CENTER FOR
Science IN THE
Public Interest
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By Electronic Submission
Docket No. FDA-2008-D-0394
Food and Drug Administration
Division of Dockets Management
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Re: Comments to Docket No. FDA-2008-D-0394 Regarding the Draft Guidance for Industry Addressing Regulation of Intentionally Altered Genomic DNA in Animals.

The Center for Science in the Public Interest (CSPI)[1] appreciates the opportunity to submit comments on the draft revised Guidance for Industry (GFI) #187 entitled "Regulation of Intentionally Altered Genomic DNA in Animals." CSPI supports science- and risk-based oversight by the Food and Drug Administration (FDA) of new products entering the food supply to ensure they are safe to humans and the environment. However, draft GFI #187 captures every single genomic altered animal and imposes the same regulatory requirements. Instead, FDA should establish a proportionate risk-based regulatory system where the degree of oversight for different genomic altered animals is based on the potential risks they pose.

I. FDA should establish a proportionate risk-based regulatory system for animals whose DNA has been intentionally altered. There should be different levels of oversight based on a product's potential risk.

The scope of the draft GFI #187 is any animal "whose genome has been intentionally altered using modern technologies, which may include random- or targeted-DNA sequence changes including nucleotide insertions, substitutions, or deletions, or other technologies that introduce specific changes to the genome of the animal." Once that condition is met, then the intentionally altered DNA is considered a "new animal drug" and must be approved by FDA. The sponsor must meet all the requirements set forth the Federal Food, Drug, and Cosmetic Act as well as draft GFI #187, which includes generating safety data and conducting a risk assessment.

FDA's proposed regulatory system is neither risk-based nor proportionate. Draft GFI #187 treats all alterations of an animal's DNA **the same** when, depending on the alteration, the potential risk could be extremely different. For example, intentionally making a single

[1] CSPI is a nonprofit education and advocacy organization that focuses on improving the safety and nutritional quality of our food supply. CSPI seeks to promote health through educating the public about nutrition; 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 600,000 member-subscribers to its *Nutrition Action Healthletter* and by foundation grants. CSPI receives no funding from industry or the federal government.

nucleotide deletion to silence a gene to mimic an existing phenotype found in nature does not have the same potential risk as introducing three new genes from a different animal that confer resistance to a disease. Clearly, the single-nucleotide deletion does not have the same risk profile and should not have to submit the same data and analysis as the addition of the three foreign genes. Similarly, silencing one gene in an animal genome does not have the same potential risk as editing 30 different genes in a single animal's genome.

FDA should establish different categories of intentionally altered animals based on their potential risk and then match its regulatory requirements to the potential risk of the products in each category. This might mean that small deletions of genomic DNA mimicking existing alleles in the animal population get little or no oversight, while animals with newly introduced genes producing new compounds or nucleotide deletions in more than a dozen genes require a more thorough pre-market approval process.

The National Academy of Sciences' (NAS) recent report on *Preparing for Future Products of Biotechnology* captured this idea of proportionate risk-based oversight when it stated that the regulatory system should make an initial determination:

> "…of whether the product is *familiar and not complex,* is *unfamiliar or complex,* or is *unfamiliar and complex* when compared to existing biotechnology products. Once a determination has been made, the appropriate processes within the relevant agency (or agencies) would be used to provide the necessary risk analysis to support the regulatory decision. For products that are *familiar and noncomplex*, an expedited process might be used (for example, a notification process). For products that are determined to be *unfamiliar or complex* or *unfamiliar and complex*, new human health and ecological risk-analysis methods might be needed to inform a regulatory decision" (p. 8).

Similarly, the NAS report on *Genetic Engineered Crops: Experiences and Prospects* similarly recommended that whether a product is subject to pre-market approval should be based on "(1) the extent to which the novel characteristics are likely to pose a risk to human health or the environment, (2) the extent of uncertainty regarding the severity of potential harm, and (3) the potential for exposure" (p. 16). FDA should follow the recommendations from those two NAS reports and set forth different categories of products based on potential risk. Then FDA should tailor its oversight for each category to what is needed to ensure that the product is safe. Not all genome edited animals have the same risk profile, and those differences need to be acknowledged and addressed in draft GFI #187.

II. FDA's oversight of intentionally altered genomic DNA in animals should be consistent with the principles set forth in the *Updated Coordinated Framework*.

The *Updated Coordinated Framework for Biotechnology* and the *National Strategy for Modernizing the Regulatory System for Biotechnology Products* both state that federal oversight of biotechnology products should be based on **potential risk** of the final product, not solely on the process by which the product is made. As stated in the *Updated Coordinated Framework*:

- "It is the characteristics of the biotechnology product, the environment into which it will be introduced, and the application of the product that determine risk (or lack thereof).
- Exercise of agency oversight within the scope afforded by statutes should be commensurate with the risk posed by the introduction of the biotechnology product and should not turn on the fact that it was created or has been altered by a particular process or technique" (pp. 7-8).

However, FDA's draft GFI #187 is not consistent with those policy statements. According to draft GFI #187, FDA will not regulate animals with altered DNA differently based on the potential risk or the scientific characteristics of the product. Instead, by capturing all possible animals whose DNA has been intentionally altered under one regulatory scheme, some products may be overregulated when they have minimal to no risk. That type of regulatory system would also waste government resources on applications with little or no risk, leaving less resources for products that raise potential risk issues. Therefore, CSPI recommends that FDA revise GFI #187 so that it defines different categories of products based on their potential risk and then matches those categories to a level of oversight commensurate with the potential risks. Such a system would benefit the public because their tax dollars would be responsibly allocated, and proportionate scrutiny would be given to new products based on potential risk.

CSPI appreciates the opportunity to provide this comment to the FDA. CSPI would welcome the opportunity to meet with the staff at FDA's Center for Veterinary Medicine to discuss the issues addressed in this letter in more detail if that would be helpful.

Sincerely,

Gregory Jaffe
Director, Biotechnology Project
Center for Science in the Public Interest
gjaffe@cspinet.org
(202)777-8369