Finding of No Significant Impact (FONSI)

In support of an Approval of a Supplemental New Animal Drug Application to allow the Grow-out of AquAdvantage Salmon at AquaBounty Technologies, Inc.'s Indiana Facility

AquaBounty Technologies, Inc. (ABT or the sponsor) has provided data and information to the Food and Drug Administration's (FDA's) Center for Veterinary Medicine (CVM) in support of a supplemental New Animal Drug Application (NADA 141-454) related to AquAdvantage Salmon, a line of genetically engineered (GE) Atlantic salmon[1] that are produced and grown only under the conditions specified in the approved application and additional conditions that may be approved in a supplemental NADA. This line of fish is designed to exhibit a rapid-growth phenotype that allows it to reach 100 g (smolt size) faster than non-GE farm-raised Atlantic salmon. In this supplemental NADA, ABT requests permission for grow-out of AquAdvantage Salmon at a land-based, freshwater aquaculture facility near Albany, Indiana (Indiana facility). All previous conditions of approval in the original NADA remain in effect.

As a part of the NADA review and approval process under the Federal Food, Drug, and Cosmetic Act (FD&C Act), and consistent with the mandates in the National Environmental Policy Act of 1969 (NEPA), 42 U.S.C. § 4321 et seq. and FDA's environmental impact considerations regulations (21 CFR part 25), FDA has thoroughly evaluated the potential environmental impacts of this proposed action[2] (the approval of a supplemental NADA for AquAdvantage Salmon) based on an environmental assessment (EA) prepared by ABT, see the attached EA dated April 20, 2018, and an FDA inspection of the Indiana facility conducted in late February, 2018. This FONSI is based on the analyses and findings presented in the sponsor's April 20, 2018 EA supporting the supplemental NADA, including a consideration and evaluation of a no action alternative (i.e., a decision not to approve the supplemental NADA for grow-out in Indiana).

FDA's November, 2015 approval of the AquAdvantage Salmon NADA was limited to the specific set of conditions enumerated and described in the NADA and the approval letter, with the GE animal remaining under FDA regulatory oversight as long as it is produced and marketed. FDA's approval of the AquAdvantage Salmon supplemental NADA would be for the specific set of conditions described in the sponsor's EA and as enumerated in FDA's approval letter. These include appropriate controls on the grow-out of the AquAdvantage Salmon, including appropriate physical and biological containment measures. Under the specific conditions of the supplemental NADA for AquAdvantage Salmon, these fish are defined as triploid[3], all-female populations that would be produced as eyed-eggs at a single specific facility on Prince Edward Island (PEI) in Canada (PEI facility). Eyed-eggs would be shipped to a specific land-based grow-out facility near Albany, Indiana, where they would be reared to market size and harvested for processing for food[4] use (e.g., preparation of eviscerated whole fish, fish fillets, steaks, etc.). The conditions that would be established in the approval of the supplemental NADA would limit breeding to one location (PEI) and

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[1] The approved NADA is for the α-form of the opAFP-GHc2 recombinant DNA construct at the a-locus in the EO-1α line of triploid, all-female Atlantic salmon under the conditions of use specified in the application. For ease of reference, this document refers to the NADA and the supplemental NADA as being for AquAdvantage Salmon.

[2] For the purposes of this FONSI, "action" and "approval" may be used interchangeably.

[3] With reference to AquAdvantage Salmon, and throughout the EA, "triploid" means that, based on sampling, at least 95% of released eyed-eggs have three complete sets of chromosomes per cell with a probability of 0.95 (i.e., the probability that these eggs are not at least 95% triploid is less than 0.05).

[4] For the purposes of this FONSI, "food" refers to food for humans and animals, including animal feed.

rearing (grow-out) of AquAdvantage Salmon to two locations (Panama and Indiana). In addition, the conditions would not include raising AquAdvantage Salmon in ocean net pens.

FDA's approval of the supplemental NADA would be for the specific set of conditions described in ABT's EA and as enumerated in FDA's approval letter. All other conditions of approval, covered by the approval letter for the original NADA dated November 19, 2015, remain in effect. No other conditions of production and use of AquAdvantage Salmon would be within the scope of the approval of the original NADA or the supplemental NADA, as no others would be approved by FDA. Any production or use outside the scope of the approval and supplemental approval would be unapproved and will result in the article, in this case AquAdvantage Salmon, being considered an unsafe new animal drug and, therefore, adulterated within the meaning of section 501(a)(5) of the FD&C Act. The sponsor must continue to notify FDA about proposed changes in any conditions established in an approved application and obtain FDA approval of a supplemental application for the change where necessary. 21 CFR 514.8. Major and moderate changes, including any additional production facilities, would require the filing and review of additional supplemental NADAs. Like this supplemental NADA, approval of any additional supplemental applications would constitute major agency actions and trigger additional environmental analyses under NEPA, unless otherwise excluded.

Social, economic, and cultural effects of the proposed action on the United States have not been analyzed and evaluated because the analysis in the EA indicates that the proposed action will not significantly affect the physical environment of the United States. Under NEPA, social and economic effects must be considered only once it is determined that the proposed agency action significantly affects the physical environment. 40 CFR 1508.14; see Olmstead Citizens for a Better Community v. U.S., 793 F.2d 201 (8th Cir. 1986) ("an impact statement generally should be necessary only when the federal action poses a threat to the physical resources of the area...."). See also Metro. Edison Co. v. People Against Nuclear Energy. 460 U.S. 766, 774 (U.S. 1983).

ABT's approach to analysis in the EA is closely based on that previously used in the FDA-prepared EA for the original NADA (NADA EA). This approach was based on a characterization of hazards, an evaluation of potential exposure pathways, and a consideration of the likelihood of any resulting risk. The environmental analysis of consequences in the EA incorporates the principles described by the National Research Council as well as the U.S. Environmental Protection Agency's (EPA) approach to ecological risk assessment. The potential hazards and harms addressed in the sponsor's EA center on the likelihood and consequences of AquAdvantage Salmon escaping, surviving, and becoming established in the environment near the Indiana facility, and subsequently causing an adverse outcome (the risk) to the environment. These hazards are addressed for grow-out at the Indiana facility within the framework of a conceptual risk assessment model, and the following series of risk-related questions:

1. What is the likelihood that AquAdvantage Salmon will escape the conditions of confinement?
2. What is the likelihood that AquAdvantage Salmon will survive and disperse if they escape the conditions of confinement?
3. What is the likelihood that AquAdvantage Salmon will reproduce and establish if they escape the conditions of confinement?
4. What are the likely consequences to, or effects on, the environment should AquAdvantage Salmon escape the conditions of confinement?

Based on this analysis, FDA considers the likelihood that AquAdvantage Salmon could escape from containment, survive, disperse, and become established in the local environment of the Indiana facility to be very low.

Information in the sponsor's EA, which was confirmed during an FDA inspection of the Indiana facility in late February 2018, indicates a high level of physical containment is present throughout the facility. Physical containment at the Indiana facility is augmented by operational containment (standard operating procedures and operational plans), security measures (e.g., perimeter fencing) and ongoing surveillance (e.g., cameras and recording devices). As described in ABT's EA (Section 5.4.2), physical containment refers to measures or barriers implemented on-site to prevent the movement or escape of fish from the facility. Containment measures can include the use of mechanical devices, either stationary or moving (e.g., tanks, screens, filters, covers, nets, etc.), or in some cases, the use of lethal temperatures or chemicals to prevent uncontrolled escape. All production units in the facility will have a minimum of five independent levels of physical containment (i.e., barriers) preventing escape of eggs or fish via effluent flow paths to the outside environment (i.e., Riley Stafford Ditch)[5], and some of the production units will have six or seven barriers in place. This number of containment levels is more than adequate and greater than the number at most fish production facilities. For comparison, the ABRAC Performance Standards[6] developed by the U.S. Department of Agriculture for facilities conducting research on genetically modified fish and shellfish call for three to five levels of containment. In addition, as substantiated during the FDA facility inspection, the majority of containment equipment (screens, filters) are either new or recently refurbished, and manufactured from heavy gauge stainless steel or other appropriate materials, so they should be reliable, durable and require minimal maintenance and repair.

Should unintentional release of AquAdvantage Salmon occur, high water temperatures and other environmental conditions in the geographic setting of the Indiana grow-out site and farther afield would afford additional means of containment of any escaped eggs or fish, given that these conditions would be generally hostile to their long-term survival, reproduction, and establishment. This is evidenced by the lack of Atlantic salmon and other salmonids (e.g., trout species), which are cold water fish species, in the vicinity of the Indiana facility even though rainbow trout have been intentionally stocked there in the past. These environmental conditions will greatly limit and essentially preclude the possibility of a complete exposure pathway by which AquAdvantage Salmon could affect Atlantic or Pacific salmon populations in the United States.

In addition, because the production process for AquAdvantage Salmon ensures that all populations produced at the PEI facility and reared at the Indiana facility will be triploid (effectively sterile), all-female animals, the possibility of their reproducing in the wild is likewise extremely remote. This was discussed at length in the FDA-prepared NADA EA.

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[5] In Section 7.2.1 of the sponsor's EA it is stated that "Five levels of physical containment are in place at each Unit except the Purge-Harvest unit which has three primary levels of containment", but that there are additional containment measures in the effluent treatment and discharge process," resulting in a total of five to seven independent levels of containment for all production units". Here we are referring to the total number of levels of containment in water flow paths between the equipment in which eggs or fish are housed (e.g., egg trays, tanks) and the Riley Stafford Ditch, which corresponds to the latter.

[6] ABRAC [Agricultural Biotechnology Research Advisory Committee] (1995). Performance standards for safely conducting research with genetically modified fish and shellfish. Document No. 95-04, Office of Agricultural Biotechnology, U.S. Department of Agriculture, 156 pp.

Because risk is the product of two probabilities, the probability of exposure, and the conditional probability of harm given that exposure has occurred (NAS 2002), if exposure is negligible, then even if the probability of harm is larger, the overall risk is negligible. The analysis in the EA indicates that there is a very low likelihood of escape from the Indiana grow-out facility. Given the additional redundant containment measures in place (e.g., physical, biological, and geographical/geophysical), the combination of these factors results in an extremely low likelihood that AquAdvantage Salmon could escape into the wild and cause effects on the environment. FDA therefore concludes that the grow-out of AquAdvantage Salmon in Indiana under the conditions specified in the supplemental NADA and as described in the accompanying EA would not result in significant effects on the quality of the human environment in the United States.

For major Federal actions, including an action to approve a supplemental NADA for grow-out of AquAdvantage Salmon at an additional facility that was not approved as part of NADA 141-454, NEPA and its implementing regulations require that environmental documents include a brief discussion of the alternatives to the proposed action, as well as the environmental impacts of these alternatives. The ABT EA in Section 4, describes the reasonable alternatives, which include the proposed action and one “no action” alternative.

The alternatives are approval of the supplemental NADA under the conditions of production and use described in the EA and that would be set forth in the approval, if the supplemental NADA is approved, and the “no action” alternative, which considers the environmental impacts of not approving the supplemental NADA. The action evaluated in the EA is the approval of the supplemental NADA, which would permit grow-out of AquAdvantage Salmon at ABT’s Indiana facility. The only other conditions of production and use of AquAdvantage Salmon would be those that are permitted under the approval of NADA 141-454, which allows commercial production of eyed-eggs for AquAdvantage Salmon at the PEI facility and the grow-out of AquAdvantage Salmon at the Panama facility. No other conditions of production and use of AquAdvantage Salmon would be within the scope of the NADA or supplemental NADA approvals. The approval of the supplemental NADA is therefore described as the preferred alternative. As described above, any changes and/or additions to the conditions of production and use for AquAdvantage Salmon that constitute a major or moderate change would require a supplemental NADA approval prior to implementation. Any supplemental approval would constitute a new agency action triggering additional environmental analysis under NEPA (see 21 CFR 25.20(m)) to address the potential and cumulative impacts of any proposed changes and/or additions.

FDA has considered the no action alternative for this action, that is, a decision not to approve the supplemental NADA for AquAdvantage Salmon. Should FDA decide not to approve the supplemental NADA to allow grow-out of AquAdvantage Salmon at the Indiana facility, ABT could either continue to produce AquAdvantage Salmon at only the PEI and Panama facilities or it could seek approval to grow-out AquAdvantage Salmon at one or more alternative grow-out facilities. The first of these outcomes would maintain the status quo and would result in no environmental impacts other than those that were evaluated in the NADA EA, which resulted in an FDA FONSI. Because this outcome would not result in a significant impact on the environment, the EA did not address it. The second of these outcomes would require submission of one or more additional supplemental NADAs that would constitute an agency action(s) requiring separate analysis under NEPA. Moreover, because production of AquAdvantage Salmon would be possible at any number of locations worldwide, under different containment conditions and levels of regulatory oversight, and potentially within areas where native Atlantic salmon or other salmonid species are present, there are far too many variables and unknowns to define specific scenarios and perform a comprehensive risk assessment for them at this time.

Section 7(a) of the Endangered Species Act (ESA) requires federal agencies to "insure that any action authorized, funded, or carried out by the agency" (the agency action) "is not likely to jeopardize" the continued existence (or result in the destruction or adverse modification of a designated critical habitat) of any species of fish, wildlife, or plants that have been determined to be threatened or endangered under Section 4 of the ESA (i.e., officially listed). In this case, the action is approval of the supplemental NADA that would allow grow-out of AquAdvantage Salmon at the Indiana facility.

Federally listed threatened or endangered species in Delaware County, Indiana, the county in which the Indiana facility is located, include four species of mollusks (the northern riffleshell, the clubshell, the rabbitsfoot, and the rayed bean mussels), one mammal (the Indiana bat), and one species of vascular plant (running buffalo clover).[7] These species are also on the Indiana list of endangered species. An additional five reptiles, five birds, and three vascular plants are state listed as endangered species.[8] No effects on any of these species are reasonably foreseeable as a result of escape or unintentional release of AquAdvantage Salmon from the grow-out facility in Indiana. None of these species serves as prey items for Atlantic salmon. Larval stages of many freshwater mussels use fish species as hosts. For the four mussel species listed, none are solely dependent on salmonid species as a host because they do not have a sole species host requirement.[9] In addition, the historical absence of salmonid species in this area of Indiana precluded them from ever being a host for these freshwater mussels. Moreover, as discussed earlier, the likelihood of escape and survival of AquAdvantage Salmon in the local watershed to an extent that they could serve as hosts for these mussel larvae is extremely remote.

Effects on threatened and endangered species in Indiana are not reasonably foreseeable given the weight of evidence that AquAdvantage Salmon are unlikely to escape from the Indiana facility, and even if they somehow were able to escape, as discussed in the EA, they could not survive for very long, disperse, reproduce, or establish in the local aquatic environment. Thus, there is no exposure pathway for AquAdvantage Salmon from the Indiana facility to interact with, or adversely affect, any threatened or endangered species in Indiana or elsewhere. It is therefore reasonable to conclude that approval of the supplemental NADA to allow grow-out of AquAdvantage Salmon at the Indiana facility will have no effect on threatened or endangered species in the area.

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[7] The endangered species listing for Atlantic salmon in the United States includes the Gulf of Maine distinct population segment (FWS, 2009). As stated in Section 7.5.1 of ABT's EA, "no complete exposure pathway exists from the grow-out site in Indiana to marine waters in the United States where populations of Atlantic and Pacific salmon live." This includes the Gulf of Maine distinct population segment of Atlantic salmon. Any interactions with wild Atlantic or Pacific salmon would require passage of AquAdvantage Salmon from the local Indiana watershed down the Wabash and Mississippi Rivers and through the Gulf of Mexico, a situation that is precluded due to the occurrence of high temperatures and other environmental conditions in these waters that are incompatible with salmon survival.

[8] http://www.in.gov/dnr/naturepreserve/files/np_delaware.pdf, Accessed 4/24.2018.

[9] Host species for northern riffleshell include banded darter, bluebreast darter, brown trout, and banded sculpin (https://www.nrc.gov/docs/ML1126/ML112650644.pdf, accessed 4/24/2018). Host species for the rabbitsfoot include whitetail shiner, spotfish shiner, and bigeye chub (Yeager and Neves, 1986). Host species for the clubshell include blackside darter, central stoneroller, logperch, and striped shiner (https://mnfi.anr.msu.edu/abstracts/zoology/Pleurobema_clava.pdf; accessed 4/24/2018). Host species for the rayed bean include Tippecanoe darter, greenside darter, mottled sculpin, and largemouth bass (Butler, 2002).

As a result of the review of the materials submitted in support of a supplemental NADA approval, FDA has made a "no effect" determination under the Endangered Species Act (ESA), 16 USC §1531et seq., i.e., that when reared under the conditions in the application, and as described within ABT's EA, AquAdvantage Salmon would not jeopardize the continued existence of United States populations of threatened or endangered species or result in the destruction or adverse modification of their critical habitat.

The North Atlantic Salmon Conservation Organization's (NASCO) Williamsburg Declaration is a non-binding resolution adopted by its members, which include the United States. In June 2003, NASCO adopted the so-called Williamsburg Resolution, Article 7 of which states that the parties should apply the Guidelines for Action on Transgenic Salmon to protect against potential impacts from transgenic or GE salmonids on wild salmon stocks. The portion of these Guidelines that is relevant to this FONSI (Williamsburg Resolution, Annex 5) states, "while there may be benefits from the introduction of such salmonids if, for example, they could not interbreed with wild stocks...," specific steps should be taken to ensure protection of the wild stocks, including utilization of "all possible actions to ensure that the use of transgenic salmonids, in any part of the NASCO Convention area, is confined to secure, self-contained, land-based facilities." FDA has determined that the Indiana facility for grow-out of AquAdvantage Salmon follows this recommendation in the NASCO guidelines in that there are no wild salmon stocks in the vicinity of the facility and it is a secure, self-contained, land-based facility.

The Council for Environmental Quality's NEPA regulations define cumulative impact as "the impact on the environment which results from the incremental impact of the present action when added to other past, present and reasonably foreseeable future actions ...." 40 CFR 1508.7. As described in the EA, because FDA found there would be no significant impact on the environment from the action to approve the original NADA, and FDA is concluding in this FONSI there would be no significant impact on the environment from the action to approve the supplemental NADA, FDA, therefore, concludes that there would be no cumulative impacts on the environment of the United States for the action to approve the supplemental NADA for the grow-out facility in Indiana.

NEPA Decision and Findings

We have carefully considered the potential environmental impacts of both the proposed agency action to approve the supplemental NADA to allow grow-out of AquAdvantage Salmon at ABT's Indiana facility (the proposed and preferred alternative) and the No Action Alternative, as described in the sponsor's EA. Based on our evaluation and analysis, and taking into consideration the specific conditions that were established in the original NADA and that would be established in the approved supplemental NADA, we have made the finding that the action to approve the supplemental NADA would not individually or cumulatively have a significant effect on the quality of the human environment in the United States. Based on that finding, FDA has decided not to prepare an environmental impact statement for this proposed action.

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Electronic Signature
Addendum for Submission ID

Signing Authority (Role)	Letter Date
Elizabeth Rettie (Office Director) - Acting	4/25/2018

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