



CENTER FOR
Science IN THE
Public Interest

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By Electronic Submission

Division of Dockets Management [HFA-305]
Food and Drug Administration
5630 Fishers Lane, rm. 1061
Rockville, MD 20853

RE: Comments on Food and Drug Administration Docket No. 2008-D-0394

The Center for Science in the Public Interest (“CSPI”)¹ hereby submits comments to the Food and Drug Administration (“FDA”) on its “Draft Guidance for Industry #187: Regulation of Genetically Engineered Animals Containing Heritable rDNA Constructs,” announced in the Federal Register on September 19, 2008 (73 FR 54407-08) (hereinafter referred to as “Draft Guidance”). That Draft Guidance sets forth FDA’s current views on how genetically engineered (“GE”) animals are regulated under the Federal Food, Drug, and Cosmetic Act and provides recommendations on how developers of GE animals can comply with existing legal obligations.

CSPI commends FDA for acknowledging that GE animals are moving toward commercialization and that regulatory oversight is necessary for those animals and their products. CSPI supports FDA’s interpretation that GE animals are regulated articles under the “new animal drug” provisions of the Federal Food, Drug, and Cosmetic Act. As engineering animals involves applying a new technology that could result in potential risks to the animals, the environment, or the food supply, it is extremely important to have a federal mandatory pre-market approval process that comprehensively ensures the safety of GE animals.

¹CSPI is a nonprofit education and advocacy organization that focuses on improving the safety and nutritional quality of our food supply and on reducing the damage caused by alcoholic beverages. CSPI seeks to promote health through educating the public about nutrition and alcohol; it represents citizens’ interests before legislative, regulatory, and judicial bodies; and it works to ensure advances in science are used for the public good. CSPI is supported by the 9000,000 member-subscribers to its Nutrition Action Healthletter and by foundation grants. CSPI receives no funding from industry or the federal government.

The legal interpretation set forth by FDA in the Draft Guidance is a good first step in providing that comprehensive federal regulatory system. According to the Draft Guidance, FDA's regulatory process for GE animals will comprehensively address any food safety concerns as well as any animal health and welfare issues. However, when discussing environmental risk issues, the Draft Guidance only mentions the National Environmental Policy Act ("NEPA"), a procedural statute. That statute only requires that FDA conduct an environmental assessment or an environmental impact statement but provides no substantive authority to FDA to actually address and mitigate any potential environmental risks. While such a review is useful, it cannot substitute for a comprehensive environmental approval conducted pursuant to a legal mandate to safeguard the environment from Congress. Therefore, either FDA needs to request the necessary legal authority to be able to ensure that GE animals don't injure the environment or the federal government needs to identify which other agencies have the legal authority to review GE animals and protect the environment.

In addition, GE animals will be controversial and any regulatory system analyzing their safety needs to be transparent and allow for public participation. The Draft Guidance, however, does not adequately address those two issues. Under the Federal Food, Drug, and Cosmetic Act, new animal drug applications cannot be revealed to the public and after approval only a limited amount of information is made public. In addition, there is no public opportunity to provide comments or information to FDA about a pending application before an agency decision is made. For GE animals, the public should have the right to review safety data and provide its input in advance of FDA's determination. The Draft Guidance provides no such opportunity. If the public is going to consider purchasing GE animal products, the public needs to be able to see the safety data and the FDA's analysis on the safety issues before those products enter the marketplace. If FDA cannot provide adequate transparency and the opportunity for public comment before a decision is made on a GE animal, then the FDA should request such powers from Congress. At a minimum, the public should have the opportunity to comment before FDA makes a determination on a new animal drug application ("NADA") before it takes any action on an investigational food use request.

In addition to the above general comments, CSPI provides the following additional comments on how FDA can improve its Draft Guidance:

I. **All Major Decisions Made by FDA and The Reasoning Behind Those Decisions Needs to be Made Public.**

All major decisions that FDA makes during the investigation new animal drug ("INAD") process and the NADA process involving a GE animal should be made public. In addition, the FDA's decision document or the analysis that supported FDA's decision should also be made public. The public is entitled to know when GE animals enter the food or feed supply, become commercially available, or produce products that are

commercially available. Therefore, the Draft Guidance should specify that the following FDA decisions will be made public once FDA has made its decision. For each instance below, the Draft Guidance should specifically state that the FDA decision will be made public to put developers on notice that this will occur.

A. Decisions to Exercise Enforcement Discretion.

The Draft Guidance provides for FDA to exempt certain GE animals from the INAD and NADA requirements. If a developer approaches FDA and requests enforcement discretion for its GE animal and FDA decides it will exercise that discretion on INAD and NADA requirements, that decision and the agency's reasoning and analysis should be made public. No GE animal or a product from a GE animal should be allowed to enter commerce without the public knowing that FDA has reviewed the situation and decided not to regulate that animal. In addition, FDA should provide a registry on its website of all individual GE animals and categories of GE animals (e.g. laboratory mice) for which enforcement discretion has been exercised.

B. Determinations to Allow Investigational GE Animals into the Food or Feed Supply.

The Draft Guidance provides a developer the opportunity to request authorization to introduce the GE animal and products from the GE animal into the food or feed supply. While, CSPI hopes this will never happen (or occur very infrequently), if FDA does decide to authorize investigational food use, that decision and FDA's reasoning and analysis should be made public. Members of the food chain and consumers have a right to know if an experimental GE animal is found safe and can enter the food chain.

C. Decisions to Approve a GE Animal.

When FDA completes its review of a NADA and makes a final decision, that final decision with its supporting documents should be made available to the public.

D. Decisions Surrounding Compliance with Requirements under the National Environmental Policy Act ("NEPA").

The Draft Guidance states that FDA will comply with NEPA by requiring an environmental assessment and a "finding of no significant impact," or an environmental impact statement. Those documents should be provided to the public.

II. **FDA's Regulatory Procedures Need to be More Transparent and Predictable.**

Both the regulated community and the public expect that the FDA regulatory process for GE animals will be transparent and predictable. The Draft Guidance should set forth the regulatory procedures in sufficient detail so that individual developers and

researchers know whether their activities are covered by the Draft Guidance and what is expected of them to ensure compliance. The public should also be able to discern when in the development stage a product is required to file an INAD and what is expected of the developer to comply with the INAD and NADA requirements.

When one reviews the Draft Guidance, however, there is currently not enough detail so that all interested stakeholders understand how the regulatory system will be applied to specific GE animals. In many instances, the Draft Guidance identifies that further guidance will be provided. CSPI supports the issuance of additional guidance but asks that it be done as soon as possible and be made public. In other instances, the Draft Guidance asks for the developer to come talk to FDA. While such a procedure is helpful to the individual developer, those discussions are conducted behind closed doors and there is no public record of the decisions made during those discussions. This prevents the public from understanding how different products are being regulated and prevents other developers from understanding what will be required from them (by understanding how other similar products have been regulated). Therefore, in addition to asking developers to “come talk to us,” FDA should provide whatever information and instruction they provide to an individual developer to the public through guidance and other agency documents. Making that information public will further transparency and understanding of the regulatory process and provide more details and predictability to the regulatory system.

Particular areas of the Draft Guidance that CSPI believes need further development are as follows:

- On page 3, the Draft Guidance states that additional guidance will describe how biopharm animals will be regulated and the relationship between the different FDA Centers when regulating those animals. We support the issuance of that guidance and hope it will be a top priority of the agency. GE animals for biopharming is an area that is moving extremely quickly to market and is likely to constitute a number of the first applications of commercial GE animals. Therefore, providing the public with details about how such products will be regulated is needed as soon as possible.
- On page 6, the Draft Guidance discusses the process that will be used by FDA to determine whether it will exercise its enforcement discretion for a particular GE animal. While CSPI is not against FDA exercising such discretion, the criteria that FDA will use to make such a determination should be made public. On the bottom of page 6 and the top of page 7, the Draft Guidance does list some of the factors it will consider for the environmental portion of its decision process. However, the Draft Guidance mentions that it will evaluate “risk factors” without explaining those in any detail. Developers and the public should know what risk factors FDA will review for such GE animals. FDA should either add that information to the Draft Guidance or issue a separate document describing the enforcement discretion process and the criteria it will use in more detail.

- On pages 9 and 10, the Draft Guidance discusses “investigational food use authorizations” and states that the developer should schedule an in-person meeting with FDA to determine “which classes of investigational animals may be suitable for consideration for food use and the nature and extent of data you will need to provide to us to make that determination.” The “classes of investigational animals” that could be introduced into the food supply is information that should be included in the Draft Guidance or otherwise made publicly available before any requests are received and reviewed by FDA. In addition, further guidance should be provided on the data that will be needed for FDA to make an investigational food use authorization decision.
- On page 17, the Draft Guidance states that FDA intends to issue further guidance on “how to meet the GMP regulatory requirements for GE animals.” CSPI supports the issuance of such guidance and requests that FDA expedites its release.
- On page 17, the Draft Guidance discusses the inclusion of an environmental assessment in the NADA application and page 23 further explains this requirement. In both places, the Draft Guidance tells the developer to contact FDA and work closely with FDA to figure out the issues that are to be addressed in the environmental assessment. While each environmental assessment of a GE animal will be unique, there are many issues and areas of inquiry that will be required for all GE animals (or at least for categories of GE animals, such as all fish applications). FDA should issue further guidance on what is to be included in the environmental assessments. The current information provided in the Draft Guidance is inadequate and does not provide a transparent and predictable regulatory procedure for this important area of inquiry.

If additional information is provided in each of these areas, the FDA’s regulation of GE animals will be more transparent and predictable, improving FDA’s overall regulatory process.

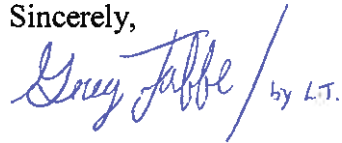
III. **Clarification on the Regulated Article Obligations.**

CSPI is supportive of the Draft Guidance’s conclusion that “all GE animals derived from the same transformation event” contain the same regulated article and only require one NADA. We also support the decision that a single INAD can be established for several different constructs and/or transformations involving the same type of animal and the same introduced gene. However, the Draft Guidance is not clear as to whether a single INAD can be established for using the same construct in different animal species or for transformations with different genes in the same species. If the same animal species is being transformed with different genes that have different phenotypes and might lead to different products, the research surrounding each distinct product using a

specific target gene should require a separate INAD. Clarifying the Draft Guidance to explain how it applies to those different situations would be helpful to both developers and the public.

CSPI appreciates the opportunity to submit comments on FDA's Draft Guidance. If FDA would like more information about any of these comments, we would be happy to meet with you at your convenience.

Sincerely,

A handwritten signature in blue ink that reads "Gregory Jaffe" followed by a diagonal slash and the initials "by L.T." in a smaller font.

Gregory Jaffe
Director, Biotechnology Project
The Center for Science in the Public Interest
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