LACK OF TRANSPARENCY IN THE PREMARKET APPROVAL PROCESS FOR *AQUADVANTAGE* SALMON

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ABSTRACT

After a lengthy premarket approval process, the Food and Drug Administration (FDA) has just deemed AquAdvantage Salmon, a fast-growing, genetically engineered salmon, safe for human consumption. AquAdvantage Salmon is the first genetically engineered animal designed for human consumption to go to market in the United States. Because there have been no significant changes to the statutory or regulatory framework governing agricultural biotechnology since it was established in the 1980s, the FDA reviews applications of genetically engineered animals under the New Animal Drug Application (NADA) provisions of the Federal Food, Drug, and Cosmetic Act (FDCA). The FDA's treatment of genetically engineered food as a new animal drug has been criticized due to potential environmental and human health risks, and because of a lack of transparency throughout the regulatory process. After providing an overview of the premarket approval process, this Issue Brief argues that even under the NADA provisions, the FDA's premarket approval risk assessment should be more transparent. In particular, the justification for trade secret status of relevant biotechnology is undermined, if not extinguished, by the need for public consideration of the biotechnology's safety and effectiveness after a certain time in the approval process. Furthermore, the comment period prior to advisory committee meetings should be lengthened to allow for greater scientific input on safety and effectiveness, and an independent body should be created to communicate with the public about food safety.

INTRODUCTION

Within the field of genetic engineering, recombinant DNA (rDNA) technology is introduced into an organism to promote a targeted

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trait.[1] A genetically engineered animal (or genetically modified organism) is one that contains an rDNA construct producing a new, desirable trait.[2] The genes and other segments of DNA that are part of the rDNA construct may be obtained from other organisms or synthesized in a laboratory setting.[3] Genetic engineering has been used in a wide array of contexts: agriculture, to produce crops resistant to pests or herbicides; medicine, to develop microbes that can produce pharmaceuticals for human or animal use; and food, to produce microorganisms that aid in baking, brewing, and cheese-making.[4] While it has not yet been commercially used to produce animals intended for human consumption, this is soon to change.[5]

AquAdvantage Salmon, produced by AquaBounty Technologies, Inc., is a genetically engineered fish intended for human consumption under active review by the FDA. In 1989, the precursor to the *AquAdvantage* Salmon line was created by injecting an Atlantic salmon egg with a gene construct containing a promoter and termination region from the ocean pout antifreeze gene and a growth hormone gene from Chinook salmon.[6] The ocean pout antifreeze promoter had been shown to continually express growth hormone in salmon, unlike the native

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[1] *Genetic Engineering*, U.S. FOOD & DRUG ADMIN. (May 23, 2011), http://www.fda.gov/AnimalVeterinary/DevelopmentApprovalProcess/GeneticEngineering/default.htm.

[2] *Id*.

[3] *General Q&A*, U.S. FOOD & DRUG ADMIN. (May 23, 2011), http://www.fda.gov/AnimalVeterinary/DevelopmentApprovalProcess/GeneticEngineering/GeneticallyEngineeredAnimals/ucm113605.htm.16, 2012).

[4] *Id*.

[5] *See, e.g.*, Jim Kozubek, *FDA Decision Will Lead to First Ever Genetically-Modified Animal for Consumption*, TMP IDEALAB (Oct. 10, 2011, 10:00 AM), http://idealab.talkingpointsmemo.com/2011/10/fda-nears-decision-on-genetically-engineered-salmon.php (stating that the FDA has completed its "evaluation of the environmental impact of the world's first genetically engineered (GE) fish for human consumption, and written a document supportive of its commercialization on the U.S. market.").

[6] *See* Anastasia Bodnar, *Risk Assessment and Mitigation of AquAdvantage Salmon*, BIOFORTIFIED (Oct. 16, 2010), http://www.biofortified.org/2010/10/salmon/. A promoter is the first region of a gene. It acts as a genetic switch, turning the gene on and off and specifying how many copies of the protein will be produced. The termination sequence, as the name indicates, follows the promoter and coding region, and signals the end of the gene so the rest of the chromosome is not read. *See, e.g.*, *Gene Regions*, AGBIOSAFETY AT THE UNIVERSITY OF NEBRASKA-LINCOLN (last visited April 8, 2012), http://agbiosafety.unl.edu/education/gene.htm.

growth hormone promoter in salmon.[7] Increased expression of the growth hormone in the transgenic[8] salmon results in fish that grow more quickly in early life than their natural comparators.[9] If approved by the FDA, *AquAdvantage* Salmon's broodstock would consist of phenotypically sex-reversed, homozygous females (that is, females having two copies of the transgene), which would cross with non-transgenic female Atlantic salmon to produce eggs with a single-copy of the transgene.[10] These eggs would be pressure-shocked to induce triploidy, which inhibits sexual development and renders them 98.9% sterile.[11] In other words, *AquAdvantage* Salmon would be mostly sterile salmon with the ability to grow to market size in less time than their non-transgenic counterparts.

The FDA regulates genetically engineered animals as animal drugs under the Federal Food, Drug, and Cosmetic Act (FDCA).[12] While this regulatory approach has certain advantages—a "new animal drug" is not generally recognized as safe,[13] and its safety must be determined with "reference to the health of man or animal"[14]—it is not without its disadvantages. Criticisms have centered on four major issues: (1) the general inadequacy and outdated mechanisms of the regulatory framework; (2) the possible environmental risks, and the related need for a comprehensive environmental impact statement; (3) the possible adverse effects on human health (for example, increased allergenicity);

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[7] *Id.*

[8] A "transgenic" animal is an organism that has had a "synthetic gene . . . constructed *in vitro* incorporated into its genome with the intended purpose of modifying its phenotype." *See* U.S. FOOD & DRUG ADMIN., BRIEFING PACKET vii (2010) [hereinafter BRIEFING PACKET], *available at* http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/VeterinaryMedicineAdvisoryCommittee/UCM224762.pdf.

[9] *See id.* at 24.

[10] AQUA BOUNTY TECHS., INC., ENVIRONMENTAL ASSESSMENT FOR *AQUADVANTAGE* SALMON 13 (2010) [hereinafter ENVIRONMENTAL ASSESSMENT], *available at* http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/VeterinaryMedicineAdvisoryCommittee/UCM224760.pdf.

[11] *Id.*

[12] U.S. FOOD & DRUG ADMIN., GUIDANCE FOR INDUSTRY: REGULATION OF GENETICALLY ENGINEERED ANIMALS CONTAINING HERITABLE RECOMBINANT DNA CONSTRUCTS 5 (2011) [hereinafter GUIDANCE FOR INDUSTRY], *available at* http://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/UCM113903.pdf.

[13] Federal Food, Drug, and Cosmetic Act § 201(v)(1), 21 U.S.C. § 321(v)(1).

[14] *Id.* at § 321(u)(1).

and (4) the lack of transparency and public input afforded under the New Animal Drug Application (NADA) provisions of the FDCA.

This Issue Brief examines the premarket approval process as applied to the *AquAdvantage* Salmon so as to explore this fourth issue—the lack of transparency within the current regulatory process. Part I will provide a brief overview of the ubiquity of genetically engineered food and the different ways in which animals have been used and are being used in genetic engineering. Part II explains the regulatory framework for NADAs in greater detail, including recently issued guidance provided by the FDA, and Part III explains how this framework has been applied to *AquAdvantage* Salmon, focusing on public meetings held in September 2010. Finally, Part IV provides reasons to increase the transparency of the premarket process and suggests several mechanisms that might achieve this goal. In particular, public disclosure of trade secrets at the public advisory committee meetings, which the FDA intends to hold for all applications for genetically engineered animals intended for human consumption, provides a reason to reduce transparency immediately before and after such disclosures. Two other mechanisms for increased public review are briefly discussed: lengthening the comment period prior to the advisory committee meetings, and creating an independent body, like the European Food Safety Authority (EFSA), to communicate with the public about food safety.

I. GENETICALLY ENGINEERED ANIMALS AS FOOD

In 1994, the first genetically engineered food item approved for human consumption, the Falvr Savr tomato (a tomato engineered to ripen slowly), was introduced to the market.[15] In 2011, 88% of all corn[16] and 94% of all soybeans[17] planted in the United States were genetically engineered. Because "many processed food products contain corn or soybean ingredients,"[18] the consumer group Food & Water Watch has estimated that 70 to 75% of processed foods on supermarket shelves

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[15] Gregory N. Mandel, *Gaps, Inexperience, Inconsistencies, and Overlaps: Crisis in the Regulation of Genetically Modified Plants and Animals*, 45 WM. & MARY L. REV. 2167, 2176 (2004).

[16] ACREAGE, NAT'L AGRIC. STATISTICS SERV., U.S. DEP'T OF AGRIC. 25 (June 2012), *available at* http://usda.mannlib.cornell.edu/usda/current/Acre/Acre-06-29-2012.pdf.

[17] *Id.* at 27.

[18] Patrick Byrne, *Labeling of Genetically Engineered Foods*, COLO. STATE UNIV. (Sept. 2010), http://www.ext.colostate.edu/pubs/foodnut/09371.html.

contain genetically engineered ingredients.[19] Despite the ubiquity of genetically engineered foods in our diet, genetic alteration of food has thus far been limited to non-animal products.[20] That is about to change, as the FDA has been reviewing a completed NADA for a genetically engineered salmon, the *AquAdvantage* Salmon, since 2010.[21] On December 20, 2012, the FDA released its draft environmental assessment of the proposed conditions of use and its preliminary finding of no significant impact (FONSI) for the *AquAdvantage* Salmon application, triggering a 60-day public comment period.[22] The preliminary FONSI concluded that food from *AquAdvantage* Salmon is "as safe as food from conventional Atlantic salmon"[23] and that the "development, production, and grow-out of AquAdvantage Salmon . . . will not result in significant effects on the quality of the human environment in the United States."[24] Once approved, the salmon will become the first genetically engineered animal approved for human consumption in the United States.[25]

Proponents of genetic engineering emphasize the many benefits genetically engineered crops and animals provide to consumers.[26] The largest class of genetically engineered animals being developed is for

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[19] Saundra Young, *Safety of Genetically Modified Salmon Debated*, CNN (Sept. 20, 2010, 8:10 PM), http://www.cnn.com/2010/HEALTH/09/20/genetically.engineered.salmon/index.html.

[20] *See* Michael B. Homer, Comment, *Frankenfish . . . It's What's for Dinner: The FDA, Genetically Engineered Salmon, and the Flawed Regulation of Biotechnology*, 45 COLUM. J.L. & SOC. PROBS. 83, 86 (2011) (listing the benefits "yielded by the widespread cultivation of [genetically engineered] food products").

[21] *See* AQUABOUNTY TECHS., INC., PROPOSED FUNDRAISE OF $2.0 MILLION (APPROXIMATELY £1.3 MILLION) BEFORE EXPENSES AND ISSUANCE OF FUNDRAISING CIRCULAR 3 (2012) [hereinafter PROPOSAL], *available at* http://www.aquabounty.com/documents/press/2012/20120222Fundraising.pdf.

[22] Draft Environmental Assessment and Preliminary Finding of No Significant Impact Concerning a Genetically Engineered Atlantic Salmon, 77 Fed. Reg. 76,050 (Dec. 26, 2012).

[23] CTR. FOR VETERINARY MED., U.S. FOOD & DRUG ADMIN. & DEP'T OF HEALTH & HUMAN SERV., PRELIMINARY FINDING OF NO SIGNIFICANT IMPACT: AQUADVANTAGE SALMON 3 (May 4, 2012), *available at* http://www.fda.gov/downloads/AnimalVeterinary/DevelopmentApprovalProcess/GeneticEngineering/GeneticallyEngineeredAnimals/UCM333105.pdf?source=govdelivery.

[24] *Id.* at 4.

[25] Paul Voosen, *Panel Advises More Aggressive FDA Analysis of Engineered Salmon*, N.Y. TIMES (Sept. 21, 2010), http://www.nytimes.com/gwire/2010/09/21/21greenwire-panel-advises-more-aggressive-fda-analysis-of-71171.html?pagewanted=all.

[26] *See* Homer, *supra* note 20, at 90–92.

biopharm purposes—animals that produce substances that can be used as human or animal pharmaceuticals.[27] For example, an environmental assessment has been prepared supporting a NADA for goats that have been genetically engineered to express recombinant human antithrombin III ("ATRYN") in the milk of lactacting does.[28] ATRYN is intended to treat patients with congenital antithrombin III deficiency in order to prevent life-threatening clot formation during high-risk situations.[29] Other genetically engineered products are intended for use as food and may be disease resistant or have improved nutritional characteristics over their natural comparators.[30] For example, scientists have engineered hens to lay low-cholesterol eggs.[31]

Despite the many advantages offered by genetically engineered animals, the premarket approval process for *AquAdvantage* Salmon has sustained heavy criticism from consumer advocacy groups and legislators.[32] The next two parts will enumerate the criticisms of the

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[27] *General Q&A*, *supra* note 3.

[28] GTC BIOTHERAPEUTICS, INC., FINDING OF NO SIGNIFICANT IMPACT FOR THE BC6 RDNA CONSTRUCT IN GTC 155-92 GOATS EXPRESSING RECOMBINANT HUMAN ANTITHROMBIN III (RHAT OR ATRYN) 2 (2009), http://www.fda.gov/downloads/AnimalVeterinary/DevelopmentApprovalProcess/GeneticEngineering/GeneticallyEngineeredAnimals/UCM163815.pdf.

[29] *Id.*

[30] *General Q&A*, *supra* note 3.

[31] Shelley Smithson, *Genetically Modified Animals Could Make It to Your Plate with Minimal Testing — and No Public Input*, GRIST (July 30, 2003, 9:00 AM), http://www.grist.org/article/and3./.

[32] For example, in early February of 2012, Food and Water Watch, Consumers Union, and the Center for Food Safety filed a petition asking the FDA to test the genetically engineered salmon as a food additive instead of as a new animal drug. *Consumer Groups Demand Rigorous Government Study of Genetically Engineered Salmon's Hazards to Human Health*, BETWEEN THE LINES (Feb. 22, 2012), http://www.btlonline.org/2012/seg/120302cf-btl-lovera.html. The groups also urged the FDA to conduct an environmental study to examine what would happen were the salmon to escape and carry disease to or breed with non-transgenic salmon species. *Id.* A handful of House Representatives voted in June of 2011 to attach an amendment to an agriculture spending bill that would ban the FDA from spending any funds on genetically engineered salmon approvals beginning in 2012. Paul Voosen, *House Moves to Ban Modified Salmon*, N.Y. TIMES (June 16, 2011), http://www.nytimes.com/gwire/2011/06/16/16greenwire-house-moves-to-ban-modified-salmon-84165.html. A month later, a group of senators asked the FDA to abandon its approval process on the application, threatening to push legislation to strip the FDA's funding to study the fish if the agency failed to comply. *Id*.

premarket approval process and the risk assessment submitted in the case of the *AquAdvantage* Salmon.

II. THE COORDINATED FRAMEWORK FOR REGULATING BIOTECHNOLOGY

As biotechnology research became more popular in the early 1980s, the application of existing statutes to biotechnology led to questions about which statutes applied to which issues and which agencies were responsible under the existing statutory and regulatory scheme.[33] In response, the Reagan Administration created the Domestic Policy Council Working Group on Biotechnology, charged with drafting an overall federal framework for regulating biotechnology.[34] The White House Office of Science and Technology Policy promulgated the Coordinated Framework for Regulation of Biotechnology (Coordinated Framework) in 1986.[35] The Coordinated Framework maintained that existing statutes were sufficient to provide agencies with jurisdiction and authority to ensure adequate regulation of biotechnology, although legislative action could be taken as the field advanced.[36]

The Coordinated Framework, while not legally binding, distributed regulatory responsibilities to three agencies—the U.S. Department of Agriculture (USDA), the Environmental Protection Agency (EPA), and the FDA—based on pre-existing statutory mandates.[37] The working group concluded that "for the most part [existing laws] as currently implemented would address regulatory needs adequately."[38] As the Pew Initiative has noted, this has encouraged

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[33] *See* PEW INITIATIVE ON FOOD & BIOTECHNOLOGY, GUIDE TO U.S. REGULATION OF GENETICALLY MODIFIED FOOD AND AGRICULTURAL BIOTECHNOLOGY PRODUCTS 5 (2001) [hereinafter PEW INITIATIVE], *available at* http://www.pewtrusts.org/uploadedFiles/wwwpewtrustsorg/Reports/Food_and_Biotechnology/hhs_biotech_0901.pdf ("[T]he application of existing statutes to biotechnology led to significant questions about overlapping authorities among the agencies, as well as uncertainties about whether the agencies would follow consistent approaches in using these authorities.").

[34] *Id.*

[35] *Id.* at 5–6; Coordinated Framework for Regulation of Biotechnology, 51 Fed. Reg. 23,302 (June 26, 1986).

[36] PEW INITIATIVE, *supra* note 33, at 6.

[37] *See* Coordinated Framework for Regulation of Biotechnology, 51 Fed. Reg. at 23,304 (stating that the agencies involved have "extensive experience with products that involve living organisms" and that new developments will be reviewed by the FDA, USDA, and EPA in the same manner for safety).

[38] *Id.* at 23,303.

agencies to reinterpret old statutes in order to fit new biotechnology products into decades-old legal frameworks.[39]

The FDA is in charge of evaluating food safety issues for all genetically engineered products intended for human consumption. Since developers first approached the FDA with genetically engineered animals, the FDA has chosen to regulate those animals under the new animal drug provisions of the FDCA.[40] On January 1, 2009, nearly eight years after AquaBounty Technologies first filed a NADA, the FDA issued a "Final Guidance Document" on regulating genetically engineered animals to alleviate confusion about the premarket approval process and the statutory scheme currently applied to genetically engineered animals intended for human consumption.[41]

Under the new animal drug provisions of the FDCA, 21 U.S.C. § 321 *et seq.*, the definition of a drug includes "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."[42] The definition of "new animal drug" in section 201(v) of the Act includes "any drug intended for use for animals other than man . . . the composition of which is such that such drug is not generally recognized . . . as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling thereof."[43] Generally, a new animal drug is "deemed unsafe" under the Act unless the FDA has approved a NADA for that particular use, or unless the drug is only for investigational use and conforms to exemptions for such use under an Investigational New Animal Drug (INAD).[44] The FDA justified this regulatory structure for genetically engineered animals on the grounds

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[39] *See* PEW INITIATIVE ON FOOD & BIOTECHNOLOGY, ISSUES IN THE REGULATION OF GENETICALLY ENGINEERED PLANTS AND ANIMALS 10–11 (2004), *available at* http://www.pewtrusts.org/uploadedFiles/wwwpewtrustsorg/Reports/Food_and_Biotechnology/food_biotech_regulation_0404.pdf.

[40] *General Q&A*, *supra* note 3.

[41] *FDA Issues Final Guidance on Regulating Genetically Engineered Animals*, U.S. FOOD & DRUG ADMIN. (Jan. 4, 2010), http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2009/ucm109066.htm.

[42] Federal Food, Drug, and Cosmetic Act § 201(g)(1), 21 U.S.C. § 321(g)(1); GUIDANCE FOR INDUSTRY, *supra* note 12, at 5.

[43] Federal Food, Drug, and Cosmetic Act § 201(v)(1), 21 U.S.C. § 321(v)(1); GUIDANCE FOR INDUSTRY, *supra* note 12, at 5–6.

[44] GUIDANCE FOR INDUSTRY, *supra* note 12, at 6. A second exception exists where the application meets the regulations promulgated under section 512(a)(4) or (5) of the Act.

that the rDNA construct in a genetically engineered animal meets the FDCA's definition of "drug" because it is intended to affect the structure or function of the body of the animal.[45] Each new animal drug approval covers all animals containing the same rDNA construct derived from the same transformation event, including animals containing the rDNA construct as a result of breeding between a non-genetically engineered animal and a genetically engineered animal.[46]

The FDA evaluates submitted NADAs to determine whether the new animal drug is safe and effective for its intended use.[47] Effectiveness of an article intended to alter a characteristic of an animal is demonstrated by showing that the genetically engineered animal has the claimed altered characteristic.[48]

Safety of an animal drug is established through a risk-based analysis centering on the molecular characterization and durability of the construct in question,[49] as well as a broader assessment, consistent with the FDA's Final Guidance Document, of food and environmental safety.[50] Food derived from a genetically engineered animal must be safe for humans or animals consuming it.[51] The Center for Veterinary Medicine (CVM) of the FDA studies toxicity by examining any relevant changes in the physiology of the animal and in the composition of edible tissues.[52] If the expression product is shown to be safe and the composition of edible tissues from the genetically engineered animal is shown to be "as safe as those from animals of the same or comparable type that are commonly and safely consumed,"[53] then there is a presumption that the food from the genetically engineered animal is safe.

When the FDA reviews and approves an INAD or NADA it must comply with the requirements of the National Environmental Policy Act (NEPA), including a review of environmental risks where required.[54] Considered environmental risks include whether the article itself poses risks to humans, animals, or the environment; whether in the event of an environmental release, the genetically engineered animal poses more risk than its non-genetically engineered counterpart; and whether there are

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[45] *Id.*
[46] *Id.* at 7.
[47] *Id.* at 13.
[48] *Id.*
[49] *Id.* at 21–23.
[50] *Id.* at 23–25.
[51] *Id.* at 23.
[52] *Id.* at 23–24.
[53] *Id.* at 24.
[54] *Id.* at 8.

any other safety questions that have not been adequately addressed by the sponsor.[55]

Following the release of its draft guidance on the regulation of genetically engineered animals in 2008, the FDA received a total of almost 29,000 comments over the sixty-day public comment period.[56] Approximately 28,000 were form letters or general statements about genetically engineered animals or the guidance.[57] The majority of comments opposed the genetic engineering of animals.[58] Approximately sixty of the remaining suggestions were "what [the FDA] consider to be substantive."[59] These comments were principally focused on eleven issues, the most salient to this discussion being: the adequacy and appropriateness of using the NADA provisions to exert regulatory oversight of genetically engineered animals; the adequacy of the FDA's approach to address animal health and safety, food safety, and environmental safety; and the need for transparency and public input in the oversight of genetically engineered animals.[60]

The FDA maintained that the statutory definition of "drug" applied to the rDNA construct intended to alter the structure or function of an animal and that it "d[id] not believe it necessary to promulgate new regulations because the existing regulatory structure is adequate to review the safety and effectiveness of [genetically engineered,] animal-related applications."[61] The FDA likewise defended its consideration of health and safety concerns, noting that the regulations require both a finding that the drug is safe for consumption and consideration of environmental risks under the broad umbrella of the National Environmental Policy Act.[62]

A number of comments noted that the NADA process does not allow for much public input.[63] The Trade Secrets Act prohibits the FDA from revealing any information acquired through the New Animal Drug

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[55] *Id.* at 8.
[56] *FDA's Response to Public Comments*, U.S. FOOD & DRUG ADMIN. (May 23, 2011), http://www.fda.gov/AnimalVeterinary/DevelopmentApprovalProcess/GeneticEngineering/GeneticallyEngineeredAnimals/ucm113612.htm.
[57] *Id.*
[58] *Id.*
[59] *Id.*
[60] *Id.*
[61] *Id.*
[62] *Id.*
[63] *Id.*

approval process.[64] Some comments posited that a lack of transparency was inappropriate for products of new and controversial technology, while others stated that developers of genetically engineered animals have the same need and deserve the same right to protect their intellectual property as do developers of "conventional human and new animal drugs."[65]

In its Final Guidance Document, the FDA stated that it was "interested in increasing the transparency of its deliberations and actions"[66] and intended to hold public advisory committee meetings prior to approving any genetically engineered animal.[67] On September 3rd, 2010, the FDA declared that *AquAdvantage* Salmon "is as safe as food from conventional Atlantic salmon."[68] From September 19th to the 21st, 2010, the FDA held two public meetings on *AquAdvantage* Salmon paneled by the agency's Veterinary Medicine Advisory Committee (VMAC).[69]

III. THE PUBLIC MEETING ON *AQUADVANTAGE* SALMON'S RISK ASSESSMENT

Because a new animal drug is deemed unsafe unless the FDA has approved a NADA for that particular use,[70] under the FDCA, the NADA must demonstrate that the regulated article is "safe and effective."[71] VMAC's charge during the public meetings was to assess the safety and efficacy of *AquAdvantage* Salmon's rDNA construct and provide advice and recommendations to the FDA.[72]

The Committee agreed with the FDA that "there is no greater effect as a result of the incorporation of [the rDNA] construct than the

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[64] *See* 21 U.S.C. § 331(j) (2006) (prohibiting information acquired under the authority of several sections related to the Animal Drug approval process from being revealed).
[65] *FDA's Response to Public Comments*, *supra* note 56.
[66] GUIDANCE FOR INDUSTRY, *supra* note 12, at 13.
[67] *Id*.
[68] *See* Andrew Pollack, *Modified Salmon is Safe, F.D.A. Says*, N.Y. TIMES (Sept. 3, 2010), http://www.nytimes.com/2010/09/04/health/policy/04salmon.html.
[69] *See* Food & Drug Admin., Veterinary Medicine Advisory Committee, Notice of Meeting, 75 Fed. Reg. 52,605 (Aug. 26, 2010).
[70] *See Charge to the VMAC for the AquAdvantage Salmon Meeting*, U.S. FOOD & DRUG ADMIN. (Sept. 16, 2010), http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/VeterinaryMedicineAdvisoryCommittee/ucm226083.htm.
[71] Federal Food, Drug, and Cosmetic Act § 201(v)(1), 21 U.S.C. § 321(v)(1).
[72] *See Charge to the VMAC for the AquAdvantage Salmon Meeting*, *supra* note 70.

normal selection process that takes place during domestication and improvement of domestic animals through selective breeding."[73] And the construct qua animal drug was unquestionably effective—the data was "straight up" that *AquAdvantage* Salmon grows faster than its conventional counterparts.[74]

Despite these conclusions, serious doubts were expressed toward the end of the meeting with regard to the adequacy of the data used.[75] Attendees raised concerns about the small sample sizes used in AquaBounty Technologies' research[76] as well as the results of these studies.[77] Dr. Jodi Ann Lapidus of the Committee, characterizing the data as "fairly suggestive [and] preliminary,"[78] and the process as "a bit ad hoc,"[79] argued that a "more rigorous experimental design [and more] rigorous epidemiologic principles" were needed to answer some of the Committee's questions.[80] Other complaints centered on the safety of the salmon and the environmental risks they posed. Generally, individuals were concerned with a few specific issues, including: disparities in the level of insulin-like growth factor 1 (IGF-1) between *AquAdvantage* Salmon and the control;[81] disparities in the level of vitamin B6 between *AquAdvantage* Salmon and the control;[82] the limited sample sizes in allergenicity tests;[83] the lack of independent, peer-reviewed studies to support some data;[84] general animal safety and health;[85] and the

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[73] U.S. FOOD & DRUG ADMIN., VETERINARY MED. ADVISORY COMM. MEETING: AQUADVANTAGE SALMON 352 (2010) [hereinafter VMAC MEETING], *available at* http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/VeterinaryMedicineAdvisoryCommittee/UCM230471.pdf.

[74] *Id*. at 378.

[75] *See id*. at 352–53.

[76] *Id*. at 352.

[77] *Id*.

[78] *Id*. at 355.

[79] *Id*. at 366.

[80] *Id*. at 355.

[81] *See, e.g.*, *id*. at 288–90 (noting a forty percent difference in IGF-1 levels between the control and the engineered fish).

[82] *Id*. at 292.

[83] *Id*. at 290–91 (noting that risk of potential allergenicity was twenty percent higher in AquAdvantage Salmon, but that this figure was not statistically significant because the sample size was only six fish).

[84] *Id*. at 293 (noting that the analysis of IGF levels looked at only two studies—a peer-reviewed publication from 1992 and an AquaBounty study from 2004—and the analysis of allergen potency focused on a 2006 study furnished by AquaBounty).

[85] *Id*. at 301–03 (noting AquaBounty's history of "extensive culling of deformed, diseased, and dying fish before any of the data in the application was

limitations of the fertilization process and the risk of salmon escaping from the facility.[86] More relevant to the issue at hand, complaints were aimed broadly toward the lack of transparency and few opportunities for public input allowed by the approval process.[87]

The notice of the September 20th meeting was published in the Federal Register on August 26th, a mere three and a half weeks before the meeting date.[88] Darrell Rogers, of the Alliance for Natural Health in the United States, noted that scientific studies have either "not been released or have been released so late in the approval process that it is impossible for the public and experts to assess whether scientific burdens have been met."[89] Jaydee Hanson, of the Center for Food Safety, added that the 180-page scientific assessment briefing packet was received by the public "only 10 days [before comments were due]."[90] Ms. Hanson further stated that "the most striking thing was how little data the company had produced over the last 15 years. Or at least how little data was being provided to us. We have discovered today that there is data that is not in this dataset."[91]

Regulating transgenic animals intended for human consumption under the FDCA ensures that the process takes place almost entirely behind closed doors. The Trade Secrets Act prohibits the FDA from sharing any information with the public before a decision is made on an application, in the interest of protecting the applicant's trade secrets.[92] The FDA does not even have the power to disclose whether an application exists until after publication of approval in the Federal Register.[93] Sponsors may disclose the application, as AquaBounty Technologies has, but even then "no data or information contained in the

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collected," as well as the fact that "a new animal drug must be evaluated for any adverse outcomes it causes for any and all animals who receive the drug," and that the FDA did not consider the health or safety of the animals excluded from the food supply).

[86] *Id*. at 306–10.

[87] *See, e.g.*, *id.* at 311 ("The FDA process for approving new animal drugs allows for neither robust public participation nor thorough consideration of environmental hazards.").

[88] Food & Drug Admin., Veterinary Medicine Advisory Committee, Notice of Meeting, 75 Fed. Reg. 52,605 (Aug. 26, 2010).

[89] VMAC MEETING, *supra* note 73, at 282.

[90] *Id.* at 297; *cf. id.* at 311 ("Until the release of the [environmental assessment] two weeks ago, the public has had no opportunity to learn more about, assess, or raise questions about potential impacts.").

[91] *Id.* at 297.

[92] 21 U.S.C. § 331(j) (2006).

[93] 21 C.F.R. § 514.11 (2012).

file is available for public disclosure before such approval is published[.]"[94] The Commissioner may, however, "in his discretion, disclose a summary of selected portions of the safety and effectiveness data as are appropriate for public consideration of a specific pending issue, e.g., at an open session of a Food and Drug Administration advisory committee[.]"[95] Regardless as to the oddity or inappropriateness of regulating rDNA constructs as animal drugs, this statutory policy is especially unsuitable for products designed for human consumption.

IV. TRANSPARENCY, PUBLIC OPINION, AND POSSIBLE REFORM

A. A *Prima Facie* Reason to Abandon Trade Secret Protection for Genetically Engineered Animals

The FDCA and The Uniform Trade Secrets Act prohibit the FDA from sharing any information about an application, absent sponsor disclosure, before a decision is made.[96] The existence of a NADA file must be publicly disclosed or acknowledged in order for the Commissioner to, in his discretion, disclose a summary of selected portions of the safety and effectiveness data as are appropriate for public consideration of a specific pending issue.[97] As a matter of policy, and in order to increase transparency, the agency intends to "hold public advisory committee meetings prior to approving any [genetically engineered] animal."[98] It follows that the FDA intends all applications to be disclosed and some data to be publicly available at advisory committee meetings prior to any approval of a new animal drug for a genetically engineered animal. The extent of such safety and effectiveness data is curbed only by "appropriate[ness] for public consideration[.]"[99]

Public support for biotechnology, including genetically engineered animal products, is on the decline.[100] A survey performed for

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[94] *Id.* at § 514.11(d).
[95] *Id.*
[96] *Id.*; 21 U.S.C. § 331(j).
[97] 21 C.F.R. § 514.11(d).
[98] GUIDANCE FOR INDUSTRY, *supra* note 12, at 13.
[99] 21 C.F.R. § 514.11(d).
[100] *See, e.g.*, Nathaniel Logar & Leslie K. Pollock, *Transgenic Fish: Is a New Policy Framework Necessary for a New Technology?*, *in* 8 ENVTL. SCI. & POL'Y 18 (2005), *available at* http://cspo.org/documents/logarpollock.pdf (citing data that "Americans' attitudes towards genetic engineering and biotechnology generally show a decline in support fur such technologies over past 5–15 years").

the Pew Initiative on Food and Biotechnology found that sixty-five percent of consumers disapproved of the idea of creating transgenic fish for human consumption.[101] Knowingly withholding data will not serve to increase public trust in the regulatory process or in the safety of the final product.

Moreover, it is not clear what the trade secret justification was for withholding data from the committee advisory meeting. First, the data provided in the 180-page briefing packet was sufficiently detailed with regard to the sequence of the rDNA construct, the purpose of the modification, the details of how the rDNA construct was assembled, and the construction of the transgenic salmon (including both the method and intermediate organisms within the process). This high level of detail would preclude the protection of many, if not most, trade secrets.[102] Second, options more sophisticated than inserting a promoter and termination sequence from ocean pout into an Atlantic salmon are being researched "that are almost ready for use in real products."[103] One scientist has claimed that "[i]f someone wanted to make AquAdvantage today, there are emerging technologies that would allow a replacement of the normal promoter for Atlantic salmon with an Atlantic salmon promoter that is always on. The resulting fish would have no possibility of unintended genetic changes and 100% DNA from Atlantic salmon."[104]

A number of commenters on the FDA's guidance noted that the bar on public disclosure "is particularly inappropriate for products of a new and controversial technology such as the genetic engineering of animals."[105] The FDA could, as a matter of policy, broadly interpret the safety and effectiveness data "appropriate for public consideration" at advisory committee meetings, at least until the genetic engineering technologies and the public perception of such data improves. Even if such data is not strictly "appropriate" for or understandable to the public,

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[101] PEW INITIATIVE ON FOOD AND BIOTECHNOLOGY AND THE GENE MEDIA FORUM, "THE GENE IS OUT OF THE BOTTLE: WHERE TO NEXT?" SURVEY HIGHLIGHTS 2 (2001), *available at* http://www.pewtrusts.org/uploadedFiles/wwwpewtrustsorg/Research/vf_biotech_gene_bottle.pdf.

[102] *See, e.g.*, BRIEFING PACKET, *supra* note 8, at 9–13 (discussing the molecular characterization of the construct, including a schematic representation for "generating the opAFP-GHc2 construct employed in the AquAdvantage Salmon").

[103] Anastasia Bodnar, Comment to *Risk Assessment and Mitigation of AquAdvantage Salmon*, BIOFORTIFIED (Oct. 18, 2010, 1:11 PM), http://www.biofortified.org/2010/10/salmon/#comment-14213.

[104] *Id.*

[105] *FDA's Response to Public Comments*, *supra* note 56.

improving the transparency of the data will allow increased opportunities for peer review, which may alleviate some of the concerns expressed by VMAC members and the public during the advisory committee meetings.

B. Public Disclosure as Abandonment of Trade Secrecy

A trade secret is "a process or device for continuous use in the operation of . . . business" and "may consist of any formula, pattern, device or compilation of information which is used in one's business, and which gives him an opportunity to obtain an advantage over competitors who do not know or use it."[106] Generally speaking, a trade secret is known only to one or a few people, and is kept secret from the general public.[107] Disclosure of a trade secret may result in an abandonment of the essential element of secrecy.[108] A number of federal and state cases bear on the issue of whether, and under what circumstances, the disclosure of a trade secret results in an abandonment of secrecy.

Courts have held that a general public disclosure of a trade secret by a party asserting a protectable interest, as in a patent application or a published material, results in abandonment of the element of secrecy and destruction of trade secret status.[109] When, as in the case of *AquAdvantage* Salmon, the FDA discloses the mechanisms by which a company creates a transgenic animal, trade secret property rights contained in the disclosure are extinguished. This "abandonment" undermines the need for secrecy throughout the premarket approval process.

The Supreme Court considered whether trade secret property right protection should continue after public disclosure of data in *Ruckelshaus v. Monsanto Co.*,[110] which concerned a statutory scheme somewhat similar to the FDCA statutory scheme described above. Provisions of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) "authorize the [EPA] to use data submitted by an applicant for registration of a pesticide [product] in evaluating the application of a

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[106] RESTATEMENT (FIRST) OF TORTS § 757, Comment b (1939).
[107] *See id.*
[108] Donald M. Zupanec, *Disclosure of Trade Secret as Abandonment of Secrecy*, 92 A.L.R.3d 138 (1979).
[109] *See BondPro Corp. v. Siemens Power Generation, Inc.*, 463 F.3d 702, 706 (7th Cir. 2006) (stating that a trade secret that becomes public knowledge, as a process was disclosed to the world in a patent application, is no longer a trade secret); *Taylor v. Babbitt*, 760 F.Supp.2d 80, 86 (D. D.C. 2011); *Saini v. Int'l Game Tech.*, 434 F.Supp.2d 913, 919 (D. Nev. 2006).
[110] 467 U.S. 986 (1984).

subsequent applicant, and to disclose publicly some of the submitted data."[111] Section 10 of FIFRA authorizes public disclosure of all health, safety, and environmental data, even though it may result in disclosure of trade secrets.[112] Monsanto, an inventor, producer, and seller of pesticides, brought suit, alleging, *inter alia*, that the data-disclosure provisions of FIFRA effected a "taking" of property without just compensation.[113]

In 1978, FIFRA was amended, revising its existing data-consideration and data-disclosure provisions. Congress added a new subsection, 7 U.S.C. § 136h(d), "that provides for disclosure of all health, safety, and environmental data to qualified requesters,"[114] except disclosure of information that would reveal "manufacturing or quality control processes" or certain details about inert ingredients "unless the Administrator has first determined that the disclosure is necessary to protect against an unreasonable risk of injury to health or the environment."[115] The District Court found that much of the health, safety, and environmental data Monsanto sought to protect "contain[ned] or relate[d] to trade secrets."[116]

The Supreme Court recognized that the extent of the property right in a trade secret "is defined by the extent to which the owner of the secret protects his interest from disclosure to others."[117] Additionally, the Court found that information that is "public knowledge or that is generally known in an industry cannot be a trade secret."[118] Because Monsanto was on notice of the ways in which the EPA was statutorily authorized to use and disclose data received from applicants for product registration, Monsanto "could not have had a reasonable, investment-backed expectation that EPA would keep the data [submitted after the

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[111] *Id*. at 990.
[112] *Id.* at 996.
[113] *Id.* at 998.
[114] *Id*. at 995–96; *see* 7 U.S.C. § 136h(d)(1) (2006) ("All information concerning the objectives, methodology, results, or significance of any test or experiment performed on or with a registered or previously registered pesticide or its separate ingredients, impurities, or degradation products, and any information concerning the effects of such pesticide on any organism or the behavior of such pesticide in the environment, including, but not limited to, data on safety to fish and wildlife, humans and other mammals, plants, animals, and soil, and studies on persistence, translocation and fate in the environment, and metabolism, shall be available for disclosure to the public.").
[115] *Ruckelshaus*, 467 U.S. at 996 (quoting 7 U.S.C. § 136(h)(d)).
[116] *Id*. at 998.
[117] *Id*. at 1002.
[118] *Id*.

1978 FIFRA amendments] confidential beyond the limits prescribed in the amended statute itself."[119] Any applicant knew that information relating to the formula of products could be revealed by the EPA to any federal agency and to the public at a public hearing when necessary to carry out their duties under FIFRA.[120] The statute also provided Monsanto notice that "much of the health, safety, and efficacy data provided by it could be disclosed to the general public at any time."[121] Thus, any voluntary submission of data in exchange for the economic advantages concomitant with product registration could not be a taking.[122]

Like the applicants under FIFRA, new animal drug applicants under FDCA are on notice that the FDA may disclose a summary of safety and effectiveness data as appropriate for public consideration at advisory committee meetings.[123] Applicants are also aware that the FDA intends to hold public advisory meetings for all applications for genetically engineered animals intended for human consumption.[124] Any trade secrets disclosed to the public through such meetings, such as those found in the *AquAdvantage* Salmon meeting materials, are likely extinguished.

All of this is not to suggest that no trade secret protection should exist for NADAs prior to the announcement of a public meeting. Biotechnology companies should be able to retain their competitive advantage during the period between the submission of an application and the VMAC meeting. It is less clear, however, why safety and effectiveness data should not be fully disclosed during the comment period prior to and after the advisory committee meetings. If the purpose of the lack of transparency is to protect trade secrets, and many, if not most of those secrets, will be extinguished through disclosure, maintaining such a high degree of secrecy outlives its purpose. As such, the FDA should more seriously consider keeping the public apprised of the status of active applications after this time, even if it means a second summary of safety findings prior to final approval.

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[119] *Id*. at 1006.
[120] *Id*.
[121] *Id*.
[122] *Id*. at 1007.
[123] 21 C.F.R. § 514.11(d) (2012).
[124] GUIDANCE FOR INDUSTRY, *supra* note 12, at 13.

C. Other Mechanisms for Increased Public Review

1. Lengthen the Comment Period Prior to Advisory Committee Meetings

In a letter to the FDA Commissioner, Jean Halloran, Director of Food Policy Initiatives for Consumers Union, wrote that her group was "concerned about trying to undertake this review [of 255 pages of technical information] in such a constrained time period when there are serious issues of food safety involved."[125] In particular, Consumers Union questioned the logic behind the fourteen days given to review the information—an "extremely brief period"—when the FDA had eleven years to review the application and there was no statutory timetable requiring particular expediency.[126] The group requested that the review period be extended from fourteen days to the standard sixty days given for pharmaceuticals or medical devices.[127]

2. Create an Independent Body to Communicate with the Public about Food Safety

On January 28th, 2002, the European Union adopted legislation authorizing the creation of a European Food Safety Authority (EFSA), an "independent source of scientific advice and communication on risks associated with the food chain."[128] EFSA was created after a call for a new authority to "contribute to a high level of consumer health protection" and to "help restore and maintain consumer confidence."[129] Premised on the belief that consumers "have the right to expect information on food quality and constituents that is helpful and clearly presented, so that informed choices can be made," one of EFSA's main goals was to directly communicate with the public in order to keep consumers informed of emerging food safety concerns and risks from certain foods.[130]

Even if risk assessment continues to be carried out by the FDA and its advisory committees like VMAC, the creation of an independent body to act as a liaison to the public and clearly communicate the goals

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[125] Jean Halloran & Michael Hansen, *Letter to Commissioner Hamburg and Deputy Commissioner Sharfstein*, CONSUMER'S UNION 1 (2010), *available at* http://www.consumersunion.org/pdf/FDA-ltr-GE-salmon.pdf.
[126] *Id*.
[127] *Id*.
[128] *About EFSA*, EUROPEAN FOOD SAFETY AUTH., http://www.efsa.europa.eu/en/aboutefsa.htm (last visited Mar. 16, 2012).
[129] COMM'N OF THE EUROPEAN CMTYS., WHITE PAPER ON FOOD SAFETY 5 (2000), *available at* http://ec.europa.eu/dgs/health_consumer/library/pub/pub06_en.pdf.
[130] *Id.* at 4.

of the regulatory process, the status of disclosed NADAs, and potential risks and benefits of genetically engineered products intended for human consumption would help restore trust in the system.

The independent authority could also serve as a go-between for agencies who share regulatory authority over genetically engineered animals. For example, the Commissioner of the FDA is required to consult with the Assistant Administrator of the National Marine Fisheries Service (NMFS) of the National Oceanic and Atmospheric Administration (NOAA) to produce "a report on any environmental risks associated with genetically engineered seafood products, including the impact on wild fish stocks."[131] Leaked e-mails between senior scientists at the U.S. Fish and Wildlife Services (FWS) and NOAA chronicle serious concerns about the FDA's treatment of genetically engineered salmon and the lack of consultation with other agencies.[132] One email from FWS staff to NOAA revealed that:

> Shortly after the Atlantic salmon was listed as endangered, several of us from USFWS and NMFS spent 2 days down in Maryland meeting with Aqua Bounty and FDA about development of genetically modified salmon and discussion around the need for FDA to engage in Section 7 consultation with the Services. We never heard a peep out of FDA or Aqua Bounty after that.[133]

Mr. Gregory Moyer, a regional geneticist from FWS, wrote a letter outlining criticisms and concerns regarding the VMAC briefing packet for *AquAdvantage* Salmon ten days after the public meetings.[134] Members of the Conservation Genetics Community of Practice of FWS wrote a letter one week later arguing that the evidence provided in the briefing packet fell short of "providing an actual risk assessment of putative environmental damages in the event of escapement."[135] Because these letters were written two to three weeks after the public meeting and

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[131] 21 U.S.C.A. § 2106.

[132] *Newly Disclosed Government Documents Conclude GE Salmon Pose a Critical Threat to Marine Environments*, CTR. FOR FOOD SAFETY, http://truefoodnow.org/2010/10/27/newly-disclosed-government-documents-conclude-ge-salmon-pose-a-critical-threat-to-marine-environments/ (last visited Mar. 16, 2012).

[133] *Id.*

[134] Gregory R. Moyer, *Letter to the U.S. Dept. of Interior* (Sept. 30, 2010), http://stopgefish.files.wordpress.com/2010/11/fws_moyers_to_fda_vmac_sept30 2010.pdf.

[135] U.S. Fish and Wildlife Service Conservation Genetics Community of Practice (COP), *Letter to the U.S. Dept. of Interior* (Oct. 6, 2010), http://stopgefish.files.wordpress.com/2010/11/cop_fws_to_vmac_oct62010.pdf.

because no information has been publicly available since that time, there is no way to tell whether these criticisms were incorporated into the FDA's subsequent analysis of safety, or whether the FDA consulted with FWS, NMFS, or NOAA. An independent authority could help ensure that the FDA meets its statutory requirements of consulting with relevant agencies to assess the safety and efficacy of NADAs.

CONCLUSION

Most complaints surrounding *AquAdvantage* Salmon have concentrated on concerns both regarding the risk posed to other fish and the environment should they escape, as well as differences between genetically engineered salmon and farm-raised salmon that could pose a risk to consumers. To increase public trust, more should be done to keep consumers apprised of the status of NADAs during premarket approval. Additionally, more needs to be done to ensure the validity of the data used to determine whether the genetically engineered animals are safe for human consumption. By focusing on improving the transparency of the process, the public will have a better understanding of which deficiencies in data are real and which are not. Such an understanding would enhance public confidence in the safety of genetically engineered food as worldwide demand for protein sources continues to increase.