

April 26, 2013

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

Re: Docket No. FDA-2011-N-0899: Draft Environmental Assessment and Preliminary Finding of No Significant Impact Concerning a Genetically Engineered Atlantic Salmon

I. Overview

The American Anti-Vivisection Society (AAVS), Animal Welfare Institute (AWI), Farm Sanctuary (FS), and the Humane Society of the United States (HSUS), on behalf of our millions of combined supporters, submit the following comments in response to Docket No. FDA-2011-N-0899.¹ As national non-profit organizations that advocate on behalf of animals, our comments will focus on the animal health, welfare, and ethical aspects of producing AquAdvantage genetically engineered (GE) salmon on a commercial scale. Due to our concerns, which we detail in these comments, and our finding that FDA's assessments continue to underestimate or ignore important harms, we do not support approval of AquAdvantage salmon.

Our organizations have commented on aspects of the AquAdvantage New Animal Drug Application (NADA) before. AAVS and FS provided in-depth comments on the animal health and safety assessment to the FDA Veterinary Medicine Advisory Committee during its Sept. 20, 2010 meeting on approval of AquAdvantage GE salmon (Docket No. FDA-2010-N-0001)² and to Docket No. FDA-2010-N-0385 Food Labeling; Labeling of Food Made from AquAdvantage Salmon; Public Hearing; Request for Comments.³ The broader animal protection community, with more than a dozen organizations representing millions of members, also submitted a position letter opposing AquAdvantage salmon.⁴ Because FDA has not responded to any of these comments, we submit them again to this docket for reference. Our current comments will focus on the latest draft Environmental Assessment (EA) released by FDA and those components of the 2010 NADA that inform the EA, particularly the animal health and safety assessment.

Genetic engineering is an experimental technology that produces unintended and unpredictable effects, and which can result in tremendous animal suffering and loss of life.⁵ Thus, we have several concerns about the health and welfare of GE salmon and the adequacy of FDA's animal safety assessment. We describe in these comments significant gaps and methodological flaws in FDA's assessment that underestimate the prevalence of health problems and leave too many questions unanswered to allow approval of AquAdvantage salmon.

¹ "Draft Environmental Assessment and Preliminary Finding of No Significant Impact Concerning a Genetically Engineered Atlantic Salmon," Federal Register / Vol. 77, No. 247 / Wednesday, December 26, 2012.

² Avail. at <http://bit.ly/15M53J3>.

³ Avail. at <http://bit.ly/10hfBHR>.

⁴ Avail. at <http://bit.ly/181lwWr>.

⁵ Mak, N. (2008). Animal Welfare for Sale: Genetic Engineering, Animal Welfare, Ethics, and Regulation.

<http://www.aavs.org/atf/cf/%7B8989C292-EF46-4EEC-94D8-43EAA9D98B7B%7D/GE-Animals-Report.pdf>

We are further concerned that approval of GE salmon for commercial-scale production would potentially “release” this experimental technology into the environment, presenting unique and unknown risks to other animals, including endangered Atlantic salmon, and to environmental integrity. Because GE salmon are intended to be raised in aquaculture facilities and to promote commercial fish farming, we are also concerned about the impacts that aquaculture practices have on the environment and animal welfare, and the possibility that GE salmon aquaculture may exacerbate those impacts. While the EA focuses on two facilities in Canada and Panama, the likelihood that AquAdvantage salmon production would be expanded to other fish farms raises additional concerns about cumulative impacts. We are also not convinced that the need for AquAdvantage salmon has been demonstrated, or that alternatives to approval that present less risk and meet with less public disapproval have been fully considered. These concerns represent basic components of an environmental review that FDA has failed to address in the EA.

The significance of the potential risks and impacts require that FDA reverse its Finding of No Significant Impact (FONSI) and instead conduct a full review as part of an Environmental Impact Statement (EIS). Approval of AquAdvantage salmon, which would be the first GE animal sold for food, would set a precedent for future approvals of other GE animals, and it is imperative that the risk assessments be done thoroughly. Refusal to conduct the requisite EIS, in the light of our detailed concerns below, would represent arbitrary and capricious action by FDA.

While we are providing comments on the AquAdvantage NADA and EA, we remain concerned that the NADA process is not appropriate for evaluating the full range of risks associated with genetically engineering animals. Particularly troubling is that, because the NADA process is normally secretive and confidential, FDA has indicated that future approvals for GE animals may not be open to public comment or subject to NEPA review. A genetic modification is conceptually different from a drug, and overall, the drug model is ill-suited for handling questions about animal health and welfare, environmental impacts, ethics, and transparency. Instead of relying on the NADA process, a new regulatory framework is needed to address the unique risks and concerns associated with genetically engineering animals.

For these reasons, we find that it is not reasonable or safe for FDA to move forward with the NADA for AquAdvantage salmon, and AquAdvantage salmon should not be approved.

II. Animal Health Impacts

AquaBounty’s AquAdvantage salmon is being regulated by FDA under the New Animal Drug provisions of the federal Food, Drug, and Cosmetics Act. As part of the NADA process, the safety of the drug (in this case, the genetic modification) for the target animal must be demonstrated. This, in theory, should allow the effects and unintended consequences of the genetic modification, and any resulting harm to the animals, to be understood.

FDA first provided information to the public on the safety of genetically engineering salmon in August 2010, when it released its briefing packet to its Veterinary Medicine Advisory Committee (VMAC). This briefing packet contained FDA’s summaries of its assessments of animal health and food safety, arguing that the genetic modification was safe and that AquAdvantage salmon should be approved.

Because approval of AquAdvantage salmon would constitute a major agency action, FDA released a draft EA (the subject of the current comment period) at the end of December 2012 to comply with NEPA regulations. In the EA, FDA discusses the health/phenotype of AquAdvantage salmon (Sec. 5.2) before going on to examine the environmental impacts associated with approval of AquAdvantage salmon. According to FDA, the 2010 health assessment of the AquAdvantage salmon “provides a baseline for the consequences assessment in Section 7 [of the EA] and for characterization of the ‘fitness’ of AquAdvantage salmon...”^{6,7}

Thus, it is important to both the NADA generally and the EA specifically that the health impacts associated with genetically engineering and producing AquAdvantage salmon be fully considered.

Description of Animal Health in EA: Significant Problems with FDA’s Assessment Remain

FDA’s assessments of animal health and safety met with significant controversy when they were released in August 2010, drawing sharp criticism during the VMAC meeting and subsequent public comment period. Environmental, consumer, and animal advocacy groups, as well as members of VMAC itself, voiced criticism and concern over the quality of data and challenged the validity of FDA’s conclusions.

Several members of VMAC, for example, identified information and studies that were missing,⁸ stating that they were not confident the data were conclusive and that there was evidence for animal health concerns.⁹ The statistician on VMAC, Dr. Jodi Lapidus, characterized FDA’s data as being “preliminary,” explaining “I would categorize all the data that we have looked at thus far given its study design, sample sizes, and mixture of fish that are not necessarily representative of the salmon that will be marketed, I would have to characterize this body of work as potentially compelling *preliminary work* that would need to be validated and confirmed in other studies particularly on the population that would be marketed.”¹⁰ Dr. James McKean felt uneasy, stating “When we get down to 60 animals to make a final safety decision in the population that I imagine to be aquaculture, that seems to be a pretty minor evaluation... [T]here are questions that have not been answered by the data that has been presented in the last two days.”¹¹ The chairman’s verbal summary of VMAC’s discussion also noted there is “serious concern” that small sample sizes and culling procedures in the studies cast doubt and uncertainty and “makes it very difficult for conclusions to be made...”^{12,13}

⁶ FDA (4 May 2012). *AquAdvantage Salmon Draft Environmental Assessment*, P. 26.

<http://www.fda.gov/downloads/AnimalVeterinary/DevelopmentApprovalProcess/GeneticEngineering/GeneticallyEngineeredAnimals/UCM333102.pdf> (Hereinafter “Draft EA.”)

⁷ See also *Transcript, Veterinary Medicine Advisory Committee Meeting: AquAdvantage Salmon* (20 Sept. 2010), P. 159, highlighting the importance of the phenotypic characterization to every other step of the risk assessment.

<http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/VeterinaryMedicineAdvisoryCommittee/UCM230471.pdf> (Hereinafter “VMAC Transcript.”)

⁸ VMAC Transcript, P. 180 Lines 7-19 (survival comparison); P. 336 Lines 6-14 (developmental disturbance); P. 338 Lines 14-16 (disease resistance); P. 340 Lines 22-24 (longer-term health effects); P. 343 Lines 2-6 (disease resistance, clinical pathology); P. 353 Lines 3-17 (summary of discussion); P. 354 Line 22 – P. 355 Line 8 (data under commercial production conditions); P. 355 Lines 10-21 (more rigorous studies); P. 357 Lines 7-12 (external validity, context to understand rates of problems in AquAdvantage salmon).

⁹ VMAC Transcript, P. 338 Lines 1-4; P. 341 Lines 9-12; P. 341 Line 15 – P. 342 Line 1; P. 342 Lines 2-5, 11-17; P. 343 Lines 2-8; P. 343 Line 13 – P. 344 Line 10; P. 344 Line 17-19; P. 351 Line 13 – P. 352 Line 3; P. 354 Line 7-14.

¹⁰ VMAC Transcript, P. 341 Lines 16-23, emphasis added.

¹¹ VMAC Transcript, P. 351 Lines 20-23; P. 354 Lines 12-14.

¹² VMAC Transcript, P. 352, Lines 15-24.

¹³ When the chairman’s written summary of the VMAC meeting was later released, however, many of the criticisms identified during the meeting were glossed over or omitted entirely.

<http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/VeterinaryMedicineAdvisoryCommittee/UCM230467.pdf>

However, in the EA,¹⁴ FDA reiterates the same disputed assertions on animal health from its 2010 assessment, clearly demonstrating that it has not taken into consideration any of the comments it received nor made changes to its preliminary assessments. To make matters worse, FDA fails to mention any of the limitations and uncertainties surrounding the studies, even those the agency itself acknowledged in its 2010 assessment. It is arbitrary and capricious for FDA to ignore entirely the comments it received and the science-based concerns that have been raised. We are resubmitting our detailed analysis of the animal health assessment to this docket, and for the purposes of these comments will highlight several unanswered questions that have bearing on the EA.

Specifically, we contend that the animal health studies relied on in the EA lack scientific and statistical rigor, that the interpretation of the data is skewed, and that the studies likely would not stand up to peer review, making FDA's conclusions of safety unfounded. The studies, by their very design, grossly underreport or fail to detect the prevalence of health problems and abnormalities in GE salmon. To properly describe the health and phenotype of AquAdvantage salmon and assess the consequences of their release into the environment, FDA must be able to address the following problems with its animal health assessment:

- 1. Health status of fish killed as part of “extensive culling”:** According to the NADA animal health data,¹⁵ Aqua Bounty engaged in “extensive culling” of deformed, diseased, and dying fish before any of the data in the application were collected. Thus, most fish with “moderate to severe malformations” were excluded from the study. To understand the full effects of the genetic modification, FDA must know what happened to those animals; an animal health evaluation cannot be considered adequate when it relies on data primarily from the healthiest fish.¹⁶ How many fish were culled, how old were they, what health problems or deformities did they exhibit, and how did AquAdvantage salmon compare to non-GE salmon in this regard?
- 2. Statistical power of safety study:** FDA's animal health assessment relied largely on only one animal safety study, and in that study, Aqua Bounty used a sample size of just 12 fish. Such a small sample essentially precludes any meaningful conclusions about animal health.¹⁷ FDA itself acknowledged this fact during the VMAC meeting: “Admittedly, it is low power, and so the effects that we did notice...would have to be with a caveat that they are likely to be powered in such a way that it would be essentially difficult to draw strong conclusions...”^{18,19} In light of this, how can FDA make strong conclusions in the EA about the health of AquAdvantage salmon? What do statistical analyses and tests of statistical power on AquaBounty's studies demonstrate in terms of the studies' ability to detect health problems with any reasonable confidence?

¹⁴ Draft EA, Section 5.2.1.2, P. 27-28.

¹⁵ FDA (20 Sept. 2010). *Briefing Packet for Veterinary Medicine Advisory Committee: AquAdvantage Salmon*. See e.g., P. 26, 27, 33, 36-37. <http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/VeterinaryMedicineAdvisoryCommittee/UCM224762.pdf> (Hereinafter “VMAC Briefing Packet.”)

¹⁶ Members of VMAC were also critical of the culling procedures and how these affected study results. See, e.g., VMAC Transcript P. 340 Lines 8-19; P. 341 Lines 5-14; P. 341 Lines 15-16; P. 352 Lines 20-24; P. 354 Lines 7-14.

¹⁷ Members of VMAC were also critical of the small sample sizes, including the statistician on the panel. See, e.g., VMAC Transcript P. 341 Lines 15-23; P.343 Line 13 – P. 344 Line 10; P. 351 Line 13 – P. 352 Line 3; P. 352 Lines 15-19.

¹⁸ VMAC Transcript, P. 193 Lines 14-18.

¹⁹ FDA claims that additional lines of evidence lend support to the findings of the main animal safety study. However, these sources of data address different questions and are of even lower quality than the main study, limiting their inferential value. Most of the studies relied on in the EA to assess health, phenotype, and fitness (Sec. 5.2.2) were not even on the AquAdvantage salmon and provided little-to-no quantitative assessment.

3. **Health status of fish across their lifetimes:** In the main animal safety study, the health of adult AquAdvantage salmon was typically examined over a 2-week period.²⁰ This is a very limited time frame in which to observe potential health problems. Further, Aqua Bounty did not provide data examining the effects of the genetic modification on the fish at different life stages or throughout their lifetimes.²¹ How can FDA approve AquAdvantage salmon, evaluate the impacts on their health, or evaluate their potential environmental impact with such limited information on how they are affected by the genetic modification?
4. **Representativeness of sample:** The main study in FDA's animal health assessment involved fish from the 2007 year-class, which, according to the historical data in Table 4 of the FDA Briefing Packet,²² means that the most healthy (least irregular) AquAdvantage salmon since 2003 were compared to the least healthy (most irregular) non-GE fish. Further, the fish were not studied in the Panama facility or under the conditions in which they would be produced and raised if approval were granted.²³ Why don't FDA's conclusions reflect this source of bias and what would data on a more representative population of fish reveal?
5. **Data on GE fish even if they do not enter food supply:** In the animal health assessment, FDA only considered animal health in the context of how it would impact marketability and food safety. Therefore, animals who would likely be excluded from the food supply (such as the culled animals mentioned above or ones who grow too slowly) did not factor into FDA's assessment, regardless of how many health problems they experienced. But a new animal drug is supposed to be evaluated for the adverse outcomes it causes for *any* animal who receives that drug (in this case, all genetically modified salmon). In addition, environmental impacts can be caused by *any* GE salmon, not just those who would enter the food supply.²⁴ Can FDA provide data on a representative sample of all animals who "received the drug," not just data on a sample of those who would enter the food supply?
6. **Evidence of increased abnormalities:** Despite the limitations of the main animal safety study, the data provide indications that AquAdvantage salmon are unhealthy animals, experiencing high rates of abnormalities and mortality. For example, FDA states that AquAdvantage salmon experience "increased frequency of skeletal malformations, and increased prevalence of jaw erosions and multisystemic, focal inflammation."²⁵ In Table 4 of the animal health assessment,²⁶ more than 30% more AquAdvantage salmon displayed slight-moderate abnormalities than non-GE salmon in 3 of the 5 years shown. In Table 5,²⁷ of 15 averages provided for survival of AquAdvantage salmon from 2001-2006, 8 showed survival rates of 50% or less, and only one showed more than 90% survival. Survival even dipped as

²⁰ VMAC Transcript, P. 185 Line 21.

²¹ The need to examine longer-term health effects was also raised at the VMAC meeting. See e.g., VMAC Transcript P. 340 Lines 22-24; P. 353 Lines 5-9.

²² VMAC Briefing Packet, Table 4. Percentage of Irregularities by Rank in Diploid (2n) and Triploid (3n) Fish for the 2003-2007 Year-Classes of ABT Salmon and Non-GE Salmon. P. 28.

²³ Members of VMAC were also critical of the lack of data under production conditions and the applicability of the study findings to the commercial setting. See e.g., VMAC Transcript P. 344 Lines 15-19; P. 354 Line 22 – P. 355 Line 8.

²⁴ FDA even acknowledges its responsibility "to determine whether any production of the GE animal poses any public health risks (risk to human health, risks to animal health, or risks to the environment)" (VMAC Briefing Packet, P. 4), despite then restricting its assessment.

²⁵ VMAC Briefing Packet, P. 45

²⁶ VMAC Briefing Packet, P. 28.

²⁷ VMAC Briefing Packet, P. 32.

low as 2% in one instance. How can these data be reconciled with a decision that the proposed genetic modification is safe?

7. **Health problems associated with “conditions of use”:** FDA dismisses most adverse outcomes from the genetic modification as being associated with fast growth or the induction of triploidy.²⁸ However, the “drug” (the genetic modification) is intended to produce the effect of fast growth and the side effects are a direct consequence of “administering the drug.” Further, induction of triploidy is considered part of the containment strategy for AquAdvantage salmon, a “condition of use” in the EA,²⁹ and effects associated with conditions of use need to be considered along with the drug itself. Several members of VMAC raised this point, expressing concern that the AquAdvantage salmon application could not be considered safe if it included requirements for triploidy or other containment measures.³⁰ FDA itself acknowledged that “the risks to the animal from any components of the biological containment strategy” should be considered as part of the phenotypic characterization,³¹ but FDA then pointedly restricted the committee to considering only the genetic modification.³² The conditions of use affect not only animal health, but also the impacts that AquAdvantage salmon can have on the environment. What is FDA’s legal basis for dismissing the health problems associated with the conditions of use for AquAdvantage salmon and how would FDA’s and VMAC’s conclusions be affected by including consideration of the conditions of use?
8. **Choice of comparator fish:** The health and behavior of AquAdvantage salmon were often compared to those of other farmed salmon. However, it is important that modern breeding and rearing practices that do not have a good history of promoting animal health and welfare or environmental stewardship, such as intensive confinement systems, and that have not been subject to risk assessment not be used as a benchmark or baseline for assessing GM animals.³³ The fact that fish raised in aquaculture are often unhealthy and deformed should not be used as a standard to justify producing a fish that will perpetuate these problems. In addition, it is not possible to understand the environmental impacts to wild fish populations if only farmed fish were used as comparators. Does FDA have data on a more appropriate set of comparators so that the full effects of producing AquAdvantage salmon can be understood?
9. **Impact of genetic background, husbandry conditions, and environment:** The data in the NADA indicate that genetics can greatly affect outcomes; for example, certain genetic crosses of AquAdvantage salmon led to 95% mortality.³⁴ FDA has also admitted that

²⁸ VMAC Briefing Packet, P. 21.

²⁹ Draft EA, P. 1-2.

³⁰ VMAC Transcript P. 337 Line 9 – P. 338 Line 8; P. 342 Lines 11-24; P. 346 Line 11-16; P. 347 Lines 2-3; P. 347 Lines 17-19; P. 348 Lines 22-23; P. 349 Line 23 – P. 35 Line 10; P. 351 Line 2 – P. 352 Line 3.

³¹ VMAC Transcript, P. 161 Lines 4-5.

³² VMAC Transcript, see e.g., P. 348 Line 25 – P. 349 Line 9.

³³ Published studies have shown, for example, that skeletal and jaw malformations are common (up to 80%) in commercial salmon farms, and that these farms can be the source of several environmental stressors such as poor water quality, contaminants, nutritional deficiencies, and disease. (VMAC Briefing Packet, P. 30)

³⁴ VMAC Briefing Packet, P. 32 Table 4 (survival to first feeding varied significantly between different crosses). See also P. 29, citing studies indicating that genotype affects survival and other performance measures.

husbandry conditions can impact health in unknown ways,³⁵ and that genotype-by-environment interactions are impossible to predict accurately.³⁶ FDA, however, has not followed standard protocols for a NADA or EA to address these issues and does not even have data on AquaAdvantage salmon raised in the Panamanian facility where production would occur.³⁷ There are also no data on the phenotype of AquaAdvantage salmon in conditions that simulate a natural environment. Why hasn't FDA provided information to fully evaluate how genetic background or environmental conditions impact the "drug's" effect (the animal's phenotype), and what is FDA's legal basis for failing to specify standards for how AquaAdvantage salmon should be bred and raised to minimize adverse outcomes?

- 10. Post-market surveillance in lieu of pre-approval safety data:** Given the limitations with AquaBounty's data, FDA asserts that it will rely on post-market surveillance to determine the rate of animal health problems in AquaAdvantage salmon.³⁸ In effect, FDA is saying it will approve first and get the safety data later, a move that some members of VMAC did not support,³⁹ one stating it gave them "heartburn."⁴⁰ How can this approach be consistent with standards for a normal drug approval process, and how can this approach adequately support an EA?

These questions cast doubt on the accuracy and reliability of FDA's conclusions about animal health and safety, as well as FDA's ability to assess potential environmental impacts. The AquaAdvantage studies were intended to examine animal health, but they specifically excluded unhealthy animals, were underpowered to detect most problems, and their sampling methodology is unclear and biased. Such a study would not meet the publication standards of any reputable scientific journal.⁴¹ Despite years of review, neither the NADA nor the EA can be valid when they rely on such a scientifically inadequate animal health assessment.

III. Direct, Indirect, and Cumulative Environmental Impacts:

FDA's proposal to approve the NADA for AquaAdvantage Salmon constitutes a major Federal action that triggers NEPA requirements to consider the environmental impacts of the proposed action. According to Sec. 1508.8 of the NEPA regulations,⁴² "impacts" are synonymous with "effects" and include "ecological (such as the effects on natural resources and on the components,

³⁵ VMAC Briefing Packet, P. 30, "The frequency of deformities in farmed fish seems to vary widely depending on fish genetics, local husbandry conditions, level of examination given and other factors." See also P. 29 (modifications to PEI facility and rearing procedures was associated with changes in animal health); and Draft EA P. 28 Note 15 (culture conditions and rearing conditions have been linked to irregularities and increased mortality).

³⁶ VMAC Transcript P. 164 Lines 21-23, Dr. Prater (FDA): "This is important. This is the environment. The expression of the phenotype relies on a given set of environmental conditions." See also Draft EA, P. 27: Noting the high degree of variability in traits displayed by salmon, "genotype-by-environment interactions will produce different phenotypes when animals with the same genetic background are exposed to different environmental conditions."

³⁷ VMAC Briefing Packet, P. 23 (FDA notes that culture conditions at the PEI facility are likely to be significantly different from the conditions at the Panama facility, with the effects on the resulting AquaAdvantage phenotype "unknown.") See also VMAC Transcript, P. 354 Line 22 – P. 355 Line 8 (comment from VMAC member voicing concern that data under commercial production conditions have not been provided).

³⁸ VMAC Briefing Packet, P. 31. See also, VMAC Transcript, P. 168 Lines 17-24.

³⁹ VMAC Transcript, e.g., P. 340 Lines 8-19.

⁴⁰ VMAC Transcript, P. 342 Line 25 – P. 343 Line 2.

⁴¹ See e.g., Nature (2013) *Reporting Checklist for Life Sciences Articles*. <http://go.nature.com/oloeip>

⁴² Council on Environmental Quality, *Regulations for Implementing the Procedural Provisions of the National Environmental Policy Act*. http://ceq.hss.doe.gov/ceq_regulations/Council_on_Environmental_Quality_Regulations.pdf

structures, and functioning of affected ecosystems), aesthetic, historic, cultural, economic, social, or health, whether direct, indirect, or cumulative.”

An EA is intended to be a relatively brief environmental review that explores the need for a more thorough Environmental Impact Statement (EIS). In preparing an EA, FDA is specifically required to consider the need for the project, alternatives to the proposed action, and the environmental impacts of the project and its alternatives.

An EIS is more comprehensive and thorough in the scope of issues and alternatives it considers than an EA, providing a full review “for major federal actions that may significantly affect the environment.”⁴³ According to the Council on Environmental Quality (CEQ), several factors are considered in determining whether an EA is sufficient or an Environmental Impact Statement (EIS) is needed. Specifically, “significantly” is defined based on consideration of the context and intensity of the potential environmental impacts, including:

- “(4) The degree to which the effects on the quality of the human environment are likely to be highly controversial.
 - (5) The degree to which the possible effects on the human environment are highly uncertain or involve unique or unknown risks.”
 - (6) The degree to which the action may establish a precedent for future actions with significant effects or represents a decision in principle about a future consideration.”
 - (7) Whether the action is related to other actions with individually insignificant but cumulatively significant impacts. Significance exists if it is reasonable to anticipate a cumulatively significant impact on the environment. Significance cannot be avoided by terming an action temporary or by breaking it down into small component parts.”
 - ...
 - (9) The degree to which the action may adversely affect an endangered or threatened species or its habitat that has been determined to be critical under the Endangered Species Act of 1973.
- [43 FR 56003, Nov. 29, 1978; 44 FR 874, Jan. 3, 1979]”⁴⁴

Environmental Review: Need for EIS

Considering the CEQ criteria for significance in the context of AquAdvantage salmon, it is clear that FDA should withdraw its FONSI and prepare an EIS to fully evaluate the potential environmental impacts of approving AquAdvantage salmon.⁴⁵ The EA for AquAdvantage salmon is insufficient, and like the animal health and food safety assessments that preceded it, seems to be designed to support a decision already made by FDA rather than truly explore potential impacts and a range of alternatives. We detail our main arguments below:

- 1. Controversial, uncertain, unique, or unknown risks and effects:** Genetic engineering, despite many years of research, is far from an exact science and remains an experimental technology. The consequences of releasing this technology out of the lab are largely

⁴³ Council on Environmental Quality, *Regulations for Implementing the Procedural Provisions of the National Environmental Policy Act*, Section 1504.1. http://ceq.hss.doe.gov/ceq_regulations/Council_on_Environmental_Quality_Regulations.pdf

⁴⁴ Council on Environmental Quality, *Regulations for Implementing the Procedural Provisions of the National Environmental Policy Act*, Section 1508.27. http://ceq.hss.doe.gov/ceq_regulations/Council_on_Environmental_Quality_Regulations.pdf

⁴⁵ Members of VMAC also called for FDA to prepare an EIS. See e.g., VMAC Transcript P. 382 Line 3 – P. 383 Line 8; and P. 383 Lines 20-23.

unstudied, and the risks that GE animals could pose to the environment if released are unique and unknown. It is rare that one gene has one effect, and the AquAdvantage salmon in particular have not been studied to determine how their health or behavior may be altered over the course of their lifetime by the genetic modification. Further, while FDA acknowledges that there can be complicated interactions between a gene and the environment, with different consequences depending on the environment in which the gene is expressed, AquAdvantage salmon have never been studied in conditions that simulate the natural environment. AquAdvantage salmon have never even been studied in the conditions of the Panamanian facilities in which they are to be grown. There also remain questions about the consequences of having up to 5% of AquAdvantage salmon remaining fertile, and FDA has not examined the stability of the sterility induced by triploidy. No data or quantitative assessments have been provided on the reproductive behavior of AquAdvantage salmon, or on other fitness characteristics such as feeding behavior. In the EA,⁴⁶ FDA largely relies on studies of other GE fish to draw inferences about potential environmental impacts from AquAdvantage salmon, despite admitting that “the extent to which these results may be applicable...to AquAdvantage salmon...are unclear,”⁴⁷ which is a weak approach to examining such critical questions.⁴⁸ There is thus little known about the implications of commercial-scale production of GE fish for the environment and animal welfare. Similarly, little is known about the impact that increasing populations of GE animals might have on environmental or ecological integrity, and no scientific consensus has been reached on these issues.

2. **Precedence of Application:** As the first GE animal intended to be produced commercially for food, approval of AquAdvantage salmon would set a precedent for how the risks associated with other GE animals would be evaluated. Thus, it is important that potential risks and impacts be fully evaluated, particularly given FDA’s lack of experience addressing these issues. An EIS is far more appropriate than an EA to examine these impacts.
3. **Cumulatively significant impact:** The Council on Environmental Quality (CEQ) defines “cumulative impact” as “the impact on the environment which results from 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 (40 CFR ~ 1508.7).”⁴⁹ Approval of the two facilities in Canada and Panama is the first step in Aqua Bounty’s stated plans to expand the locations where AquAdvantage salmon would be raised.⁵⁰ Though “significance” should not be avoided “by terming an action temporary or by breaking it down into small component parts,” FDA narrowly

⁴⁶ Draft EA, Sec. 5.2.2, P. 29-34.

⁴⁷ Draft EA, P. 27.

⁴⁸ Members of VMAC also expressed uncertainty regarding the effects AquAdvantage salmon might have on the environment. See, e.g., VMAC Transcript, P. 386 Lines 12-17; P. 386 Lines 22-24 (“It seems to me the big data gap is, even though the chance may be small if these fish get out into the environment, what happens once they are out there and might be able to survive.”)

⁴⁹ Council on Environmental Quality, *Regulations for Implementing the Procedural Provisions of the National Environmental Policy Act*, Section 1508.7. http://ceq.hss.doe.gov/ceq_regulations/Council_on_Environmental_Quality_Regulations.pdf

⁵⁰ See, e.g., AquaBounty Technologies, Inc. (15 Feb. 2013). *Proposed Fundraising and Collaboration Agreement*, P. 4: “Once approval has been obtained, the Company plans to begin the process of preparing for and implementing customer field trials. If FDA approval is received before the end of 2013, the Company believes eggs could be supplied to field trials in January 2014. If the outcome of these trials is successful, the Company expects that sales and shipments of eggs could increase over the next two years. After FDA approval is received, the Company expects to focus on those significant fish farming markets where it believes it will have greater success in gaining approval and consumer acceptance. Currently, the Company expects to market AAS in five countries after receipt of FDA approval: the US, Canada, Argentina, Chile, and China.” <http://www.aquabounty.com/documents/press/2013/201302.15-ProposedFundraising.pdf>

focuses the EA on only the two facilities in Canada and Panama, failing to consider the cumulative impacts associated with growing AquAdvantage salmon in additional facilities. FDA uses the narrow construction of the EA to claim that AquAdvantage salmon would have no significant environmental impacts, and then incorrectly argues that because the action is individually insignificant, there would be no “incremental impact” from approval.⁵¹

In addition, FDA describes in its No Action Alternative that one consequence of no action (denying approval of AquAdvantage salmon) is that the fish could be raised in other locations in the world and under different production methods. However, this is the case *with or without* FDA approval, since FDA has no oversight of AquAdvantage fish farms if the fish are not sold in the U.S. In fact, it is arguably *more likely* that AquAdvantage fish farms may appear around the world if FDA grants approval, as FDA approval is seen as an important signpost. In addition, approval of AquAdvantage salmon would send a positive signal to developers of other GE animals, several of which are already in the pipeline. Taken together, approval of AquAdvantage salmon will likely result in greater numbers of GE salmon, and potentially other GE animals, being produced commercially in the foreseeable future, possibly in less secure or more vulnerable environments. It may also result in increased aquaculture production. FDA, however, incorrectly asserts that, “because this is the first approval for AquAdvantage salmon, there would be no cumulative impacts.”⁵² The potential for cumulatively significant environmental impacts and the animal welfare implications associated with these scenarios need to be evaluated.

4. **Effects on endangered species:** Among the risks associated with AquAdvantage salmon is the threat they pose to Atlantic salmon, which are listed as endangered. Though FDA has met with the National Oceanic and Atmospheric Association (NOAA), it is not reassuring that NOAA merely “does not disagree” with FDA’s proposal. It is also troubling that, though the Fish and Wildlife Service (FWS) officially supports FDA’s plan for approval, at least some FWS agents have expressed concerns about the potential for AquAdvantage salmon to negatively impact the environment. For example, according to the assistant regional director for fisheries for the Fish & Wildlife Service’s Northeast region, James Geiger, “Although AquaBounty claims their fish are sterile, that sterilization process is not 100 percent. There is the possibility that some of these fish could escape and reproductively interact with wild native salmon...Any potential offspring could reduce the biological and ecological fitness of the native wild salmon...any potential escape, no matter how little,” Geiger states, has the potential to harm endangered wild salmon populations.⁵³ A formal consultation with NOAA and FWS as part of an EIS is necessary to fully examine the potential of AquAdvantage salmon to adversely affect Atlantic salmon.
5. **Need for AquAdvantage salmon:** A full environmental review of AquAdvantage salmon needs to address gaps in the draft EA. FDA, for example, claims that AquAdvantage salmon benefits “commercial salmon farming by significantly reducing time-to-market and improving economics of land-based production.” (Sec. 2.1, P. 5). However, the only data that FDA presents to substantiate this claim show that one generation of AquAdvantage salmon grow faster to 100g than a comparator salmon. 100g is the size of young smolts, whereas market size is 2-5kg. FDA has provided no data on AquAdvantage salmon growth

⁵¹ Draft EA, P. 97.

⁵² Draft EA, P. 97.

⁵³ Szaniszlo, M. (2013). “Fishing for compliance: Genetically engineered salmon co. raises concerns,” Boston Herald, Jan. 2, 2013.

to market size, nor has it provided other pertinent information regarding issues such as feed efficiency, waste, and antibiotic use. There is also no comparison between AquAdvantage salmon and selectively-bred, non-GE farmed salmon, which, according to one company, can rival AquAdvantage growth rates. The sufficiency of the data on the relative nutrient quality of AquAdvantage salmon has also been called into question by consumer and food safety groups. Without these facts, it is impossible to assess FDA's claim regarding the benefits of AquAdvantage salmon, as well as certain potential environmental and public health impacts.

6. **Environmental impacts of aquaculture:** The EA considers the risks posed by potential escape or release of AquAdvantage salmon into the environment, but it does not consider the impacts of actually producing AquAdvantage salmon. AquAdvantage salmon are intended to be raised in aquaculture facilities and to generally help promote aquaculture, which is industrialized fish farming. However, there is overwhelming scientific evidence regarding the environmental problems associated with aquaculture, ranging from impacts on fish stocks to provide feed to pollution from waste water discharge. While aquaculture facilities already exist, these have not been the subject of FDA approval or an EA or any other risk assessment. Therefore, their existence cannot be used to dismiss consideration of the impacts of aquaculture in the context of the AquAdvantage salmon application. In addition, production of AquAdvantage salmon raise additional concerns related to water contamination since the fish are treated with androgen hormone as part of the process of creating neomales (sex-reversed females), and AquAdvantage salmon may also be treated with greater quantities of antibiotics due to potentially increased susceptibility to disease. The impacts associated with production of AquAdvantage salmon should be evaluated in an EIS, as well as whether production of GE farmed salmon may impact the environment differently than production of non-GE farmed salmon.

IV. Use of NADA Approval Process to Regulate GE Animals

The problems noted here and elsewhere with the animal health assessment, environmental review, and overall lack of transparency underscore the difficulties of using the New Animal Drug rubric to regulate AquAdvantage salmon and other GE animals. Genetically engineering an animal is conceptually different from treating an animal with a drug.

A drug is typically designed to provide some benefit to animal health, against which FDA would weigh potential risks (cost-benefit analysis).⁵⁴ Genetic modifications, at least the kind under evaluation with the AquAdvantage salmon, do not benefit the animal in any way. It is unclear how FDA can make an approval decision for a "drug" that has no benefit but does carry risk of harm, and no such risk-benefit calculation has been provided by FDA.

Genetically modifying an animal, and then producing it on a commercial scale where it can potentially interact with the environment, also raises a fundamentally different set of issues than producing traditional pharmaceuticals, which are not alive. The NADA process was not designed to handle the unique animal health, welfare, ethical, societal, and environmental implications of genetically engineering living beings who can think, feel, suffer, and interact with the environment.

⁵⁴ See e.g., VMAC Transcript P. 127 Lines 18-19 ("And our safety standards...for animal safety, it is a balance of risk and benefit for animal health.")

In addition, the NADA process is normally confidential, with the public only learning of the existence of a drug once it is approved for sale. FDA has indicated that it may not allow for public comment for future GE animal applications,⁵⁵ and it is unclear when environmental reviews would be undertaken. Changes to approved NADAs, such as the production of GE animals in additional locations or under different containment measures, would likely only require that a supplemental NADA be filed, and it is unclear for these, too, whether they will be open to public scrutiny and environmental review.

Not only are the animal health and environmental assessments for the AquAdvantage salmon NADA incomplete and inadequate, but the entire approval process is inappropriate to address the full range of risks associated with producing GE animals. We therefore request that FDA withhold approval of AquAdvantage salmon. Rather than move forward with regulating AquAdvantage salmon and other GE animals as New Animal Drugs, a new regulatory framework should be established that can address the unique risks and concerns associated with genetically engineering animals. However, if FDA proceeds with the NADA process, an EIS must be prepared, and we are confident that it will clearly demonstrate that the AquAdvantage salmon application should be rejected.

Sincerely,



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American Anti-Vivisection Society



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⁵⁵ FDA (2009). Guidance for Industry #187: Regulation of Genetically Engineered Animals Containing Heritable Recombinant DNA Constructs, P. 13.
<http://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/UCM113903.pdf>