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Food and Drug Administration  
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Rockville, MD 20852

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**Re: Docket No. 2003N-0573; Department of Health and Human Services, Food and Drug Administration; Draft Animal Cloning Risk Assessment; Proposed Risk Management Plan; Draft Guidance for Industry; 72 Fed. Reg. 136 (Jan. 3, 2007)**

Dear Sir/Madam:

The Biotechnology Industry Organization (BIO) provides the following comments on the documents referenced above. BIO represents more than 1,100 biotechnology companies, academic institutions, state biotechnology centers and related organizations across the United States and 31 other nations. BIO members are involved in the research and development of healthcare, agricultural, industrial and environmental biotechnology products.

BIO members provide industry leadership for the ethical application of animal biotechnology to improve animal and human well-being. The industry seeks to improve global food supply and quality through the application of animal cloning, and thereby provide solutions to issues important to humankind—hunger, health and a sustainable environment. BIO appreciates the opportunity to comment on the Draft Animal Cloning Risk Assessment; Proposed Risk Management Plan; and Draft Guidance for Industry recently published by the United States Food and Drug Administration's Center for Veterinary Medicine (FDA or the Agency). In addition to general comments, specific comments on each of these documents are provided.

## General Comment

BIO supports and agrees with the science-based conclusions of FDA's Draft Animal Cloning Risk Assessment (the Draft Risk Assessment). Edible products from healthy clones and progeny of clones of cattle, swine and goats, pose no additional food consumption risks relative to corresponding products from other sexually-derived animals. In this matter, FDA is in agreement with the National Academy of Sciences, which, in "2002 Animal Biotechnology: Science-Based Concerns," concluded that "The products of offspring of clone(s)...were regarded as posing no food safety concern because they are the result of natural matings," and "In summary there is no current evidence that food products derived from adult somatic cell clones or their progeny present a food safety concern." ([www.nap.edu/books/0309084393/html/](http://www.nap.edu/books/0309084393/html/))

The Draft Risk Assessment recognizes somatic cell nuclear transfer (SCNT) as an assisted reproductive technology (ART) that falls on a continuum of other technology-assisted breeding methods used today in animal agriculture, including artificial insemination, embryo transfer and in vitro fertilization. It is estimated that 75 percent of the milk and 80 percent of the pork produced in the United States comes from animals bred with the use of artificial insemination. The use of embryo transfer has been valuable in capturing the desirable traits of superior females. In vitro fertilization is increasingly being used in production of superior animals eventually used as founder sires. As these examples show, ARTs have been successfully practiced in the agriculture sector. Cloning is simply another ART, which will continue to improve the health of agricultural animals that produce safe meat and milk.

Animal cloning allows for the rapid distribution of the best genetics from proven animals to provide consistent, healthful, and safe meat and milk for human consumption in a reliable manner. The FDA and the food industry are focused on maintaining the highest possible safety, quality, and affordability in the food supply; livestock cloning will contribute dramatically to that goal.

The U.S. companies that have developed cloning technology for agricultural animals share the safety and quality concerns of FDA and the food industry. BIO members recognize the importance of a rigorous, science-based risk assessment process designed to protect the safety of the food supply. The cloning technology providers have continuously improved the technology, collaborated in their research, shared data with FDA and other federal agencies, and openly provided information about the animals and the technology to many different stakeholder groups.

Similarly, BIO supports the FDA's efforts to date in maintaining a transparent dialogue with stakeholders, including the international scientific community. We encourage FDA to continue that transparent dialogue, by collaborating among US federal agencies, and sharing results of the Draft Risk Assessment with international governmental agencies.

BIO supports the responsible use of this technology. Therefore, BIO members will continue to abide by FDA's request to voluntarily withhold the sales of foods and food products from livestock clones and their progeny. However, BIO anticipates that the FDA will end this voluntary moratorium once the Agency publishes a final Risk Assessment.

BIO urges the rapid completion and release of a final Risk Assessment. BIO members believe that governmental support and encouragement of technological advances such as cloning contributes to our competitive advantage both domestically and in global markets. We encourage FDA to proceed without delay.

BIO strongly recommends that, along with the final Risk Assessment, FDA release an industry guidance document setting forth the Agency's position on the labeling of food products from animal clones and their progeny. Consistent with well-established law and longstanding FDA policy regarding food labeling, in the absence of any demonstrated material differences between meat and milk from livestock clones or their progeny, labeling that would specifically target the meat and milk from these animals would be inappropriate, confusing and potentially misleading. FDA has determined that food products from animal clones that pass government food safety inspections would be considered as safe as food derived from sexually reproduced animals. The Draft Risk Assessment further concludes that food from any progeny of a clone poses no more risk than food from any other sexually-reproduced animal. Accordingly, labeling that could imply otherwise should be avoided.

## **Specific Comments**

### **1) Draft Animal Cloning Risk Assessment**

BIO supports and agrees with FDA's conclusion in the Draft Risk Assessment that edible products from healthy clones and progeny of clones of cattle, swine and goats, pose no additional food consumption risks relative to corresponding products from other sexually-derived animals. The Draft Risk Assessment includes detailed reviews of both the health of livestock clones to date, and the relative food safety risks of food produced from clones and their progeny compared with food produced from animals bred through other ARTs. BIO applauds the process conducted by the FDA in compiling the Draft Risk Assessment. In 2003, FDA presented the draft Executive Summary of the Draft Risk Assessment to the Veterinary Medicine Advisory Committee (VMAC) for their critical scientific review. Since that time, the agency has met the VMAC recommendation to include additional data. Subsequently, the agency compiled over 400 scientific references, including data from decades of research, both published and raw. Taking these data, FDA then conducted its own independent statistical analysis, which contributed to the weight of the scientific evidence, and thus, the Agency's conclusion of safety. The Draft Risk Assessment then underwent peer review and approval by three independent scientific experts, whose comments were available on the FDA web site. One of the experts is current Chairperson of the VMAC, a valid linkage to the important role of the agency's advisory committee. Moreover, the conclusions of the Draft Risk

Assessments were reviewed and accepted for publication in a scientific journal (Rudenko, L. and J. C. Matheson. The US FDA and Animal Cloning: Risk and Regulatory Approach. *Theriogenology* 2007; 67: 198-207).

BIO endorses FDA's objectives in performing the risk assessment which were to determine whether cloning introduced any unique hazards to animals involved in the cloning process, and whether the meat and milk derived from them posed different risks from those posed by foods produced by current agricultural practices. The basis for the scientific review was a risk assessment/risk management/risk communication paradigm. This paradigm is not well understood by many, but is a valid means to develop and communicate science-based decisions. The Draft Risk Assessment is therefore, the result of a qualitative analysis that identified and characterized the nature of the hazards that may be introduced into animals as the result of cloning.

BIO strongly supports the two-pronged approach used by FDA to evaluate the potential risks associated with the food products of animal clones. BIO has reviewed the Comprehensive Biological Systems Approach developed by the FDA and finds it to be a valid assessment approach to systematically evaluate all data on animals involved in cloning on a developmental stage basis. Additionally, BIO has critically evaluated the Compositional Analysis Method. These procedures were validated via peer review and acceptance for publication in a scientific journal: L. Rudenko, J. C. Matheson, A. L. Adams, E. S. Dubbin, K. J. Greenlees. Food consumption risks associated with animal clones: what should be investigated? [Cloning Stem Cells, 2004;6\(2\):79-93](#).

In BIO's estimation, the FDA has established the most extensive review to date of the publicly available animal health and food composition data on animal clones and their progeny. BIO strongly supports that the agency's scientific review was a consideration of the weight of the evidence, evaluating all available information in the appropriate context, rather than relying on a single key study, as the basis for the Draft Risk Assessment. These procedures were validated via peer review and acceptance for publication in a scientific journal: L. Rudenko, J. C. Matheson, S. F. Sundlof. Animal cloning and the FDA—the risk assessment paradigm under public scrutiny [Nature Biotechnology, January 2007; 25\(1\):39-43](#). Therefore, using the four steps of this systematic approach, over 400 scientific, peer-reviewed, published references were evaluated from the standpoint of the empirical evidence, considering the biological assumptions, for coherence of the observations with predictions based on molecular mechanisms, and for consistency of observations across all of the species considered, including the mouse model system. It is inappropriate, therefore, to cherry-pick portions of individual research studies and elicit mis-leading interpretations.

FDA discontinued adding new data to the Draft Risk Assessment in 2006. Additional scientific data have been published since that time regarding SCNT that support the conclusions FDA reached in the Draft Risk Assessment. BIO recommends that the results from all recent SCNT studies -- whether positive or negative -- should be included in a final Risk Assessment.

Among the data that should be included in a final Risk Assessment include those recently presented at an international scientific symposium. The International Embryo Transfer Society held a symposium in Kyoto, Japan on January 6, 2007 that focused on cloning technology, "Assisted Reproductive Technologies and Food Safety in Farm Animals." The presenters were from seven different countries. All of the data at that symposium are in agreement with the Draft Risk Assessment conclusions, and include:

- H. Ortegon, D.H. Betts, L. Lin et al. Genomic Stability and Physiological Assessments of Life Offspring Sired by a Bull Clone, Starbuck II. *Theriogenology* 2007; 67: 116-126 ("Offspring of a cloned bull had a normal chromosomal stability, growth, physical, hematological and reproductive parameters.").
- Y. Heyman, P. Chavatte-Palmer, V. Berthlot et al. Assessing the Quality of Products from Cloned Cattle: An Integrative Approach. *Theriogenology* 2007; 67: 134-141 ("In clone and control groups, most parameters measured for health and development of the animals as well as evaluation of milk and meat products were within the normal range for the breed. ..Slight significant difference was observed in fatty acid composition... Nutritional evaluation of milk and meat using the rat model did not reveal any difference between products derived from clones versus controls.").
- M. Panarace, J.I. Aguero, M. Garrote et al. How Healthy are Clones and Their Progeny: 5 years of Field Experience. *Theriogenology* 2007; 67: 142-151 ("In conclusion, cloning had no risks qualitatively different from those encountered in animals involved in modern agricultural practices, although the frequency of the risks appeared to be increased in cattle during the early portion of the life cycle of cattle clones.").
- M. Yamaguchi, Y. Ito, S. Takahashi. Fourteen-Week Feeding Test of Meat and Milk Derived From Cloned Cattle in the Rat. *Theriogenology* 2007; 67: 152-165 (Long-term rat feeding study found "no significant differences in general conditions, death loss, growth, battery of functional observation tests and estrous cycles among groups given diets containing meat and milk powder from non-clone, embryonic clone and somatic clone cattle. Furthermore, no significant changes attributed to consumption of clone meat or milk were detected in urinalysis, hematological and blood chemical, gross pathological or histological examinations. Therefore, we concluded that the physiologic conditions of the rats were not affected by consumption of meat and milk from bovine clones.").
- G. Laible, B. Brophy, D. Knighton et al. Compositional Analysis of Dairy Products Derived from Clones and Cloned Transgenic Cattle. *Theriogenology* 2007; 67: 166-177 (Compositional differences, associated with milk and cheese derived from cloned and transgenic cows, were assessed. "Based on gross composition, fatty acid and amino acid profiles and mineral and vitamin contents,

milk produced by clones and conventional cattle were essentially similar and consistent with reference values from dairy cows farmed in the same region under similar conditions.”).

- S.C. Walker, R.K. Christenson, R.P. Reeves et al. Comparison of Meat Composition from Offspring of Cloned and Conventionally Produced Boars. *Theriogenology* 2007; 67: 178-184 (“Meat composition from offspring of cloned and conventionally produced boars was compared. The “data indicated that meat from the offspring of clones was not chemically different than meat from controls.”).

BIO also recommends that a final Risk Assessment include references that provide clarity on interpretation of the science-based risk assessment process with regard to regulatory approaches. These papers could be provided in an appendix to a final Risk Assessment. Such papers include, but are not limited to:

- H.P.S. Kochlar and B.R. Evans. Current Status of Regulating Biotechnology-Derived Animals in Canada. *Animal Health and Food Safety Considerations*. *Theriogenology* 2007; 67: 188-197.
- L. Rudenko and J.C. Matheson. The US FDA and Animal Cloning: Risk and Regulatory Approach. *Theriogenology* 2007; 67: 198-207.
- L. Rudenko, J. C. Matheson, S. F. Sundlof. Animal cloning and the FDA—the risk assessment paradigm under public scrutiny *Nature Biotechnology*, January 2007; 25(1):39-43.

Finally, BIO recommends that FDA monitor, and consider including in a final Risk Assessment, results from international risk assessments, as other countries complete and publicly report their findings on the safety of food from cloned animals. Both New Zealand and France have released government risk assessments attesting to the safety of foods from livestock clones and their progeny. (New Zealand Food Safety Authority, 2007. Food from cloned animals. Available online at <http://www.nzfsa.govt.nz/policy-law/publications/policy-statements/food-cloned-animals/food-from-cloned-animals-final.htm>; Agence Francaise de Securitie Sanitaire des Aliments, 2005. Risks and benefits related to livestock cloning applications. Available online at [www.afssa.fr/Ftp/Afssa/33773-33774.pdf](http://www.afssa.fr/Ftp/Afssa/33773-33774.pdf)).

## **2) Proposed Risk Management Plan**

With regard to FDA's Proposed Risk Management Plan for Clones and their Progeny (the Proposed Risk Management Plan), BIO supports the FDA's assertion that the Draft Risk Assessment is strictly a science-based evaluation and that the Proposed Risk Management Plan, therefore, need not address any ethical or other non-science-based concerns regarding animal cloning. We strongly support a scientific basis for any risk management proposal, which should be driven by scientifically identified risk or uncertainties. We urge the Agency to remain steadfast in execution of its authority in this regard. BIO supports the risk management approaches presented by FDA, and recognizes that they assist in building public confidence and thus, the success of the technology.

As FDA correctly states in the Proposed Risk Management Plan, many systems (federal, state and local laws and regulations) are in place in the United States to assure the safety of human food. Foods from animal clones would be subject to the same food safety systems as food from any other animal. Therefore, as FDA recognizes, clones that pass the appropriate food safety inspections would be considered as safe as any other animals that pass those inspections. In addition, BIO supports FDA's conclusion that there are no feed risks unique to clones that have been identified.

Similarly, BIO strongly supports the Proposed Risk Management Plan's conclusion that food products from the progeny of clones are suitable to enter the food and feed supply under the same controls as those applied to any other animal that is produced via sexual reproduction. As FDA recognizes, most of the food products resulting from cloning technology will be derived from progeny of animal clones.

BIO members who are cloning technology providers look forward to continuing communications with FDA regarding such issues as the state of the science and changing technology in this area, as well as the development of an international database on animal clone and progeny health and production. We appreciate FDA's commitment to encourage the development of standards of care for animals involved in the cloning process. BIO members welcome the opportunity to work with FDA to develop standards that will encourage the participation of animal owners and the advancement of the technology to continually improve the processes involved.

## **3) Draft Guidance for Industry Number 179**

BIO supports FDA's positions as set forth in the Draft Guidance for Industry Use of Edible Products from Animal Clones or Their Progeny for Human Food or Animal Feed (the Draft Guidance), specifically:

- a) FDA does not recommend any additional measures related to the use of clones for the production of feed for animals that are based on the fact that the animals are derived from cloning.

- b) There is no science-based reason to recommend any additional safeguards or any additional measures related to the use of products from cattle, swine, or goat clones as human food.
- c) No recommendations are necessary regarding the use of the progeny of clones for production of food for humans or feed for animals based on the fact that these are progeny of clones.

Regarding the labeling of food products from livestock clones and their progeny, BIO strongly encourages the Agency to release a guidance document for industry regarding labeling along with the issuance of a final Risk Assessment. Such guidance should specifically address issues of consumer confusion and accuracy that may arise in the course of voluntary labeling.

Based on FDA's failure to find any material safety or nutritional differences between meat and milk from clones and their progeny for which adequate data was available and meat and milk from livestock produced through more conventional breeding methods, and in agreement with the National Academy of Sciences (2004, Safety of Genetically Engineered Foods: Approaches to Assessing Unintended Health Effects, [http://books.nap.edu/openbook.php?record\\_id=10977&page=232](http://books.nap.edu/openbook.php?record_id=10977&page=232) ) mandatory labeling of meat, milk or any food products from these livestock clones (cattle, swine and goats) or their progeny is not appropriate. Moreover, any voluntary labeling regarding the presence or absence of meat or milk products derived from these clones or their progeny would also be subject to the relevant federal law requiring that food labeling be truthful and non-misleading. The food industry would benefit from clarification from the Agency regarding the law's requirements as to labeling, and a guidance document for industry on this topic would be appropriate. Of course, enforcement of the law in this area is critical, and BIO encourages the agency to enforce its labeling policy, as cloning technology is adopted and various labels may be developed by the food industry. BIO also recognizes the labeling policy of the United States Department of Agriculture (USDA), Food Safety and Inspection Service (FSIS), which is in agreement with FDA's policy. Therefore, as appropriate, BIO supports coordination between FDA and FSIS regarding labeling of foods.

#### **4) Support for Coordination Among Federal Agencies and International Outreach**

BIO strongly urges the FDA to coordinate with other federal agencies by sharing the results of the Draft Risk Assessment among its sister agencies and advising them with respect to implementation, leading up to the release of the final Risk Assessment and thereafter. Similarly, BIO encourages FDA's international outreach, education, and communication in order to develop and implement harmonized regulatory processes (ie, the use of risk assessment) to minimize trade implications. FDA can play an important role, in concert with the United States Department of Agriculture (USDA) and the United States Trade Representative (USTR), which will, along with others, lead the U.S. government international outreach efforts. BIO recommends that FDA offer briefings on the status of the science and the final Risk Assessment.

FDA should also leverage its significant scientific and regulatory contacts in other countries, and via international standard setting bodies, to assist other agencies to ensure that science-based regulatory regimes are developed in other countries, that allow the marketing of food from clones and progeny in those countries.

BIO supports continued coordination by FDA with the USDA, FSIS on elements of the Proposed Risk Management Plan and Draft Guidance for Industry regarding USDA's important role in regulation of food safety and food labeling.

## **Conclusion**

BIO members are committed to continuing interaction with the FDA, as set forth in the Proposed Risk Management Plan, to continue to improve this technology for the benefit of human and animal health and well-being. BIO also supports and agrees with FDA's risk assessment process and their conclusion, as stated in the draft Risk Assessment, that edible products from healthy clones and progeny of clones studied pose no additional food consumption risks relative to corresponding products from other animals. Accordingly, no new measures or safeguards specific to clones or progeny of clones of cattle, swine or goat are necessary. Bolstered even further by the more recent supporting health and safety data described above, BIO supports the timely release of a final Risk Assessment to help drive forward the success of this technology.

Once the final Risk Assessment is released, BIO supports the lifting of the current voluntary moratorium on the sale of products from livestock clones and their progeny into the food supply. At that time, to ensure that the Risk Assessment's message is made clear to consumers, we strongly recommend that FDA release industry guidance on labeling. Based on FDA's findings as set forth in the Draft Risk Assessment, BIO would strongly oppose the mandatory labeling of meat, milk or any food products from cattle, swine or goat clones or their progeny. Throughout this process, BIO asserts that FDA has an important outreach role to play both domestically and internationally, to ensure compliance and understanding among federal and state regulatory bodies in this country, and to promote science-based regulatory regimes in other countries that will allow the marketing of food from clones and progeny abroad.

BIO appreciates this opportunity to comment on the Draft Animal Cloning Risk Assessment; Proposed Risk Management Plan; and Draft Guidance for Industry. We look forward to further deliberation, and would be pleased to work with the FDA to provide further input or clarification of our comments, as needed.

Sincerely,



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