Dr. Stephen Ostroff, M.D
Acting Commissioner
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

May 28, 2015

Dear Commissioner,

We are writing today to inform the FDA that a newly released environmental assessment drafted by the Canadian Department of Fisheries and Oceans (DFO) contains scientific data and risk determinations that conflict with the FDA's risk determinations and the underlying data found in the briefing packet and environmental assessment (EA) of AquaBounty Technologies' AquAdvantage Salmon (AAS).

The 2013 Canadian review, which recently became publicly available, conflicts with FDA's risk assessment work in these ways:

--Scientists at the DFO determined that AquAdvantage Salmon (AAS) are more susceptible to a type of disease-causing bacteria than are domesticated salmon, which indicates unique animal health problems and also raises environmental and public health concerns. This contradicts FDA's assertion that AAS do not exhibit a difference in disease susceptibility.

--The DFO review indicates that AAS have dramatically diminished growth rates in the company's commercial facility compared to the company's experimental facility. This finding casts more doubt on AquaBounty's highly dubious growth rate claims which FDA affirmed based on very limited data from the company's experimental facility—not its commercial facility.

--The DFO found that AquaBounty's ongoing breeding program is producing AAS with a variable phenotype, including inconsistent growth rates, raising serious questions about the stability and durability of AAS—in contradiction to FDA's favorable determinations, which were based on very limited data.

--The DFO found that there is no scientific evidence demonstrating that AAS do not grow larger than conventional Atlantic salmon, which presents a variety of risk questions, including serious environmental concerns about the impact of potential escapes that FDA has entirely ignored.

The information we provide in this letter shows that FDA's risk determinations to date are based on information about AAS that is incomplete, inaccurate or incorrect. Troublingly, this is not the first time that FDA has been confronted with scientific data and facts that openly contradict the agency's assertions, data and determinations.

This includes news that AquaBounty experienced a major mechanical failure that lead to "lost" salmon at its Panamanian facility in 2008 and a major disease outbreak at its Canadian facility in 2009, neither of which were documented in the agency's 2010 EA, which asserted that AquaBounty's facilities were disease-free and biosecure.[1] FDA also failed to document that AquaBounty's Panamanian facility was operating without a variety of legally required permits and inspections, including those related to the safe operation of the facility.[2] At one point, AquaBounty handed over all management and operational oversight of its Panamanian grow-out facility, including key safety measures, to an independent salmon producer, which directly contradicts the very explicit terms and conditions of the company's New Animal Drug Application (NADA).[3]

FDA has also failed to accurately or adequately evaluate the performance and environmental risks of AAS. Independent scientists have noted AAS's ability to interbreed with another species of fish, the brown trout, producing highly competitive hybrids—a risk that FDA never considered.[4] Similarly, FDA's determination that AAS offer a growth-rate benefit over non-engineered Atlantic salmon has long been openly contradicted by several Atlantic salmon companies and a variety of independent data.[5]

Many of these discrepancies are due to the extremely weak risk assessment process that FDA is conducting through its use of an EA and NADA. However, some of these discrepancies appear due to AquaBounty's failure to disclose all of the relevant information and data that FDA may have asked of the company. Such apparent failures by AquaBounty give the public zero confidence in validity or accuracy of any of the data package that AquaBounty furnished to the FDA and, once again, highlight how the agency's dependence on sponsor data presents a major conflict of interest.

Whatever the case, FDA's routine failure to consider or even document major risk dimensions of AAS gives the public zero confidence that the agency can adequately assess the risks of this fish using a narrow risk assessment tool like the EA. The discrepancies and contradictions in the FDA's EA, which continue to emerge, are too myriad and too damning for the FDA to continue down its pathway toward regulatory approval.

Given AquaBounty's clear track record of failing to maintain biosecurity at its facility, the strong indications that AAS suffers unique animal health problems, the variety of evidence that has emerged demonstrating environmental and food safety concerns, and the wholly elusive benefits of the fish, the only proper course of action for the FDA to take is to deny AquaBounty's NADA.

As a far less desirable course of action, the agency should conduct a thorough risk assessment using an Environmental Impact Statement (EIS), which consumers and scientists—including the agency's own advisory committee—have long requested. FDA should make every effort to collaborate with DFO and attempt to secure a clean copy of the DFO draft risk assessment (and any other Canadian risk assessment documents), as currently available public documents are highly redacted.

Disease Susceptibility

DFO scientists concluded with "reasonable certainty that AAS is more susceptible to *A. salmonicida* than domesticated comparators…"[6] The DFO draft risk assessment also notes that the "difference in *A. salmonicida* infection and mortality between AAS and domesticated controls can be attributed to the presence of the transgene…"[7]

Aeromonas salmonicida is a bacteria that causes furunculosis in salmon, which can be treated with several antibiotics approved by FDA.[8] The use of antibiotics to treat furunculosis in salmon aquaculture has already led to the emergence of antibiotic-resistance bacteria.[9]

The DFO review also noted "it is highly certain that AAS is highly susceptible to ISAV [infectious salmon anemia virus],"[10] and that "we have no data on the relative susceptibility of AAS to other disease agents of environmental significance [compared to wild Atlantic salmon]."[11]

AquaBounty has already experienced at least one major, accidental disease outbreak (ISAV) at its Canadian facility in the third quarter of 2009. The FDA indicates that the ISA virus entered the facility in 2008.[12] The company stated as late as 2011 that it did not know how the disease entered its supposedly biosecure operation, which casts enormous doubts on the company's ability to mitigate future disease outbreaks.[13]

The several biosecurity lapses that have occurred during the short history of AquaBounty's operations—and the company's inability to determine the cause in one case—clearly indicates the potential, and even the likelihood, for future accidents, including disease outbreaks. If and when domestic or international commercial producers commence production of AAS, these facilities will face similar biosecurity problems, including potential exposure to bacteria or disease. It is unlikely that FDA will not have resources to monitor or even document these problems.

In 2010, FDA stated it reviewed the "limited information on disease resistance" provided by AquaBounty, yet, inexplicably, the agency failed to document the 2009 ISAV.[14] In fact, the FDA told the public that AquaBounty's facilities have been certified as being "disease-free."[15] In response to a Freedom of Information Act request, the FDA indicated that it did not know about AquaBounty's ISAV outbreak in 2010.[16]

Likewise, at the 2010 VMAC meeting, AquaBounty President Ron Stotish brazenly vilified traditional sea-cage operations for their ISAV problems, never mentioning his own company's grave struggles with the same disease.[17] The company's apparent failure to truthfully disclose highly relevant events in the company's operations raises very grave questions about what other major biosecurity lapses have occurred in AquaBounty's operations, which AquaBounty has not disclosed and which FDA failed to detect.

Only after a public-interest group discovered and publicized the ISAV outbreak in 2011 did FDA and AquaBounty acknowledge the biosecurity failure, which was briefly

described in the 2012 EA; still, the agency offered no meaningful scientific analysis of disease resistance in AAS—only a "limited study of 20 gram" AAS, furnished by AquaBounty.[18]

Faced with limited data but a clear indication of potential disease resistance problems, the FDA made favorable risk-assessment determination about AAS, asserting that the agency "found no evidence that AquAdvantage Salmon have any altered resistance to disease or parasites."[19] Such a determination illustrates how the FDA routinely conflates the absence of evidence about risks with the evidence of absence of risks—and how this can lead to errors of great significance.

That scientific evidence has emerged challenging FDA's assertions about disease resistance is a wholly predictable consequence of the agency's head-in-the-sand approach to risk assessment throughout its environmental assessment.

Dramatically Diminished Growth Performance

Canadian regulators also observed that the so-called growth-rate advantage of AquAdvantage Salmon is dramatically diminished in the company's commercial facility, located in Panama, compared to the fish's performance in company's experimental, laboratory setting, located in Canada. AAS "are approximately 1.5 times greater in size than non-transgenic fish at 20 months when grown at the Panama site…and 4 or more times greater in size at 15-18 months when grown at the PEI Facility."[20] One of the data sources referenced in the DFO review is redacted, but it would appear that AAS growth rates would be nearly two-thirds lower in Panama.

This extreme reduction in growth rate provides one more indication of the highly elusive, totally unsubstantiated growth-rate benefit of AAS, which has bearing on the FDA's statutory requirement to assess the "effectiveness" of new animal drugs.

There have long been doubts about the so-called growth-rate advantages of AAS. Non-engineered, commercial varieties of Atlantic salmon, whether produced in in-land facilities and conventional open-water facilities, grow equally fast or even more quickly than AquAdvantage Salmon.[21]

Unfortunately, FDA's extremely limited, extremely weak benefit-claim analysis fails to acknowledge the preponderance of evidence that AAS actually offers no real-world growth-rate benefit. Most critically, FDA's assessment fails to acknowledge that AquaBounty's growth-rate trials lack a key measure of external validity: the non-engineered comparator salmon used in growth-rate trials are especially slow-growing varieties of Atlantic salmon that have undergone very limited domestication and are totally unrepresentative of the kinds of Atlantic salmon widely grown in commercial aquaculture. In view of this fact, AquaBounty's growth-rate trials are essentially meaningless for the purposes of FDA's "effectiveness" review.

It should also be noted that AquaBounty's corporate studies lack independence, are heavily biased through the company's role in the experiments, and are not supported by independent, peer-reviewed literature.

The diminished growth-rate finding also raises other concerns. If there are dramatic differences in growth rates in AAS in Panama compared to Canada, it stands to reason that there may also be other dramatic differences, perhaps related to animal safety, nutritional content, or even food safety.

This point was highlighted by VMAC members in 2010 who noted the limitations of the experimental data FDA was assessing, which came from AquaBounty's experimental laboratory in Canada.[22] One VMAC member told the FDA, "We ought to be looking at the final product, not something out of a laboratory setting. But let's look at some animals out of [the commercial facility in] Panama after we have raised them, we have fed them, and their structures, those numbers are going to look at little different."[23]

The FDA cannot advance regulatory approval of AAS based on experimental data about fish that do not conform to the definition, terms or conditions laid out in the NADA, as it has attempted to do to date.

Maximum Size

Canadian regulators determined that "there is no evidence to support the claim that AAS does not grow larger than their non-transgenic counterparts"[24] and that "the maximum size of the AAS therefore remains unknown."[25]

The DFO review also notes, "Should AAS reach a larger size than its wild conspecifics, they could potentially predate upon larger species not normally preyed upon by wild Atlantic salmon."[26] This raises obvious ecological questions about the impacts that escaped salmon on the entire marine ecosystem, including competing with native populations of wild species for food.

The potential, unique environmental risks associated with AAS remain totally unaddressed by FDA, and the uncertainties around this scientific question presents a major gap in FDA's risk assessment. Indeed, given that AquaBounty has been developing AAS for more than 20 years, it is troubling that the company is unable to provide fundamental scientific data about the phenotype of AAS.

Beyond phenotypic characterization questions and environmental concerns, a larger-than-normal Atlantic salmon could also present animal health issues or even food safety issues, which also remain unaddressed by FDA.

Durability Issues

The scientific review performed by DFO raises questions about the durability of AquAdvantage salmon—and contradicts FDA's determination that AAS has

demonstrated phenotypic durability and FDA's assumption that the AAS product the agency is reviewing will be equivalent to AAS product that AquaBounty eventually commercializes.

The DFO assessment notes variability in the performance of AAS, which indicates the gene construct does not appear to be presenting a predictable, consistent phenotype.[27] DFO scientists noted that there "is limited data on the stability of accelerated growth over generations..,," that "there appears to be noteworthy variation in growth rate of AAS fish between generations..,[28]" and that "further work is required to determine the phenotypic stability of high growth in AAS fish across standard culture conditions." DFO concluded, "Taken together, size and growth rate appears to vary to a degree between and within generations in AAS fish than in non-transgenic fish, although further work is required to confirm this."[29]

DFO's findings echo public comments submitted to FDA in 2013, which noted the abundant evidence demonstrating the highly variable growth rates and animal health characteristics of different generations of AAS.[30] Even researchers associated with AquaBounty have noted—in both scientific presentations and published scientific literature—that AAS experience variable performance.[31] The lack of phenotypic durability can also be seen in the data package that AquaBounty submitted to FDA, as public comments provided to FDA have explained in great detail previously.[32]

In contradiction to this evidence, FDA determined as early as 2010 that the AquAdvantage Salmon "phenotype is stable over at least six generations" and that "both the genotype and phenotype of AquAdvantage Salmon are durable…"[33]

FDA articulates that it has in place a durability assessment "to ensure that future animals in commerce are equivalent to those evaluated for safety and effectiveness during the pre-market review…"[34] FDA's Guidance 187 is clear in stating the agency's legal requirement to establish that genetically engineered animals exhibit a durable phenotype and genotype, stating that the durability assessment

> *"addresses some additional components of the manufacturing requirements codified in 21 CFR 514.1(b)(5). It is intended to provide information to ensure that the rDNA construct in the GE animal resulting from the specific transformation event and defining (identifying) the GE animal being evaluated is durable — that there is a reasonable expectation that the rDNA construct is stably inherited, and the phenotype is consistent and predictable."*[35]

Given that FDA's risk assessment looks at widely disparate data from several generations of AAS—for example looking at food safety data from 2001-era AAS and growth-rate data from 2007-era AAS[36]–there are very serious questions about whether the AAS product that FDA has reviewed can be in any way equivalent to the AAS product that Aquabounty commercializes.

The uncertainties that DFO notes regarding the phenotypic durability of AAS is notable given that AquaBounty has been developing the fish for more than 20 years.

Maintenance and Operations

The DFO review presents problems in the management and operations that are of relevance to the FDA, including DFO statement that "the absence of internal compliance documentation, such as a daily check-list to ensure that all relevant mechanical barriers are in place and functioning properly." [37] Because of the "absence of operational oversight documentation," DFO considered the likelihood of AAS fry escape to be "low," but not negligible.[38]

AquaBounty's failure to carry out basic safeguards and/or recordkeeping related to its operations and management provide additional evidence that the company lacks the responsibility, competency and wherewithal to produce AAS. It is notable that DFO's July 2, 2013 review was written with the understanding that AquaBounty will be exercising ""singular and direct control" over both the PEI and Panama facilities, which we know is false. In fact, according to lease signed in June 2013, AquaBounty ceded operations and management of its Panamanian facility, including critical safety measures to an independent fish grower.[39] The current terms and conditions remain unknown, but it seems unlikely that they conform in any way to the terms and conditions spelled out in AquaBounty's NADA.

The fact that regulators in both Canada and the United States appear to be conducting risk assessments based on terms and conditions that do not line up with the facts on the ground once again strongly indicates that AquaBounty has not been forthcoming with all relevant information. AquaBounty's track record of apparently failing to provide comprehensive, truthful information to regulators gives the public zero confidence that FDA's trust-but-don't-verify approach to risk assessment can work.

Environmental Risks

The DFO reviewers notes that "the reported increased oxygen consumption in AAS could lead to an increased uptake and subsequently to higher bioconcentration factors of waterborne contaminants in AAS compared to wild conspecifics. We conclude with reasonable certainty that the increased oxygen consumption could increase bioconcentration of waterborne contaminants in AAS."[40]

Such risks would appear to be of particular concern under AquaBounty's stated business plans to sell AAS eggs for production is places like China,[41] a country whose vast aquaculture production has long been noted for the toxic waters in which fish are sometimes grown.[42]

It is not apparent in any of FDA's review materials that the agency has considered this risk—neither examining the heavy metal or toxicant content of the water that

AquaBounty is using nor considering how water-quality issues may impact potential, future commercial production of AAS.

Missing and Weak Data: Scientific Uncertainty on Key Safety Issues

The DFO review provides a litany of notes about gaps and weaknesses in the available data on AAS, echoing comments from VMAC and many independent scientists about problems in the data related to hormone levels, body composition, animal safety, food safety and environmental impacts. Again, it is notable that AquaBounty has been developing this fish for more than 20 years yet is unable to provide basic scientific data about the AAS. It is also notable that FDA, in the face of scientific uncertainty, has consistently moved forward with favorable scientific determinations.

Examples of gaps and weaknesses in the available data on AAS, as quoted from the DFO review, include:

Growth Hormones

Regarding hormone expression in AAS, the DFO notes: "The available data does not provide a complete temporal and tissue expression profile of the transgenic GH protein levels through the life cycle of the AAS. No data on plasma GH levels are available…Available data is limited to transgene mRNA expression at varying levels in several tissues in two juvenile fish of unknown position in the AAS genealogy and in muscle and skin samples of eight AAS progenies at market size using methodologies with different sensitivities."[43]

"Knowing that levels of plasma GH vary with life stages and environmental factors.., we conclude that the available information about the GH levels in AAS might not be representative of potential highest levels."[44]

"Consequently….we conclude that the characterization of GH levels in AAS is insufficient to conclude that GH levels do not increase above normal range for non-transgenic or wild counterparts throughout lifespan…."[45]

Molecular Characterization

"The exact location of the [gene construct] integrant in the host genome is not known…uncertainty remains about the potential for the integrant to disturb surrounding genes."[46]

Animal Health

"AquaBounty's statement that there was 'no indication of serious health issues deriving specifically from AquAdvantage transgenesis that would be cause to prevent the deployment of the AquAdvantage Salmon line in commercial production…is less certain given the short comings of the study design and lack of additional diagnostic work-up

done for the pre-study and enrolled fish at the time of post mortem or Necropsy, respectively."[47]

"Specific pathological changes that were associated with AquAdvantage (transgenic) fish, included 'increased presence of focal inflammation, especially among diploid fish, and a low occurrence of jaw erosions among both male and female diploids….These changes are somewhat unusual (especially the inflammation) but ultimately were not considered further by the authors….However, the study was restricted to such a small number of animals at one point in time. The issue of determining whether there are health or welfare concerns with transgenic fish that are to be cultured in a commercial setting would have benefitted from a more wide ranging study involving fish selected from different ages and sizes throughout a grow-out cycle, under actual commercial conditions.[48]

"…The study design was too restrictive in scope to provide a satisfactory answer" to the question of whether the overall health of AAS may be compromised in a commercial setting.[49]

Body Composition and Tolerance to Physical Factors

"There is no empirical data on range of temperature, salinity and pH tolerance of the AAS compared to non-transgenic Atlantic salmon."[50]

"…Whether AAS differs from non-transgenic fish in body composition during other life stages, or under different environmental conditions or diets has not been assessed."[51]

"We also conclude that in the context of the environmental risk assessment, the body composition of the AAS at other life stages, including highly predated upon juvenile stages, and the body composition of the AAS based on a diet representative of what would be found in nature also remains unknown."[52]

Nutritional and Food Safety Differences

The DFO review cited AquaBounty research showing "71% higher fat, 13% lower pantothenic acid, 21% lower vitamin B1, and lower 30% vitamin C content in AAS compared to the non-transgenic control salmon.[53] These differences are based on an analysis of a redacted dataset. Notably, these differences, and, one would presume, the underlying nutritional data, do not line up with FDA's data analysis, suggesting that there may be two different sources of nutritional data about AAS, which say two different things.[54]

There may even been three sources of data, as the DFO review includes another dataset with nutritional information, which is unredacted. Though the description of this dataset matches the description of the dataset FDA used – market-sized AAS (2.0-7.5kg), sponsor control Atlantic salmon, and a farm control Atlantic salmon, fed a Moore-Clarke

commercial diet with the same range of protein and fat content—many of the nutritional data points are different from what FDA reports.[55]

The DFO analysis raises many questions about the quality and thoroughness of FDA's review of nutritional content, but also drives home the important point that AAS exhibits significant differences in nutritional content compared to non-engineered salmon raised in the same environment, fed the same food.

On the issue of food safety, DFO also notes "knowledge gaps and uncertainties related to human health hazard endpoints," including allergenicity of AAS and the likelihood of pleiotropic effects that will emerge with AquaBounty's ongoing selective breeding efforts. Other problems include "a lack of experimental data on AAS (e.g. altered susceptibility to pathogens of human importance)…"[56]

Conclusion

Given AquaBounty's clear track record of failing to maintain biosecurity at its facility, the strong indications that AAS suffers unique animal health problems, the variety of evidence that has emerged demonstrating environmental and food safety concerns, and the wholly elusive benefits of the fish, the only proper course of action for the FDA to take is to deny AquaBounty's NADA.

As a far less desirable course of action, the agency should conduct a thorough risk assessment using an Environmental Impact Statement (EIS), which consumers and scientists—including the agency's own advisory committee—have long requested. FDA should make every effort to collaborate with DFO and attempt to secure a clean copy of the DFO draft risk assessment (and any other Canadian risk assessment documents), as currently available public documents are highly redacted.

Thank you for your consideration of this important issue. If you have questions or need more information, please contact Patty Lovera at Food & Water Watch, (202) 683-2500.

Wenonah Hauter
Executive Director
Food & Water Watch

Jaydee Hanson
Senior Policy Analyst
Center for Food Safety

Dana Perls
Food and Technology Campaigner
Friends of the Earth

[1] LeVaux, Ari. "The genetically engineered salmon that could soon run wild." *Outside Online*. June 6, 2012; Living Oceans Society. [Press Release]. "ISA virus confirmed in AquaBunty's genetically-engineered salmon." December 20, 2011.
[2] Autoridad Nacional del Ambiente Administracion Regional de Chiriqui. Resolucion ARACH 071-2014. July 30, 2014.
[3] AquaBounty Technologies. SEC Filing. Form 10. July 23, 2014 at Exhibit 10.9.
[4] Oke, Krista et al. "Hybridization between genetically modified Atlantic salmon and wild brown trout reveals novel ecological interactions." *Proceedings of the Royal Society*. May 29, 2013.
[5] "Salmon egg producer questions AquaBounty's claims." *Intrafish.* November 1, 2011; Personal Correspondence with Marine Harvest.
[6] Department of Fisheries and Oceans Canada, Office of Aquatic Biotechnology. "Environmental and indirect human Health Risk assessment of the AquAdvantage Salmon." Draft in Revision. July 2, 2013 at 99.
[7] Department of Fisheries and Oceans Canada, Office of Aquatic Biotechnology. "Environmental and indirect human Health Risk assessment of the AquAdvantage Salmon." Draft in Revision. July 2, 2013 at 102.
[8] FDA CVM. Approved Drugs for Aquaculture. Available at http://www.fda.gov/AnimalVeterinary/DevelopmentApprovalProcess/Aquaculture/ucm132954.htm and on file. Accessed March 20, 2015; FDA CVM. New animal drug application 141-246. Freedom of Information summary. Aquaflor. October 26, 2007; FDA CVM. New animal drug application 125-933. Finding of no significant impact for Romet-30 medicated premix for salmonid fish (trout and salmon). September 28, 2004; FDA CVM. New animal drug application 038-439. Freedom of Information summary. TERRAMYCIN 200 for Fish. June 30, 2006.
[9] Benbrook, Charles. The Northwest Science and Environmental Policy Center. "Antibiotic drug use in U.S. aquaculture." Institute for Agriculture and Trade Policy. February 2002 at 12. 14; Inglis, V. et al. "Antibiotic resistance of *Aeromonas salmonicida* isolated from Atlantic salmon, *Salmo salar* L., in Scotland." *Journal of Fish Diseases*. April 7, 2006 at Abstract.
[10] Department of Fisheries and Oceans Canada, Office of Aquatic Biotechnology. "Environmental and indirect human Health Risk assessment of the AquAdvantage Salmon." Draft in Revision. July 2, 2013 at 99.
[11] Department of Fisheries and Oceans Canada, Office of Aquatic Biotechnology. "Environmental and indirect human Health Risk assessment of the AquAdvantage Salmon." Draft in Revision. July 2, 2013 at 305.
[12] Food and Drug Administration Center for Veterinary Medicine. "Draft Environmental Assessment for AquAdvantage® Salmon." May 4, 2012 at 33.
[13] Stotish, Ron. Response to questions by Mark Begich. U.S Senate Subcommittee on Oceans, Atmosphere, Fisheries, and Coast Guard Oversight Hearing on the Environmental Risks of Genetically Engineered Fish." December 15, 2011 at 73.
[14] Food and Drug Administration. Transcript of Veterinary Medicine Advisory Committee Meeting on AquAdvantage Salmon. Monday, September 20, 2010 at 174.
[15] Food and Drug Administration Center for Veterinary Medicine. Veterinary Medicine Advisory Committee. "Briefing Packet: AquAdvantage Salmon." September 20, 2010 at 23.
[16] Rudenko, Larisa. FDA CVM. In Correspondence received in a FOIA to Jaydee Hanson. February 8, 2012.
[17] Food and Drug Administration. Transcript of Veterinary Medicine Advisory Committee Meeting on AquAdvantage Salmon. Monday, September 20, 2010 at 101-102, 110.
[18] Living Oceans Society. [Press Release]. "ISA virus confirmed in AquaBounty's genetically-engineered salmon." December 20, 2011; Food and Drug Administration Center for Veterinary Medicine. "Draft Environmental Assessment for AquAdvantage® Salmon." May 4, 2012 at 32.
[19] Food and Drug Administration Center for Veterinary Medicine. "Draft Environmental Assessment for AquAdvantage® Salmon." May 4, 2012 at 32.
[20] Department of Fisheries and Oceans Canada, Office of Aquatic Biotechnology. "Environmental and indirect human Health Risk assessment of the AquAdvantage Salmon." Draft in Revision. July 2, 2013 at 125.

[21] Summerfelt, Steven et al. The Conservation Fund's Freshwater Institute. "Freshwater growout trial of St. John River strain Atlantic Salmon in a commercial-scale, land-based closed-containment system." January 2013 at 13, 24; "Salmon egg producer questions AquaBounty's claims." *Intrafish.* November 1, 2011; Personal Correspondence with Marine Harvest.
[22] Food and Drug Administration. Transcript of Veterinary Medicine Advisory Committee Meeting on AquAdvantage Salmon. Monday, September 20, 2010 at 119, 163, 170.
[23] Food and Drug Administration. Transcript of Veterinary Medicine Advisory Committee Meeting on AquAdvantage Salmon. Monday, September 20, 2010 at 362.
[24] Department of Fisheries and Oceans Canada, Office of Aquatic Biotechnology. "Environmental and indirect human Health Risk assessment of the AquAdvantage Salmon." Draft in Revision. July 2, 2013 at 81.
[25] Department of Fisheries and Oceans Canada, Office of Aquatic Biotechnology. "Environmental and indirect human Health Risk assessment of the AquAdvantage Salmon." Draft in Revision. July 2, 2013 at 84.
[26] Department of Fisheries and Oceans Canada, Office of Aquatic Biotechnology. "Environmental and indirect human Health Risk assessment of the AquAdvantage Salmon." Draft in Revision. July 2, 2013 at 324.
[27] Department of Fisheries and Oceans Canada, Office of Aquatic Biotechnology. "Environmental and indirect human Health Risk assessment of the AquAdvantage Salmon." Draft in Revision. July 2, 2013 at 38.
[28] Department of Fisheries and Oceans Canada, Office of Aquatic Biotechnology. "Environmental and indirect human Health Risk assessment of the AquAdvantage Salmon." Draft in Revision. July 2, 2013 at 123-125.
[29] Department of Fisheries and Oceans Canada, Office of Aquatic Biotechnology. "Environmental and indirect human Health Risk assessment of the AquAdvantage Salmon." Draft in Revision. July 2, 2013 at 125.
[30] *SEE* Food & Water Watch Public comments. 2013. Docket FDA-2011-N-0899-0685 and Docket FDA-2011-N-0899-0003.
[31] AquaBounty Technologies. Annual report and accounts. 2012 at 4; Xu, Quigheng et al. "Family-specific differences in growth rate and hepatic gene expression in juvenile triploid growth hormone (GH) transgenic Atlantic salmon (*Salmo salar*)." Comparative Biochemistry and Physiology Part D. Genomics and Proteomics." Vol 8, Iss 4. December 2013 at Abstract; Plouffe, Debbie et al. "Reproductive Confinement for the Safe Cultivation of Genetically Improved Lines of Atlantic Salmon." Presentation at World Aquaculture Society conference. Nashville, Tennessee. February 24, 2013; Hori, Tiago. "Functional Genomic Analaysis of Immune-Relevant Transcript Expression Response to Triploidization in Growth Hormone (GH) Transgneic Atlantic Salmon." Presentation at World Aquaculture Society conference. Nashville, Tennessee. February 24, 2013.
[32] *SEE* Food & Water Watch Public comments. 2013. Docket FDA-2011-N-0899-0685 and Docket FDA-2011-N-0899-0003.
[33] Food and Drug Administration Center for Veterinary Medicine. Veterinary Medicine Advisory Committee. "Briefing Packet: AquAdvantage Salmon." September 20, 2010 at 47, 60.
[34] Food and Drug Administration. Transcript of Veterinary Medicine Advisory Committee Meeting on AquAdvantage Salmon. Monday, September 20, 2010 at 265, 267.
[35] Food and Drug Administration. Guidance 187 for Industry Regulation of Genetically Engineered Animals Containing Heritable Recombinant DNA Constructs. January 15, 2009 at 22.
[36] Food and Drug Administration Center for Veterinary Medicine. Veterinary Medicine Advisory Committee. "Briefing Packet: AquAdvantage Salmon." September 20, 2010 at 78 and 133.
[37] Department of Fisheries and Oceans Canada, Office of Aquatic Biotechnology. "Environmental and indirect human Health Risk assessment of the AquAdvantage Salmon." Draft in Revision. July 2, 2013 at 226.
[38] Department of Fisheries and Oceans Canada, Office of Aquatic Biotechnology. "Environmental and indirect human Health Risk assessment of the AquAdvantage Salmon." Draft in Revision. July 2, 2013 at 226.
[39] AquaBounty Technologies. SEC Filing. Form 10. July 23, 2014 at Exhibit 10.9.

[40] Department of Fisheries and Oceans Canada, Office of Aquatic Biotechnology. "Environmental and indirect human Health Risk assessment of the AquAdvantage Salmon." Draft in Revision. July 2, 2013 at 302.
[41] AquaBounty. U.S. Securities and Exchange. Form 10. November 17, 2014 at 8.
[42] Barboza, David. "In China, farming fish in toxic waters." *New York Times*. December 15, 2007.
[43] Department of Fisheries and Oceans Canada, Office of Aquatic Biotechnology. "Environmental and indirect human Health Risk assessment of the AquAdvantage Salmon." Draft in Revision. July 2, 2013 at 73-74.
[44] Department of Fisheries and Oceans Canada, Office of Aquatic Biotechnology. "Environmental and indirect human Health Risk assessment of the AquAdvantage Salmon." Draft in Revision. July 2, 2013 at 75.
[45] Department of Fisheries and Oceans Canada, Office of Aquatic Biotechnology. "Environmental and indirect human Health Risk assessment of the AquAdvantage Salmon." Draft in Revision. July 2, 2013 at 299.
[46] Department of Fisheries and Oceans Canada, Office of Aquatic Biotechnology. "Environmental and indirect human Health Risk assessment of the AquAdvantage Salmon." Draft in Revision. July 2, 2013 at 69.
[47] Department of Fisheries and Oceans Canada, Office of Aquatic Biotechnology. "Environmental and indirect human Health Risk assessment of the AquAdvantage Salmon." Draft in Revision. July 2, 2013 at 114.
[48] Department of Fisheries and Oceans Canada, Office of Aquatic Biotechnology. "Environmental and indirect human Health Risk assessment of the AquAdvantage Salmon." Draft in Revision. July 2, 2013 at 115.
[49] Department of Fisheries and Oceans Canada, Office of Aquatic Biotechnology. "Environmental and indirect human Health Risk assessment of the AquAdvantage Salmon." Draft in Revision. July 2, 2013 at 115.
[50] Department of Fisheries and Oceans Canada, Office of Aquatic Biotechnology. "Environmental and indirect human Health Risk assessment of the AquAdvantage Salmon." Draft in Revision. July 2, 2013 at 115.
[51] Department of Fisheries and Oceans Canada, Office of Aquatic Biotechnology. "Environmental and indirect human Health Risk assessment of the AquAdvantage Salmon." Draft in Revision. July 2, 2013 at 328.
[52] Department of Fisheries and Oceans Canada, Office of Aquatic Biotechnology. "Environmental and indirect human Health Risk assessment of the AquAdvantage Salmon." Draft in Revision. July 2, 2013 at 120.
[53] Department of Fisheries and Oceans Canada, Office of Aquatic Biotechnology. "Environmental and indirect human Health Risk assessment of the AquAdvantage Salmon." Draft in Revision. July 2, 2013 at 118.
[54] Food and Drug Administration Center for Veterinary Medicine. Veterinary Medicine Advisory Committee. "Briefing Packet: AquAdvantage Salmon." September 20, 2010 at Tables 21-24.
[55] Department of Fisheries and Oceans Canada, Office of Aquatic Biotechnology. "Environmental and indirect human Health Risk assessment of the AquAdvantage Salmon." Draft in Revision. July 2, 2013 at 120.
[56] Department of Fisheries and Oceans Canada, Office of Aquatic Biotechnology. "Environmental and indirect human Health Risk assessment of the AquAdvantage Salmon." Draft in Revision. July 2, 2013 at 296-297.