 16 U.S.C. § 1536(b)(3)(A). If the biological opinion concludes that the action is not likely to jeopardize the continued existence of a listed species, and will not result in the destruction or adverse modification of critical habitat, NOAA Fisheries and/or FWS must

provide an "incidental take statement," specifying the amount or extent of such incidental taking on the listed species, any "reasonable and prudent measures" that they consider necessary or appropriate to minimize such impact, and setting forth the "terms and conditions" that must be complied with by FDA to implement those measures. 16 U.S.C. § 1536(b)(4); 50 C.F.R. § 402.14(i). In order to monitor the impacts of incidental take, FDA must monitor and report the impact of its action on the listed species to the Services as specified in the incidental take statement. 16 U.S.C. § 1536(b)(4); 50 C.F.R. §§ 402.14(i)(1)(iv), 402.14(i)(3). If during the course of the action the amount or extent of incidental taking is exceeded, FDA must reinitiate consultation with the Services immediately. 50 C.F.R. § 402.14(i)(4).

Federal agencies have an independent and substantive obligation to insure that their actions are not likely to jeopardize the continued existence of endangered or threatened species or adversely modify critical habitat. *See Pyramid Lake Paiute Tribe of Indians v. United States Dep't of the Navy*, 898 F.2d 1410, 1415 (9th Cir. 1990). Indeed, a "no jeopardy" biological opinion from NOAA Fisheries or FWS does not absolve the action agency of its independent duty to insure that its actions comply with the ESA. *Res. Ltd., Inc. v. Robertson*, 35 F.3d 1300, 1304 (9th Cir. 1994). Federal agencies also have a continuing duty under Section 7 of the ESA to re-initiate consultation whenever "new information reveals effects of the action that may affect listed species or critical habitat in a manner or to an extent not previously considered," where the action in question is "subsequently modified in a manner that causes an effect to the listed species or critical habitat that was not considered in the biological opinion," or where "a new species is listed or critical habitat designated that may be affected by the identified action." 50 C.F.R. § 402.16(b)-(d).[3]

Finally, Section 9(a) of the ESA, 16 U.S.C. § 1538(a), prohibits the "take" of an endangered species by any person. This prohibition has generally been applied to many species listed as "threatened" through the issuance of regulations under Section 4(d) of the ESA, 16 U.S.C. § 1533(d); 50 C.F.R. § 17.31(a).[4] "Take" includes actions that kill, harass, or harm a protected species. 16 U.S.C. § 1532(19). "Harass" is defined to include acts that create the likelihood of injury to wildlife by annoying it to such an extent as to significantly disrupt normal behavioral patterns. 50 C.F.R. § 17.3. "Harm" includes significant habitat modification or degradation that actually kills or injures wildlife by significantly impairing essential behavioral patterns. *Id.*; 50 C.F.R. § 222.102.

III. FACTUAL BACKGROUND AND LEGAL VIOLATIONS

FDA has now approved GE salmon pursuant to authority it asserts under a unique and unlawful interpretation of its Federal Food Drug and Cosmetic Act (FFDCA) duty to regulate "new animal drugs." 80 Fed. Reg. 73,104 (Nov. 24, 2015). The GE salmon is the first GE fish (and the first GE animal for human consumption) that FDA has approved. In doing so, FDA has made an erroneous determination that its approval action will have "no effect" on threatened or protected species or their critical habitat. *See* FDA, Finding of No Significant Impact at 6-7 (Nov. 12, 2015). Endangered species such as imperiled Atlantic salmon (*Salmo salar*) (and in the predictable future, Pacific salmon), may be affected by the approval. FDA was therefore required to consult with the expert wildlife agencies under the ESA before reaching any decision.

A. Affected Species and Critical Habitat

The protected species and critical habitat that may be affected by FDA's approval action include, but are not limited to, the Gulf of Maine Distinct Population Segment of Atlantic salmon (*Salmo salar*) and Pacific salmonids, including certain populations of Chinook salmon (*Oncorhynchus tshawytscha*), chum salmon (*Oncorhynchus keta*), coho salmon (*Oncorhynchus kisutch*), sockeye salmon (*Oncorhynchus nerka*), and steelhead trout (*Oncorhynchus mykiss*).[5]

Wild Atlantic salmon populations have experienced steep declines due to a variety of human-induced pressures including overexploitation, degradation of water quality, and damming of rivers.[6] In 2000, NOAA Fisheries and FWS issued a final rule designating the Gulf of Maine Distinct Population Segment (GOM DPS) as endangered under the ESA.[7] The Services subsequently published a final rule in 2009 listing the expanded GOM DPS, updating the geographic boundaries of the freshwater range of the Atlantic salmon population to include the Androscoggin, Kennebec, and Penobscot River basins.[8] A final rule designating critical habitat for the GOM DPS was published in the Federal Register on June 19, 2009.[9]

According to NOAA's Office of Protected Resources, "[t]he populations of Atlantic salmon present in the Gulf of Maine DPS represent the last wild populations of U.S. Atlantic salmon."[10] NOAA recognizes aquaculture practices as one of the threats facing the remaining Atlantic salmon population as they "pose ecological and genetic risks."[11] The same is true for transgenic salmon, which have been banned off the coast of Maine since 2003.[12]

Pacific salmonid populations have also faced significant declines on the west coast of the United States.[13] Pacific salmonid species are vulnerable to a number of significant natural and human threats, among them: aquaculture,[14] hydropower, agriculture, flood control, natural resource extraction, and fishing.[15]

According to NOAA's Office of Protected Resources, the majority of all fish listed as endangered or threatened under the Endangered Species Act are Pacific salmonids, including certain populations of Chinook salmon (*Oncorhynchus tshawytscha*), chum salmon (*Oncorhynchus keta*), coho salmon (*Oncorhynchus kisutch*), sockeye salmon (*Oncorhynchus nerka*), and steelhead trout (*Oncorhynchus mykiss*).[16] NOAA Fisheries has issued a final rules designating critical habitat for 25 species of West Coast salmon and steelhead under the ESA.[17]

B. FDA Has Taken Action that "May Affect" Listed Species and Their Designated Critical Habitat Without Consulting with the Services.

Pursuant to the FDA approval, AquaBounty would manufacture its GE salmon at a facility located on Prince Edward Island, Canada, and transport, by land and air, the resulting eggs to a separate facility located in Panama, where they would be grown to maturity before being processed for sale in the United States. Like its approval decision, FDA's conclusion concerning endangered or threatened species rests on an extremely limited inquiry that failed to adequately consider the significant risks of harm to listed species related to the production and proliferation of AquaBounty's GE fish at the Prince Edward Island and Panama facilities, as well as from AquaBounty's ongoing efforts to expand these operations and produce GE salmon at numerous additional facilities around the world.

Both the Prince Edward Island (PEI) and Panama facilities where GE salmon will be engineered, grown, and housed create risks of escape, and potential harm to endangered and threatened species. The ESA requires FDA to consult on these potential impacts, even under FDA's unlawfully narrow scope of review. These threats, and the risks of escape from these sites, are detailed in numerous comments to FDA, including those from NOAA Fisheries and FWS[18] and many independent scientists.[19] This evidence also demonstrates that transgenic salmon are capable of surviving outside either facility. The PEI facility, for example, is near water bodies that historically have held salmonid species and is within the current range of the species' marine habitat. *See* Final EA at 75-6. The GE salmon's transgenic nature makes it more likely to survive because of its more aggressive nature and enhanced growth rate.[20] Studies have found that GE fish may be more competitive (Devlin et al., 1999), less discriminate in choosing prey (Sundström et al., 2004), more likely to attack novel prey (Sundström et al., 2004), and better at using lower quality food (Raven et al., 2006) when compared to wild relatives. The great weight of evidence of past experiences with invasive species and escapes further supports this conclusion.[21] When the GE salmon do escape, the impacts on the environment may be significant and irreversible, in the form of, *inter alia*, (1) ecological impacts on native species via predation and/or competition; and (2) genetic impacts via hybridization and genetic introgression.[22]

Scientists at FWS expressed these very concerns. Commenting on the FDA's 2010 EA and Briefing Packet, FWS's Northeast Region explained:

- Transgenic fish, regardless of where they are, pose a clear and present danger to wild fish populations. Given the extremely low populations of wild Atlantic salmon in the Maine DPS, any interaction between wild and transgenic salmon must be considered a serious threat, which can disrupt runs of wild fish, compete with wild fish for available food and habitat, interbreed with wild fish, transfer disease and/or parasites, and degrade benthic habitat. The scientific literature is full of actions indicating that interactions of wild fish and aquaculture escapees (read transgenic escapees) may lead to decreased numbers of wild fish and in the worst scenario, lead to extirpation of the remaining stocks in the U.S.

- History dictates it is reasonable to assume that fish held in aquaculture facilities, either land- or water-based, will escape unless strict quarantine/water treatment/screening/ bioengineering modifications are in place and aggressively monitored. And even then, it must be assumed that escape will still occur, and protocols must be in place to deal with such a non-native organism released into the environment, and its subsequent effect on native species, habitat, and aquatic communities. Transgenic fish, whether reproductively viable or sterile, must be maintained only in biosecure (zero discharge) land-based facilities ideally positioned outside of any wild fish watersheds until appropriate laboratory and field research has been undertaken to ensure that the risk of adverse effects on wild fish has been minimized.

- [AquaBounty Technologies (ABT)] appears to have established several physical and biological containment mechanisms to prevent the escape of AquAdvantage salmon. However, there is still risk of escapement and we think this risk is most prevalent at the PEl facility. If the brood stock from the PEI facility were released either accidentally or

with malicious intent, we do not feel enough evidence has been provided to conclude the risks to natural populations of Atlantic salmon in Canada and the U.S. are negligible. Additional experimentation needs to be conducted to verify that any escapees from the PEI facility will not be able to tolerate the brackish water in the vicinity of the facility. Also, the lack of information on the transport procedures from PEI to Panama is troublesome. It is during this stage of the operation that malicious activities could result in these fish being lost from the direct control of ABT.

- If there is an escape event, competition from the GMO salmon would negatively impact the wild stocks. Research has shown that aquaculture-raised salmon can outcompete wild salmon, and given the already endangered status of the wild stocks, any additional threat is amplified in their impacts. References are available.

- Aside from the potential spread of the GMO growth gene if they escape and successfully reproduce, the genetic origin of the broodstock that has been developed is likely genetically distinct from Maine salmon. The concern is if escape and reproduction occurs, this could lead to a disruption of the locally adapted gene complexes of the endangered populations. In the FDA report-petition, we didn't see reference to the origin of the broodstock.[23]

FWS's Conservation Genetics Community of Practice[24] sent FDA a letter in October 2010 noting these same risks and the need for FDA to conduct more thorough analyses:

> [T]he biological containment at either the PEI or Panama facilities along with the possible interaction of AquAdvantage salmon with endangered wild salmon stocks is of great concern to the COP. To this regard, AquaBounty Technologies has established several physical and biological containment mechanisms to prevent the escape of AquAdvantage salmon and the [EA] indicated escapement risk and establishment risks were low. However, history dictates that fish held in aquaculture facilities, either land- or water-based—escape. In addition, the information provided by AquaBounty Technologies for the likelihood of establishment relies on the assumption that farmed Atlantic salmon have not established themselves in North America. This assumption is clearly violated because Atlantic salmon juveniles have been found in several streams in the state of Washington as well as British Columbia. While interactions of these fish with native salmon are unknown[,] any interaction between wild and transgenic salmon must be considered a serious threat. Numerous scientific publications have documented that interactions of wild and introduced fish have led to decreased numbers of wild fish (for ESA listed Atlantic stocks this is of great concern).[25]

Dr. Gregory Moyer, a FWS Regional Geneticist also sent FDA a letter in October 2010 outlining "several criticisms and concerns" regarding the Briefing Packet, specifically the environmental risk analysis.[26] Dr. Moyer noted that the Briefing Packet "falls short of providing an actual risk assessment of putative environmental damages in the event of escapement."[27] He explained that the "environmental analysis should provide an overview of the general risks associated with escapement or hybridization of GE and wild type individuals" which "would

provide readers with an understanding of the potential harm and the degree of harm posed by GE organisms even when the risk of escapement is low."[28] He urged FDA to "more accurately quantif[y]" both the risk of escapement and degree of harm if escaped. Dr. Moyer added that he was concerned with phrases like "are unlikely to survive if exposed to high salinity and low temperature" "when no data have been collected on AquAdvantage salmon to evaluate the likelihood of these scenarios," and that although AquaBounty currently has "in place various standard operating procedures to minimize escapement and test for durability of the gene construct," he "fail[s] to see any policy in place for monitoring or enforcement of these SOPs by the [FDA]."[29]

Likewise, NOAA Fisheries recognized that "[p]reventing escapes is essential to minimizing the risks to genetic deterioration of wild fish populations, especially endangered and threatened salmonids whose effective populations are particularly vulnerable to the effects of interbreeding."[30] A memo from NOAA Fisheries notes that while it may not be likely, it is possible that AquAdvantage salmon will escape from the PEI and Panama facilities, and when they do, "they will likely [] reproduce in the wild because hatchery released fish and hatchery sterilized fish continue to behave similar to wild fish (Trested et al., 2002)."[31] This memo also warns that "successfully sterilized salmon would be attractive mates for wild fish and may reduce wild population fitness." It goes on to explain that, *inter alia*:

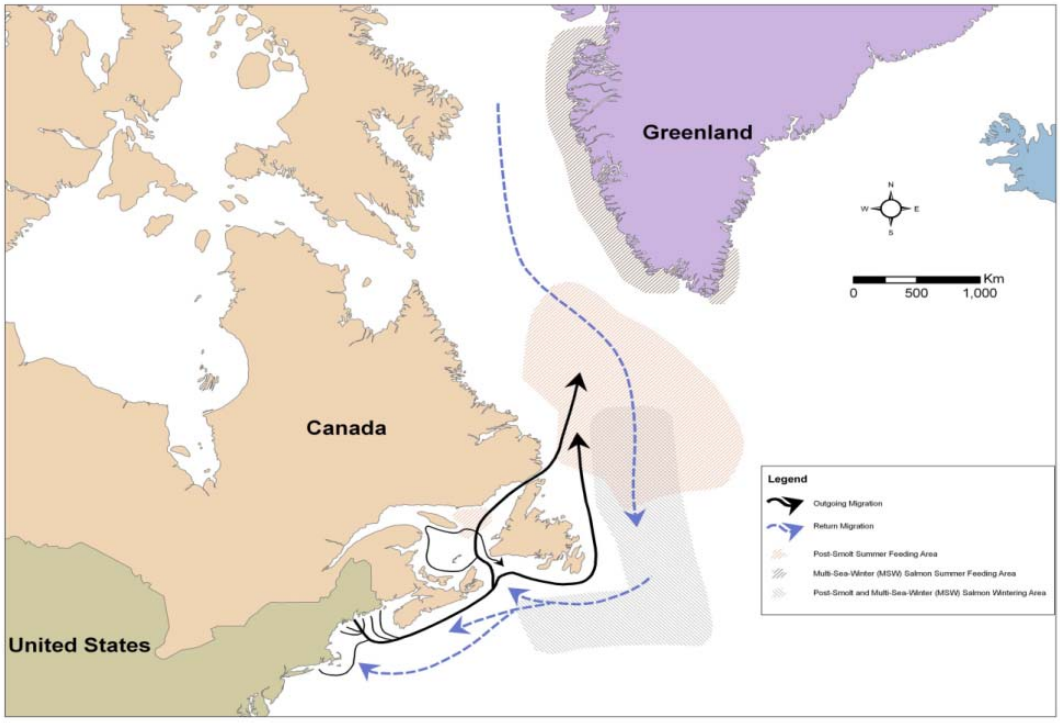
- An introduction of genetically engineered Atlantic salmon could pose catastrophic threats to wild listed species.

- The egg production facility may pose a threat to wild Atlantic salmon, including Gulf of Maine DPS Atlantic salmon.

- Any fish introduced along the Pacific Coast would have the potential to affect Pacific salmonids through hybridization.[32]

NOAA Fisheries has long recognized the potential harms associated with transgenic fish. In 2003, it issued an ESA Section 7 Biological Opinion (BiOp) for the Army Corps of Engineers regarding aquaculture fish pens within the state of Maine, banning transgenic salmonids in aquaculture sites off the coast of Maine due to the risks they could pose to wild, endangered Atlantic salmon populations.[33] There, NOAA Fisheries expressly referenced the potential risks associated with FDA's consideration of the AquaBounty NADA, and relied on studies by Dr. Kapuscinski to call for more research "to identify the impacts [] escaped transgenic salmon would have on natural populations and their habitat before use for commercial aquaculture is considered."[34]

FDA claims that it is "highly unlikely that [GE salmon] or diploid ABT salmon would affect" endangered Atlantic salmon from the Gulf of Maine or from Maine rivers because the "environmental conditions [surrounding the Prince Edward Island facility] are hostile to survival [of salmon], as evidenced by the lack of self-sustaining salmon populations in an environment that used to possess plentiful salmon runs." Final EA at 115. But, as shown by the following map from NOAA, endangered Atlantic salmon from Maine rivers and the Gulf of Maine migrate in and around the waters surrounding Prince Edward Island:[35]



Because containment measures cannot guarantee that GE salmon will not escape into the wild,[36] and because survival and reproduction of escaped GE salmon is possible, such an escape or release event would be significant and irreparable.[37] Indeed, FDA itself recognized the seriousness of these potential risks when it previously acknowledged that it would formally consult with the Services if these fish were grown in net pens.[38] These likely impacts far exceed the low threshold for actions that "may affect" listed Atlantic and Pacific species and trigger FDA's duty to consult with FWS and NOAA Fisheries regarding its approval of AquaBounty's application. As explained above, for an action that *may* affect any species or its critical habitat—"whether beneficial, benign, adverse, or of an undetermined character"—FDA *must*, at a minimum, seek the Services' expertise through consultation. *Western Watersheds Project v. Kraayenbrink*, 632 F.3d 472, 496 (9th Cir. 2010). "[A]ctions that have *any chance of affecting* listed species or critical habitat—even if it is later determined that the actions are 'not likely' to do so—require at least some consultation under the ESA." *Karuk Tribe of California v. U.S. Forest Service*, 681 F.3d 1006, 1027 (9th Cir. 2012) (en banc) (emphasis added). FDA's failure to complete consultation with the expert fish and wildlife Services violates the ESA.

For the same reasons, FDA also violated its independent duty to consult on the potential effects to any habitat designated as "critical" pursuant to ESA § 4(a)(3)(A), 16 U.S.C. § 1533(a)(3)(A). The legal standard for triggering FDA's duty to consult where its approval "may affect" a listed species' designated critical habitat is identical to the requirement to consult where the action "may affect" the species itself. *Karuk Tribe*, 681 F.3d at 1027 ("[A]ctions that have *any chance of affecting* listed species or *critical habitat*—even if it is later determined that the actions are 'not likely' to do so—require at least some consultation under the ESA.") (emphases added); *id*. ("Any possible effect, whether beneficial, benign, adverse or of an undetermined character" triggers the requirement) (citations omitted).

C. FDA's "No Effect" Determination Is Arbitrary and Did Not Use the Best Available Scientific and Commercial Data Available.

Rather than consult with the Services after a may affect determination, FDA instead relied entirely on its own internal assessments of the risks to conclude that its approval of GE salmon will have "no effect" on any listed species or designated critical habitat. FDA's "no effect" conclusion—and the process by which it reached that conclusion—violates the ESA.

As a threshold matter, FDA carries a heavy burden to demonstrate that its "no effect" determination is justified. Indeed, the ESA requires FDA to prove its approval will not jeopardize any listed species, nor adversely affect any critical habitat, and it has not met that burden. *See, e.g., Wash. Toxics Coalition v. Envtl. Prot. Agency*, 413 F.3d 1024, 1035 (9th Cir. 2005) ("Placing the burden on the acting agency to prove the action is non-jeopardizing is consistent with the purpose of the ESA and what we have termed its 'institutionalized caution mandate[].'"). Consistent with these requirements, FDA may decline to undergo consultation with the expert agencies *only* if it legitimately determines that its action will have no chance of affecting any listed species or critical habitat. This means *none*; any effect, however minor, compels consultation. *See supra.*

FDA, however, based its conclusions on its own inexpert—and fatally flawed—assumptions regarding the risk that GE salmon may escape into the environment and unilaterally concluded that the affected species have absolutely no chance of possibly being harmed.

First, as detailed above and extensively in the comments FDA received from Dr. Kapuscinski and other independent experts, the agency's assumption that GE salmon will not escape from AquaBounty's facilities is not based on the best available scientific and commercial data, including the standard practice of conducting a quantitative failure mode risk analysis. Instead, FDA relied on outdated risk analysis methods when considering risk of escapes and the direct and indirect environmental effects of AquaBounty's GE salmon on listed species. FDA cannot rely on outdated and inaccurate information to determine the potential effects on listed species. 16 U.S.C. § 1536(a)(2) (requiring agencies to use only the best available scientific and commercial data available).

Second, FDA arbitrarily limited the geographic scope of its inquiry to just the immediate vicinity of PEI and Panama sites. However, under the ESA, the "action area" is expressly defined as "all areas to be affected directly or <u>indirectly</u> by the federal action and not merely the immediate area involved in the action." 50 C.F.R. § 402.02 (emphasis added). The agency's approval will affect substantially more than just areas in Panama and PEI, due to the highly mobile and migratory nature of the species, its presence throughout the Gulf of Maine and in rivers in New England and throughout Atlantic Canadian provinces, and because of the likely proliferation of GE salmon in other locations, including within the United States, as reflected by pending requests for importation of AquaBounty's GE salmon eggs and AquaBounty's stated plans for expansion following this initial approval decision.

In addition, the area affected by any GE salmon that may be released or that may escape is far greater than just the immediate area around the facility—these fish could enter any number of marine environments that are home to endangered or threatened aquatic species.[39] FDA's "no effect" determination is based on its unlawfully restricted view of the action area as limited to just the areas immediately around the facilities.

Third, FDA similarly arbitrarily limited the scope of the "action" and the "effects" it considered. Under the ESA, "'agency action' is to be construed broadly." *See Karuk Tribe*, 681 F.3d at 1020. "[T]he scope of the agency action is crucial because the ESA requires the biological opinion to analyze the effect of the entire agency action." *Conner v. Burford*, 848 F.2d 1441, 1453 (9th Cir. 1988). Courts "interpret the term 'agency action' broadly," because "caution can only be exercised if the agency takes a look at all the possible ramifications of the agency action." *Id.*

Moreover, the "effects" of the broad action that must be considered under the ESA include not just direct, but also "indirect effects of an action on the species or critical habitat, together with the effects of other activities that are interrelated or interdependent with that action…." *Wild Fish Conserv. v. Salazar*, 628 F.3d 513, 525 (9th Cir. 2010) (quoting 50 C.F.R. § 402.02). "Indirect effects are those that are caused by the proposed action and are later in time, but still are reasonably certain to occur. Interrelated actions are those that are part of a larger action and depend on the larger action for their justification. Interdependent actions are those that have no independent utility apart from the action under consideration." *Id. See, e.g.*, *National Wildlife Federation v. Federal Emergency Management Agency*, 345 F. Supp. 2d 1151 (W.D. Wash. 2004) (rejecting agency argument that it could limit its scope to just the issuance of floodplain insurance and holding that the agency must also assess the impacts of later housing construction that the insurance would facilitate). FDA's duties under the ESA thus require it also consider its action's indirect effects, and the effects of all activities "interrelated or interdependent" with that action. 50 C.F.R. § 402.02.

Yet, FDA has defined the action and its effects to include only those effects it believes are directly associated with the production of the GE salmon in PEI and Panama. FDA unlawfully ignored the reasonably foreseeable direct, indirect, and cumulative impacts of its decision. Evidence in the record shows that petitions are already being submitted to grow these transgenic salmon elsewhere. Indeed, AquaBounty's own public statements admit that they plan to grow them elsewhere. And as commenters have observed, it is not economically feasible to grow these fish at just these two small facilities. AquaBounty's current application is thus just a foot in the door; AquaBounty is clearly dependent on future growth to justify its operation.[40]

Fourth, FDA's "no effect" determination is arbitrary and contrary to law because FDA did not consider impacts to threatened or endangered aquatic species and their habitats other than Atlantic salmon. As expert scientists have noted, the introduction of GE fish like AquaBounty's GE salmon could affect entire ecosystems.[41] Given, in particular, the foreseeable proliferation of GE salmon and the risks of escape inherent in the current application, FDA was required to consider possible effects on Pacific salmon and other salmonids, such as steelhead and trout.[42]

Indeed, just a short time after the close of the comment period on FDA's draft EA, a new study was published on June 3, 2013 in the Proceedings of the Royal Society, further belying the agency's assumptions and concluding that the AquaBounty GE salmon can successfully cross-breed with brown trout.[43] The scientists who authored the study "…suggest that interspecific hybridization be explicitly considered when assessing the environmental consequences should transgenic animals escape to nature." The study also concluded that the GE hybrid offspring could outgrow wild salmon, non-GE hybrid offspring, and even GE salmon.[44] The GE hybrids also outcompeted wild salmon in simulated stream environments. Although acknowledging this study in its Final EA, FDA dismissed the possibility of cross-breeding between brown trout and escaped GE salmon, and failed to discuss the potential of any effects from such cross-breeding on threatened and endangered species, including the GOM DPS Atlantic salmon. Final EA at 40-41 and 100, 104.

Finally, FDA violated its "rigorous" duty to "insure" against jeopardy by relying entirely on AquaBounty's third-party, uncertain measures to mitigate any harm. *See, e.g.*, *Ctr. for Biological Diversity v. Rumsfeld*, 198 F. Supp. 2d 1139, 1152 (D. Ariz. 2002) (holding that mitigation measures must be "certain to occur," "subject to deadlines or otherwise-enforceable obligation," and "must address the threats to the species in a way that satisfies the jeopardy and adverse modification standards"). Rather than being included as enforceable mitigation measures, the containment measures are merely described as "conditions of production and use," not even "conditions of approval." FDA fails to describe, and apparently has failed to consider, how it would enforce or monitor AquaBounty's purported protective measures to prevent escapes or otherwise prevent environmental harm.[45] FDA cannot avoid consultation by relying on mitigation measures not within its control. *See Nat'l Wildlife Fed'n v. Nat'l Marine Fisheries Serv*., 254 F. Supp. 2d 1196, 1213-14 (D. Or. 2003) (Biological Opinion inadequate where it relied on non-federal mitigation actions not reasonably certain to occur); *Sierra Club v. Marsh*, 816 F.2d 1376, 1385 (9th Cir. 1987) ("This reliance on the proposed actions of [others] does not satisfy [FDA]'s burden of insuring that its actions will not jeopardize the continued existence of the [endangered species]."). Without any provision for enforcement, these "mitigation measures" must be considered as being outside FDA's control and unlawfully uncertain.

IV. CONCLUSION

In sum, FDA's "no effect" finding and failure to consult is arbitrary and capricious and violates the ESA, because it fails to follow the ESA's mandated procedures, fails to use the best scientific and commercial data available, fails to consider significant aspects of the issue, and offers an explanation that runs counter to the evidence before the agency. As more fully detailed above, FDA is hereby notified that it has violated Section 7 of the ESA, 16 U.S.C. § 1536(a)(2), in at least the following ways:

Prior to approving the GE salmon, FDA failed to request from the expert agencies whether any threatened or endangered species, or designated critical habitat, may be present within or near the areas of the proposed actions. 16 U.S.C. § 1536(c)(1); 50 C.F.R. § 402.12.

Prior to approving the GE salmon, FDA failed to prepare a "biological assessment" to determine whether any threatened and endangered species that may be present within or near the

areas of the proposed actions may be affected. 16 U.S.C. § 1536(c)(1); 50 C.F.R. § 402.12.

Prior to approving the GE salmon, FDA failed to consult with the expert fish and wildlife Services regarding the potential adverse effects of the GE salmon on threatened and endangered species, and/or their critical habitat. 16 U.S.C. § 1536(a); 50 C.F.R. §§ 402.13-14.

FDA has failed to insure, in consultation with the expert agencies, that its action is not likely to jeopardize the continued existence of any threatened or endangered species or result in the destruction or adverse modification of the critical habitat of such species. 16 U.S.C. § 1536(a)(2).

FDA has failed to insure that the agency or AquaBounty will not make any irreversible or irretrievable commitment of resources with respect to the GE salmon prior to initiating and completing consultation with NOAA Fisheries. 16 U.S.C. § 1536(d).

FDA has failed, in consultation with the expert agencies, to utilize its authorities in furtherance of the purposes of the ESA by carrying out programs for the conservation of endangered and threatened species, in violation of the ESA. 16 U.S.C. § 1536(a)(1). More specifically, FDA has failed to utilize its authorities to carry out programs for the conservation of the threatened and endangered species located in areas where GE salmon will be foreseeably farmed, in violation of the ESA. 16 U.S.C. § 1536(a)(1).

FDA's determination that its approval of AquaBounty's GE salmon NADA will have "no effect" on listed species is arbitrary and fails to use the best available science.

For the above stated reasons, FDA has violated and remains in ongoing violation of Section 7 of the ESA. If these violations of law are not cured within sixty days, the listed organizations intend to file suit against the responsible agency/agencies and officials to enforce the ESA, seeking declaratory and injunctive relief, as well as attorney and expert witness fees and costs. 16 U.S.C. § 1540(g)(4). This notice letter was prepared based on good faith information and belief after reasonably diligent investigation. If you believe that any of the foregoing is factually erroneous or inaccurate, please notify us promptly. Further, during the notice period we are available to discuss effective remedies and actions that will assure future compliance with the ESA.

Sincerely,

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[1] This letter is substantively identical to a letter dated December 22, 2015 sent on behalf of Cascadia Wildlands, Center for Biological Diversity, Center for Food Safety, Ecology Action Centre, Food & Water Watch, Friends of the Earth, Golden Gate Salmon Association, Institute for Fisheries Resources, and Pacific Coast Federation of Fishermen's Associations. This letter is provided as notification only that Friends of Merrymeeting Bay and Kennebec Reborn intend to join in any action initiated pursuant to the original December 22, 2015 letter and does not amend, supersede, or otherwise alter the original letter.

[2] "Jeopardize" means taking action that "reasonably would be expected, directly or indirectly, to reduce appreciably the likelihood of both the survival and recovery of a listed species in the wild by reducing the reproduction, numbers, or distribution of that species." 50 C.F.R. § 402.02. A species' "critical habitat" includes those areas identified as "essential to the conservation of the species" and "which may require special management considerations or protection." 16 U.S.C. § 1532(5)(A).

[3] Section 7(a)(1) of the ESA requires FDA, in consultation with and with the assistance of the Services, to utilize its authorities in furtherance of the purposes of the ESA by carrying out programs for the conservation of endangered and threatened species. 16 U.S.C. § 1536(a)(1).

[4] NOAA has adopted rules pursuant to ESA § 4(d) that extend the take prohibition to Pacific salmon and steelhead species that are listed as "threatened." 16 U.S.C. § 1533(d); Endangered and Threatened Species: Final Listing Determinations for 16 ESUs of West Coast Salmon, and Final 4(d) Protective Regulations for Threatened Salmonid ESUs, 70 Fed. Reg. 37,160 (June 28, 2005) (updating 4(d) rules for Pacific salmon species); Endangered and Threatened Species: Final Listing Determinations for 10 Distinct Population Segments of West Coast Steelhead, 71 Fed. Reg. 834 (Jan. 5, 2006) (incorporating updated 4(d) rules for steelhead).

[5] The specific listed species include: California coastal chinook salmon, Central Valley spring-run chinook salmon, Lower Columbia River chinook salmon, Puget Sound chinook salmon, Sacramento River winter-run chinook salmon, Snake River fall-run chinook salmon, Snake River spring/summer-run chinook salmon, Upper Columbia River spring-run chinook salmon, Upper Willamette River chinook salmon, Columbia River chum salmon, Hood Canal summer run chum salmon, Central California Coast coho salmon, Southern Oregon and Northern Coastal California coho salmon, Lower Columbia River coho salmon, Oregon Coast coho salmon, Snake River sockeye salmon, Central California Coast steelhead, California Central Valley steelhead, Lower Columbia River steelhead, Middle Columbia River steelhead, Northern California steelhead,

Snake River Basin steelhead, South-Central California Coast steelhead, Southern California steelhead, Upper Columbia River steelhead, and Upper Willamette River steelhead. 70 Fed. Reg. 37,160 (June 28, 2005) (listing salmon); 71 Fed. Reg. 834 (Jan. 5, 2006) (listing steelhead).

[6] Office of Protected Resources, NOAA Fisheries, Atlantic salmon (*Salmo salar*), http://www.nmfs.noaa.gov/pr/species/fish/atlanticsalmon.htm (last visited Dec. 21, 2015).

[7] Endangered and Threatened Species; Final Endangered Status for a Distinct Population Segment of Anadromous Atlantic Salmon (*Salmo salar*) in the Gulf of Maine, Final Rule, 65 Fed. Reg. 69,459 (Nov. 17, 2000).

[8] Endangered and Threated Species; Designation of Critical Habitat for Atlantic Salmon (*Salmon salar*) Gulf of Maine Distinct Population Segment: Final Rule, 74 Fed. Reg. 29,300 (June 19, 2009).

[9] *Id.*

[10] Office of Protected Resources, NOAA Fisheries, Atlantic salmon (*Salmo salar*), *supra* n.6.

[11] *Id.*

[12] Endangered Species Act Section 7 Consultation, Biological Opinion, Proposed modification of existing ACOE permits authorizing the installation and maintenance of aquaculture fish pens within the State of Maine (November 19, 2003), attached to this letter as Attachment 1.

[13] *See generally* Endangered and Threatened Species: Listing of Several Evolutionary Significant Units (ESUs) of West Coast Steelhead, 62 Fed. Reg. 43,937 (Aug. 18, 1997); Endangered and Threatened Species: Threatened Status for Two ESUs of Steelhead in Washington, Oregon, and California, 63 Fed. Reg. 13,347 (Mar. 19, 1998); Endangered and Threatened Species: Threatened Status for Two ESUs of Steelhead in Washington and Oregon, 64 Fed. Reg. 14,517 (Mar. 25, 1999); Endangered and Threatened Species; Threatened Status for Three Chinook Salmon Evolutionarily Significant Units (ESUs) in Washington and Oregon, and Endangered Status for One Chinook Salmon ESU in Washington, 64 Fed. Reg. 14,308 (Mar. 24, 1999); Endangered and Threatened Species: Threatened Status for Ozette Lake Sockeye Salmon in Washington, 64 Fed. Reg. 14,528 (Mar. 25, 1999).

[14] *See, e.g.*, R. L. Naylor, *et al.*, *Salmon aquaculture in the Pacific Northwest a global industry with local impacts*, Environment: Science and Policy for Sustainable Development 45(8) (2003) 18-39.

[15] *Id.*

[16] Office of Protected Resources, NOAA Fisheries, Endangered and Threatened Marine Species under NMFS' Jurisdiction, http://www.fisheries.noaa.gov/pr/species/esa/listed.htm#fish (last visited Dec. 21, 2015).

[17] Endangered and Threatened Species; Designation of Critical Habitat for 12 Evolutionarily Significant Units of West Coast Salmon and Steelhead in Washington, Oregon, and Idaho, Final Rule, 70 Fed. Reg. 52,630 (Sept. 2, 2005); Endangered and Threatened Species; Designation of Critical Habitat for Seven Evolutionarily Significant Units of Pacific Salmon and Steelhead in California, 70 Fed. Reg. 52,488 (Sept. 2, 2005) (designation of Critical Habitat for California Coastal Chinook salmon, Northern California Steelhead, Central California Coast Steelhead; South Central Coast Steelhead; Southern California Steelhead; Central Valley spring run Chinook salmon; and Central Valley Steelhead); Designated Critical Habitat; Snake River Sockeye Salmon, Snake River Spring/Summer Chinook Salmon, and Snake River Fall Chinook Salmon, 58 Fed. Reg. 68,543 (Dec. 28, 1993); Designated Critical Habitat; Central California Coast and Southern Oregon/Northern California Coasts Coho Salmon, 64 Fed. Reg. 24,049 (May 5, 1999); Endangered and Threatened Species: Final Threatened Listing Determination, Final Protective Regulations, and Final Designation of Critical Habitat for the Oregon Coast Evolutionarily Significant Unit of Coho Salmon, 73 Fed. Reg. 7,816 (Feb. 11, 2008).

[18] After FDA changed course and found that its approval would have "no effect" on listed species, FWS and NOAA sent separate letters to FDA in which the agencies did not object to FDA's determination. *See* Final EA, Appendix D. Neither of these letters discusses any of these agencies' previous findings and comments, or the scientific evidence concerning risks posed by the release of GE salmon from the PEI, Panama, or any other facilities. To the extent that FDA interprets these letters to support its "no effect" determination, the letters have no legal significance in the ESA's consultation process, and to the extent that FDA believes they represent any conclusions by the Services, the positions articulated in those letters are not based on the best available science and are themselves arbitrary and capricious.

[19] *See* Dr. Jon Rosenfield Comments, attached to this letter as Attachment 2.

[20] *Id.*

[21] *Id.*

[22] *Id.*

[23] FWS Region 5 Fisheries Program Comments on FDA approval process for Aqua Bounty Technologies, Inc. (ABT)/AquAdvantage GMO salmon (emphases added), attached to this letter as Attachment 3.

[24] This is FWS's coalition of fish conservation genetics experts. *See* http://www.fws.gov/ConservationGeneticsCOP/index.html.

[25] FWS Conservation Genetics Community of Practice Letter to FDA (Oct. 6, 2010) (emphases added), attached to this letter as Attachment 4.

[26] Dr. Gregory Moyer Letter to FDA (Sept. 30 2010), attached to this letter as Attachment 5.

[27] *Id*.

[28] *Id*.

[29] *Id*.

[30] NMFS, Talking Points for Senate Commerce Committee Staff Briefing on S. 1717 "Prevention of Escapement of Genetically Altered Salmon in the United States Act" (Dec. 5, 2011), attached to this letter as Attachment 6.

[31] NMFS Concerns Memo and Letter from Therese Conant, NMFS Acting Division Chief, Endangered Species Division, to Larissa Rudenko (Nov. 30, 2011), attached to this letter as Attachment 7.

[32] *Id*.

[33] 2003 BiOp, *supra* n.12.

[34] *Id*. at 74-75.

[35] http://www.nefsc.noaa.gov/press_release/2008/MediaAdv/MA0807/2Saunders_MigrationRoute.jpg.

[36] Anne Kapuscinski and Fredrik Sundstöm, *Comments on Environmental Assessment for AquAdvantage Salmon and Briefing Packet on AquAdvantage Salmon for the Veterinary Medicine Advisory Committee* at 4 (2010) ("As scientists, we cannot agree with this approach because it assumes 100% achievement of multiple confinement without presenting the failure mode analysis that is standard practice in technology risk assessment. Even if actual exposure is very close to zero, it is still necessary to assess ecological consequences…."), attached to this letter as Attachment 8.

[37] See, Dr. Jonathan Rosenfeld Comments, *supra* n.18; *see also* FWS Region 5 Comments, *supra* n.23, FWS COP letter, *supra* n.25, NFMS Concerns Memo and Letter, *supra* n.30.

[38] 2009 FDA denial of 2001 CFS petition, attached to this letter as Attachment 9.

[39] As NOAA Fisheries previously indicated, because FDA's action contemplates the selling of eyed eggs commercially and rearing fertile adult males at the PEI facility, the action area must include the United States. *See* NOAA Fisheries Concern Memo, *supra* n.30 and Letter to FDA from Therese Conant, *supra* n.31.

[40] FDA may not rely on the potential to consult later to addresses these fatal flaws in its "no effect" conclusion. The precautionary approach embodied in Section 7(a)(2) requires consultation before an action begins, not to conduct a post mortem years later. *See, e.g., Wild*

Fish Conservancy v. Salazar, 628 F.3d 513, 524 (9th Cir. 2010) (intent to consult later does not cure failure to complete consultation at the outset concerning action's full extent).

[41] Dr. Jonathan Rosenfeld Comments, *supra* n.18. *See also* NMFS Concerns Memo, *supra* n.31 ("Any fish introduced along the Pacific Coast would have unknown potential for affecting Pacific salmonids through hybridization.").

[42] *Id.* Accidental or other release of fish from aquaculture facilities is plainly "reasonably certain to occur;" indeed, it is already in progress in many parts of the United States and elsewhere in the world. *See, e.g.*, Fischer, et al., *Occupancy dynamics of escaped farmed Atlantic salmon in Canadian Pacific Coastal Salmon Streams: Implications for Sustained Invasions*, Biological Invasions, Vol. 16, Issue 10, pp 2137-2146 (October 2014), *available at* https://goo.gl/QpRWsD; Morris, et al., *Prevalence and Recurrence of Escaped Farmed Atlantic Salmon in Eastern North American Rivers*, Can. J. Fish. Aquat. Sci. Vol. 65 (2008), *available at* http://0101.nccdn.net/1_5/165/1c4/1be/morrisetal2008.pdf.

[43] K. B. Oke, *et al. Hybridization between genetically modified Atlantic salmon and wild bran trout reveals novel ecological interactions*, The Royal Society (May 2013), *available at* http://rspb.royalsocietypublishing.org/content/280/1763/20131047.

[44] Rebecca Morelle, *GM salmon can breed with wild fish and pass on genes*, BBC News (May 29, 2013), http://www.bbc.co.uk/news/science-environment-22694239.

[45] *See 2010* Kapuscinski and Sundström VMAC Comments at 2, *supra* n.36 (questioning how FDA will oversee the facilities; "How will FDA assure and audit the company's implementation of this 'integrated confinement system'"?).