U.S. Food and Drug Administration

For Public Comment

Preliminary
FINDING OF NO SIGNIFICANT IMPACT

AquAdvantage® Salmon

In support of a proposed agency action on
a New Animal Drug Application for
the integrated α-form of the *opAFP-GHc2* gene construct
at the α-locus in the EO-1α line of triploid, all-female genetically engineered
Atlantic salmon (AquAdvantage Salmon) to be produced as eyed-eggs and
grown-out only in the physically-contained freshwater culture facilities
specified in the sponsor's application

4 May 2012

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

Preliminary
Finding of No Significant Impact (FONSI)
for AquAdvantage Salmon

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 New Animal Drug Application (NADA) for a genetically engineered (GE) Atlantic salmon[1] to be produced and grown under specified conditions in physically-contained freshwater culture facilities specified in the sponsor's application. This line of fish, named AquAdvantage Salmon, is designed to exhibit a rapid-growth phenotype that allows it to reach smolt size (100 g) faster than non-GE farmed Atlantic salmon.

The AquAdvantage Salmon founder animal was generated in 1989 by micro-injecting a recombinant deoxyribonucleic acid (rDNA) construct, *opAFP-GHc2,* composed of a promoter from an ocean pout antifreeze protein (AFP) gene and a protein-coding sequence from a chinook salmon growth hormone (GH) gene into the fertilized eggs of wild Atlantic salmon. Subsequent selection and breeding led to the establishment of the AquAdvantage Salmon line, which has been propagated for eight generations. Under the conditions proposed for the NADA, AquAdvantage Salmon would be produced as triploid, all-female populations with eyed-eggs as the product for commercial sale and distribution. These eggs would be produced in the sponsor's facility on Prince Edward Island (PEI) in Canada. After confirming the genetic integrity of the broodstock used for manufacture and effective induction of triploidy in the eyed-eggs, these eggs would be shipped to a land-based grow-out facility in the highlands of Panama, where they would be reared to market size and harvested for processing.

Under the proposed action, AquAdvantage Salmon would not be produced or grown in the United States, or in net pens or cages, and no live fish would be imported for processing.

As a part of the NADA review and approval process, and consistent with the mandates in the National Environmental Policy Act of 1969 (NEPA), 42 U.S.C. § 4321 et seq. and FDA's regulations (21 CFR part 25), CVM has thoroughly evaluated the potential environmental impacts of approving an NADA for AquAdvantage Salmon, and has prepared the attached draft Environmental Assessment (EA) dated May 4, 2012 in relation to this proposed action.

FDA approvals for articles regulated under the new animal drug provisions of the Federal Food, Drug, and Cosmetic Act (FD&C Act) may be for a specific set of conditions where such conditions are proposed in the drug sponsor's NADA, or are required by FDA to mitigate potential risks, and are explicitly set forth in the conditions of approval. Any other uses are not approved. The sponsor must notify FDA about each proposed change in each condition established in an approved application and obtain FDA approval of a supplemental application for the change where necessary. 21 CFR 514.8. Approvals by FDA of NADAs related to GE

[1] The NADA is for approval of the integrated α-form of the *opAFP-GHc2* gene construct at the α-locus in the EO-1α line of triploid, female Atlantic salmon under the conditions of use specified in the application. However, for ease of reference, this document refers to the application as being for approval of the AquAdvantage Salmon.

animals are limited to a very specific set of conditions with the GE animal remaining under regulatory oversight as long as it is produced and marketed. FDA has determined that for the proposed action, conditions of use should include appropriate and redundant mitigation measures such as use of physical, biological, and geographical/geophysical forms of containment. For the proposed action (i.e., approval of an application for AquAdvantage Salmon), the conditions proposed in the materials submitted in support of an NADA would limit production of eyed-eggs to a single specific facility on Prince Edward Island (PEI), Canada, for delivery to a single, specific, land-based facility in Panama for grow-out (i.e., rearing to market size), with harvesting and processing (e.g., preparation of fish fillets, steaks, etc.) in Panama prior to retail sale in the United States. The specific proposed limitations on the production and use (grow-out) of AquAdvantage Salmon, including the production of triploid, all-female fish populations, are designed to mitigate potential adverse environmental impacts.

As part of the NADA review process, but separate from the environmental analysis itself, CVM has evaluated both the direct and indirect food safety impacts of AquAdvantage Salmon and any potential impacts of the rDNA insertion on target animal safety. With respect to food safety, FDA has concluded that food from AquAdvantage Salmon is as safe as food from conventional Atlantic salmon, and that there is a reasonable certainty of no harm from consumption of food from triploid AquAdvantage Salmon. Further, FDA has concluded that no significant food safety hazards or risks have been identified with respect to the phenotype of the AquAdvantage Salmon.

As the proposed action would only allow production and grow-out of AquAdvantage Salmon at facilities outside of the United States, the areas of the local surrounding environments that are most likely to be affected by the action lie largely within the sovereign authority of other countries (i.e., Canada and Panama). Because NEPA does not require an analysis of environmental effects in foreign sovereign countries, effects on the local environments of Canada and Panama have not been considered and evaluated in this draft EA except insofar as it was necessary to do so in order to determine whether there would be significant effects on the environment of the United States due to the origination of exposure pathways from the production and grow-out facilities in Canada and Panama.

In addition, social, economic and cultural effects of the proposed action on the United States have not been analyzed and evaluated because the analysis in the draft EA preliminarily indicates that the proposed action will not significantly affect the physical environment of the United States. Courts have held that under NEPA, social and economic effects must be considered only once it is determined that the proposed agency action significantly affects the physical environment.

FDA's approach in the draft environmental assessment is one based on a characterization of hazards, an evaluation of potential exposure pathways, and the likelihood of any resulting risk. The environmental analysis of consequences in the draft 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 draft EA center on the likelihood and consequences of AquAdvantage Salmon escaping, surviving, and becoming established in the environment, dispersing or migrating (i.e., evaluating whether there is an exposure pathway to the United States), and subsequently causing

an adverse outcome (the risk). These hazards are addressed for the production of eyed-eggs and grow-out to market size, 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 of the United States should AquAdvantage Salmon escape the conditions of confinement?

As discussed at length in the draft EA, AquAdvantage Salmon would be produced and grown-out in secure facilities with multiple and redundant forms of physical containment that have been verified and validated by FDA. As a result, the possibility that GE fish could escape from containment, enter the local environments of PEI or Panama, and survive to reproduce is extremely remote. In addition, because the production process for AquAdvantage Salmon would ensure that populations produced will be triploid (effectively sterile), all-female animals, the possibility of their reproducing in the wild is likewise extremely remote. Finally, the environmental conditions found around the egg production and grow-out facilities represent types of geographical/geophysical containment that further reduce the possibility of survival, establishment and spread. Based on the evidence collected and evaluated by FDA, FDA has made the preliminary determination that it is reasonable to believe that approval of the AquAdvantage Salmon NADA will not have any significant impacts on the quality of the human environment of the United States (including populations of endangered Atlantic salmon) when produced and grown under the conditions of use for the proposed action. FDA preliminarily concludes that the development, production, and grow-out of AquAdvantage Salmon under the conditions proposed in the materials submitted by the sponsor in support of an NADA, and as described in the attached draft EA, will not result in significant effects on the quality of the human environment in the United States.

FDA has considered the no action alternative for this action, that is, denial of the NADA for AquAdvantage Salmon. There are two general likely scenarios to consider as a result of the no action alternative: (1) cessation of production of AquAdvantage Salmon, and (2) production of AquAdvantage Salmon at suitable locations outside the United States. There are no potential environmental impacts arising from the first general scenario. If no AquAdvantage Salmon are produced, there will be no production sites and no potential for escape or release of these fish to the environment, and therefore no effects on the environment of the United States. For the second general scenario, production of AquAdvantage Salmon at locations outside the United States, an assessment of potential effects on the environment becomes highly uncertain. Because production of AquAdvantage Salmon would be possible at any number of locations worldwide, under different containment conditions, and potentially within areas where native Atlantic salmon are present, there are too many variables and unknowns to perform a comprehensive risk assessment and make any predictions with respect to potential environmental impacts on the United States. NEPA does not require an analysis of effects in foreign sovereign countries.

However, to the extent that production would occur with less restrictive containment conditions than those proposed (e.g., fish might not be triploid, might not be reared in land-based facilities, or might not be subjected to multiple and redundant forms of physical containment), it is expected that adverse environmental impacts to the United States might be more likely to occur than under the conditions of production and grow-out for the proposed action.

FDA, having reviewed the materials submitted in support of an NADA for AquAdvantage Salmon, has made a "no effect" determination under the Endangered Species Act (ESA), 16 USC § 1531 et seq., that approval of the AquAdvantage Salmon NADA will not jeopardize the continued existence of United States populations of threatened or endangered Atlantic salmon, or result in the destruction or adverse modification of their critical habitat, when produced and reared under the conditions described within the attached draft EA. The two federal agencies responsible for administering the ESA, the National Marine Fisheries Service (NMFS) of the National Oceanic and Atmospheric Administration (Department of Commerce) and the U.S. Fish and Wildlife Service (FWS) of the Department of Interior, have been provided with this "no effect" determination and underlying information in support of it, provided within the attached draft EA. Both of these agencies have either concurred with, or indicated no disagreement with, FDA's "no effect" determination. [See Appendix D to the draft EA]

Conclusion

FDA has carefully considered the potential environmental impacts of the proposed action and at this time has made a preliminary determination that this action would not have a significant effect on the quality of the human environment in the United States. Therefore, FDA has made a preliminary determination that an environmental impact statement will not be prepared.

Attachment:
Draft Environmental Assessment for AquAdvantage Salmon dated 4 May 2012