Amended Finding of No Significant Impact (FONSI)

For
the production of AquAdvantage® Salmon at the
Bay Fortune and Rollo Bay Facilities on Prince Edward Island, Canada

In support of the
New Animal Drug Application related to AquAdvantage® Salmon,
which are triploid, hemizygous, all-female Atlantic salmon (Salmo salar)
bearing a single copy of the α-form of the opAFP-GHc2 recombinant DNA construct
at the α-locus in the EO-1α lineage
Owned by
AquaBounty Technologies, Inc.
Harvard, MA

Prepared by
Center for Veterinary Medicine
United States Food and Drug Administration
Department of Health and Human Services

September 2024

Background

On November 19, 2015, the United States (US) Food and Drug Administration (FDA) approved new animal drug application (NADA) 141-454 concerning AquAdvantage Salmon (AAS).[1] AAS are triploid, hemizygous, all-female Atlantic salmon (*Salmo salar*) bearing a single copy of the α-form of the *opAFP-GHc2* recombinant DNA (rDNA) construct at the α-locus in the EO-1α lineage. AAS is designed to exhibit a rapid-growth phenotype that allows it to reach smolt size (100 g) faster than farm-raised Atlantic salmon without the *opAFP-GHc2* construct. The November 19, 2015, NADA approval allowed for the AAS to be produced at a facility on Prince Edward Island (PEI), Canada, and grown at a facility in Panama,[2] and allowed for sale of food harvested from AAS in the US.

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's Center for Veterinary Medicine (CVM) prepared an environmental assessment (EA) dated November 12, 2015, for the original

[1] The NADA is for approval of a single copy of the α-form of the *opAFP-GHc2* recombinant DNA construct at the α-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 generally refers to the application as being for approval of the AquAdvantage Salmon (AAS).
[2] The AquaBounty Technologies, Inc. (ABT) facility in Panama was closed in 2019 and is no longer approved under NADA 141-454.

approval of AAS.[3] Based on the EA and the specific conditions that were established in the NADA, FDA determined the action would not individually or cumulatively have a significant effect on the quality of the human environment in the US. Therefore, FDA prepared a FONSI.[4] Based on the findings in the EA, FDA also made a "no effect" determination under the Endangered Species Act (ESA), 16 USC § 1531, et seq., concluding that AAS, when produced and reared under the conditions in the application, and as described in the EA, would not affect US populations of threatened or endangered Atlantic salmon or their critical habitat.

Following the original approval, several organizations filed suit in the US District Court, Northern District of California, challenging, among other things, FDA's evaluations under NEPA and the ESA for the 2015 NADA approval. While the Court upheld FDA's jurisdiction to regulate this product under the FD&C Act and left the NADA approval in place, on November 5, 2020, the Court remanded the EA for the 2015 original approval to FDA and ordered FDA to evaluate the potential harm to endangered Atlantic salmon in the unlikely event that AAS escaped, survived and established in the natural environment.[5] In addition, it ordered FDA to reconsider its "no effect" determination under the ESA.

Following the original approval in November 2015, FDA approved two supplements under NADA 141-454 allowing for grow-out of AAS at a land-based, freshwater aquaculture facility near Albany, Indiana (approval date April 26, 2018), and the production of AAS eyed-eggs[6] in a Hatchery Unit at a second, new land-based aquaculture facility on PEI, known as the Rollo Bay facility (approval date November 5, 2019). EAs were also prepared for these supplemental approvals, which resulted in FONSIs. These approvals and EAs were not challenged in the lawsuit.

In order to address the outstanding issues outlined in the Court's November 5, 2020, decision, FDA prepared an amended EA, dated September 2024, titled "Amended Environmental Assessment for Production of AquAdvantage® Salmon at the Bay Fortune and Rollo Bay Facilities on Prince Edward Island, Canada." A copy of the EA is attached. FDA determined that the September 2024 amended EA provides sufficient evidence to support a FONSI, which is described in greater detail below.

September 2024 Amended EA

Summary

The September 2024 amended EA focuses on addressing the directives in the November 5, 2020, Court opinion: to evaluate the potential harm to endangered Atlantic salmon in the unlikely event that AAS escaped, survived and established in the natural environment. FDA was also ordered to reconsider its "no effect" determination under the ESA. As directed by the Court, FDA expanded its assessment in the September 2024 amended EA beyond that in the 2015 EA in order to conduct an exhaustive analysis of the likelihood of harms that could occur from the

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[3] https://animaldrugsatfda.fda.gov/adafda/app/search/public/document/downloadEA/2243 (accessed September 6, 2024)
[4] https://animaldrugsatfda.fda.gov/adafda/app/search/public/document/downloadFonsi/2223 (accessed September 6, 2024)
[5] *Inst. for Fisheries Res. v. United States Food and Drug Adm'n*, 499 F. Supp. 3d 657, 660 (N.D. Cal. 2020) (emphasis added).
[6] Eyed-eggs are a life stage where black spot(s) of the eyes are visible through the membrane of the fertilized egg.

assumed presence of Atlantic salmon containing the rDNA construct (collectively referred to as ABT salmon[7]) in the natural environment.

To achieve this goal, FDA conducted an amended risk assessment that qualitatively determined the risk of harms (consequences) occurring based on the likelihood of exposure and likelihood of harm assuming exposure occurs. To determine the likelihood of exposure, FDA outlined the pathways necessary for ABT salmon to escape confinement from the PEI facilities and migrate to and establish a persistent population in the US. The potential pathways for pathogen/parasite transmission from ABT salmon and the ABT facilities on PEI to wild fish populations, including endangered US Atlantic salmon, were also evaluated. Then, FDA identified and evaluated the potential harms (consequences) to the US environment[8] and the endangered Atlantic salmon population if these highly unlikely exposure scenarios were to occur. As part of this expansive evaluation, FDA considered the maximum current and planned production of all Atlantic salmon reared at all ABT facilities[9] located on PEI (including future planned changes at the Bay Fortune facility and expansion at the Rollo Bay facility). Using this information, FDA re-evaluated whether there is a potential for significant impacts on the US environment under NEPA, and whether the action would result in effects on endangered Atlantic salmon and their critical habitat in the US under the ESA.

Based on this assessment, FDA has concluded that this action will not have a significant impact on the quality of the human environment and, therefore, an environmental impact statement (EIS) will not be prepared. The information and analyses in the amended EA reflect comments and input received from the National Marine Fisheries Service (NMFS) and the Fish and Wildlife Service (FWS) during an ESA technical assistance review initiated in June 2022 with initial discussions beginning in March 2021. FDA also took into consideration oral comments received from the public during a public meeting held on December 15, 2022, and written comments sent to a public docket and received during a public comment period from November 16, 2022, to January 17, 2023.

Analysis

In the September 2024 amended EA, FDA used the same risk assessment approach as that used in the 2015 EA, but revised the conceptual model and the risk-related questions and expanded the analysis. The amended EA not only considers the production of AAS eyed-eggs at the Bay Fortune facility, which was the subject of the 2015 EA and November 2020 Court order, but also expands that analysis to include approved egg production in the Hatchery Unit at the Rollo Bay facility, which was evaluated in the 2019 EA. Further, this assessment also includes the planned expansion at the Rollo Bay facility of two new broodstock units, to be known as Broodstock Units 1 and 2, as well as planned future changes to consolidate egg incubation at the Bay Fortune facility within a new egg incubation room.

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[7] ABT salmon will be used collectively herein when referring to triploid and diploid AAS and all AquAdvantage broodstock, including neomales and AquAdvantage female broodstock (see Section 6.3 of the amended EA for definitions of the types of Atlantic salmon with the rDNA construct held at ABT's facilities).
[8] In this assessment, FDA only evaluates potential impacts to the US environment as required under NEPA. Evaluating potential impacts to the Canadian environment is the responsibility of the Canadian government. See footnote (fn) 25 and 26 of the amended EA for additional reasoning.
[9] Atlantic salmon without the rDNA construct are reared at the ABT facilities on PEI and, therefore, were considered in the assessment.

The amended EA focuses only on the approved production of AAS at facilities on PEI, Canada; it does not evaluate production at the former Panama facility or the Indiana facility. ABT did not renew its lease of the Panama facility and, as of November 5, 2019, that facility is no longer part of FDA's approval of NADA 141-454. In addition, an EA and FONSI were prepared for grow-out at the ABT Indiana facility, which found that there is no valid exposure pathway for AAS raised at the Indiana facility[10] to affect endangered Atlantic salmon in the US.

The expanded conceptual model used by FDA is presented in Figure 4-1 of the amended EA. To characterize the risk of impacts from the production of ABT salmon at the facilities on PEI, FDA used the National Research Council (NRC) (2002)[11] simple risk model, R = $P(E) \times P(H|E)$, where risk (R) is the joint probability of exposure [$P(E)$], and the conditional probability of harm assuming that exposure has occurred [$P(H|E)$]. The revised risk-related questions used to determine risk are as follows:

1. What is the likelihood that AquAdvantage Salmon or AquAdvantage Broodstock will escape the conditions of confinement?
2. What is the likelihood that AquAdvantage Salmon or AquAdvantage Broodstock will survive and disperse if they escape the conditions of confinement?
3. What is the likelihood that AquAdvantage Salmon or AquAdvantage Broodstock will reproduce and establish if they escape the conditions of confinement, survive, and disperse?
4. What are the identified potential harms to, or effects on, the US environment if AquAdvantage Salmon or AquAdvantage Broodstock establish and/or are present? What is the likelihood of these potential harms occurring assuming exposure in the US environment has occurred?
5. What is the risk that the potential harms to, or effects on, the US environment would occur given the likelihood of exposure in the US environment?

Risk-related questions 1-3 are similar to those used in the 2015 EA; however, FDA's responses to Questions 1-3 from the 2015 and 2019 EAs are expanded in Section 9.2 of the amended EA to give context to the discussion in the risk characterization.

FDA revised and expanded Risk-related Question 4 from the 2015 EA and provided revised responses in Section 9.3 of amended EA. FDA addressed the Court's order by identifying and evaluating the potential harms (the term "harms" is synonymous with "consequences," "effects," and "impacts") to the US environment, specifically the environment of Maine, that could result from the highly unlikely event of escape and establishment of ABT salmon. The potential for exposure via transmission of pathogens and/or parasites from ABT salmon and the ABT production facilities on PEI is also identified, and the potential for harm, i.e., disease, is evaluated. FDA used a qualitative ranking scale (negligible, low, moderate high likelihood) in Sections 9.2 and 9.3 to rank $P(E)$ and $P(H|E)$.

FDA also created a new risk-related question (Question 5) that re-evaluates the risk of these potential harms occurring in the US, including potential effects on endangered Atlantic salmon of the Gulf of Maine Distinct Population Segment (DPS), based on the potential for exposure in

[10] ABT stopped shipping and growing AAS at the Albany, Indiana facility in 2024. The facility is currently for sale.
[11] NRC. (2002). Animal Biotechnology: Science-based Concerns. Board on Agriculture and Natural Resources, Board on Life Sciences, The National Academies Press, Washington, DC, pp. 200.

the US environment, including from establishment and/or presence of ABT salmon in the US environment, and from pathogen/parasite transmission to wild US Atlantic salmon. In Section 9.4 of the amended EA, FDA used the NRC (2002) risk model, R = *P(E)* × *P(H|E)*, and the answers (rankings) to Risk-related Questions 1-4 to determine the risk of significant harms occurring in the US environment, including to endangered Atlantic salmon of the Gulf of Maine DPS, from the production of ABT salmon at the PEI facilities (including known future planned expansions and changes). It was found that the likelihood of exposure [*P(E)*] is extremely negligible, i.e., approaching zero. Thus, the overall risk of significant harms (adverse consequences, effects, or impacts) occurring is also close to zero regardless of the value for *P*(*H*|*E*). This concept is displayed visually in the amended EA using risk matrices (see Figures 9-3 and 9-4 of the amended EA).

FDA also considered the severity of the harms in the risk analysis assuming a worst-case exposure scenario for each potential harm pathway. As stated above, the exposure is negligible for all types of ABT salmon (diploid and triploid AAS and AquAdvantage broodstock); therefore, the risk is also negligible for all potential harms. Because the risk (probability of harm) is negligible for these harms under a worst-case exposure scenario, the likely impact of harms will also be negligible, regardless of their possible severity. Thus, significant harms (impacts) are not expected to occur in the US environment due to the production of ABT salmon at the facilities on PEI, Canada.

FDA concluded in the amended EA that significant environmental impacts are not expected in the US environment from maximum current and known future planned production of ABT salmon at the Bay Fortune (including the planned future incubation room) or Rollo Bay (Hatchery Unit and future planned Broodstock Units 1 and 2) facilities. Furthermore, based on an evaluation of the uncertainties associated with the exposure and harms analysis, it was found that there is high certainty in the outcome of this assessment.

Determination under the Endangered Species Act

Section 7(a)(2) of the ESA states that each Federal agency shall, in consultation with the Secretary of Interior or Commerce, as appropriate, insure that any action they authorize, fund, or carry out is not likely to jeopardize the continued existence of a listed species or result in the destruction or adverse modification of designated critical habitat. Because of the close proximity of the PEI facilities to the Gulf of Maine, it was necessary to evaluate the potential risk of harm to endangered Atlantic salmon of the Gulf of Maine DPS, and their critical habitat, due to the production of AAS and AquAdvantage broodstock on PEI.

The amended EA was prepared to address FDA's NEPA obligations, but was also prepared to assist in FDA's re-evaluation of its ESA decision per the 2020 Court order, i.e., to re-evaluate whether the production of AAS and AquAdvantage broodstock at the PEI facilities, including planned changes to the Bay Fortune facility and expansion at the Rollo Bay facility, may affect US populations of threatened or endangered Atlantic salmon or their critical habitat. The information from Risk-related Questions 1-5 in Section 9 of the amended EA was used when reassessing the ESA determination for the original approval relating to AAS.

As described in Appendix I of the amended EA, FDA concludes that, when produced and reared under the conditions in the application, and as described in the amended EA, the production of AAS and AquAdvantage broodstock at the PEI facilities (including future planned changes and expansions described in Section 7 of the amended EA) may affect but are not likely to adversely

affect US populations of endangered Atlantic salmon or their critical habitat due to discountable effects[12]. As required under Section 7 of the ESA, FDA requested initiation of an informal consultation with NMFS. Due to joint jurisdiction over endangered Atlantic salmon of the Gulf of Maine DPS, FDA also initiated an informal consultation with FWS; however, FWS chose to defer the final concurrence to NMFS. On April 24, 2024, NMFS provided an ESA Letter of Concurrence with FDA's assessment that the action may affect, but is not likely to adversely affect endangered Gulf of Maine Atlantic salmon or their critical habitat. The letter is included in Figure I-2 of the amended EA.

NEPA Decision and Findings

We have conducted a hard look at, and carefully considered, the potential environmental impacts of the production of ABT Salmon at all ABT facilities on PEI, including planned modifications and expansions at these facilities, as described and evaluated in the EA. Based on our expanded evaluation and comprehensive analysis, and taking into consideration the specific conditions that were established in the original NADA, as modified by the subsequent supplemental NADAs, we have made the finding that the production of ABT salmon at the Bay Fortune and Rollo Bay facilities (including planned changes and expansions), as described in the EA, would not individually or cumulatively have a significant effect on the quality of the human environment in the US. Based on that finding, FDA has decided not to prepare an EIS for the action.

{see appended electronic signature page}

Matthew Lucia, DVM
Director
Office of New Animal Drug Evaluation
Center for Veterinary Medicine
U.S. Food and Drug Administration

[12] Discountable effects "are those extremely unlikely to occur. Based on best judgment, a person would not: … expect discountable effects to occur." FWS and NMFS. (1998). Endangered Species Act Consultation Handbook. Procedures for Conducting Section 7 Consultations and Conferences. https://www.fws.gov/sites/default/files/documents/endangered-species-consultation-handbook.pdf

Electronic Signature Addendum for Submission ID

N-141454-Q-0048-OT

Signing Authority (Role)	Letter Date
Matthew Lucia (Office Director)	9/26/2024

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