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IN THE UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF CALIFORNIA
SAN FRANCISCO DIVISION

INSTITUTE FOR FISHERIES RESOURCES, *et al.*,

Plaintiffs,

v.

ALEX M. AZAR II, *et al.*,

Defendants,

and

AQUABOUNTY TECHNOLOGIES, INC.,

Intervenor-Defendant,

Case No. 3:16-cv-01574-VC

FEDERAL DEFENDANTS' MOTION FOR JUDGMENT ON THE PLEADINGS ON CLAIMS 1, 8, 12, AND 13

Date: November 8, 2018
Time: 1:30 p.m.
Location: Courtroom 4 - 17th Floor
Judge: Hon. Vince Chhabria

NOTICE OF MOTION FOR JUDGMENT
ON THE PLEADINGS ON CLAIMS 1, 8, 12, AND 13

PLEASE TAKE NOTICE that on November 8, 2018, at 1:30 p.m., or as soon thereafter as counsel may be heard, Defendants Alex M. Azar II, Secretary of the Department of Health and Human Services, the U.S. Food and Drug Administration ("FDA"), and Scott Gottlieb, M.D., Commissioner of the FDA ("Federal Defendants"), by and through undersigned counsel, will bring for hearing their Motion for Judgment on the Pleadings on Claims 1, 8, 12, and 13 of the Amended Complaint, in the Courtroom of the Honorable Vince Chhabria, United States District Judge, U.S. District Court for the Northern District of California, San Francisco Division, Courtroom 4 - 17th Floor, 450 Golden Gate Avenue, San Francisco, California 94102.

Pursuant to Fed. R. Civ. P. 12(c) and Civil L.R. 7, Federal Defendants move for Judgment on the Pleadings on Claims 1, 8, 12, and 13 of the Amended Complaint. The Court lacks jurisdiction over Plaintiffs' challenges to Guidance for Industry 187 in Claims 1, 8, 12, and 13 because the Guidance is not final agency action, and Plaintiffs lack standing to challenge it. Moreover, Plaintiffs' challenge in Claim 1 to FDA's authority under the Federal Food, Drug, and Cosmetic Act ("FDCA" or "Act") to approve Intervenor-Defendant AquaBounty Technologies, Inc.'s new animal drug, which is intended to alter the genome in a line of Atlantic salmon to accelerate growth, their challenge in Claim 12 to FDA's consideration of environmental safety under the National Environmental Policy Act and not the FDCA, and their procedural challenge to the Guidance in Claim 13, fail on the merits as a matter of undisputed fact and law under the plain language of the Act and its implementing regulations.

In support of this Motion, Federal Defendants rely upon the attached Memorandum of Points and Authorities, Plaintiffs' Amended Complaint, documents referenced in Plaintiffs' Amended Complaint, and matters subject to judicial notice.

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The claims at issue turn on the U.S. Food and Drug Administration ("FDA")'s authority to regulate drugs intended to alter an animal's genome to create a genetically engineered animal. In November 2015, almost 20 years after Intervenor-Defendant AquaBounty Technologies, Inc.'s ("AquaBounty") corporate predecessor first approached FDA about its proposed new animal drug, the agency approved AquaBounty's application. That now-approved drug is an rDNA construct as integrated in the genome of a line of Atlantic salmon, known as AquAdvantage Salmon, that is intended to cause the fish to reach an important growth marker faster than their conventional counterparts.[1] FDA has previously exercised its new animal drug approval authority over integrated rDNA constructs intended to alter an animal's genome,[2] but this was FDA's first approval of such a drug for an animal intended for use as food.[3] Federal Defendants now seek judgment on the pleadings on four counts in the Amended Complaint that raise five threshold issues related to this approval. Resolving these issues now and on the pleadings will simplify this case for summary judgment.

First, Plaintiffs challenge FDA's approval of this new animal drug on the ground that FDA has no authority to regulate new animal drugs that create genetically engineered animals (Claim 1). But the text of the Federal Food, Drug, and Cosmetic Act ("FDCA" or "Act") plainly gives FDA

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[1] Specifically, the new animal drug or "article" that FDA approved is "[a] single copy of the [alpha]-form of the *opAFP-GHc2* recombinant deoxyribonucleic acid (rDNA) construct at the [alpha]-locus in the EO-1 [alpha] lineage of triploid, hemizygous, all-female Atlantic salmon (*Salmo salar*)." 21 C.F.R.§ 528.1092(a).

[2] FDA's first such approval was for a drug that intentionally alters the genome of an animal to produce a biopharmaceutical product to treat a rare clotting disorder. In February 2009, FDA's Center for Veterinary Medicine approved an rDNA construct as integrated in the genome of a line of lactating goats that directs the expression of recombinant human antithrombin (an anticoagulant) in their milk. FDA's Center for Biologics Evaluation and Research licensed the resulting biologic for use in patients with hereditary antithrombin deficiency, who are at high risk of blood clots during medical procedures. FDA also has approved an rDNA construct as integrated in a line of genetically engineered chickens that produce a protein in their egg whites that is used to treat a rare enzyme disorder in pediatric and adult patients.

[3] Plaintiffs do not challenge the food safety of AquAdvantage Salmon.

that authority. That Act defines "drugs" to include "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)—language that easily encompasses the new animal drug at issue here, which alters the structure and function of the genome in an animal.[4]

Second, Plaintiffs challenge FDA's January 2009 issuance of a Guidance for Industry ("Guidance") (Claims 1, 8, 12, 13),[5] but the Guidance is not final agency action and so cannot be challenged here. It is, rather, a guidance document that explains the FDCA's new animal drug provisions, describes FDA's implementing regulations and how they apply to genetically engineered animals, and recommends ways in which developers of genetically engineered animals can satisfy these requirements. Review under the Administrative Procedure Act ("APA") is limited to "final agency action" and thus excludes challenges to this sort of agency guidance.

Third, Plaintiffs' asserted harms arise solely from FDA's approval of AquaBounty's new animal drug application—rather than the Guidance—such that Plaintiffs would not have standing

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[4] It is not clear what Plaintiffs hope to accomplish through a lawsuit that vigorously opposes FDA's approval of AquaBounty's new animal drug and seeks to strip FDA of its jurisdiction not only to require premarket approval of a construct that creates a genetically engineered food animal but, indeed, of its authority to require premarket approval concerning all genetically engineered animals until some unknown future date (that may never arrive) when Congress enacts a new regulatory regime lodging authority in a different agency more to Plaintiffs' liking. *See* Am. Compl., ¶ 13 (requesting injunction against "[FDA's] assertion of jurisdiction over GE animals" and "further FDA action on AquaBounty's GE salmon application or any other application for commercialization of a genetically engineered food animal until Congress provides explicit statutory authority governing regulation of such products and vests clear authority for such regulation in a named agency of the Executive Branch of the United States"). If successful, Plaintiffs' claim would eliminate FDA premarket new animal drug approval as a requirement for marketing AquAdvantage Salmon, thus eliminating the "major federal action" that triggers environmental review under the National Environmental Policy Act ("NEPA") and making it easier to bring that product to market without environmental or other review—the precise opposite outcome from what Plaintiffs purport to seek.

[5] Guidance for Industry 187 Regulation of Genetically Engineered Animals Containing Heritable Recombinant DNA Constructs. Ex. 1 at FDA-G187-00568. Cited documents are attached as exhibits. The referenced Bates-numbers are the pages cited within each exhibit.

to challenge the Guidance even if it were somehow reviewable under the APA (Claims 1, 8, 12, 13).

Fourth, to the extent Plaintiffs' challenge relies on the argument that FDA must consider potential environmental impacts in evaluating the safety of a new animal drug under the FDCA, that claim also fails. The FDCA is the statutory apparatus for regulating the safety of food, drugs, devices, tobacco products, and cosmetics; it is not an environmental statute. Assessing environmental impacts is, rather, the domain of NEPA, and there is no basis to backdoor that environmental-regulatory apparatus into the approval process for new animal drugs (Claim 12).

Finally, Plaintiffs' claim that FDA was required to engage in formal notice-and-comment rulemaking before it could issue the Guidance fails because, again, the Guidance is not a final agency action (Claim 13).

As demonstrated below, Federal Defendants are entitled to judgment on the pleadings on Claims 1, 8, 12, and 13.[6] Resolving this motion now will streamline the case going forward. If the Court grants the motion, it will leave for decision only Plaintiffs' environmental challenges to FDA's Environmental Assessment and Finding of No Significant Impact under NEPA (Claims 2-7); and FDA's determination under the Endangered Species Act that its approval of AquaBounty's new animal drug application would have "no effect" on endangered species or their habitat (Claim 10).

I. GOVERNING STATUTES AT ISSUE

A. The Federal Food, Drug, and Cosmetic Act (21 U.S.C. § 301, *et seq.*)

The FDCA authorizes FDA to regulate drugs sold in interstate commerce. 21 U.S.C. § 331. As noted above, the term "drug" is defined to include "articles (other than food) intended to affect the structure or any function of the body of man or other animals." *Id.* § 321(g). A "new animal

[6] For purposes of this motion only, Federal Defendants accept as true all well-pleaded material factual allegations in the Amended Complaint. *See* Section III.A., *infra*.

drug" includes "any drug intended for use for animals other than man" that is not generally recognized as safe and effective for the conditions prescribed, recommended, or suggested in the labeling or that has not been used to a material extent or for a material time for such conditions. *Id.* § 321(v). A new animal drug is "deemed unsafe" unless FDA has approved the drug for the particular use at issue. *Id.* § 360b(a)(1). To obtain approval, a sponsor must demonstrate, *inter alia*, that its new animal drug is safe and effective for its intended use. *Id.* § 360b(a)(1); *see* FDA-G187-00578. FDA's regulations implementing these statutory provisions are set forth at 21 C.F.R. § 514, *et seq.*

B. The FDA Modernization Act of 1997 (21 U.S.C. § 371(h)(1)(A))

The FDA Modernization Act of 1997, which amended the FDCA, provides that FDA may issue guidance documents "with public participation and [shall] ensure that information identifying the existence of such documents and the documents themselves are made available to the public." 21 U.S.C. § 371(h)(1)(A). Such documents, however, "shall not create or confer any rights for or on any person, although they present the views of the Secretary on matters under the jurisdiction of the [FDA]." *Id.*

C. The National Environmental Policy Act (42 U.S.C. § 4221, *et seq.*)

"NEPA is a procedural statute that does not 'mandate particular results, but simply provides the necessary process to ensure that federal agencies take a hard look at the environmental consequences of their actions.'" *Sierra Club v. Bosworth*, 510 F.3d 1016, 1018 (9th Cir. 2007). NEPA directs federal agencies to prepare a detailed Environmental Impact Statement for every "major Federal action[] significantly affecting the quality of the human environment." 42 U.S.C. § 4332(C).

D. The Administrative Procedure Act (5 U.S.C. § 551, *et seq.*)

Plaintiffs' claims for violations of the FDCA, the FDA Modernization Act, and NEPA are brought under the APA. To sustain an action under the APA, two requirements must be met. First, where a statute does not provide a private right of action (like the statutes here), the challenged

"agency action" must be "final agency action." 5 U.S.C. § 704; *Northcoast Envtl. Ctr. v. Glickman*, 136 F.3d 660, 668 (9th Cir. 1998). For claims under NEPA, this means that the challenged agency action must be both a major Federal action ***and*** final agency action. *Northcoast Envtl*, 136 F.3d at 668; *Delta Smelt Consol. Cases v. Salazar*, 686 F. Supp. 2d 1026, 1033 (E.D. Cal. 2009). Second, the plaintiffs must establish that they have suffered a legal wrong, or will be adversely affected or aggrieved within the meaning of a relevant statute. *Id.*

II. BACKGROUND, THE GUIDANCE, AND CLAIMS 1, 8, 12, AND 13

A. Case Study No. 1 Growth-Enhanced Salmon

Since at least 2001, the FDA has publicly asserted its authority to regulate rDNA constructs that are intended to affect the structure or function of an animal under the new animal drug provisions of the FDCA. That year, the Council on Environmental Quality and the White House Office of Science and Technology Policy published a case study on growth-enhanced salmon authored by various federal agencies, including FDA, the National Marine Fisheries Service, and the Department of the Interior. Ex. 3 at FDA-2001CP-00012 n.12.[7] This case study, "one of a series of case studies aimed at elucidating the adequacy of federal environmental regulations pertaining to transgenic organisms," addressed the potential aquaculture production of Atlantic salmon genetically engineered to contain an additional fish growth hormone gene intended to make

[7] The U.S. Fish and Wildlife Service, a bureau within the Department of the Interior, and the National Marine Fisheries Services, are responsible for protecting endangered species under the Endangered Species Act. Case Study No. 1 is an exhibit to a Citizen Petition submitted to FDA by Plaintiffs Center for Food Safety, Friends of the Earth, Institute for Fisheries Resources, Pacific Coast Federation of Fishermen's Association, and others in May 2001. Because the Citizen Petition and FDA's denial of that petition are referenced in paragraphs 79 and 82 of the Amended Complaint—and for the reasons discussed below in Section III.A—they may be considered by the Court without converting Federal Defendants' motion for judgment on the pleadings into a motion for summary judgment. *See, e.g., Knievel v. ESPN*, 393 F.3d 1068, 1076 (9th Cir. 2005).

the Atlantic salmon grow faster and use feed more efficiently. *Id.* at 80.[8] As explained in the study, such

> transgenic Atlantic salmon are subject to FDA oversight because they are considered to contain a "new animal drug." The [FDCA] . . . defines a "drug" to include "articles . . . intended to affect the structure or any function of the body of man or other animals." 21 U.S.C. § 321(g). Because an introduced genetic construct will of necessity "affect the structure or . . . function" of transgenic animals, the genetic construct is a "drug."

Ex. 2 at FDA-2001CP-00091 (footnote omitted).[9] As further explained in the case study, "[a]ll subsequent generations of the salmon contain the inserted genetic construct . . ., and therefore all contain a new animal drug." *Id.* at 92. The case study also noted that "[t]he best known example of such a transgenic Atlantic salmon under investigation is the AquAdvantage variety being developed by Aqua Bounty." *Id.* at 80.

B. Plaintiffs' 2001 Citizen Petition

In May 2001, after Case Study No. 1 was published, several Plaintiffs in this case submitted a Citizen Petition acknowledging and embracing FDA's authority to regulate articles that intentionally alter animals' genomes under its new animal drug authority, but requesting that FDA impose a moratorium on the domestic marketing, importation, and exportation of transgenic fish "until the FDA establishes a comprehensive regulatory framework under the mandate of the [FDCA] to evaluate and fully address the human health and environmental impacts caused by the

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[8] The case study assumed that genetically engineered Atlantic salmon would—unlike the AquAdvantage Salmon at issue here—be raised in ocean net pens in or near the Atlantic or Pacific coastal waters of the United States, Ex. 2 at FDA-2001CP-00079, and that escapes would occur, *id.* at 101.

[9] The Case Study defined transgenic fish as "fish that have been modified to contain copies of new genetic constructs introduced into their genome by modern genetic techniques (specifically, recombinant DNA techniques)." Ex. 2 at FDA-2001CP-00080.

commercialization of transgenic fish." Ex. 3 at FDA-2001CP-00001 at 2, 14.[10] They further requested that this regulatory framework include adoption of regulations "addressing the safety and efficacy of transgenic fish by requiring all transgenic fish producers to complete a full review of transgenic fish *as a new animal drug* pursuant to the requirements of 21 U.S.C. § 360b and accompanying implementing regulations." *Id.* at 2 (emphasis added).

The Citizen Petition specifically considered the impact of an approval on the environment under NEPA, but never suggested that the FDCA required its own environmental analysis. *Compare id.* at 14 ("FDA Is Required Under the [FDCA] To Review The Human Health Impacts From Consuming Transgenic Fish") *with id.* at 22 ("FDA Is Required Under [NEPA] To Review The Impacts To Human Health And The Environment"). They argued that,

> FDA must comply with NEPA before approving the commercialization of transgenic fish and allowing transgenic fish to be grown in ocean pens. FDA's decision on whether or not to approve transgenic fish as an animal drug . . . is a major federal action that may significantly affect the environment. Therefore, before this decision is reached, FDA is required to fully and completely consider the human health and environmental impacts as part of the NEPA process.

Id. at 23; *see also id.* at 24 ("FDA must comply with NEPA before transgenic fish are approved as a safe food product.").

C. Issuance of the Guidance

On September 19, 2008, FDA announced the availability of a draft version of the Guidance and provided a public comment period. Ex. 4 at FDA-G187-00001; Ex. 5 at FDA-G187-00026.[11]

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[10] Like Case Study No. 1, Plaintiffs' petition defined transgenic fish to include genetically engineered fish that have been intentionally altered at the molecular or cellular level by rDNA techniques, as well as the progeny of such fish that possess any of the altered molecular or cellular characteristics, and further described AquAdvantage Salmon as transgenic fish. Ex. 3 at FDA-2001CP-00002 n.4, 11.

[11] FDA's issuance of the draft Guidance and provision of notice and opportunity to comment is referenced in paragraphs 80 and 263 of the Amended Complaint. The notice of availability of the draft Guidance was published at 73 Fed. Reg. 54407 (Sept. 19, 2008).

The draft Guidance was issued as a Level 1 draft guidance, pursuant to FDA's Good Guidance Practices regulation, 21 C.F.R. § 10.115, implementing FDA's responsibilities under the FDA Modernization Act. Ex. 5 at FDA-G187-00026. Level 1 guidance documents include guidance documents that set forth initial interpretations of statutory or regulatory requirements, complex scientific issues, or cover highly controversial issues, and generally may be issued only after providing an opportunity for public comment. 21 C.F.R. § 10.115(c)(1) & (g). Plaintiff Center for Food Safety and other public interest groups submitted extensive comments on the draft Guidance. Am. Compl. ¶ 80.

On January 15, 2009, FDA issued the final version of the Guidance. *Id.* ¶ 81; Ex. 1 at FDA-G187-00568.[12] The Guidance explains the statutory provisions giving FDA authority over new animal drugs and how those provisions apply to genetically engineered animals. *Id.* at 71 to -73. Consistent with Case Study No. 1, the Guidance explains that the FDCA's new animal drug provisions authorize FDA to regulate in this context because "[t]he rDNA construct in a GE animal that is intended to affect the structure or function of the body of the GE animal … meets the [FDCA] drug definition." *Id.* at 572.[13]

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[12] The Guidance was revised in minimal and largely administrative ways in June 2015. *Compare* Ex. 1 at FDA-G187-00568 (Jan. 2009 Guidance) *with* Ex. 6 at FDA-G187-00594 (June 2015 revision). The revision to the Guidance was a Level 2 change under FDA's Good Guidance Practices. *See* 21 C.F.R. § 10.115(c)(2), (g) (Level 2 guidance documents are ones that set forth existing practices or minor changes in interpretation or policy and generally are not subject to public comment prior to issuance). Level 1 changes to update the guidance and broaden its scope to encompass more current technology were proposed in January 2017, but have not been finalized. 82 Fed. Reg. 6,167 (Jan. 19, 2017); 82 Fed. Reg. 17,844 (April 13, 2017) (extending comment period). The citations to the Guidance herein are to the 2009 version.

[13] The Guidance defines genetically engineered animals as "those animals modified by rDNA techniques, including the entire lineage of animals that contain the modification." Ex. 1 at FDA-G187-00569. For ease of reference, in the Guidance and at times here, FDA "refer[s] to [its] regulation of the article in . . . GE animals [*i.e.*, the rDNA construct as integrated in the animal's genome] as regulation of the GE animal." *Id.* at FDA-G187-00573.

The Guidance also explains the statutory requirements for applications seeking approval of new animal drugs, set out in 21 U.S.C. § 360b(b)(1); describes the requirements for approval in each implementing provision of FDA's regulations, *i.e.*, in each subpart of 21 C.F.R. § 514.1; discusses how these requirements apply to developers of rDNA constructs intended to affect the structure or function of animals' bodies; and suggests ways in which such developers can satisfy each of those regulatory requirements and obtain approval of such new animal drugs. *See* Ex. 1. The Guidance further explains the various steps that FDA intends to follow in its review process. *See id*. at FDA-G187-00579 to -586. The Guidance states that it "represents [FDA]'s current thinking [and] does not create or confer any rights for or on any person and does not operate to bind FDA or the public. [A sponsor] can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations." *Id.* at 569 (emphasis omitted).

In addition, the Guidance acknowledges FDA's obligation to comply with NEPA when approving a new animal drug application, *id.* at 574; summarizes the requirement in 21 C.F.R. § 514.1(b)(14) that a new animal drug application include either a claim for categorical exclusion or an environmental assessment, *id.* at 585; and sets forth FDA's expectation that, "at least until we have more experience, most [genetically engineered] animal applications would have to be evaluated to determine whether such an application individually or cumulatively affects the environment," *id.* at 590-91.

D. FDA's Denial of the 2001 Citizen Petition

On January 15, 2009, FDA denied the 2001 Citizen Petition. Ex. 7 at FDA-2001CP-000805. In its denial letter, FDA explained that "it already has 'a comprehensive regulatory framework' in place that addresses potential impacts to human health and the environment of GE fish and, because GE fish must comply with the requirements of this regulatory framework," there was "no need for a 'moratorium' on the domestic marketing and importation of GE fish." *Id.* at 806. FDA explained that this comprehensive regulatory framework consists of "FDA's existing [new animal drug application] regulations [that] apply to GE animals, including GE fish." *Id.*

at 809. FDA noted that "it is accomplishing what petitioners request since the application of the new animal drug statutory and regulatory provisions will address the safety and efficacy of GE fish and the human food safety of food animal fish.[14] Therefore, the necessary regulatory framework is in place and no new regulations are necessary." *Id.* FDA further noted that the Guidance provided guidance on how the FDCA's new animal drug provisions and its implementing regulations apply to genetically engineered animals. *Id.* at 805.[15]

With respect to environmental issues, citing its regulation and echoing the Guidance, FDA explained that its new animal drug application approvals "are subject to the requirements of NEPA"; and that a new animal drug application "must include either an environmental assessment or a claim for categorical exclusion (which excuses certain categories of actions from the preparation of an [environmental assessment] where the agency has determined that that category of action does not individually or cumulatively have a significant effect on the human environment, 40 CFR § 1508.4). 21 CFR § 514.3(b)(14)." Ex. 7 at FDA-2001CP-00811.[16] As FDA further explained, "NEPA is a procedural requirement and does not give us new authority, such as to prohibit an activity solely because it would harm the quality of the environment." *Id.* at 813.

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[14] In its denial of the citizen petition, FDA noted that "new animal drugs must be found safe for use in food for the drug to be approved for use in food animals," and that the food safety of genetically engineered salmon would have to be established for FDA to approve a new animal drug application concerning such fish. Ex. 7 at FDA-2001CP-00809. As noted above, Plaintiffs do not challenge FDA's conclusion that AquAdvantage Salmon is safe to eat.

[15] In rejecting an additional request in the citizen petition that FDA establish regulations requiring that all genetically engineered fish undergo review under the food additive provisions of the FDCA in addition to review under the new animal drug provisions, *see* Ex. 3 at FDA-2001CP-00002, -15, FDA explained that "[n]ew animal drugs are excluded from the definition of food additives and so cannot be regulated as food additives." Ex. 7 at FDA-2001CP-000809 (citing 21 U.S.C. § 321(s)(5), which defines "food additive" to "not include . . . a new animal drug"). Under this clear exclusionary language, as the citizen petition itself acknowledged, *see* Ex. 3 at FDA-2001CP-00015 n.27, an article regulated as a new animal drug cannot *also* be regulated as a food additive.

[16] The reference to Section 514.3(b)(14) rather than Section 514.1(b)(14) is a typographical error.

E. FDA's Approval of AquaBounty's New Animal Drug Application

On November 19, 2015, FDA approved AquaBounty's new animal drug application for an rDNA construct as integrated in the genome of a line of triploid, all-female genetically engineered Atlantic salmon, known as "AquAdvantage Salmon." Ex. 8. Under the approval, AquAdvantage Salmon are to be produced in Canada and grown out in Panama, where the fish will be harvested and processed for food use and sale in the United States. Am. Compl. ¶¶ 2, 5, 112-14.

F. Claims 1, 8, 12, and 13

Claim 1 of the Complaint challenges FDA's approval of AquaBounty's new animal drug application and issuance of the Guidance under the FDCA and the APA as *ultra vires*. Plaintiffs allege that FDA lacks statutory authority under the FDCA's new animal drug provisions to regulate the rDNA construct as integrated in the genome of genetically engineered animals because it does not meet the FDCA's definition of a "drug" or "new animal drug." *Id.* ¶¶ 11, 156-66. Specifically, Plaintiffs allege that the FDCA "does not explicitly grant FDA authority to regulate GE animals," *id.* ¶ 11; "Congress never intended or provided a means for FDA to regulate twenty-first century GE animals using its 1938 authority over veterinary animal drugs," *id.*; the Guidance "interpret[s] the definition of 'new animal drug' under the []FDCA to include GE animals," *id.*; and "FDA's approval of AquaBounty's application and the issuance of [the Guidance] represent an unlawful effort to extend FDA's regulatory reach far beyond the statutory mandates of the []FDCA," *id.*

Claim 8 challenges the Guidance under NEPA and the APA. Plaintiffs allege that the Guidance adopted a new "regulatory framework for GE animal approvals," and, therefore, "is a major federal action significantly affecting the human environment," requiring FDA to prepare a programmatic environmental impact statement on the effects of this new "framework" before issuing the Guidance and approving AquaBounty's new animal drug application. *Id.* ¶ 219-20, 222.

Claim 12 challenges the Guidance and new animal drug application approval under the FDCA and APA. Plaintiffs allege that FDA was required to consider environmental safety in

determining the safety and effectiveness of AquaBounty's new animal drug. *Id.* ¶¶ 11, 247-55. Specifically, Plaintiffs allege that FDA, in the Guidance, "expressly interpreted the [FDCA] to include environmental risks as a relevant factor when evaluating the safety and effectiveness of a drug," but "fails to rationally explain what factors FDA will consider relevant to this determination and how FDA will weigh or consider such factors when it evaluates whether an application is 'safe and effective' in its approvals and decisionmaking." *Id.* ¶¶ 249-50, 253. Plaintiffs further allege that FDA failed to consider environmental safety as part of the FDCA's "safety and effectiveness" requirement in approving AquaBounty's new animal drug application. *Id.* ¶¶ 248, 254.

Claim 13 challenges FDA's issuance of the Guidance under the FDA Modernization Act of 1997 and the APA on procedural grounds. *Id.* ¶¶ 256-65. Plaintiffs allege that FDA was required to follow notice and comment rulemaking in issuing the Guidance. *Id.* Specifically, Plaintiffs allege that FDA in its draft Guidance "formally announced for the first time that the agency would extend its jurisdiction to cover GE animals, including those produced for food like AquaBounty's GE salmon," *id.* ¶ 80, *see id.* ¶ 260; the Guidance is a *de facto* amendment to FDA's new animal drug regulations "because it confers legal rights to entities seeking approval of GE animals and binds FDA to accept and review those applications," *id.* ¶ 261; prior to issuance of the Guidance, "[n]o regulatory pathway for GE animals existed," *id.* ¶ 262; and although FDA provided notice and opportunity to comment prior to issuing the Guidance, its failure to offer notice and comment "in the APA formal rulemaking context deprived stakeholders, including Plaintiffs, of the formality and finality in FDA's determination and interpretation of its authority," *id.* ¶ 263.

III. CONTROLLING LEGAL STANDARDS AND SCOPE OF REVIEW

A. Federal Rule of Civil Procedure 12(c)

Judgment on the pleadings is appropriate when there are no disputed issues of material fact and the movant is entitled to judgment as a matter of law. Fed. R. Civ. P. 12(c); *Fleming v. Pickard*, 581 F.3d 922, 925 (9th Cir. 2009); *Knappenberger v. City of Phx.*, 566 F.3d 936, 939 (9th Cir. 2009). The court must accept as true all the material facts alleged in the complaint and draw all

reasonable inferences in favor of the non-moving party, *Fleming*, 581 F.3d at 925, and may, without converting the motion into one for summary judgment, take judicial notice of facts when appropriate to do so and consider any document referenced in or integral to a plaintiff's complaint. *Knievel*, 393 F.3d at 1076; *Shame on You Productions, Inc. v. Banks*, 120 F. Supp. 3d 1123, 1144-45 (C.D. Cal. 2015).

B. Deference under the APA

An agency action may only be set aside under the APA if "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law"; "in excess of statutory jurisdiction, authority, or limitations, or short of statutory right"; or "without observance of procedure required by law." 5 U.S.C. § 706(2)(A), (C), (D). This standard is highly deferential to the agency. *See Northwest Ecosystem Alliance v. U.S. Fish and Wildlife Serv.*, 475 F.3d 1136, 1140 (9th Cir.2007). The reviewing court must determine whether the agency's decision was based upon consideration of the relevant factors and whether there has been a clear error of judgment. *Northcoast Envtl. Ctr. v. Glickman*, 136 F.3d 660, 666 (9th Cir. 1998). But the court "may not substitute [its] judgment for that of the agency," *id.* (internal quotations omitted), and must uphold the agency's action so long as it is "rational, based on consideration of the relevant factors, and within the scope of the authority delegated to the agency by the statute." *Motor Vehicle Mfrs. Ass'n, Inc., v. State Farm Mut. Auto. Ins. Co.*, 463 U.S. 29, 42 (1983). In addition, "the party challenging an agency's action as arbitrary and capricious bears the burden of proof." *George v. Bay Area Rapid Transit*, 577 F.3d 1005, 1011 (9th Cir. 2009) (citing *City of Olmsted Falls v. FAA*, 292 F.3d 261, 271 (D.C. Cir. 2002)).

Agencies receive deference for their interpretations of the statutes they are tasked with administering. *Chevron, U.S.A., Inc. v. Natural Res. Def. Council, Inc.*, 467 U.S. 837, 865 (1984); *see also United States v. Mead Corp.*, 533 U.S. 218, 227–28 (2001) (recognizing "that considerable weight should be accorded to an executive department's construction of a statutory scheme it is entrusted to administer"). The first question under *Chevron* is "whether Congress has directly

spoken to the precise question at issue." *Chevron*, 467 U.S. at 842. "If the intent of Congress is clear, that is the end of the matter." *Id.* at 842-43. Put another way, the Court must initially decide "whether the statute unambiguously forbids the Agency's interpretation." *Barnhart v. Walton*, 535 U.S. 212, 218 (2002). If, however, the statute "is silent or ambiguous with respect to the specific issue," the Court proceeds to the second prong of *Chevron*, under which "the question for the court is whether the agency's answer is based on a permissible construction of the statute." *Chevron*, 467 U.S. at 843. The court need not find that the agency's construction was the only one it permissibly could have adopted or even the reading the court would have reached; rather, so long as the agency's reading is permissible, it must be sustained. *See Chevron*, 467 U.S. at 843–44 & n.11; *Cnty. of L.A. v. Shalala*, 192 F.3d 1005, 1012–13 (D.C. Cir. 1999).

Moreover, even when an agency is interpreting its own regulations, the agency is entitled to "substantial deference." *Thomas Jefferson Univ. v. Shalala*, 512 U.S. 504, 512 (1994); *Auer v. Robbins*, 519 U.S. 452, 462 (1997); *see also Alaska Wilderness League v. Jewell*, 788 F.3d 1212, 1221-22, 1224 (9th Cir. 2015) *and Novartis Pharms. Corp. v. Leavitt*, 435 F.3d 344, 349 (D.C. Cir. 2006) ("We have held on a number of occasions that FDA interpretations of the [FDCA] receive deference, as do its interpretations of its own regulations unless plainly erroneous or inconsistent with the regulations."). A court's task "is not to decide which among several competing interpretations best serves the regulatory purpose. Rather, the agency's interpretation must be given controlling weight unless it is plainly erroneous or inconsistent with the regulation." *Thomas Jefferson Univ.*, 512 U.S. at 512 (internal quotation and citation omitted). Deference is especially appropriate when the statutory and regulatory regimes implemented by the agency are complex. *See Actavis Elizabeth LLC v. FDA*, 625 F.3d 760, 766 (D.C. Cir. 2010).

IV. FEDERAL DEFENDANTS ARE ENTITLED TO JUDGMENT ON CLAIMS 1, 8, 12, AND 13 AS A MATTER OF LAW

A. This Court Lacks Jurisdiction over Plaintiffs' Challenge to the Guidance in Claims 1, 8, 12, And 13

Plaintiffs' challenge to the Guidance in Claims 1, 8, 12, and 13 fails on jurisdictional

grounds for two reasons.[17] The Guidance is not final agency action, and even if it were, Plaintiffs would lack standing to challenge it.

1. The Guidance is not final agency action

The Guidance is not final agency action because it merely summarizes the new animal drug provisions of the FDCA and implementing regulations, explains how those provisions apply to particular new animal drugs concerning genetically engineered animals, and provides suggestions to potential sponsors and FDA's current thinking on how they can comply with those provisions' technical requirements. Claims 1, 8, 12, and 13 challenge the Guidance in whole or in part, and thus, to the extent they do so, they fail as a matter of law.[18]

"As a general matter, two conditions must be satisfied for agency action to be 'final.'" *Bennett v. Spear*, 520 U.S. 154, 177 (1997). "First, the action must mark the 'consummation' of the agency's decision[-]making process, --it must not be of a merely tentative or interlocutory nature." *Id.* at 177-78 (internal citation omitted). "And second, the action must be one by which rights or obligations have been determined, or from which legal consequences will flow." *Id.* (internal quotation marks omitted). Finality is a jurisdictional requirement for obtaining judicial review of agency action. *Navajo Nation v. U.S. Dep't of Interior*, 819 F.3d 1084, 1090 (9th Cir. 2016); *see City of San Diego v. Whitman*, 242 F.3d 1097, 1098 (9th Cir. 2001).

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[17] The D.C. Circuit concluded in *Vietnam Veterans of America v. Shinseki*, 599 F.3d 654, 661 (D.C. Cir. 2010) that the APA's reviewability provision, Section 704, is not jurisdictional. Courts in the Ninth Circuit have held that it is jurisdictional, however, because it limits the scope of the APA's waiver of sovereign immunity. *See Tucson Airport Auth. v. General Dynamics Corp.*, 136 F.3d 641, 645 (9th Cir. 1998); *Gallo Cattle Co. v. USDA*, 159 F.3d 1194, 1198-99 (9th Cir. 1998). While there is some tension in the Ninth Circuit's precedents as to whether Section 704 poses a jurisdictional barrier to constitutional claims, *see Gros Ventre Tribe v. United States*, 469 F.3d 801, 809 (9th Cir. 2006) (contrasting *Gallo Cattle* and *Presbyterian Church v. United States*, 870 F.2d 518 (9th Cir. 1989)), there is no doubt that it poses an independent limitation on APA claims – the only claims at issue in this motion.

[18] Claims 1 and 12 also challenge the approval.

Neither *Bennett* prong is satisfied here. The Guidance—unlike FDA's approval of AquaBounty's new animal drug application—does not mark the consummation of any decision-making process. *See Navajo Nation*, 819 F.3d at 1092 ("the decision to follow Interior's solicitor's guidance" and "to apply NAGPRA [the Native American Graves Protection and Repatriation Act] to these [human] remains and objects . . . constituted a final agency action").

The requirements for approval of a new animal drug application are established by statute, 21 U.S.C. § 360b(b), and implementing regulations, 21 C.F.R. Part 514. Section 514.1 sets forth the requirements for new animal drug applications. On its face, the Guidance does not create any new requirements. Rather, as set forth above, it summarizes the requirements of each subpart of section 514.1 and provides guidance on how new animal drug applications can address those requirements. *See* Ex. 1, FDA-G187-00579 to -86. In order to facilitate FDA's evaluation of new animal drugs under the existing regulatory framework, the Guidance also sets forth FDA's recommendations concerning the information a sponsor can submit to satisfy these regulatory requirements and the FDCA's safety and effectiveness requirements with respect to rDNA constructs intended to affect the structure or function of animals' bodies. *Id.* at 586-91.[19] And it explains FDA's "current thinking" on regulation of genetically engineered animals containing heritable rDNA constructs as of the date of issuance. *Id.* at 569. The Guidance is thus advisory only. *See U.S. Army Corps of Engineers v. Hawkes Co.*, 136 S. Ct. 1807, 1813 (2016) (distinguishing preliminary jurisdictional determination of whether "waters of the United States"

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[19] To illustrate, the Guidance summarizes the regulatory requirements for safety and effectiveness, explaining that 21 C.F.R. § 514.1(b)(8) "requires that [a new animal drug application] include data/information to permit evaluation of the safety and effectiveness of the new animal drug product for the use as suggested in the proposed labeling" and "also requires that sponsors supply all information relevant to safety and effectiveness for a new animal drug, favorable and unfavorable." Ex. 1 at FDA-G187-00583-84 (section IV.B.8.). The Guidance then refers sponsors to the discussion in section IV.C. of the related steps in FDA's review process, including target animal safety (Step 4), food and feed safety (Step 6), and effectiveness/claim validation (Step 7), and discusses an approach that sponsors can follow to satisfy section 514.1(b)(8)'s regulatory requirements for each step. *Id.* at 586.

are on a parcel of property that is "'advisory in nature'" from an approved determination that constitutes final agency action).

The second *Bennett* prong also is not satisfied because, unlike the approved jurisdictional determination at issue in *Hawkes*, the Guidance has no legal consequences, as it itself states. Any legal consequences flow from the FDCA, implementing regulations, and approval of a new animal drug pursuant thereto—*not* the Guidance. Ex. 1 at FDA-G187-00569, 571; 21 C.F.R. § 10.115(d). Because the Guidance does not have "the status of law or comparable legal force," *Oregon Natural Desert Ass'n v. U.S. Forest Service*, 465 F.3d 977, 986-87 (9th Cir. 2006), "impose an obligation, deny a right, or fix some legal relationship," *Ukiah Valley Med. Ctr. v. FTC*, 911 F.2d 261, 264 (9th Cir. 1990), or "give[] rise to 'direct and appreciable legal consequences,'" *Hawkes*, 136 S. Ct. at 1814, it is not final agency action.

Because issuance of the Guidance is not "final agency action," it is not reviewable under the APA. Claims 1 and 12 thus fail to the extent they challenge the Guidance, while Claims 8 and 13 (which challenge the Guidance but not the approval), fail as a matter of law.

2. Plaintiffs also lack standing to challenge the Guidance

Plaintiffs' challenge to the Guidance in Claims 1, 8, 12, and 13 also fails on jurisdictional grounds because they have not alleged that (1) the Guidance has or will injure them in any concrete or particularized way, or that (2) an order setting aside the Guidance would have any effect on the only harms about which they complain, *i.e.*, injuries to their "recreational, scientific, aesthetic, cultural, spiritual, subsistence, and commercial" interests in salmon and salmon habitats. *See* Am. Compl. ¶¶ 17-18, 29-30. Plaintiffs nowhere allege that these harms are attributable to the Guidance. Nor would any such allegation be plausible because the Guidance simply summarizes the law; it does not extend FDA's authority. "Enjoining" this Guidance document would do nothing to redress Plaintiffs' alleged harms and they thus lack standing to challenge it.

To establish standing under Article III's "case" or "controversy" provision, a plaintiff must establish as to each claim "that (1) [it] suffered an injury in fact, *i.e.*, one that is sufficiently

'concrete and particularized' and 'actual or imminent, not conjectural or hypothetical,' (2) the injury is 'fairly traceable' to the challenged conduct, and (3) the injury is 'likely' to be 'redressed by a favorable decision.'" *Bates v. United Parcel Serv.*, 511 F.3d 974, 985 (9th Cir. 2007) (quoting *Lujan v. Defenders of Wildlife*, 504 U.S. 555, 560-61 (1992)); *see Washington Envtl. Council v. Bellon*, 732 F.3d 1131, 1139-40 (9th Cir. 2013); *Schmier v. U.S. Court of Appeals for Ninth Circuit*, 279 F.3d 817, 820-21, 823 (9th Cir. 2002).

Plaintiffs do not allege that any of their claimed injuries are fairly traceable to the Guidance. They allege, rather, that it is "FDA's *approval* of [AquaBounty's new animal drug application that] harms Plaintiffs' and their members' . . . enjoyment of salmonids and salmonid habitat by allowing production of GE salmon to proceed without adequate regulation and analyses of associated . . . environmental and ecological impacts." Am. Compl., ¶ 30 (emphasis added); *see id.*, ¶ 139 ("Of particular concern to Plaintiffs are the potential impacts of FDA's approval of [AquaBounty's new animal drug application] upon already vulnerable wild fish populations"). Plaintiffs' actual dispute is with FDA's approval of the new animal drug at issue—not the Guidance. Their asserted harms are neither traceable to the Guidance nor redressable via an injunction against the Guidance, such that they lack standing.

Indeed, even if this Court were to enjoin the Guidance, that injunction would not constrain FDA's approval authority, because that authority comes from the FDCA itself. The Guidance merely advises sponsors on how they may satisfy preexisting statutory and regulatory requirements. "Relief that does not remedy the injury suffered cannot bootstrap a plaintiff into federal court." *Steel Co. v. Citizens for a Better Env't*, 523 U.S. 83, 107 (1998). Accordingly, Claims 1 and 12, to the extent they challenge the Guidance, and Claims 8 and 13 (which challenge only the Guidance and not the approval) fail on jurisdictional grounds as a matter of law.

B. Federal Defendants Are Entitled to Judgment on the Merits of Claims 1, 12, and 13's Challenge to the Guidance and Approval as a Matter of Law

1. Judgment on Claim 1 is warranted because FDA has authority to regulate the integrated rDNA construct under the plain language of the FDCA

Under the plain language of the FDCA, FDA has authority to regulate new animal drugs intended to affect the structure or any function of the body of animals, including through genetic engineering. Plaintiffs nonetheless challenge FDA's approval of AquaBounty's new animal drug application and issuance of the Guidance on the ground that the FDCA "does not explicitly grant FDA authority to regulate GE animals," and that "Congress never intended or provided a means for FDA to regulate twenty-first century GE animals using its 1938 authority over veterinary animal drugs." Am. Compl. ¶ 11 (Count 1). Neither assertion is correct. The FDCA's new animal drug provisions easily encompass the rDNA construct as integrated in the genome of AquAdvantage Salmon. Congress, moreover, has acknowledged FDA's statutory authority with respect to genetically engineered animals and ratified that authority on a number of occasions.

Foremost, the FDCA defines "drug" to include "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)(C). "Congress fully intended that the [FDCA's] coverage be as broad as its literal language indicates." *United States v. Article of Drug Bacto-Unidisk*, 394 U.S. 784, 798 (1969). It is undisputed that the AquAdvantage Salmon rDNA construct at issue has been integrated into the genome of a line of Atlantic salmon in order to affect the animal's structure or function, *i.e.*, to stimulate faster growth.[20] Because the construct is intended to affect the structure or function of the salmon into whose genome the construct has been integrated, it meets the FDCA's definition of a drug. *See*

[20] Paragraph 77 of the Amended Complaint alleges that, "The ocean pout promoter acts like a switch, keeping the growth hormone protein from turning off, which allows for continued growth of the fish"). *See also* Ex. 3 at FDA-2001CP-00016 ("The growth hormone transgene affects the characteristics of the fish by causing it to grow . . . faster than wild salmon.").

Ex. 2 at FDA-2001CP-00091 (Case Study No. 1); Ex. 7 at FDA-2001CP-000805 to -806 (denial of 2001 Citizen Petition); Ex. 1 at FDA-G187-00571 (the Guidance); Ex. 8 at FDA-023113 (approval of AquaBounty's new animal drug application).

An animal drug is defined as a "new animal drug" unless it is both generally recognized as safe and effective and has been used to a material extent and for a material time, as defined in the FDCA. 21 U.S.C. § 321(v); *see* Section I.A., *supra*. Because the rDNA construct as integrated in the genome of AquAdvantage Salmon is not generally recognized as safe and effective for this intended use and has not been used to a material extent or for a material time, it is a new animal drug under 21 U.S.C. § 321(v). Under the Act, with exceptions not applicable here, a new animal drug is generally "deemed unsafe" unless FDA has approved a new animal drug application for a particular use. *See* 21 U.S.C. §§ 360b(a)(1), (a)(3), (a)(4), (a)(5). FDA thus has the authority to review, and if appropriate approve, a new animal drug application such as AquaBounty's under the FDCA's new animal drug provisions.

Even if the new animal drug provisions of the FDCA were ambiguous, which they are not, *Chevron* requires deferring to FDA's reasonable construction of the Act here because that construction is plainly permissible and there is no "clear expression of congressional intent to the contrary." *San Francisco BayKeeper v. Whitman*, 297 F.3d 877, 885 (9th Cir. 2002) **(**absent "a clear expression of congressional intent to the contrary, courts should defer to reasonable agency interpretations" of the laws they are charged with enforcing) (internal quotation marks omitted); *see Chevron*, 467 U.S. at 843-44; *Fournier v. Sebelius*, 718 F.3d 1110, 1118 (9th Cir. 2013).

Indeed, amendments to the FDCA as far back as 1988 reflect Congress' recognition that FDA has authority to regulate rDNA constructs under its new animal drug authority, making clear that FDA's authority is not limited to the technologies of the 1930s, but is sufficiently broad to encompass new medical and scientific developments such as genetic manipulation. *See Chevron*, 467 U.S. at 842 (rejecting "static" definition of statutory term when Congress had not commanded that definition). The Generic Animal Drugs and Patent Term Restoration Act of 1988, Pub. L. No.

100-670, Title I, § 106, 102 Stat. 3984, amended the FDCA to create an expedited approval system for certain generic new animal drugs, but excepted new animal drugs primarily manufactured using rDNA or other processes involving site specific genetic manipulation techniques (biotechnology), thereby requiring such drugs to go through the full new animal drug application process.[21] Similarly, the Minor Use and Minor Species Animal Health Act of 2004, 21 U.S.C. § 360ccc, amended the FDCA to permit "conditional approval" of an animal drug to treat minor animal species and uncommon diseases in major animal species in specified circumstances, but excepted a drug "that is contained in, or is a product of, a transgenic animal."[22] In addition, Section 1007 of the Food and Drug Administration Amendments Act of 2007, 21 U.S.C. § 2106, directed FDA to consult with the National Marine Fisheries Service to produce a report on environmental risks associated with genetically engineered seafood products. Most recently, in the Animal Drug and Generic Animal Drug User Fee Amendments of 2018, Congress amended Section 740(d) of the FDCA to exempt from certain user fee provisions sponsors of an application or investigational submission "if such application or submission involves the intentional genomic alteration of an animal that is intended to produce a drug, device, or biological product subject to fees." This provision has the effect of exempting from fees submissions and applications for genetically engineered animals that are intended to produce human medical products, such as the genetically engineered goat that produces a human biological product in its milk. *See* n.2, *supra*. These statutory provisions would have been unnecessary—indeed they would make no sense—if the new animal drug provisions of the FDCA did not encompass new animal drugs manufactured through

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[21] Plaintiffs address this exclusion in their 2001 Citizen Petition. *See* Ex. 3 at FDA-2001CP-00014 to -15.

[22] "Transgenic animal" is defined as "an animal whose genome contains a nucleotide sequence that has been intentionally modified in vitro, and the progeny of such an animal," but further provided that it "does not include an animal of which the nucleotide sequence of the genome has been modified solely by selective breeding." 21 U.S.C. § 360ccc(j). For purposes of AquAdvantage Salmon, the terms genetically engineered and transgenic are interchangeable.

the use of rDNA or other forms of biotechnology. *See U.S. v. Regenerative Sciences, LLC*, 741 F.3d 1314, 1319-20 (D.C. Cir. 2014) ("The [FDCA's] breadth—and, more specifically, its applicability to doctors—is evident in the fact that the FDCA carves out certain exceptions from its requirements for doctors who manufacture and administer drugs in the course of their professional practice. Those exceptions would be unnecessary if the FDCA did not otherwise regulate the distribution of drugs by licensed physicians." (internal citations omitted)).

Likewise, bills introduced in Congress attempting to amend the new animal drug provisions of the FDCA to *prevent* FDA from approving drugs that are intended to alter the genome of fish through the use of bioengineering would have been unnecessary if FDA lacked authority under the Act to do so. *See* Ex. 9 at FDA-2011CP-040 (S. 230, to amend the FDCA to prevent the approval of genetically engineered fish by deeming it unsafe); Ex. 10 at FDA-2011CP-043 (H.R. 521, same).[23] Congress is presumed to be knowledgeable about existing law pertinent to the legislation it enacts (and proposes). *Goodyear Atomic Corp. v. Miller*, 486 U.S. 174, 184-85 (1988); *see Columbia Riverkeeper v. U.S. Coast Guard*, 761 F.3d 1084, 1093 (9th Cir. 2014). The above examples "'provid[e] further evidence . . . that Congress intended the Agency's interpretation, or at least understood the interpretation as statutorily permissible.'" *Fournier*, 718 F.3d at 1122, (ellipses in original)(quoting *Barnhart v. Walton*, 535 U.S. 212, 220 (2002)).

In sum, the plain and unambiguous language of the new animal drug provisions of the FDCA requires entry of judgment in the government's favor on the merits of Claim 1. But if even that text were ambiguous, FDA has consistently construed those provisions—in its 2001 Citizen Petition denial, the Guidance, and the approval of AquaBounty's new animal drug application—as encompassing an rDNA construct as integrated in the genome of an animal. That long-standing construction is undoubtedly permissible, and eminently reasonable. Thus, the agency is entitled

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[23] These bills are exhibits to the 2011 Citizen Petition, referenced in the Amended Complaint, which Plaintiffs Center for Food Safety, Friends of the Earth, and Food and Water Watch, among others, submitted to FDA. Am. Compl., ¶ 137.

to judgment on Count 1.

2. Judgment on Claim 12 is warranted because environmental safety is considered under NEPA, not the FDCA

Claim 12's challenge to the Guidance and FDA's approval of AquaBounty's new animal drug application rests on the legally incorrect premise that the FDCA requires environmental safety to be considered in determining whether a new animal drug is "safe and effective" for its intended use. Under the plain language of the Act, FDA considers whether a drug is safe for humans and animals, *e.g.*, whether it is safe for the target animal and whether it is safe for humans to eat food from the animal, not whether it is safe for the environment. *See* 21 U.S.C. § 360b(a)(1), (b)(1)(H), (d)(1)-(2), (i). Even if the Act were ambiguous, the agency's implementing regulations, which address environmental safety under NEPA, are reasonable and entitled to *Chevron* deference. *Compare* 21 C.F.R. § 514.1(b)(8) (evidence to establish safety and effectiveness) *with* 21 C.F.R. § 514.1(b)(14) (environmental assessment), and FDA-G187-00589 to -90 (food/feed safety) *with* FDA-G187-00590 to -91 (environmental safety); *see also* 21 C.F.R. §§ 511.1(b)(10).

Plaintiffs' assertion in paragraph 249 of their Amended Complaint that FDA in the Guidance "expressly interpreted the [FDCA] to include environmental risks as a relevant factor when evaluating the safety and effectiveness of a drug" is flatly contradicted by the Guidance itself. The allegation appears to be based on the Guidance's inclusion of its assessments of both "*Food/Feed Safety*" and "*Environmental Safety*" in the same step (Step 6) of FDA's new animal drug approval review process. Ex. 1 at FDA-G187-00589 to -90.[24] But the *Food/Feed Safety*

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[24] The Guidance states:

> ***Step 6: The Food/Feed Safety and Environmental Safety Assessments***
>
> *Food/Feed Safety*
>
> This part of Step 6 addresses the food and feed safety requirements in 21 CFR 514.1(b)(8). It focuses on the issue of whether food or feed derived from a GE animal is safe for humans or animals consuming edible products from the animals.

assessed in the first "part of Step 6 addresses the food and feed safety requirements in *21 CFR 514.1(b)(8),*" and "focuses on the issue of whether food or feed derived from a GE animal is safe for humans or animals consuming edible products from the animals." Ex. 1 at FDA-G187-00589 (emphasis added). The *Environmental Safety* assessed in the second part of Step 6, in contrast, "addresses the environmental component of [a new animal drug application]," and cites *21 C.F.R. § 514.1(b)(14)*, not 21 C.F.R. § 514.1(b)(8). Ex. 1 at FDA-G187-00589 to -90.[25] As the discussion of 21 C.F.R. § 514.1(b)(14) in Step 6 and the plain language of the provision itself make clear, (b)(14) is intended to implement FDA's obligations under NEPA to assess environmental safety, not any purported obligations under the FDCA. *See* Ex. 1 at FDA-G187-00585.[26]

. . .

> *Environmental Safety*
>
> This portion of Step 6 addresses the environmental component of your [new animal drug application]. 21 CFR 514.1(b)(14). We expect that, at least until we have more experience, most GE animal applications would have to be evaluated to determine whether such an application individually or cumulatively affects the environment (i.e., whether an extraordinary circumstance exists). 21 CFR 25.21. An [environmental assessment] that demonstrates the GE animal will not significantly affect the quality of the human environment leads to a finding of no significant impact (FONSI).

Ex. 1 at FDA-G187-00589 to -90 (emphasis in original).

[25] 21 C.F.R. § 514.1(b)(14) provides: "*Environmental Assessment*. The applicant is required to submit either a claim for categorical exclusion under § 25.30 or § 25.33 of this chapter or an environmental assessment under § 25.40 of this chapter."

[26] The discussion in the Guidance addresses Section 514.1(b)(14)'s requirement that a sponsor prepare an environmental assessment unless the action at issue is categorically excluded, citing FDA's regulations implementing NEPA, 21 C.F.R. Part 25. Ex. 1 at FDA-G187-00585. It notes that an environmental assessment "is a public document that provides sufficient information to allow FDA to either prepare an environmental impact statement (EIS) or issue a finding of no significant impact (FONSI)", and "recommend[s] that the [environmental assessment] focus on environmental issues and potential impacts related to the use and disposal of the GE animal and its final product, if relevant." *Id.*

The *Food/Feed Safety* and *Environmental Safety* assessments are both included in Step 6, not because FDA interprets the FDCA to include environmental risks as a relevant factor in evaluating the safety and effectiveness of a new animal drug, but because this is the point in the review process at which FDA expects to have the information necessary to determine whether the drug will be safe for humans and animals, a determination required under the FDCA, and whether FDA's approval of the drug will have a significant impact on the environment, a determination required under NEPA. The only remaining step, "*Effectiveness/Claim Validation*," provides no new information relevant to environmental considerations. *See* Ex. 1 at FDA-G187-00591. Judgment on the merits of Claim 12, accordingly, is warranted as a matter of law.

3. Judgment on Claim 13 is warranted because the Guidance is not a rule subject to notice and comment rule making

Plaintiffs' procedural claim that the Guidance could be issued only after formal notice and comment rulemaking also must be dismissed because it rests on the demonstrably false premise that the Guidance is more than advisory. *See* Am. Compl., ¶ 261. As demonstrated in section IV.A.1. above, the Guidance does not create or confer any rights; any "rights" relating to approval of a new animal drug application concerning a genetically engineered animal are created by the FDCA and FDA's implementing regulations (21 C.F.R. Part 514). Moreover, as required by the FDA Modernization Act, before issuing the Guidance, FDA provided notice and an opportunity to comment, of which several Plaintiffs availed themselves. The Guidance thus fits squarely within the scope of the FDA Modernization Act, which authorizes the Secretary of HHS to "develop guidance documents with public participation" that do not "create or confer any rights for or on any person, although they present the views of the Secretary on matters under the jurisdiction of the [FDA]." 21 U.S.C. § 371(h)(1)(A). Judgment on the merits of Claim 13 is thus also warranted as a matter of law.

CONCLUSION

For the foregoing reasons, the Court should enter judgment on Claims 1, 8, 12, and 13 in Federal Defendants' favor.

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ATTESTATION

Pursuant to Local Rule 5-1(i)(3), I attest that I am the ECF user whose user ID and password are being used in the electronic filing of this document. I further attest that I have obtained the concurrence in the filing of the document from the other signatories.

/s/ Mary M. Englehart
MARY M. ENGLEHART

CERTIFICATE OF SERVICE

I hereby certify that on this 30th day of August, a true and correct copy of the foregoing document was filed electronically with the Clerk of the Court using CM/ECF. I also certify that the foregoing document is being served on all counsel of record via transmission of Notices of Electronic Filing generated by CM/ECF.

/s/ Mary M. Englehart
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