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RE: **Docket No. FDA-2010-N-0001**, VMAC Meeting on approval of AquAdvantage genetically engineered salmon

Genetically Engineered AquAdvantage Salmon: Animal Health and Welfare Concerns

EXECUTIVE SUMMARY

The American Anti-Vivisection Society and Farm Sanctuary, representing over 250,000 members and supporters across the United States who are concerned about the welfare of animals, are opposed to the approval of Aqua Bounty's AquAdvantage salmon genetically engineered for faster growth.

We are particularly concerned about the impacts that production of AquAdvantage salmon have on animal health and welfare. As part of the New Animal Drug Application (NADA) for the AquAdvantage salmon, Aqua Bounty is required to demonstrate the safety of its genetic modification to the animals involved. However, it is not possible to assess animal health impacts when fish who are severely deformed or unhealthy are precluded from the study, samples involve just 6-12 fish, and very limited data are collected.

The little data that are provided, however, clearly indicate that fish reared in aquaculture facilities, which are intensive confinement systems used to factory farm fish, are prone to abnormalities, more susceptible to disease, and have low rates of survival. The AquAdvantage salmon fare no better, and possibly worse, in these conditions, and production of AquAdvantage salmon can be associated with a large loss of life.

The adverse outcomes experienced by AquAdvantage salmon are particularly concerning given research that demonstrates that fish experience pain, fear, and distress. The importance of assuring the well-being of these animals should not be dismissed.

We are further concerned about the FDA's regulatory process for genetically engineered animals. The FDA cannot adequately address the risks associated with genetically engineering animals, particularly the animal health and welfare concerns, using the New Animal Drug (NAD) rubric. The FDA's attempt to apply the NAD rubric to AquAdvantage salmon is

especially flawed, employing faulty logic, overlooking several factors that impact animal health, and failing to specify requirements to minimize risks. The AquAdvantage salmon application does not meet the standards of a traditional NADA and furthermore sets a dangerous precedent for future applications involving genetically engineered animals.

This report, “Genetically Engineered AquAdvantage Salmon: Animal Health and Welfare Concerns,” details our concerns as outlined above and comprehensively examines the animal health data presented in the AquAdvantage salmon NADA. On the basis of these concerns, and those shared by numerous other stakeholders, we request that the application for approval of AquAdvantage salmon be denied. We further request that the FDA discontinue review of any other applications for genetically engineered animals under the New Animal Drug rubric.

BACKGROUND

Aqua Bounty Technologies, Inc. has genetically engineered Atlantic salmon to grow faster than normal. The GE salmon (AquAdvantage salmon) are intended to be raised in aquaculture facilities, which are highly intensive factory farms for fish. The AquAdvantage salmon contain a growth hormone gene from Chinook salmon under the control of regulatory sequences derived from ocean pout. In addition, they have undergone procedures to induce triploidy (containing three sets of chromosomes rather than the normal two sets) to reduce fertility.

Aqua Bounty has applied to the FDA for approval to grow the AquAdvantage salmon commercially. If approved, the AquAdvantage salmon would be the first genetically engineered animals to be sold as food for human consumption.

The AquAdvantage salmon is only one of several GE animals nearing approval. Aqua Bounty has several other GE fish in the pipeline, and other companies have also filed applications with the FDA for approval of other GE animals. Many of these GE animals have been designed to facilitate factory farming. The EnviroPig, a pig genetically engineered to produce less phosphorous in its waste, and cows genetically engineered to be resistant to mad cow disease are among the GE animals in development. Goats genetically engineered to produce a blood clotting pharmaceutical, ATryn, in their milk have already received approval from the FDA.

The FDA currently regulates genetically engineered animals as “drugs” using the New Animal Drug rubric. Specifically, the FDA considers the rDNA construct in the genetically engineered animal to meet the definition of a “drug,” as it is an article that is intended to alter the structure or function of an animal.

There are numerous shortcomings with the FDA’s use of the New Animal Drug rubric to regulate genetically engineered animals. Animal health and welfare, in particular, are not adequately considered. In this specific instance, the New Animal Drug Application for the AquAdvantage salmon, and the FDA’s assessment of the NADA, raise numerous concerns regarding animal health safety and the FDA regulatory process.

ANIMAL HEALTH

The safety of a New Animal Drug must be demonstrated before it can receive approval. The studies and data submitted by Aqua Bounty, however, are inadequate to demonstrate that their proposed AquaAdvantage genetic modification is safe for animals. The FDA's analysis, moreover, is scientifically unsound and fails to give due consideration to animal health and welfare.

To understand how the health of fish is affected by the proposed genetic modification, it is important to know the health status of AquaAdvantage salmon at all life stages.¹ In particular, it would be concerning if, at any point from egg through adulthood, the AquaAdvantage salmon are more likely to experience health problems, deformities, or disease, require medical treatment or intervention (e.g., with antibiotics), or die than conventionally farmed fish or wild-type fish. The impact of environmental conditions and genetic background must also be considered, as these have the potential to influence the effects of the genetic modification.

The procedures used to produce the AquaAdvantage salmon also need to be examined. Genetic engineering has a high failure rate, producing unpredictable and unintended consequences. Typically, hundreds to thousands of animals are used to establish (or re-establish) a line of genetically engineered animals, and it is common for animals to turn out deformed or diseased as a result of the genetic modification attempt going awry.²

Once a genetically engineered line of animals has been established, there are additional concerns related to the production of subsequent animals. In the case of the AquaAdvantage salmon, production of future generations of fish is dependent on treating fish with androgen, a hormone used to induce sex reversal; killing males to strip them of their milt (sperm); pressure shocking eggs to induce triploidy (having three sets of chromosomes instead of the normal two sets) to reduce fertility; and destroying entire lots of fish if they are found to be "out of specification." Triploidy has been documented as compromising animal health and welfare in numerous ways, including causing spinal and jaw deformities and increased mortality.³ Extensive, on-going culling also occurs, as fish are killed who are unhealthy, do not have the desired characteristics, or are considered "excess inventory."

The NADA for AquaAdvantage salmon, however, does not evaluate most of these risks, and the FDA wrongly dismisses any findings of concern. Nevertheless, fish are sentient animals, capable of experiencing pain, fear, and distress.⁴ The potential for adverse outcomes and massive loss of life associated with the production of AquaAdvantage salmon cannot be ignored.

1. Main Animal Safety Study

Most of the data that FDA relies on to declare the proposed genetic modification safe for animals comes from one study, conducted by Aqua Bounty, which the FDA refers to as the "animal

¹ Levesque et. al, *Myogenesis and Muscle Metabolism in Juvenile Atlantic Salmon (Salmo salar) Made Transgenic for Growth Hormone*, 211 J. EXPERIMENTAL BIOLOGY 128 (2008).

² American Anti-Vivisection Society, *Animal Welfare for Sale: Genetic Engineering, Animal Welfare, Ethics and Regulation* (2008).

³ See, e.g., FDA, *Briefing Packet on AquaAdvantage Salmon* 29, 31-32 (Sept. 20, 2010).

⁴ See *infra* notes 12-14 and accompanying text.

safety study.” However, the study is characterized by several major limitations and flaws that raise serious doubts about the reliability, accuracy, and usefulness of the data and conclusions.

1.a. Culling prevents measurement of serious health problems.

In the animal safety study, Aqua Bounty engaged in extensive culling of deformed, unhealthy, and otherwise undesirable fish, thus removing these individuals from inclusion in the study without collecting any data on them. As stated by the FDA:

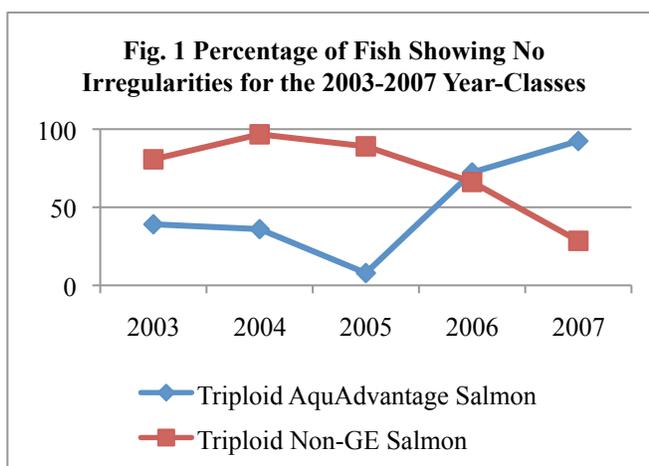
“For the safety study, it is not known whether culling was comparable for all four study groups, but, in general, this practice would be expected to remove those fish with moderate to severe malformations from all sample populations well before actual enrollment in the study began. This may explain why most morphological changes in the study, independent of the study group examined, were classified as “slight” in nature.” (P. 27)

Any findings regarding the health of AquaAdvantage salmon would therefore grossly underestimate the incidence of adverse outcomes and mortality and would essentially be meaningless.

1.b. Small, unrepresentative samples have little statistical power.

The study involved samples of only 6-12 adult animals, which is far too few to demonstrate an increased prevalence of health problems and does not address health problems at earlier life stages. Importantly, no statistical analyses were presented, nor was a test provided to demonstrate the statistical power of the study. For example, is it a statistically significant difference if an abnormality occurs 33% of the time compared to 25% of the time? When 4 of 12 animals exhibited the abnormality compared to 3 of 12 animals? From the outset, the study was not designed to detect differences between AquaAdvantage salmon and comparators, nor was it capable of detecting the occurrence of less frequent, but still potentially significant, health problems.

Further reducing the utility of the main animal safety study, it appears that these animals came from a cohort that, according to historical data provided by Aqua Bounty (P. 28), does not appear to be representative of AquaAdvantage salmon generally (Fig. 1). Indeed, this cohort, from the 2007 year-class, had by far the highest percentage of AquaAdvantage salmon with no irregularities in the five years of data that were provided. For triploid AquaAdvantage salmon, the 2007 year-class had 92.4% with no irregularities (Rank 1), whereas the 2003-2006 year-classes had 7.9-72.3% with no irregularities. In addition, the 2007 year-class of comparator non-GE salmon had the lowest percentage with no irregularities: 28.5% with no irregularities in 2007, compared to 66.2-96.7% with no irregularities in 2003-2006. Therefore,



use of the 2007 year-classes of AquAdvantage and non-GE salmon for the main animal safety study means that an AquAdvantage population with the most normal fish were compared against a non-GE salmon population with the least normal fish, diminishing the possibility of detecting differences between these populations.

1.c. Lack of key information precludes independent interpretation of results.

As part of the main animal safety study, Aqua Bounty presented data on size, weight, behavior, gross external abnormalities (jaw, operculum, gills, fins, spine, etc), nine internal organs, hematology and serum chemistry values, and other related parameters. However, in many instances, only a summary of the data or conclusions were provided, precluding independent interpretation of the results.

Other key information necessary to interpret the results was also lacking, including information on the make-up of the population from which fish were selected, the sampling methodology used to enroll fish in the study, the rationale behind what data would be collected, the data collection and processing methodology, husbandry conditions, and genetic backgrounds, even though differences in these factors can greatly affect results.

1.d. Evidence provides basis for concern about animal health.

Despite the limitations of the main animal safety study, the data provide some indication that AquAdvantage salmon are unhealthy animals, experiencing high rates of abnormalities and mortality, which are made worse by the induction of triploidy and aquaculture practices used for commercial production.

For example, ten of 12 adult fish who were most similar to the AquAdvantage salmon under review had external abnormalities, most with the gills and/or fins, and AquAdvantage salmon had more slight-moderate abnormalities than comparators in three of the five year-classes studied. Fourteen of 22 hematology and serum chemistry values were significantly different in AquAdvantage salmon, and AquAdvantage salmon showed an increased incidence of jaw erosions and inflammation in various tissues. Looking at historical data, of 15 averages provided for survival of AquAdvantage salmon to first feeding from 2001-2006, 13 showed survival rates of 75% or less, 8 showed survival rates of 50% or less, and only one showed more than 90% survival. Survival even dipped as low as 2% in one instance.

Contrary to the FDA's conclusion, the main animal health study does not adequately demonstrate that there are no risks to animal health associated with the proposed genetic modification.

2. Historical/Retrospective Data

In addition to the main animal safety study, Aqua Bounty also provided five sets of historical data. These data suffer from many of the same limitations that characterized the main animal safety study.

2.a. Percentage of irregularities, 2003-2007.

Fish from 2003-2007 year-classes, with sample sizes ranging from 38-2368, were ranked on a scale of 1-3 regarding the extent of external abnormalities present. As acknowledged by the

FDA, more (>30%) slight-moderate abnormalities were found in triploid AquAdvantage salmon than comparators in three of the five year-classes.

The FDA goes on to conclude that irregularities decrease over time, in both rate and severity. However, the data do not support this conclusion, as there were large fluctuations in percentages of abnormalities reported over the five years (highly variable data), and no clear trends.

As with the main study, no information was provided on culled fish, how samples were selected (and why sample sizes were so variable), what life-stages and sizes of fish were observed, or how data were collected. No statistical analyses were presented either, further limiting the usefulness of this data set.

2.b. Average survival to first feeding, 2001-2006.

The average survival (percentage) to first feeding of AquAdvantage salmon compared to non-GE salmon was provided for 2001-2006 year-classes. The FDA concluded that survival rates were similar on average between the two groups.

However, there was significant variation in survivability/mortality from year to year and between different crosses in the same year (as admitted by FDA), meaning that survivability ranged from 2-98%. With this kind of data, averages are not useful as a means of comparison, and statistical analyses, which were completely lacking, are critical.

In addition, as with other studies, there was extensive culling by Aqua Bounty, and no data were collected on morbidity and malformation for culled fish, so the data are likely unrepresentative of the general AquAdvantage salmon population.

Nonetheless, it is clear that all of the fish raised by Aqua Bounty experienced high rates of mortality. Of the 15 averages provided for survival of AquAdvantage salmon to first feeding, 13 showed survival rates of 75% or less, 8 showed survival rates of 50% or less, and only one showed more than 90% survival. In comparison, of 11 averages provided for survival of non-GE salmon to first feeding, 9 showed survival rates of 75% or less, 4 showed survival rates of 50% or less, and two showed more than 90% survival.

The variability uncovered in this study in terms of potential adverse health outcomes resulting from “administration” of the “drug” should be concerning. In several instances, more than 95% of fish from a particular cross died. In others, more than 95% survived. Yet the FDA does not really probe the factors contributing to greater or lesser survivability and has no adequate explanation for the variability. The implications in terms of animal health and welfare are significant, yet the FDA does not consider how the risks could be mitigated.

2.c. Percentage of irregularities, 2004.

Aqua Bounty provided the FDA with retrospective data on the entire 2004 breeding season’s fish, which included 19,000 AquAdvantage fry and 6,000 “wild-type” fry. The FDA claims that the data indicated no increase in mortality or developmental irregularities in AquAdvantage fish.

However, key information necessary to interpret the results was lacking, including information on the study design, data collection methodology, and whether or not culling occurred. In

addition, it is unclear how these data relate to the historical data provided on survival to first feeding from 2001-2006. According to the historical data set, there was 46-76% mortality in AquAdvantage fish and 41-43% mortality in non-GE fish in 2004, but according to the retrospective data set, there was 8.7% mortality for AquAdvantage salmon and 18.5% mortality for comparator fish.

Perhaps these measurements of mortality occurred at different life stages, but that explanation would only highlight the importance of understanding the impact of the genetic modification throughout the fish's life.

2.d. Macroscopic and microscopic observations, 2001-2005.

Macroscopic and microscopic observations were conducted on certain fish from the 2001-2005 year-classes as part of routine health evaluations. According to the FDA, "As fish were found dead, moribund, or culled, selected individuals were subject to necropsy and diagnostic histopathology and bacteriology as deemed necessary...." (P. 36, emphasis added.)

However, no specific data were presented, nor was information provided as to the data collection and processing methodology (e.g., what criteria were employed to deem analysis necessary) or sample size. In addition, the data were collected from fish produced from a variety of crosses and raised under a variety of husbandry conditions, which could greatly affect the results and limit interpretation.

Nevertheless, spontaneous skeletal deformities, including lateral and dorsoventral deviations of the vertebral column, malformations of the head, primarily of the lower jaw, and inflammatory and degenerative lesions were observed in AquAdvantage salmon, further demonstrating that these animals experience significant health problems.

In addition, the FDA acknowledged that "...significant morbidity and mortality could be masked as a result of the rigorous culling practices..." (P. 37), raising further concerns about the health of AquAdvantage salmon.

2.e. Disease resistance.

Aqua Bounty conducted a highly limited study to partially evaluate the susceptibility of AquAdvantage salmon to disease. It was not a comprehensive disease challenge study. Instead, this study looked at the onset of mortality in 20g fish exposed to furunculosis (*Aeromonas salmonicida*).

AquAdvantage salmon succumbed to disease sooner than comparators (12-15 days vs 14-21 days). No other data were presented, no information was provided on the number of fish studied, and no details were provided regarding study design, limiting the usefulness of this study.

The FDA inappropriately concluded that there is no indication of significant change in disease resistance in AquAdvantage salmon, but this conclusion is not supported by the data. Not only is there insufficient data to conclude anything with any reasonable amount of certainty, the data that do exist indicate the possibility that AquAdvantage salmon have increased susceptibility to disease.

3. FDA Analysis

The FDA's conclusion that there are no significant adverse outcomes associated with production of AquaAdvantage salmon is unsupported by the data. In several instances, it appears, in fact, that the FDA accepts Aqua Bounty's data uncritically, warping the data to fit with what seems to be a foregone conclusion to support approval of AquaAdvantage salmon.

3.a. FDA does not take animal well-being into consideration.

The studies provided by Aqua Bounty are too limited and flawed to draw any meaningful conclusions, with deformed and unhealthy fish (those of most interest in determining adverse outcomes) excluded from the studies. Nonetheless, there are indications that AquaAdvantage salmon experience high rates of abnormalities and mortality. Indeed, the extensive, on-going culling itself indicates that unhealthy and undesirable animals are common.

The FDA, however, fails to consider the implications of these findings for animal health and welfare, even though doing so is an explicit requirement of the New Animal Drug rubric. According to the FDA's reasoning, the health of AquaAdvantage salmon is of concern only to the degree that it affects the marketability of the fish or human food safety; deformed, unhealthy, or culled fish, regardless of how many, are inconsequential since they would likely be excluded from the food supply.

3.b. FDA does not attribute adverse outcomes to genetic modification.

The FDA dismisses most adverse outcomes as being associated with triploidy or fast growth, rather than the genetic modification itself. However, the FDA admits that the data suggest that "induction of triploidy may not be the sole causative agent for the increased regularities" (P. 29).

In addition, these fish would not exhibit triploidy or fast growth if they had no been subjected to genetic modification and other procedures to produce the AquaAdvantage salmon under review. Indeed, the "drug" is intended to produce the effect of fast growth, and the side effects associated with that effect need to be considered as they are a direct consequence of "administering" the "drug."

3.c. FDA disregards factors affecting health outcomes, fails to set standards.

The FDA fails to specify standards to promote animal health and minimize adverse outcomes, even though the data indicate that certain aquaculture conditions, procedures, or genetic crosses may increase the occurrence of adverse outcomes (P. 30).

For example, husbandry conditions such as water temperature, ambient light, and diet, are known to affect the occurrence of developmental abnormalities (P. 30), and Aqua Bounty reported that use of Combi-tanks increased survival of AquaAdvantage salmon (P. 32). Aqua Bounty also attributed an increase in severe irregularities in AquaAdvantage salmon to changes in incubation procedures (P. 29), and Deitch et al (2006) demonstrated that transgenic salmon have increased oxygen requirements and a decreased tolerance for low oxygen concentrations.⁵

⁵ Deitch et. al, *Cardiorespiratory Modifications, and Limitations, in Post-Smolt Growth Hormone Transgenic Atlantic Salmon salar*, 209 J. EXPERIMENTAL BIOLOGY 1310 (2006).

In addition, the FDA acknowledges that different genetic crosses and the underlying genetics of broodstock families can affect the incidence of abnormalities (P. 29), and data from Aqua Bounty showed drastically different rates of survival for different crosses in a given year (P. 32).

The FDA further admits that it does not know how different husbandry conditions would affect the health of AquAdvantage salmon (P. 23), but does not see this as a barrier to approval of the NADA despite its implications for animal health.

3.d. FDA is setting a dangerous precedent.

The FDA's animal safety assessment for AquAdvantage salmon is neither rigorous nor scientifically sound. The most unhealthy animals were not even studied, and few potential risks to animal health were adequately examined.

The FDA's assertion that it will accept such limited and highly flawed data, and instead rely on post-market surveillance to better determine the rate of abnormalities and mortality in AquAdvantage salmon, is wholly unacceptable and inconsistent with standards for a normal drug approval process.

REGULATORY PROCESS

Application of the New Animal Drug rubric to the regulation of genetically engineered animals does not adequately address all the concerns associated with this technology. Use of the NAD rubric is akin to trying to fit a square peg into a round hole, since a genetic modification is conceptually different from a drug and raises novel issues.

The NAD rubric is particularly ill-suited for handling impacts to animal health and welfare associated with genetic engineering. Typically, a drug is designed to provide some benefit to animal health, against which the FDA would weigh potential risks. Genetic modifications, at least the kind under evaluation with the AquAdvantage salmon, do not benefit the animal in any way. The FDA has not indicated how it can make approval decisions for a drug that has no benefit but does carry risk of harm.

The FDA, moreover, when applying the NAD rubric to genetically engineered animals, does not even meet the standards and requirements of a normal drug approval for demonstrating animal safety. For example, the FDA does not consider the animal health impacts associated with "administration of the drug," i.e., the production of the genetically engineered line of animals, even though this uses a substantial number of animals and abnormalities are common.

In addition, the FDA only evaluates those animals who would enter commerce, even though a greater number of animals contain the "drug," and those animals excluded from commerce are most likely to be unhealthy in some way.

The FDA also has not demonstrated concern for individual animals or their welfare when evaluating NADAs for genetically engineered animals. Animal health has been a concern only to the degree that it affects the marketability of the animals or human food safety.

The New Animal Drug regulatory process raises additional concerns because it is confidential, providing little to no opportunity for broad, informed public participation in the decision-making process. Data on the AquAdvantage salmon, for example, were provided at the discretion of the FDA and only made available to the public two weeks prior to the advisory committee meeting. After 10 years of review, the FDA has provided only 1.25 hours for public comment on the approval of the AquAdvantage salmon.

There are no requirements that data be provided and public input be solicited prior to approvals of future applications of genetically engineered animals. Furthermore, the FDA has reserved the right to waive the NADA requirements entirely for certain genetically engineered animals.

Due to the limitations of the NADA process in general and problems with the FDA's review of the AquAdvantage NADA in particular, it is clear that the NAD rubric is inadequate to protect animal health and welfare from the risks associated with genetic engineering. No approvals for genetically engineered animals should be granted using the NAD provisions.

AQUACULTURE

Aquaculture is the fastest growing agriculture industry worldwide, with nearly half of fish consumed globally raised on factory farms.⁶ Developed for rapid growth rate, AquAdvantage salmon further support the industrial farming model and promote intensive confinement in U.S. aquaculture despite known animal health and welfare implications.

High stocking density, poor husbandry practices, and other adverse conditions in aquaculture are known to significantly affect the health and welfare of farmed fish. Adverse responses caused by aquaculture conditions and practices include increased aggression, injury, disease and distress.⁷ Negative environmental conditions, including poor water quality, inadequate nutrition, improper lighting and unsuitable water temperatures, are common in aquaculture facilities.⁸ The FDA's limited evaluation concludes that husbandry conditions for AquAdvantage salmon are consistent with those in commercial freshwater aquaculture facilities, despite the significant welfare concerns associated with existing facilities.

Scientists studying the welfare of fish in modern aquaculture facilities further conclude that a review of conditions and husbandry practices must be species specific.⁹ However, the FDA's study merely compares GE salmon to normal Atlantic salmon under industrial fish farming conditions, without taking into consideration differences between the fish.

The FDA should not merely accept the similarities between GE salmon and normal salmon under factory farming conditions. Because AquAdvantage salmon grow larger twice as fast, comparison with normal Atlantic salmon in aquaculture facilities is insufficient and unlikely to

⁶ Rosamond L. Naylor et. al, *Feeding Aquaculture in an Era of Infinite Resources*, 9 PROC. NAT'L ACAD. SCI. 15103 (Sept. 8, 2009); U.S Dep't Agric. Econ Res. Serv., *U.S. Seafood Market Shifts to Aquaculture*, AMBER WAVES (Apr. 2004).

⁷ T. Håstein, *Animal Welfare Issues Relating to Aquaculture*, in Global Conference on Animal Welfare 219 (Feb. 2004).

⁸ *See id.*

⁹ Scientific Opinion of Panel on Animal Health and Welfare, *General Approach to Fish Welfare and the Concept of Sentience in Fish*, 954 EUR. FOOD SAFETY AUTHORITY J. 1, 6 (Jan. 29, 2009).

produce an accurate reflection on the fish's health and welfare. Review procedures should also evaluate those conditions specific to AquAdvantage salmon.

As the FDA acknowledged in its recent Draft Guidance # 209, titled *Judicious Use of Medically Important Antimicrobial Drugs in Food Producing Animals*, the already existing overuse and misuse of antimicrobial drugs in animal agriculture may pose a serious public health threat.¹⁰ Scientists warn that GE salmon farming would require extensive administration of antibiotics because transgenic fish may be more susceptible to disease. Accordingly, approval of AquAdvantage salmon is likely to significantly add to the already existing risks of drug-resistant bacteria and viruses associated with animal agriculture.¹¹

Clearly, modern aquaculture practices have already proven problematic in relation to animal health and welfare. Because approval of Aqua Bounty's application would increase the number of fish maintained in intensive confinement in the U.S. and abroad, the effects of GE salmon approval on aquaculture systems, and the corresponding implications for fish health and welfare, must be considered.

FISH SENTIENCE

The high incidence of health problems and mortality experienced by AquAdvantage salmon is concerning given current research on fish sentience, which has demonstrated that not only do fish experience pain, fear, and stress, they are also capable of learning and retaining information.¹²

A report by the Animal Health and Welfare Panel in Europe concludes that there is sufficient evidence demonstrating that fish experience pain, fear and distress and that the brain structures of fish indicate they are likely sentient.¹³ Other studies have demonstrated memory in fish lasting for significant periods of time, from weeks up to months, further supporting the concept that fish are sentient.¹⁴ As a result, scientists conclude that the concept of welfare for fish is the same as for mammals and birds and that welfare protections for fish should be adequately considered, within the regulatory context.¹⁵

Studies comparing fish in natural settings to those on fish farms indicate sentience and suggest adverse emotional, behavioral, and physical response to stressors inherent on fish farms.¹⁶ Natural swimming, feeding, anti-predatory and reproductive behaviors are often lacking in fish raised in aquaculture facilities.¹⁷ Factory-farmed fish exhibit chronic stress responses including

¹⁰ FDA, *Draft Guidance #209: The Judicious Use of Medically Important Antimicrobial Drugs in Food Producing Animals* (June 28, 2010).

¹¹ William Muir et al., *Possible ecological risks of transgenic organism release when transgenes affect mating success*, 96 PROC. NAT'L ACAD. SCI. 13853 (Nov. 23, 1999); Rebecca Goldberg, *Murky Waters: The Environmental Effects of Aquaculture in the U.S.* 44, Env'tl. Defense Fund (1997).

¹² Lucy Odling-Smee, *The Role of Learning in Fish Orientation*, 4 FISH & FISHERIES 235 (2003).

¹³ Panel on Animal Health and Welfare, *supra* note 4.

¹⁴ Gilson L. Voplato, *Challenges in Assessing Fish Welfare*, 50(4) INST. LABORATORY ANIMAL RES. 334 (2009).

¹⁵ *Id.*

¹⁶ T. Håstein, *supra* note 8, at 219-23.

¹⁷ Panel on Animal Health and Welfare, *supra* note 9, at 8.

reduced immune function, growth and reproduction and increased death, similar to responses observed in mammals and birds used in agriculture.¹⁸

The Animal Health and Welfare Panel report recommends that despite limited research on fish sentience currently available, enough information exists to require that welfare indicators for fish should be “species-specific, validated, reliable, feasible and auditable.”¹⁹ Based on the existing evidence demonstrating fish sentience, the FDA’s regulatory process of evaluating AquAdvantage salmon as NADs is inappropriate. Furthermore, evaluation of Aqua Bounty’s application should encompass the health and welfare of fish beyond the extent of commercial fitness and human food safety.

CONCLUSION

One of the key provisions of the New Animal Drug rubric is that the safety of the proposed drug to the animal be demonstrated. The AquAdvantage salmon NADA, however, fails to demonstrate animal safety and, in fact, is wholly lacking in scientific rigor. In addition, the FDA’s approach to and analysis of the AquAdvantage NADA raises serious questions about the agency’s commitment to protecting animal health.

Fish are sentient animals, and the risks of the proposed genetic modification, in terms of health and mortality, should not be ignored. The NADA for AquAdvantage salmon should be rejected, and reviews of any other genetically engineered animals under the NAD rubric should be halted.

Sincerely,



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¹⁸ *Id.*

¹⁹ *Id.* at 9.