April 28, 2015 Blog

Transgenic Salmon: A Primer on FDA Food Safety Regulations

"Earth & Table" Law Reporter

When Meriwether Lewis tasted his first roasted morsel of a fresh Chinook salmon at a Shoshone camp along the Lemhi River (in modern day Idaho), he ate it with "very good relish." It convinced him that "we were on the waters of the Pacific Ocean."

For centuries, native tribes and later settlers in the Pacific Northwest have revered the Chinook (or King) salmon as an iconic symbol of life and regeneration. Celilo Falls, along the Columbia River bordering Washington and Oregon, was once the greatest salmon fishing site in North America, and perhaps the world.

Some 200 years later, the Atlantic and Pacific salmon fisheries have merged in the form of the first transgenic salmon. An AquAdvantage® salmon[1] is what you create when you take an Atlantic salmon and insert a Chinook salmon growth hormone gene and an ocean pout fish regulatory gene sequence into it through the use of recombinant DNA technology. An AquAdvantage salmon can grow to market size in land-based tank farms in half the time of conventional salmon. It is never, ever supposed to swim in either ocean.

Whether or not the AquAdvantage salmon achieves final regulatory approval and market acceptance, its current fate squarely pits the much

Related People

Paul D. Swanson
swansonp@lanepowell.com

Related Practices & Industries

Food, Beverage & Hospitality

vaunted concept of ***sustainability*** against the other two most heralded words in the modern food vocabulary, ***natural*** and ***organic***.

This article provides a brief survey of how the FDA evaluates the food safety of transgenic animals as "new animal drugs." It then discusses an alternative, more rigorous means of assessing genetically altered animals as "food additives," the analytical approach favored by Food & Water Watch in a recently filed FDA citizen's petition. It closes with an animal scientist's perspective regarding the sustainability of transgenic animals as food sources.

"Our First Precision Bred Fish"

AquAdvantage salmon is the first animal to be genetically engineered for potential human food consumption. AquaBounty Technologies touts it as "our first precision bred fish" which is "an environmentally sustainable alternative to current farmed salmon." This transgenic salmon variety is slated to "be grown as sterile, all-female populations in land-based facilities with redundant biological and physical containment." Hence, the risk of AquAdvantage salmon escaping and posing a threat to wild salmon populations is supposedly nil.

Even more so than transgenic plants (*e.g.*, soybeans and corn), genetically altering animals for food consumption purposes pushes a host of cultural hot-buttons. We champion recombinant DNA technology when it offers up breakthroughs in medical treatment. However, we are much more wary of gene-splicing technology when it transforms longstanding food habits and expectations.

Choosing what to eat is essentially a nostalgic, backward-looking act, relying on deeply ingrained family, cultural and religious norms for determining what should and should not be served around the dinner table. The act of swallowing food itself is imbued with physical and psychological triggers. In this consumer realm, transgenic salmon become *frankenfish* and fodder for dystopian horror films. Pejorative labels reflect intense popular discomfort with genetically modified food.

How Are Transgenic Animals Regulated by the FDA?

The Food and Drug Administration (FDA) seeks to regulate food safety from a strictly scientific standpoint; it is not an arbiter of consumer ingestion preferences. Yet, how the FDA analyzes and regulates transgenic animals intended for human consumption is hardly common knowledge.

As a bellwether, the laboratory-to-table regulatory journey for AquAdvantage salmon began over 20 years ago and is ongoing. In the meantime, AquaBounty's U.S. patent rights for this invention expired in March 2014. To an outside observer, the vocabulary associated with the FDA's regulatory review of transgenic salmon will seem arcane.

Evaluating Transgenic Salmon as a "New Animal Drug"

For regulatory review and approval purposes, the FDA defines a genetically engineered (GE) animal intended for food consumption as a "new animal drug" and compares the GE animal to its "natural" counterpart" in order to analyze its food safety and potential environmental impacts.

Treating transgenic salmon as a "new animal drug" appears to be an indirect—some would argue, a *misdirected*—way of regulating GE animals at first blush. That regulatory pathway flows from the statutory structure of the federal Food, Drug and Cosmetic Act of 1938 (FDCA), codified at 21 U.S.C. 321 *et seq* (as amended). "Food" itself is defined statutorily as articles used for food or drink for man or other animals, chewing gum, and articles used for components of any such article. 21 U.S.C. 321(f).

When conventional food is altered or mislabeled, it can be classified as a "drug" under federal law. The FDCA defines "drugs" as including "articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals," and "articles (other than food) intended to affect the structure or any function of the body of man or other animals." 21 U.S.C. 321(g)(1).

Under the "new animal drug" analysis, the recombinant DNA (rDNA) construct—a genomic sequence—is intended to affect the structure or function of the body of the GE animal and therefore meets the foregoing definition of a "drug." As applied to AquAdvantage salmon, the rDNA construct is composed of the protein-coding sequence from a Chinook

salmon growth hormone gene and a promoter of an ocean pout antifreeze protein gene. This rDNA construct is micro-injected into the fertilized eggs of wild Atlantic salmon and renders the salmon growth cycle continuous rather than seasonal.

Under AquaBounty's new animal "new animal drug application" (NADA) proposal, the AquAdvantage salmon would be produced as triploid, all-female populations. "All-female fish are unable to interbreed with each other and triploidy results in sterility." These "eyed-eggs" would then be shipped to a land-based grow-out facility where they would be reared to market size and harvested for processing.

Under the FDCA, a new animal drug is generally "deemed unsafe" unless the FDA approves a NADA for a particular use. The FDA reviews NADA applications to determine whether the new animal drug is safe and effective for its intended use. Through this process, the FDA preliminarily determined that AquAdvantage salmon "is as safe as food from conventional Atlantic salmon and that there is a reasonable certainty of no harm from consumption of food" from them.

Pursuant to environmental laws and regulations, the FDA also reviewed the NADA application for its environmental impacts and concluded that AquAdvantage salmon "will not jeopardize the continued existence of United States populations of threatened or endangered Atlantic salmon, or result in the destruction of adverse modification of their critical habitat" because of the land-based nature of its commercial production.

Regulating Transgenic Salmon as a "Food Additive"

At least one non-profit food group vigorously disagrees with the how the FDA conducted it review of AquAdvantage salmon as a new animal drug. A recent citizen petition submitted by Food & Water Watch0 (F&WW) would instead evaluate (1) the novel transgenic fish and (2) the gene expression product (GEP) used to make it both as "food additives" under the FDCA. In this regard, the GEP is the biochemical material, primarily the Chinook salmon growth hormone, that results from inserting the rDNA construct into an Atlantic salmon.

F&WW contends that neither the AquAdvantage salmon nor the GEP are generally recognized as safe (GRAS) for human consumption. Rather,

food additives are presumed to be *unsafe* and the food processor's burden is to demonstrate that the food additive is GRAS. F&WW further argues that the food safety of AquAdvantage salmon cannot be predicated upon the food safety data already prepared and presented by AquaBounty because that data is incomplete, biased and unreliable.

To understand this food additive argument, a brief historical FDA digression is necessary. The Food Additives Amendment of 1958 arose out of concern about that U.S. food safety was being compromised by a host of chemicals and other substances being added willy-nilly to food without any pre-market safety testing or approval. To regulate food additives going forward, the Act grandfathered in conventional foods or additives that had already been consumed by the public before 1958 without any apparent untoward effect on health. Those food products or additives would be generally recognized as safe or GRAS and they would therefore need no pre-market FDA review or approval.

The statutory definition of a "food additive" added in 1958 reads in key part:

The term "food additive" means any substance the intended use of which results or may reasonably be expected to result, directly or indirectly, in its becoming a component or otherwise affecting the characteristics of any food (including any substance intended for use in producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food; and including any source of radiation intended for any such use), if such substance is not generally recognized, among experts qualified by scientific training and experience to evaluate its safety, as having been adequately shown through scientific procedures (or, in the case of a substance used in food prior to January 1, 1958, through either scientific procedures or experience based on common use in food) to be safe under the conditions of its intended use. 21 U.S.C. 321(s).

If a subject food additive cannot be grandfathered in, qualified experts must generally recognize its food safety in order to avoid the FDA food additive screening process.

In its citizen's petition, F&WW acknowledges that statutory roadblock for engaging in this proposed food additive review exists. A new animal drug

is expressly excluded from the definition of a food additive per 21 U.S.C. 321(s)(5). The FDA interprets this statutory exclusion as foreclosing any resort to an additional "food additive" analysis of AquAdvantage salmon. F&WW, in contrast, maintains that the FDA review process is not so bracketed and confined by this definitional exclusion and that the FDA has the statutory authority to review and assess this salmon creation as a food additive if it chooses to do so.

Were AquAdvantage salmon evaluated as a novel food additive, it arguably would be subject to more rigorous scientific scrutiny of its food safety. That regulatory track would place the onus on AquaBounty Technologies to affirmatively prove the food safety of its product. The FDA would not be able to simply compare the transgenic salmon with its counterpart Atlantic salmon. That type of "substantial equivalency" testing already shows that AquAdvantage salmon exhibits elevated allergenic potential and has higher levels of growth hormones than Atlantic salmon. However, those risks are prone to exaggeration.1

F&WW submits that assessing AquAdvantage salmon as a novel fish product comports most closely with the internationally recognized food safety guidelines set forth in the Codex Alimentarius (Latin for "Book of Food"). The Codex is formed through international consensus and forms the basis for the food laws of many countries around the world. The Codex's more rigorous safety assessment approach is necessary, the F&WW's citizen petition argues, because genetic modification may change the characteristics of a food in unpredictable ways. Were the FDA to apply its food additive regulations and the Codex guidelines, the end result would and should be the banning of AquAdvantage salmon from the public marketplace—according to F&WW's citizen petition.

Whither Marketplace Acceptance of Transgenic Animals?

Even if AquAdvantage salmon eventually does make it into grocery store display cases, it faces the momentous hurdle of marketplace acceptance. Food retailers (such as Target, Whole Foods and Trader Joe's) have already stated that they will not stock AquAdvantage salmon even if it receives final FDA approval.2

Even those in favor of GE animal consumption acknowledge that consumer concerns must be addressed and satisfied. One

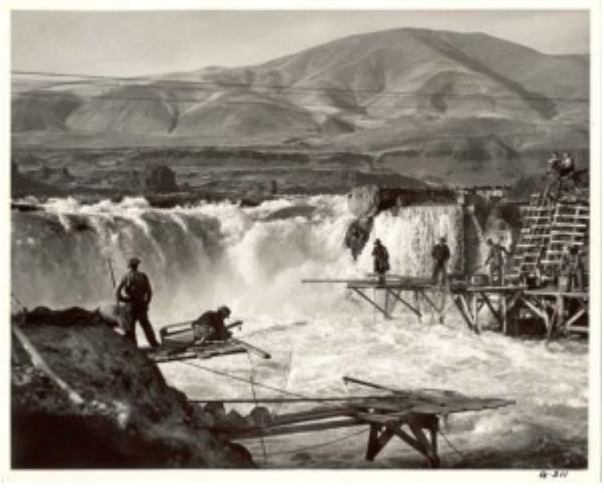
scientist/author concludes that the "human health risks are not greater than that posed by other meats and animal products," but that "feeding studies comparing AquAdvantage salmon to commonly eaten salmon species may be needed to assuage consumer concerns."3 She further notes that "voluntary labeling such as 'wild caught' and 'not genetically engineered' will allow for different products to prove themselves in the marketplace."

A Scientific Perspective on Sustainability

From the perspective of animal science professors, the regulatory review process for transgenic salmon focuses on "risks with little consideration of attendant benefits."4 As two animal science professors note:

Subjecting conventionally bred and GE [genetically engineered] animals to different regulatory standards is inconsistent from a scientific perspective and places an excessive regulatory burden on the development of GE technologies. Assessing potential risks in the absence of considering concomitant benefits and those risks associated with alternative food production systems gives disproportionate emphasis to the risk side of the GE food animal equation. Few, if any, technologies could survive a risk-only analysis. Wild-caught fish deplete oceanic stocks and do not present a long-term, ecologically sustainable solution to rising global fish demand.5

Conclusion



AquAdvantage salmon remains in regulatory limbo. The FDA's preliminary draft environmental approval and its "Preliminary Finding of No Significant Impact" are steps towards final regulatory approval. In contrast to its Chinook predecessors swimming upstream against the mighty currents of the Columbia River,

AquAdvantage salmon are swimming around in tanks while a tide of contentious public opinion swirls around them.

---

[1] The name *AquAdvantage* is a registered U.S. trademark. To promote readability, the registration symbol is not further used in this article.

[2] *See* http://aquabounty.com/our-salmon/.

[3] *See* U.S. Patent No. 5,545,808 ("Transgenic Salmonid Fish Expressing Exogenous Salmonid Growth Hormone"), issued on August 13, 1996.

[4] *See generally,* "Guidance for Industry: Regulation of Genetically Engineered Animals Containing Heritable Recombinant DNA Constructs" (issued on January 29, 2008 and revised on May 17, 2011), available online at http://tinyurl.com/249xse7.

[5] A. Van Eenennaam and W. Muir, "Transgenic salmon: a final leap to the grocery shelf?, *Nature Biotechnology,* Vol. 29, No. 8, at 706 (August 2001).

[6] *See* "Preliminary Finding of No Significant Impact for AquAdvantage® Salmon," available online at http://tinyurl.com/os23eat.

[7] *Id.* at 3.

[8] *Id.* at 5.

[9] This Food & Water Watch citizen petition is available online and is identical to a separate Food Additive Petition that F&WW filed. *See* http://www.regulations.gov/#!documentDetail;D=FDA-2015-P-1094-0001.

[10] Food & Water Watch describes itself as a "national non-profit consumer organization that advocates to ensure that food, water and fish is safe, accessible and sustainably produced."

[11] *See generally,* A. Bodnar, "Risk assessment and mitigation of AquAdvantage salmon," The Biofortified Blog (October 16, 2010), available online at http://www.biofortified.org/2010/10/salmon/.

[12] http://www.foodnavigator-usa.com/Markets/GM-salmon-Target-joins-58-other-retailers-to-say-no-to-GM-fish.

[13] *See* fn. 11.

[14] *See* fn. 5, p. 709.

[15] *Id.*