DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

January 15, 2008

Mr. William Rostov
Mr. Joseph Mendelson III
Center for Food Safety
660 Pennsylvania Ave, SE
Suite 302
Washington, DC 20003

Re: Docket No: 2006P-0415

Dear Mr. Rostov and Mr. Mendelson:

This letter is in response to the citizen petition dated October 12, 2006, and the supplement dated December 6, 2006, submitted by you on behalf of Center for Food Safety and several other petitioners[1] requesting that the Food and Drug Administration (FDA) take various actions related to animal cloning. Specifically, the petition requests that FDA take the following actions:

1. Issuance of an interpretive rule requiring all producers of animal clones to comply with the Federal Food and Drug Cosmetic (sic) Act's new animal drug requirements and FDA's implementing regulations before permitting the sale of any cloned animals or cloned food products, including reviewing the health risks from consuming milk or meat products from the offspring of cloned animals.

2. Conversion of its voluntary moratorium on food or feed from cloned animals into a mandatory moratorium until each product of cloning completes the new animal drug process.

3. Preparation of an Environmental Impact Statement ("EIS") evaluating the environmental and health effects of each new animal drug petition.

4. Creation of an Advisory Committee to address the ethical issues of animal cloning by the Health and Human Services Department.

[1] The other petitioners include the American Anti-Vivisection Society, the Center for Environmental Health, the Consumer Federation of America, the Food & Water Watch, the Friends of the Earth, the Humane Society of the United States, and the Religious Coalition for Reproductive Choice.

We have considered the petition, its supplement, and the public comments received on the petition. In accordance with 21 C.F.R. § 10.30(e)(3), this letter advises you that FDA is denying your petition.

Background

A. Animal Cloning

FDA has been involved in an extensive evaluation of the safety of animal cloning since the late 1990's when it first became apparent that animal cloning could have commercial agricultural applications.

> Since the beginning of livestock agriculture, selection criteria have been applied to foster the propagation of animals with traits more desirable to humans. The expansion of herds with desirable traits has been limited, however, by the reproductive capacity of the species or breed and the prevalence of particular versions of genes (or sets of genes) responsible for those traits in the available gene pool.
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> To help overcome some of these complications, various forms of assisted reproductive technologies (ARTs) have been adopted in animal agriculture for over a century, and at least one (artificial insemination) has been used for several hundred years. These technologies form a continuum that ranges from the fairly minimal assistance provided to animals engaged in natural service through those containing components of significant *in vitro* manipulation such as *in vitro* fertilization and embryo splitting, to the more recent development of somatic cell nuclear transfer (SCNT), or what is colloquially referred to as "cloning."
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> Cloning, or somatic cell nuclear transfer, is a process by which animals are reproduced asexually.... In cloning, a differentiated somatic cell (a non-germ line cell from an existing animal) is introduced to an oöcyte (a cell that is the immediate precursor of a mature egg) that has had its nucleus (and thus its genome) removed, and then, following some manipulations, is induced to start replicating. If all goes well, the dividing cell is implanted into a female animal (dam), continues to develop normally, and is delivered just as any newborn. See FDA's Animal Cloning: A Final Risk Assessment, Chapter II (http://www.fda.gov/cvm/cloning.htm).

B. Regulation of New Animal Drugs

Under the Federal Food, Drug, and Cosmetic Act (Act), the definition of drug in section 201(g) includes "articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals" and "articles (other than food) intended to affect the structure or any function of the body of man or other animals." 21 U.S.C. §§ 321(g)(1)(B); 321(g)(1)(C).

Section 201(v) of the Act defines "new animal drug" as follows:

> any drug intended for use for animals other than man ... (1) the composition of which is such that such drug is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of animal drugs, as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling thereof...; or (2) the composition of which is such that such drug, as a result of investigations to determine its safety and effectiveness for use under such conditions, has become so recognized but which has not, other than in such investigations, been used to a material extent or for a material time under such conditions. 21 U.S.C. § 321(v).

Section 512 of the Act sets out the regulatory scheme for new animal drugs. That section provides for the submission of new animal drug applications to obtain FDA's approval of a new animal drug. In general, section 512 provides for new animal drugs to be approved by FDA based on the demonstration of the safety and effectiveness of the drugs. New animal drugs for food-producing animals require a showing of safety of the edible products from the treated animals. Section 512(a)(1) provides, with certain limited circumstances, that an unapproved new animal drug is unsafe for purposes of section 501(a)(5) and section 402(a)(2)(C)(ii) of the Act. Section 512(a)(1) also provides that an approved new animal drug, with certain limited circumstances, that is used in a manner inconsistent with its approved labeling or that is used in a manner not conforming to its approval is unsafe for purposes of section 501(a)(5) and 402(a)(2)(C)(ii) of the Act. 21 U.S.C. § 360b.

Section 501(a)(5) of the Act provides that a drug is deemed adulterated if it is an unsafe new animal drug. 21 U.S.C. § 351(a)(5). Section 402(a) (2)(C)(ii) specifies that food[2] is adulterated if it bears or contains an unsafe new animal drug. 21 U.S.C. § 342(a)(2)(C)(ii). Section 301 sets out the prohibited acts with regard to adulterated and misbranded food and drugs, many of which require some nexus with interstate commerce. See 21 U.S.C. § 331.

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[2] "Food" is defined in section 201(f) of the Act as "(1) articles used for food or drink for man or other animals, ... (3) articles used for components of any such article." 21 U.S.C. § 321(f).

II. Agency Response to Requested Actions

We address your requests in the same order as they appear in the petition.

A. Your first request is that FDA "issu[e] ...an interpretive rule requiring all producers of animal clones to comply with the Federal Food and Drug Cosmetic (sic) Act's new animal drug requirements and FDA's implementing regulations before permitting the sale of any cloned animals or cloned food products, including reviewing the health risks from consuming milk or meat products from the offspring of cloned animals." We are denying this request.

The petition argues that (1) each of the three steps of somatic cell nuclear transfer, i.e., animal cloning, as well as animal clones themselves fit within the statutory definition of "drug" because each is intended to affect the structure or function of an animal; (2) each of these further fits the definition of "new animal drug" because it is not generally recognized as safe or effective; and (3) each fits the definition of "new animal drug" because it has not been used to a material extent or for a material time. The petition also argues that regulating animal cloning and animal clones as new animal drug is consistent with FDA's regulation of human cloning and genetically engineered animals.

We deny your request to issue an interpretive rule to require the regulation of animal cloning and animal clones as new animal drugs.[3] To the extent that animal clones meet the necessary statutory requirements to be regulated as new animal drugs, at this time, FDA intends to exercise its enforcement discretion. That is, assuming, without here deciding that animal clones could be regulated as new animal drugs, at this time, FDA does not intend to regulate animal clones as new animal drugs. FDA does not actively regulate all products that may fall within its jurisdiction. It considers a number of factors in determining the appropriate regulatory/enforcement strategy it will use for various products and sometimes decides to exercise its enforcement discretion. That is the case here. See Guidance for Industry #179, which sets out FDA's intent to exercise enforcement discretion for animal cloning/animal clones to the extent that they meet the statutory requirements for regulation as new animal drugs.

We think that clones of non-food species do not present any public health concerns. There are no data that show that such animals introduce any new heritable traits into other animals, and such clones are already in distribution, or being used for the preservation of endangered species. For clones of food-producing species, our intent to exercise enforcement discretion is based on (i) the conclusions in the Risk Assessment that edible products from cattle, swine, and goat clones and the progeny of clones of species traditionally consumed as food are as safe as products from conventionally bred animals; (ii) our observation that the voluntary moratorium has been sufficient to protect the public health during the agency's evaluation of clones of food-producing species; and (iii) our conclusion that a continuation of the voluntary moratorium is sufficient to protect the public health as to species other than cattle, swine, and goats.

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[3] For brevity, throughout the remainder of the response, where appropriate, we will use the term "animal clones" to refer each of the three steps of somatic cell nuclear transfer and the resulting animal clone.

We note that with regard to FDA's intent to exercise its enforcement discretion, decisions as to whether to exercise enforcement discretion are made on a case-by-case basis. An FDA decision about whether to regulate (and if so, when and how to regulate) a particular product is the type of decision that falls within FDA's expertise and discretion. FDA has primary jurisdiction to determine whether an article is properly regulated according to the new drug provisions of the Act. See Weinberger v. Hynson, Westcott & Dunning, Inc., 412 U.S. 609 (1973); CIBA Corp. v. Weinberger, 412 U.S. 640 (1973). The Act vests the authority to approve new animal drugs in the Secretary of Health and Human Services, e.g., 21 U.S.C. §§ 360b(b); 360b(n), who, in turn, has delegated that authority to FDA. Through this delegation, FDA has the authority to determine whether a new animal drug is safe and effective under the Act. 21 U.S.C. § 360b. In addition, the agency's decisions about whether, when, and how to regulate a product, and in particular, whether to take enforcement action against a product are committed to the complete discretion of the agency and are not subject to judicial review under the Administrative Procedure Act (APA).

When "agency action is committed to agency discretion by law," judicial review is unavailable. 5 U.S.C. § 701(a)(2). Section 701(a)(2) of the APA precludes review when "the statute is drawn so that a court would have no meaningful standard against which to judge the agency's exercise of discretion [in a particular case]. In such a case, the statute ('law') can be taken to have 'committed' the decisionmaking to the agency's judgment absolutely." Heckler v. Chaney, 470 U.S. 821,830 (1985). In Chaney, plaintiffs sought review of FDA's decision not to bring an enforcement action against the use of certain unapproved new drugs to effect capital punishment. The plaintiffs argued that such drugs had not been shown to be safe and effective for that specific use. When the statute does not provide clear substantive standards, the agency instead makes policy decision relying on its specialized knowledge and expertise and by balancing numerous considerations. As the Court in Chaney explained:

> [The] agency decision [failure to take enforcement action against an unapproved new drug] ... involve[d] a complicated balancing of a number of factors which are peculiarly within its expertise. Thus, the agency must not only assess whether a violation has occurred, but whether agency resources are best spent on this violation or another, whether the agency is likely to succeed if it acts, whether the particular enforcement action requested best fits the agency's overall policies, and indeed, whether the agency has enough resources to undertake the action at all. An agency generally cannot act against each technical violation of the statute it is charged with enforcing. The agency is far better equipped than the courts to deal with the many variables involved in the proper ordering of its priorities.

Chaney, 470 at 831-32.[4]

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[4] See also Community Nutrition Institute v. Young, 818 F.2d 943, 950 (D.C. Cir. 1987), citing Chaney ("FDA enjoys complete discretion not to employ the enforcement provisions of the FDC Act, and those decisions are not subject to judicial review.").

The District Court for the District of Columbia considered similar questions regarding the agency's discretion not to regulate a product as a new animal drug. The plaintiffs challenged, among other decisions, FDA's decision not to regulate a genetically engineered ornamental fish as a new animal drug. The district court dismissed the claims against FDA. See Int'l Ctr. for Tech. Assessment v. Thompson, No. 04-0062 (RMU), Memorandum Opinion (D.D.C. Mar. 30, 2005). The district court later denied the plaintiffs' motion to alter or amend the judgment, reaffirming its previous dismissal of plaintiffs' claim that FDA had improperly refused to regulate the fish. See Int'l Ctr. for Tech. Assessment v. Thompson, 421 F. Supp. 2d 1 (D.D.C. 2006), see also Int'l Ctr. for Tech. Assessment v. Leavitt, 468 F. Supp.2d 200 (D.D.C. 2007) (denying motion for relief from judgment based on newly discovered evidence). The Court quoted its statement from its earlier opinion that "FDA's 'enforcement decisions relating to unapproved new animal drug products are discretionary and are not subject to judicial review under the APA.' Mem. Op. at 18" 421 F. Supp. 2d at 8.

B. Your second request is that FDA "conver[t] ...its voluntary moratorium on food or feed from cloned animals into a mandatory moratorium until each product of cloning completes the new animal drug process." We are denying your second request. We have concluded, per our final risk assessment, that food from cattle, swine, and goat clones, and the progeny of a clone from any species traditionally consumed as food, is as safe as food we eat every day (http://www.fda.gov/cvm/cloning.htm). With regard to other food-producing species, we do not believe that there is a need for a mandatory moratorium. In 2001, FDA asked producers to voluntarily withhold edible products from animal clones and their progeny from the human food and animal feed supply while the agency obtained scientific data on any food safety risks from such products. FDA again made this request when it released the draft risk assessment in January 2007. See 72 FR 136 (January 3, 2007). Producers have agreed to FDA's request. Because the voluntary moratorium has worked well, we are continuing to ask producers of food-producing species other than cattle, swine, and goats to voluntarily refrain from introducing edible products from animal clones into the food or feed supply. See Guidance for Industry #179.

C. Your third request is that FDA "prepar[e] ... an Environmental Impact Statement ("EIS") evaluating the environmental and health effects of each new animal drug petition." The petition indicates that an EIS is necessary to address the effects on animal disease rates given the biodiversity of cloned animals. The National Environmental Policy Act (NEPA) requires federal agencies to consider the environmental consequences of "major Federal actions significantly affecting the quality of the human environment." 42 U.S.C. § 4332(2)(C). Because we are merely adopting a policy that we intend to exercise our enforcement discretion over animal cloning/animal clones to the extent that it meets the statutory requirements for regulation as a new animal drug, we are not taking any "major Federal action." An EIS is not necessary, and we therefore deny this request.

D. Your final request is that FDA "creat[e] ...an Advisory Committee to address the ethical issues of animal cloning by the Health and Human Services Department." The petition states that those issues would include the ethics of animal cloning with regards to

animal welfare, religious concerns, and ways to inform consumers if food is the product of cloned animals or progeny of cloned animals. Your request appears to be directed at the Department of Health and Human Services or to request that FDA take some action on behalf of the Department. We are also denying this request. We do not believe we are required by law to establish an advisory committee on ethical or religious issues related to animal cloning nor do we believe that it is necessary to do so. Nor do we believe we are required to establish an advisory committee to consider animal welfare or consumer information on products. We note that we have considered the animal health impacts of animal cloning. They are discussed in the Risk Assessment. Also the Risk Management Plan discusses the measures FDA is taking to work with other groups to minimize the impacts of the risks to animal health (http://www.fda.gov/cvm/cloning.htm).

III. Conclusion

In summary, for the reasons discussed above, we are denying all the requests in the petition. We again note that the agency's current policy on its intent to exercise enforcement discretion for animal cloning/animal clones can be found in the Guidance for Industry #179 at http://www.fda.gov/cvm/cloning.htm. That guidance also contains our recommendations regarding the use of edible products from clones and their progeny as human food or animal feed. Also on the Web site, you can find our final risk assessment on the food safety risks from clones and their progeny and our risk management plan.

Sincerely,

Randall W. Lutter, Ph.D.
Deputy Commissioner for Policy

cc: Division of Dockets Management (HFA-305)