



November 18, 2008

Docket No. FDA-2008-D-0394  
Dockets Management (HFA-305)  
Food and Drug Administration  
5630 Fishers Lane, rm. 1061  
Rockville, MD 20852

**RE: Docket No. FDA-2008-D-0394 Guidance for Industry: Regulation of Genetically Engineered Animals Containing Heritable rDNA Constructs**

To Whom It May Concern:

The National Milk Producers Federation (NMPF) and the U.S. Dairy Export Council (USDEC) are submitting the following comments to the Food and Drug Administration's (FDA) Notice of Availability entitled Guidance for Industry: Regulation of Genetically Engineered Animals Containing Heritable rDNA; Docket Number FDA-2008-D-0394. NMPF, based in Arlington, VA, develops and carries out policies that advance the well being of dairy producers and the cooperatives they own. The members of NMPF's 31 cooperatives produce the majority of the U.S. milk supply, making NMPF the voice of more than 40,000 dairy producers on Capitol Hill and with government agencies. USDEC is a non-profit, independent membership organization that represents the export trade interests of U.S. milk producers, proprietary processors, dairy cooperatives, and export traders. Its mission is to increase the volume and the value of U.S. dairy product exports.

Dairy producers have routinely been at the forefront of technological innovation in reproduction to enhance the genetic merit of dairy animals. Artificial insemination was first commercialized in the dairy industry over 60 years ago and is used routinely on dairy farms today. Although not as common as artificial insemination, *In vitro* fertilization and embryo transfer have nearly three decades of proven efficacy allowing dairy producers to select their best cows to serve as the foundation for future generations of dairy cattle. Cloning has been conducted on a limited basis in the dairy industry for twenty years, initially in the form of embryo splitting which results in two or more identical offspring from the same zygote. Genetically engineered animals containing heritable rDNA (GE animals) is a future step in the technological innovation in reproduction for dairy animals.

We understand that GE animals that may be developed can be divided into six broad classes based on the intended purpose of the genetic modification: (1) to enhance food quality or agronomic traits; (2) to improve animal health; (3) to produce products intended for human therapeutic use (“biopharm” animals); (4) to enrich or enhance the animals’ interactions with humans; (5) to develop animal models for human diseases; and (6) to produce industrial or consumer products. While the first two uses are of most interest to the dairy industry, our comments are applicable to the use of dairy animals in all of these circumstances. **We support a comprehensive mandatory pre-market approval process for GE animals regardless of their intended use.**

The present debate on GE animals and FDA’s notice of availability of documents refers specifically to the regulatory approval process for these animals. We have carefully reviewed the documents FDA has requested comment on and will provide comments in the following areas: (1) the Draft Guidance for Industry (Draft Guidance); (2) labeling guidance; (3) interagency consultation; and (4) market impacts.

#### **DRAFT GUIDANCE FOR INDUSTRY**

*Approval Process* – We support the use of the New Animal Drug Application (NADA)<sup>1</sup> process as an appropriate mandatory pre-market approval process for the regulation of GE animals. The dairy industry is familiar with the NADA process because it serves as a rigorous standard for the approval of animal drugs allowing the use of approved drugs by veterinarians and producers. This process will assure dairy producers and their customers and consumers about the health and safety of the GE animal and any products that may be derived from its milk.

This NADA process requires a demonstration that the GE construct in the GE animal is both safe and effective for its intended use. The safety of the GE construct in the GE animal would apply to both the health and safety of the animal and any resulting products from that animal that may enter the food or feed supply. We believe that the detailed process outlined by FDA in the Draft Guidance provides an appropriate path.

We caution FDA to be prudent when evaluating the safety of GE animals used for non-food purposes (i.e. “biopharm” animals) to include the risk of accidental introduction of meat or milk into the food system, or the transgene into the larger animal population. In 2002, material from a “biopharm” GE corn that had been test planted was inadvertently mixed with 500,000 bushels of soybeans, resulting in quarantine by USDA to keep the “biopharm” GE corn out of the food supply. An accidental introduction of a “biopharm” animal product into food or transgene into the larger animal population would likely cause adverse market conditions for dairy products (detailed in **Market Impacts**). Prior to any GE animal being approved for non-food purposes, there must be strong safety mechanisms to ensure that they are not accidentally introduced into the food system or the transgene into the larger animal population.

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<sup>1</sup> Federal Food Drug and Cosmetic Act (21 U.S.C. 321 et seq.).

Enforcement Discretion – We encourage FDA to be extremely cautious in the use of Enforcement Discretion (i.e. not regulate) certain GE animals including those that may be regulated by other government agencies and GE animals of non-food species as this would prohibit a review of environmental risks under the National Environmental Policy Act (NEPA).

Investigational Use – We support that the development of GE animals constitutes a clinical investigation requiring where the research is subject to the Investigational New Animal Drug (INAD) process. While in the Draft Guidance FDA encourages a researcher/company to submit an INAD notice early in the developmental stage (only requiring prior to shipment of a GE animal), we believe that for food-producing animals (with transgenes for both food and non-food production) should be required to open an INAD immediately upon production of an investigational GE animal.

Post Approval – We concur with FDA that once a GE animal has been approved through the NADA process the sponsors have “*on-going responsibilities including registration and drug listing, recordkeeping, filing supplements, and periodic reporting*” under the Federal Food Drug and Cosmetic Act.<sup>2</sup>

## **LABELING GUIDANCE FOR INDUSTRY**

We believe it is important for FDA to provide labeling guidance on food products derived from approved GE animals. We wish to make a distinction between milk and meat products from GE animals if it is indistinguishable from milk and meat from conventionally-bred animals (no labeling requirement) from milk and meat products from GE animals that are different from that of conventionally-bred animals (labeling requirement).

Mandatory Labeling – We oppose labeling which differentiates between milk and meat from GE animals if it is indistinguishable from milk and meat from conventionally-bred animals. FDA reached a similar conclusion concerning rbST whereby there could be no special requirement to label milk from cows administered rbST.<sup>3</sup> In the case of *IDFA v. Amestoy*,<sup>4</sup> the court found that consumer interest alone could not justify mandatory label disclosures when there is no human safety or health concerns associated with food products derived from cows administered rBST. However if the GE construct causes the milk and meat from an approved GE animal to be materially different (although established as safe through the NADA process) from that of conventionally-bred animals, FDA should examine if and how these products may be labeled.

Negative Labeling Claims – While negative (or absence) claims are allowed by FDA on some products, the statements must not be false or misleading. For those milk and meat products from GE animals that are indistinguishable from those of conventionally-bred

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<sup>2</sup> Federal Food Drug and Cosmetic Act (21 USC 360, 21 USC 356a, 21 CFR 514.80, 21 CFR 514.8

<sup>3</sup> 59 FR 6279.

<sup>4</sup> 92 F.3d 67 (2d Cir. 1996).

animals any negative claim which leads a consumer to believe that milk and meat from that GE animal are different will be false and misleading. We have great concern that such statements may be allowed in the marketplace with the intention to lead consumers to the belief that milk and meat products from certain GE animals are different when they are not and recommends that FDA pursue vigorous enforcement of labeling requirements. For example, the proliferation of misleading label claims about rBST has prompted several states (including Utah, Kansas, Pennsylvania, Ohio, New York, and New Jersey) to consider label restrictions on milk from cows not treated with rBST. We oppose the allowance of negative label claims because of the propensity for them to be false or misleading.

*Federal Preemption* – As previously stated, we oppose labeling which differentiates between milk and meat from GE animals if it is indistinguishable from milk and meat from conventionally-bred animals. This opposition includes efforts at the state or local level to require mandatory labeling.

The Nutrition Labeling and Education Act (NLEA) established most Federal food labeling requirements as national uniform standards through Federal preemption of state requirements. Under NLEA, no state can directly or indirectly establish any requirement that is not identical to a Federal requirement under the provisions of the Federal Food Drug and Cosmetic Act which is given preemptive effect. Any product introduced into interstate commerce is subject to FDA regulations. In practice courts have interpreted the scope of interstate commerce broadly to include a products ingredients and packaging materials, so we believe milk and milk products from GE animals if it is indistinguishable from milk and meat from conventionally-bred animal would be subject to Federal preemption. We recommend that FDA actively enforce Federal preemption for food labeling requirements milk and milk products involved in interstate commerce.

*Organic Standards* – We believe that the National Organic Program is the preferred alternative for consumers to be able to purchase milk and meat products derived from non-GE animals if it is indistinguishable from milk and meat from conventionally-bred animal rather than a system of misleading negative label claims.

We believe that GE animals (and thereby food products derived from GE animal) are already excluded by the National Organic Program. Under Excluded Methods<sup>5</sup> a “variety of methods used to genetically modify organisms or influence their growth and development by means that are not possible under natural conditions or processes and are not considered compatible with organic production. Such methods include cell fusion, microencapsulation and macroencapsulation, and **recombinant DNA technology** (emphasis added) (including gene deletion, gene doubling, introducing a foreign gene, and changing the positions of genes when achieved by recombinant DNA technology).” Clearly the technologies that produce GE animals are an Excluded Method in the National Organic Program.

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<sup>5</sup> 7 CFR § 205.2

## INTERAGENCY CONSULTATION

Under Executive Order 12866 *Regulatory Planning and Review*,<sup>6</sup> an agency must determine whether a regulatory action<sup>7</sup> is “significant” and therefore subject to Office of Management and Budget (OMB) review and the requirements of the Executive Order. The Executive Order defines a “significant regulatory action” as one that is likely to result in a rule that may: (1) Have an annual effect on the economy of \$100 million or more or adversely affect in a material way the economy, a sector of the economy, productivity, competition, jobs, the environment, public health or safety, or State, local, or Tribal governments or communities; (2) Create a serious inconsistency or otherwise interfere with an action taken or planned by another agency; (3) Materially alter the budgetary impact of entitlements, grants, user fees, or loan programs or the rights and obligations of recipients thereof; or (4) Raise novel legal or policy issues arising out of legal mandates, the President’s priorities, or the principles set forth in the Executive Order.

We have determined that the Draft Guidance is a “significant regulatory action” under the terms of Executive Order 12866. Specifically, we believe that the proposed use of the NADA process may be inconsistent or otherwise interfere with actions that may be planned by other agencies. For example, the U.S. Department of Agriculture (USDA) published a request for information in the *Federal Register* on GE animals indicating the possibility of future regulatory actions regarding GE animals.<sup>8</sup> We also have concern that the annual effect on the dairy sector of the economy may be greater than \$100 million annually (detailed in **MARKET IMPACTS**). Prior to this action being finalized, we recommend that it be submitted to OMB for review with any changes made in response to OMB suggestions or recommendations documented in the public record. During OMB review, we recommend that the U.S. Department of Agriculture, U.S. Environmental Protection Agency, and the Office of the U.S. Trade Representative be included in interagency consultation (detailed in **MARKET IMPACTS**).

## MARKET IMPACTS

*International Markets* – Exports have become an important outlet for U.S. dairy production. In 2007, U.S. dairy exports reached a record of over 17 billion pounds of milk equivalent. This record volume represented 9.1 percent of total U.S. milk production, an all-time high and nearly triple the percentage of just 10 years ago.<sup>9</sup>

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<sup>6</sup> Executive Order 12866 of September 30, 1993, as amended by E.O. 13258 of February 26, 2002 and E.O. 13422 of January 18, 2007.

<sup>7</sup> FDA’s Draft Guidance to Industry demonstrates FDA’s authority to be regulate GE animals under the Food Drug and Cosmetic Act, a regulatory action which subjects any action by FDA on GE Animals to requirements of Executive Order 12866.

<sup>8</sup> 73 FR 54360

<sup>9</sup> Table 50 in 2009 Dairy Producer Highlights. October 2008. National Milk Producers Federation. Arlington, Virginia.

A factor on international markets identified by USDEC is those policies that might be adopted by national regulatory authorities in other countries regarding products from GE animals. For example, if other major suppliers of dairy products such as New Zealand, Australia or the European Union do not permit the commercial sale of such products, then U.S. dairy products would be put at a very significant disadvantage in a number of markets around the world. A similar negative effect could be felt if important buyers such as Japan or leading reference points (such as the EU) for many developing countries do not adopt similar policies to that presented by the FDA. Conversely, if the United States takes into account progress in other key markets in coordinating its approval and commercial release of these products, it is possible that this could help to mitigate what would otherwise be a considerably negative impact on U.S. dairy exports.

Many world-wide buyers are already leery of cloned products and have reported as such to USDEC. The prospect of commercial release of GE products is expected to generate much greater concern given its groundbreaking nature. International efforts are just beginning to address products from GE animals in the marketplace. Codex has recently adopted a Guideline for the Conduct of Food Safety Assessment of Foods Derived from Recombinant-DNA Animals. It is essential that FDA decision-making on GE animal products entering commerce be harmonized with international efforts to attempt to avoid significant negative consequences in international market access for U.S. dairy products.

*Domestic Markets* – While consumer acceptance of new technology is not a mandatory consideration under FDA’s regulatory purview, FDA in the past has recognized the importance of ensuring consumer confidence in new technologies affecting food production.<sup>10</sup> With the impending introduction of rbST, OMB concluded that the need for credible nutrition information and education on rBST is substantial, and could likely reduce consumer concerns about rbST.<sup>11</sup> We believe that the same principles to ensure consumer confidence apply to products derived from GE animals. Strong enforcement to prevent misleading and untruthful labeling is one avenue to maintain consumer confidence (see **LABELING GUIDANCE FOR INDUSTRY**). A negative consumer reaction to milk and milk products due to lack of confidence in safety of GE animals will have a decisive impact on all segments of the dairy industry. We encourage FDA to take all steps necessary to prevent a negative consumer reaction.

## CONCLUSIONS

We support a comprehensive mandatory pre-market approval process for GE animals regardless of their intended use. The FDA Draft Guidance provides a clear pre-market approval process for GE animals through the New Animal Drug Application provisions of the Federal Food Drug and Cosmetic Act. In addition, this process provides for appropriate post-approval monitoring and surveillance necessary for GE animals. Prior to any GE animal being approved for non-food purposes, there must be strong safety

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<sup>10</sup> Executive Branch of the Federal Government (USA). 1994. Use of Bovine Somatotropin (BST) in the United States: its potential effects. Office of the Management of the Budget, Washington, DC.

<sup>11</sup> IBID.

mechanisms to ensure that they are not accidentally introduced into the food system or the transgene into the larger animal population.

We believe it is important for FDA to provide labeling guidance on food products derived from approved GE animals. We wish to make a distinction between milk and meat products from GE animals which is indistinguishable from milk and meat from conventionally-bred animals (no labeling requirement) from milk and meat products from GE animals that are different from that of conventionally-bred animals (labeling requirement).

Finally, domestic and international market implications for the approval of a GE animal are an important consideration. In fact, the Federal government in the past has recognized the importance of ensuring consumer confidence in new technologies affecting food production. We believe that the same principles to ensure consumer confidence apply to products derived from GE animals.

Thank you for the opportunity to submit these comments. If you have any questions or require any clarification about these comments, please contact Jamie Jonker (NMPF Director of Regulatory Affairs) via telephone at 703-243-6111 or email at [jjonker@nmpf.org](mailto:jjonker@nmpf.org).

Sincerely,



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