Food Safety Review

A PUBLICATION OF THE CENTER FOR FOOD SAFETY (updated April 2018)

Genetically Engineered Salmon: The Next Generation of Industrial Aquaculture

Plagued by decades of over-fishing, pollution, agricultural runoff, and deficient management, our marine ecosystems and the fisheries that depend upon them stand at a crossroads. States like Alaska have taken bold steps to ensure the longevity of their wild fish stocks by prohibiting the factory farming of fish such as salmon or tuna, and instead investing in proper fisheries management. Other states such as Washington and Maine have invested considerably in industrial aquaculture as a way to supplement diminishing returns of their wild stocks. The next chapter in this unfolding drama is the private development of genetically engineered (GE) fish, which are designed to be raised under industrial aquaculture conditions. The Food and Drug Administration, entrusted with oversight of GE animals, approved in 2015 a GE salmon engineered to grow faster for industrial fish farming. The "AquAdvantage" salmon developed by AquaBounty Technologies, Inc. would be the first-ever GE animal approved for human consumption. AquaBounty has echoed the false promises made by other biotechnology companies regarding feeding the world or minimizing environmental hazards, but alarming red flags suggest quite the contrary, including threats to food safety, the environment, the economic wellbeing of fishermen, animal welfare, and the international marketplace. These risks are exacerbated by the fundamentally flawed oversight model FDA is applying to this unprecedented transgenic organism. The Center for Food Safety has sued the FDA for its faulty review of the environmental and health effects of the AquAdvantage GE salmon. As of April 2018, an amendment to the FDA Appropriations bill by Senator Murkowski (R-AK) makes it illegal to import or grow the fish in the US.

GE FISH AND THE "AQUADVANTAGE SALMON"

Genetic Engineers are currently experimenting on over 58 species of fish, including trout, catfish, tilapia, striped bass, carp, flounder, and salmon. By selecting genes from a variety of organisms (including other fish, coral, mice, bacteria, and even humans) companies hope to produce new breeds of transgenic or genetically engineered (GE) fish that grow faster, produce larger muscles, are disease resistant, and tolerate a wide range of temperatures. Through manipulating certain genes, industry claims these fish will be better suited for industrial aquaculture systems, also referred to as fish farming.

The "AquAdvantage" salmon approved by the Food and Drug Administration (FDA) was developed by AquaBounty Technologies, Inc. The transgenic salmon is an Atlantic salmon (*Salmo salar*) that has had its DNA spliced with a growth hormone gene from the unrelated Chinook salmon (*Oncorhynchus tshawytscha*) and anti-freeze DNA from an Arctic eelpout (*Zoarces americanus*). Normally, an Atlantic salmon's growth hormone stimulates growth in the fish during certain months of the year, and will "turn off" growth during other months to devote its resources toward survival. However, due to the introduction of the eelpout's anti-freeze DNA, the GE salmon produces growth hormone year-round, thus creating a fish that its developer claims can grow up to twice as fast as conventionally raised Atlantic salmon. However, other salmon breeders have produced salmon that grow as fast without genetic engineering.[1]

On November 19, 2015, FDA approved of the GE salmon based on a draft risk assessment.[2]

FDA SWIMMING IN A DANGEROUS DIRECTION

The Problems with the AquAdvantage salmon begin with how our government assesses its risks: with the wrong agency, old laws, and an unacceptable level of analysis. If a transgenic animal is a square peg, the U.S. is attempting to shove it through a round hole.

In 2009, FDA announced in a guidance document that it would regulate novel GE animals pursuant to its veterinary animal drug authority. FDA declared that companies who seek Federal approval must file a New Animal Drug Application (NADA). The agency decided to do this rather than pursue other more robust regulatory mechanisms. For instance, it could have used its food authority (in

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whole, or in part), sought new legislative authorities from Congress to address these novel products, or implemented specific binding regulations under its existing authority.

Transgenic animals are plainly very different from veterinary animal drugs, presenting new difficulties in assessment and regulation. However, FDA equates approval of an engineered animal, and its risks, with the approval of a drug injected into animals. This unprecedented mismatch creates numerous inherent oversight problems.

SCOPE: Animals drugs are approved if safe and effective for intended use, with safe referring to man and the animal. Essentially, review asks whether the "drug" works and its whether its claims are accurate. The environmental risks resulting from GE animals are nowhere contemplated by FDA's statutory process, nor are broader socioeconomic risks.

EXPERTISE: Even if the scope of review were comprehensive, FDA lacks any expertise in the disciplines needed to adequately address impacts.

TRANSPARENCY: Because it is a confidential "drug" approval process, there is a severe lack of transparency and meaningful, timely public participation. FDA cannot even publicly announce what NADAs may be pending until it proposes approval. Nor is labeling of the food necessarily required, likely leaving consumers in the dark if GE animals are approved for human consumption.

FUTURE APPROVALS: Once initial approval is given, subsequent approvals may be granted through supplemental applications, which are limited and ill-suited to cover emerging GE animal risks.

The AquAdvantage salmon is the first GE animal being considered by FDA for human consumption, and the agency has continued to use the inadequate NADA review process despite overwhelming opposition from the public, scientific community, and Members of Congress. These regulatory shortcomings leave much to be concerned about when considering not only the 58 GE fish species currently in development, but also the numerous other GE animals that are possibly under review by FDA, including cattle, chickens, and pigs. The approach also stands in sharp contrast to the approach of other governments, such as the European Union (EU), which show it is possible for transgenic animal oversight to be comprehensive, precautionary in nature, and specifically designed to apply to GE organisms.

ENVIRONMENTAL IMPACTS

GENETICALLY ENGINEERED FISH pose serious risks to wild populations of fish and the marine environment. Each year, an estimated two million salmon escape from open-water net pens into the North Atlantic, outcompeting wild populations for resources and straining ecosystems.[3] The risks of escaped GE salmon include the transgenic contamination of wild fish stocks, out-competing wild fish for food and mates, spreading lethal diseases and parasites, and disrupting food webs in local environments. While AquaBounty has promised to raise its GE salmon in land-based facilities, the United Nations Food and Agriculture Organization recommends that the introduction of species for aquaculture be considered as introductions to the wild, even if the facility is considered a closed system.[4]

Scientists have hypothesized that GE salmon escapes would not just wreak havoc on local ecosystems, but could lead to the eventual extinction of wild populations as a result of the "Trojan gene effect." That is, the introduction of fast- growing transgenic fish with enhanced mating success but reduced adult viability into a wild population may result in a rapid population decline. Research published in the *Proceedings of the National Academy of Sciences* concluded that a release of just sixty GE fish into a wild population of 60,000 would lead to the extinction of the wild population in less than 40 generations.[5]

Even though AquaBounty makes the claim to FDA that it will only produce sterile female fish, information presented in FDA's own draft Environmental Assessment indicated that up to 5% of the fish could be fertile and able to reproduce.[6] AquaBounty will also keep large stocks of fertile fish to produce offspring, and fish are known to change sex, raising additional concerns about fish escaping and reproducing in the wild.[7] A 2011 study published by Canadian scientists concluded that if GE Atlantic salmon were to escape from captivity, they could succeed in breeding and passing their genes into the wild.[8]

Knowing that these foreseeable impacts would cause significant regulatory scrutiny, AquaBounty claims that it will only produce its fish in a scheme involving: growing the eggs at its Prince Edward Island facility in Canada, flying them to a land-based facility in Panama to be raised, and finally shipping the processed salmon to U.S. markets. Yet we know that it is not economically viable to farm salmon in this way. Salmon are commercially farmed in open-water net pens, where escapes are a regular occurrence. AquaBounty' s smokescreen is intended to breach the regulatory door, and it has stated its future plans to grow the fish elsewhere in the U.S.[9]

In 2010, the FDA convened a meeting of its Veterinary Medicine Advisory Committee (VMAC) to review its GE salmon risk assessment. The only scientist with expertise in fisheries explicitly called for the agency to produce a much more rigorous risk assessment.[10] To date, the agency has claimed it is not obligated to consider the full range of impacts that GE salmon would have on the environment, and claimed it need not even formally consult with our expert wildlife agencies—the Fish and Wildlife Service and the National Oceanic and Atmospheric Administration—on

those potential impacts. Previously hidden documents surfaced during a Canadian investigation that revealed that AquaBounty's Prince Edward Island facility was contaminated in 2009 with a new strain of Infectious Salmon Anemia (ISA)[11], the deadly fish flu that is devastating fish stocks around the world. This information was hidden from the public and the VMAC.

FOOD SAFETY CONCERNS

FDA never required or conducted any studies to assess the possible long-term health impacts of eating GE animals; however, several independent studies have produced findings that leave cause for serious concern. For instance, the routine use of antibiotics to control disease in factory farm operations (like the AquAdvantage salmon conditions) may adversely impact human health.[12] Research suggests transgenic fish may be even more susceptible to diseases than conventional farmed fish.[13] Increased disease susceptibility could mean transgenic fish may then require more antibiotics. Human health could also be jeopardized as a result of antibiotic-resistant bacteria, and exposure to certain classes of antibiotics that may cause allergic reactions.[14]

Genetically Engineered salmon also presents problems for consumers who have certain allergies. Allergenicity con- cerns are twofold: the possible allergenicity with newly expressed protein(s); and endogenous allergenicity that comes from the insertion of a growth hormone construct possibly changing the level of allergenic proteins normally found in Atlantic salmon. Consumers need to know if this new fish is more likely to cause allergic reactions. Even the small sample sizes used by the company in their allergenicity tests (only 6 fish) showed that GE fish were likely to cause heightened allergic responses.

In 2009, a study commissioned by the E.U. indicated several potential food safety concerns with GE fish and their ability to grow faster and possess a higher tolerance to environmental toxins.[15] The study's authors expressed concerns that both toxins and growth hormones had a high potential to end up in consumers' bodies and called for further tests to determine safety. This demand for additional data is critical in light of FDA's 2010 data release, where results indicated that GE salmon possess 40% higher levels of the hormone called IGF-1 (insulin-like growth factor 1), which has been shown to increase the risk of certain cancers.[16] Finally, nutritionally speaking, GE salmon lack many of the beneficial qualities that salmon boast: specifically, wild salmon have 189% higher levels of beneficial omega fats than GE salmon can produce.[17]

ECONOMIC IMPACTS

Another Clear Deficiency in FDA's review is the absence of any assessment of economic impacts. Wild salmon

Serving Size: 1 AquAdvantage Frankenfish

Nutrition Facts: [Hazard Factor UNKNOWN]

% Difference to Non-GE Salmon*			
Total Fat	+ 57.8%	Omega 3/6 Fatty Acids+	- 65.4%
Protein	- 5.1%	Sodium	- 9.2%
Total Carbohydrate	+ 2.7%		

Vitamin C	- 25.1%	Folic Acid	- 12.0%
Calcium	- 8.2%	Iron	+ 8.3%
Zinc	- 1.9%	Phosphorous	- 4.4%
Thiamin	- 12.5%	Riboflavin	- 4.4%
Vitamin B6	+ 6.5%		

Essential Amino Acids			
Histidine	- 3.6%	Phenylalanine	- 6.3%
Isoleucine	- 4.4%	Threonine	- 5.3%
Leucine	- 6.6%	Tryptophan	- 5.3%
Lysine	- 6.2%	Valine	- 5.6%
Methionine	- 5.1%		

* % Difference to Non-GE Salmon based on GE AquAdvantage Salmon and AquaBounty's non-GE sponsor control data, available at: www.fda.gov/downloads/Advisory Committees/CommitteesMeeting-Materials/VeterinaryMedicineAdvisoryCommittee/UCM224762.pdf

+ Omega 3/6 Fatty Acids based on data compared to Wild Salmon.

INGREDIENTS: GENETICALLY ENGINEERED ATLANTIC SALMON, INDUCED GROWTH HORMONE GENE FROM CHINOOK SALMON (ONCORHYNCHUS TSHAWYTSCHA), ANTI-FREEZE DNA FROM OCEAN POUT (ZOARCES AMERICANUS). GROWN AND PROCESSED IN A TOP SECRET FACILITY IN PANAMA.

are a crucial economic and public resource for commercial, recreational, and subsistence fishers throughout California, the Pacific Northwest, and Alaska. Thousands of men and women depend on salmon fishing for their livelihoods. While some Pacific salmon fisheries are healthy, many are already threatened with extinction. Similarly, in the past several decades, significant investments have been made to restore wild salmon populations in the Northeast U.S., where Atlantic salmon is currently listed as an endangered species and commercial fishing is restricted. On both coasts, approval of GE salmon and its subsequent entrance into the market will pose serious threats to our nation's marine economy.

These economic concerns are especially alarming for states like Alaska, where the seafood industry is the state's largest private sector employer and creates 56,600 direct and 22,000 indirect jobs annually (more jobs than the oil, gas, and mining industries combined).[19] A 2010 study published in the *Journal of Bioeconomics* found that the success of wild fish-

eries can also cause positive economic ripples in other sectors, such as agriculture, forestry, manufacturing, and financial services.[19] Given these serious threats to our nation's fishing industry and the economic market as a whole, FDA must complete a comprehensive analysis of these impacts.

There are also significant market ramifications to be considered in terms of consumer opinion. Since the U.S. does not yet require labeling for GE foods, there is likely to be consumer confusion about which salmon or fish at the supermarket are in fact genetically engineered, perhaps resulting in consumers not purchasing any salmon or farmed fish entirely. In an international context, this lack of labeling could impede foreign markets and result in trade disparities with governments that *do* require labeling for GE foods (such as the EU). A 2008 Consumer Reports poll indicated that 95% of respondents felt food from genetically engineered animals should be labeled.[20] These findings are supported by a 2010 poll from Lake Research Partners, indicating that 91% of Americans felt FDA should *not* introduce GE fish and meat into the marketplace.[21]

ANIMAL WELFARE ISSUES

Numerous Factors must be considered when assessing the animal welfare and health issues associated with genetic engineering. These include the likelihood of GE fish experiencing more health problems; increased likelihood of disease; high rates of physical deformities and other abnormalities; and premature death, especially when compared to conventionally farmed fish. FDA data and reports from AquaBounty indicate that GE salmon have already suffered deformities, such as jaw erosions and inflamed tissues. Numerous animal welfare issues are were not analyzed by FDA in their review process and the health of the Aquabounty's salmon through its full life cycle remains unknown.

CONCLUSION

Our Fisheries are at a crossroads. While some companies are looking to genetic engineering as a panacea, the solution to declining fisheries is not to engineer salmon to "fit" more efficiently in our factory farm systems. The solution is to bring our wild salmon populations back to sustainability. The Center for Food Safety is suing the FDA to get the agency to address the real questions : do we continue down the road to industrial aquaculture, consolidation, and ecological degradation? Or can we muster the political will to reject the notion that a single technology, like genetic engineering, will solve the complex problems that face our fisheries, and instead advocate for policy changes that will effectively protect them?[i]

[1] See chart in "Salmobreed Challenges GMO Salmon", Newsletter from Salmobreed, Year 7, nr. 5, November 2011 available at: http://www.salmobreed.no/newsletters/en/newsletter_5_2011.pdf

[2] https://www.fda.gov/animalveterinary/developmentapprovalprocess/geneticengineering/geneticallyengineeredanimals/ucm466214.htm; Federal Register, Vol. 77, No. 247. "Draft Environmental Assessment and Preliminary Finding of No Significant Impact Concerning a Genetically Engineered Atlantic Salmon." Docket No. FDA–2011–N–0899, Wednesday, December 26, 2012.

[3] Schiermeier Q. 2003. Fish farms' threat to salmon stocks exposed. Nature 425:753; and Naylor, R et al. "Fugitive Salmon: Assessing the Risks of Escaped Fish from Net Pen Aquaculture," *Bioscience*. May 2005.

[4] FAO, 1995, Code of Conduct for Responsible Fisheries, United Nations Food and Agriculture Organisation, Rome, Italy, 41pp.

[5] William Muir et al., Possible ecological risks of transgenic organism release when transgenes affect mating success: Sexual selection and the Trojan gene hypothesis, 96 PNAS 13853-13856, at 13853 (Nov. 23, 1999).

[6] U.S. Food and Drug Administration Center for Veterinary Medicine. "Draft Environmental Assessment: AquAdvantage Salmon." May 4, 2012 (published December 26, 2012), at page 86.

[7] James J. Nagler et al., "High Incidence of a Male-Specific Genetic Marker in Phenotypic Female Chinook Salmon from the Columbia River." *Environmental Health Perspectives*, Vol. 109, no. 1, January 2001.

[8] Darek T. R. Moreau, Corinne Conway, Ian A. Fleming. (2011) "Reproductive performance of alternative male phenotypes of growth hormone transgenic Atlantic salmon (Salmo salar)." *Evolutionary Applications*, Blackwell Publishing, Ltd.

[9] Suzanne Goldenberg, Obama Administration "bailed out" GM Salmon Firm, The Guardian (UK) October 18, 2011 available at: http://www.guardian.co.uk/environment/2011/oct/18/gm-salmon-aquabounty According to the article, the company president, Ron Stotish said the company had prospective fish farmers lined up for the GM Salmon in South Dakota, West Virginia, Wisconsin and Ohio. "We have people in the in the United States who are interested in growing these fish right now."

[10] Veterinary Medicine Advisory Committee Meeting Transcript, Center for Veterinary Medicine, Food and Drug Administration. Recorded by Audio Associates at the Double Tree Hotel in Rockville, MD, Sept. 20, 2010, p. 383.

[11] Living Oceans Society, Media Release. "ISA virus confirmed in AquaBounty's genetically-engineered salmon." Reposted on December 20, 2012. Available at: http://www.livingoceans.org/media/releases/salmon-farming/isa-virus-confirmed-aquabounty's-genetically-engin

[12] Ian Phillips et al., "Does the use of antibiotics in food animals pose a risk to human health? A critical review of published data." *Journal of Antimicrobial Chemotherapy* vol. 53, 28–52. DOI: 10.1093/jac/dkg483. December 4, 2003.

[13] William Muir et al., "Possible ecological risks of transgenic organism release when transgenes affect mating success: Sexual selection and the Trojan gene hypothesis," *96 PNAS* 13853-13856, at 13853. November 23, 1999.

[14] Rebecca Goldberg and Tracy Triplett. "Murky Waters: The Environmental Effects of Aquaculture in the U.S." (p.44). *Environmental Defense Fund*, 1997.

[15] Centre for Aquaculture and Environmental Research (2009) "Ecological Risk Assessment of Transgenic Salmon." Study commissioned by the European Union, the Swedish Research Council Fromas and the University of Gothenburg. Vancouver, Canada.

[16] Yu H. and T. Rohan. "Role of the Insulin-Like Growth Factor Family in Cancer Development and Progression." *Journal of the National Cancer Institute*, vol. 92, iss. 18. September 20, 2000; and Moschos, S. and C. Mantzoros. "The Role of the IGF System in Cancer: From Basic to Clinical Studies and Clinical Applications." *Oncology*, vol. 63 iss. 4. November 4, 2002.

[17] U.S. Food and Drug Administration (FDA) Center for Veterinary Medicine. Veterinary Medicine Advisory Committee. "Briefing Packet: AquAdvantage Salmon." September 20, 2010, at Table 28.

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[20] Consumer Reports. 11/11/08 http://www.greenerchoices.org/pdf/food-poll2008.pdf

[21] Lake Research Partners, Commissioned by Food and Water Watch. September 20, 2010. Available at: http://documents.foodandwaterwatch.org/release-FWW-Omnibus.pdf

[22] http://www.centerforfoodsafety.org/press-releases/4131/fda-approves-first-genetically-engineered-animal-for-human-consumption-over-the-objections-of-millions