

# Exploring the Regulatory and Commercialization Issues related to Genetically Engineered Animals

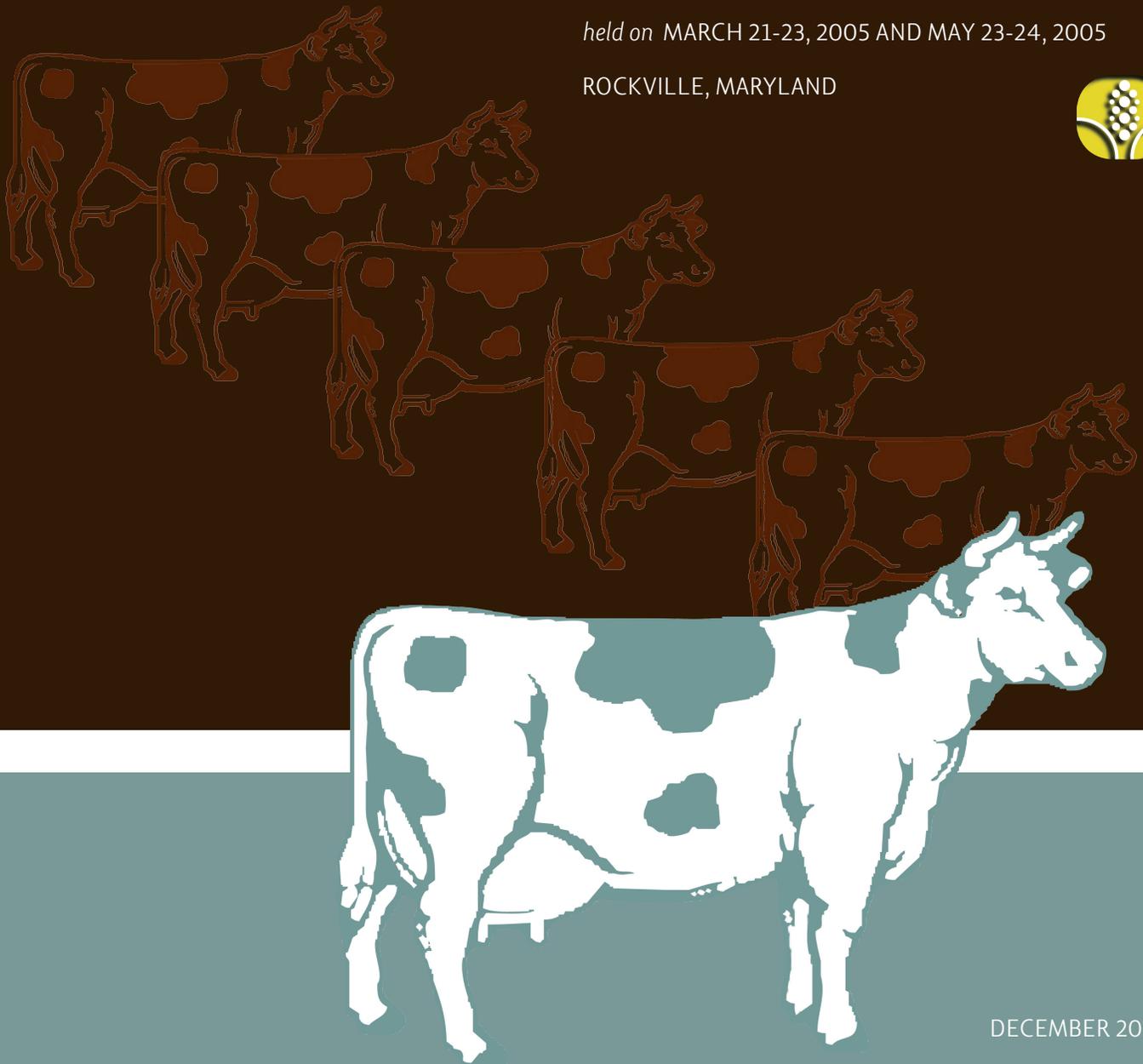
SUMMARY OF TWO MULTI STAKEHOLDER WORKSHOPS

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THE PEW INITIATIVE ON FOOD AND BIOTECHNOLOGY

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The regulatory system for genetically engineered (GE) organisms is not consistent for different products. For example, the U.S. Department of Agriculture (USDA), U.S. Environmental Protection Agency (EPA), and U.S. Food and Drug Administration (FDA) have issued regulations, policy statements, and guidances governing the testing and commercialization of GE plants and have sanctioned 65 such plants for commercial use. Though aspects of this regulatory system are technically voluntary, it is widely believed that all GE plants in commercial production today have gone through the appropriate agency's system.

By contrast, the regulatory system governing GE animals is not as firmly established. The federal government has stated in various documents (such as case studies and letters) that GE animals are currently being regulated, and may continue to be regulated, under the "new animal drug" provisions of the Food, Drug, and Cosmetic Act (FDCA). (Under this scenario, the introduced genetic construct is technically the "drug.") Numerous types of GE animals are currently being developed in university and private laboratories around the country in accordance with the FDA's rules governing research on new animal drugs. Nonetheless, the FDA has issued no formal guidance explaining how the new animal drug rubric applies specifically to GE animals, nor has the agency issued any regulations specific to GE animals. Also, it remains unclear what other agencies and statutory authorities may play a role in the regulation of GE animals. Thus, the formal pathway to the commercialization of GE animals remains somewhat ambiguous and open to speculation.

In July 2004, the Pew Initiative on Food and Biotechnology held a meeting of diverse stakeholders to discuss animal biotechnology. At that meeting, participants pinpointed three key issues relating to GE animals—ethics, regulation, and commercialization—as being of interest for future discussion. We at the Pew Initiative thus set out to sponsor a series of workshops among diverse parties on these topics. The first workshop, held in January 2005, covered ethical and moral considerations relating to GE animals. A summary of that workshop is available on our web site ([www.pewagbiotech.org](http://www.pewagbiotech.org)).

The second and third workshops, held in March and May 2005, covered both regulatory and commercialization issues. This report summarizes both workshops. It contains summaries of the ten presentations given, plus a brief overview of the views and ideas that were expressed by participants in the discussions that followed. Participants did not seek consensus, so the report simply captures the range of issues and opinions that were raised. We hope that this summary will help to forward continuing discussions regarding the regulation and commercialization of genetically engineered animals in the United States.



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## SECTION 1

# INTRODUCTION

THE STARTING POINT FOR THE FEDERAL GOVERNMENT'S REGULATION OF GENETICALLY ENGINEERED (GE)\* PLANTS AND ANIMALS IS THE COORDINATED FRAMEWORK, WHICH WAS ARTICULATED IN 1986 BY THE REAGAN ADMINISTRATION. The Framework's basic principles, which still guide the regulatory system today, are as follows:

(1) Biotechnology as a process is not uniquely risky; (2) regulation should be based on the nature and intended use of the product (i.e., a product-based, not process-based, policy perspective); and (3) existing laws are adequate to regulate the products of biotechnology.

Under the Coordinated Framework, the White House Office of Science and Technology Policy (OSTP) coordinated the efforts of three regulatory agencies—the Food and Drug Administration, the Environmental Protection Agency, and the U.S. Department of Agriculture. The USDA was given responsibility for reviewing GE plants that could be plant pests. The EPA was given lead responsibility for GE microorganisms, pesticides, and pesticide residues. And the FDA was considered responsible for the safety of food, food additives, animal feed, animal drugs and human drugs, biologics, and devices derived from GE plants and animals.

The federal government next communicated about the regulation of animal biotechnology in 2001, when the OSTP and the Council on Environmental Quality (CEQ) released several case studies that illustrated how certain products of biotechnology would be handled within the regulatory system. These case studies were published at the close of the Clinton administration. They have no legal effect, but they have served as an informal guide for how products of biotechnology would be regulated. One case study stated that the FDA would regulate GE salmon as containing a “new animal drug” under the federal FDCA. Another case study said that a transgenic goat that produced a human drug would be looked at as containing both a new animal drug (the rDNA construct) and a human biologic (the resulting human pharmaceutical).

To date, the FDA has not issued any formal policy statements, guidelines, or regulations specific to GE animals. The agency has made several statements in the past few years, however, that have solidified the notion that the agency will regulate GE animals under the “new animal drug” rubric of the FDCA. In May 2003, for example, the FDA sent a letter to university researchers reminding them of the requirements of the FDCA with regard to transgenic animals in research. In October 2003, the FDA announced that the University of Illinois was being

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\*The terms *genetically engineered* (GE), *genetically modified* (GM), and *transgenic* are used interchangeably in this report.

investigated for allowing transgenic pigs into the food supply without regulatory approval. And in December 2003, the FDA announced that GloFish™, a transgenic aquarium fish engineered to glow in the dark, would not be subject to regulation because “...they pose no threat to the food supply” and “[t]here is no evidence that [they] pose any more threat to the environment than their unmodified counterparts which have long been widely sold in the United States.” The GloFish is currently the only GE animal in commercial trade in the United States.

So, while numerous types of GE animals remain in development in public and private laboratories around the United States—guided by the FDA’s regulations governing research on new animal drugs—none have yet gone through the new animal drug approval process from beginning to end and been commercialized.

The lack of concrete FDA guidance or regulations specific to transgenic animals has led to speculation, questions, and concerns about how a regulatory system designed for drugs will function when applied to live animals. For example, consumer advocates—while generally supportive of the mandatory pre-market approval aspect of the new animal drug rubric—have raised concerns about the law’s strict confidentiality provisions, which appear to preclude transparency and public participation in the regulatory review process. Environmental advocates have raised concerns about the lack of a specific environmental mandate in the FDCA. Questions remain, too, about how other agencies’ statutes will be interpreted to apply to GE animals, and how the multiple agencies will work together in the regulatory system.

The Pew Initiative on Food and Biotechnology has undertaken a number of activities relating to GE animals, in an effort to foster understanding and information exchange regarding how the FDA’s regulatory system will function. For example, the Pew Initiative in 2002 sponsored a conference about animal biotechnology regulation entitled “Biotech in the Barnyard.” And the Pew Initiative has issued several reports on the topic, including *Future Fish* (January 2003), *Bugs in the System?* (January 2004), and *Issues in the Regulation of GE Plants and Animals* (April 2004). All of these reports, and the proceedings from the conference, are available at [www.pewagbiotech.org](http://www.pewagbiotech.org).

The Pew Initiative also sponsored a Stakeholder Forum on Food and Biotechnology, the diverse members of which met ten times in plenary sessions from 2001 to 2003. The Stakeholder Forum had three working groups, including one on GE animals. The Animals Working Group was a small but well-balanced group, with members from industry, the public interest sector, and academia. It focused on environmental and food safety issues relating to transgenic animals intended for the food

supply. The group looked at a number of issues and legal authorities, including the new animal drug provisions of the FDCA, the food safety provisions of the FDCA, and the USDA's Animal Health Protection Act.

In order to continue its efforts to foster learning and an information exchange about issues relating to animal biotechnology, the Pew Initiative in July 2004 brought together a diverse array of interested parties to explore how to forward the policy discussions surrounding GE animals. Participants in that meeting agreed that it would be productive to hold a series of workshops on key issues in 2005. The January 2005 workshop covered ethical issues relating to animal biotechnology; a summary of that forum can be found at [www.pewagbiotech.org](http://www.pewagbiotech.org). The March and May workshops covered issues relating to the regulation and commercialization of the products of animal biotechnology. This document summarizes the March and May workshops.

For all three workshops, the approximately 40 participants included animal biotechnology researchers from academia and industry; other representatives from the biotechnology, food, and agriculture industries; consumer, environmental, and animal welfare advocates; ethicists; and federal agency officials. The workshops were convened and sponsored by the Pew Initiative and facilitated by mediators from RESOLVE, a nonprofit dispute resolution and public policy organization based in Washington, D.C. (See Appendices B and C for a full list of participants and staff.)

The scope of the discussions included GE animals and animal clones designed for use in agricultural production. Participants did not address issues specific to "laboratory animals" (i.e., mice, rats, rabbits, and primates) or invertebrates, or marker-assisted breeding. Also not discussed were the distributional impacts of animal biotechnology, such as its possible effects on small farmers or its potential to help reduce world hunger.

The first two days of the March workshop were composed largely of presentations from ten experts. These presentations gave participants a strong grounding in the statutory authorities of the various federal agencies that may regulate GE animals and in the issues relating to the commercialization and marketing of those animals. In the remainder of the March workshop and all of the May workshop, participants then proceeded to share their views on an array of issues relating to the regulation and commercialization of GE animals, in both large group and small group settings. The remainder of this report includes summaries of the presentations and a brief overview of the issues and views raised in the discussions.

## SECTION 2

# PRESENTATIONS

THIS SECTION CONTAINS PARAPHRASED SUMMARIES OF THE PRESENTATIONS GIVEN ON THE FIRST TWO DAYS OF THE MARCH WORKSHOP. The question and answer sessions following each presentation are also summarized. The first day's presentations concerned possible regulatory authorities for governing genetically engineered animals. The Pew Initiative's founding Executive Director Mike Rodemeyer began the day with an overview of the Coordinated Framework and the Pew Initiative Stakeholder Forum; his remarks were used as the basis for the introduction to this report and thus are not paraphrased here. Mike Taylor of Resources for the Future (and formerly with the Food and Drug Administration) spoke next about the 2002 National Academy of Sciences report on science-based concerns relating to animal biotechnology. In the next four presentations, current or former federal agency officials described for workshop participants the legal authorities implemented by those agencies that may relate to transgenic animals. These speakers included Holly Wheeler of the U.S. Department of the Interior; Tom Bundy, formerly with the U.S. Department of Agriculture; Fred Degnan, formerly with the Food and Drug Administration; and Larry Culleen, formerly with the Environmental Protection Agency.

The presentations on the second day covered topics relating to the potential commercialization and marketing of transgenic animals. First, Jim MacDonald of the USDA's Economic Research Service gave an overview of the U.S. marketing structure for livestock. A three-member panel of speakers then talked from the perspective of specific product or service providers in the livestock markets. These speakers included Cari Wolfe of the American Jersey Cattle Association, Jim Riddle of the USDA's Organic Standards Board, and Will Pape of AgInfoLink Global, Inc. Steve Tanner of the USDA's Grain Inspection, Packers, and Stockyards Administration then spoke about lessons that can be learned from the grain industry regarding the tracking and identification of GE animals. The final presentation was a short talk given by Tom Bundy and Mike Rodemeyer, at the request of workshop participants, on the National Environmental Policy Act.

## ► MICHAEL TAYLOR

### OVERVIEW OF THE NAS REPORT ANIMAL BIOTECHNOLOGY: SCIENCE-BASED CONCERNS

MIKE TAYLOR is a Senior Fellow at Resources for the Future; he formerly served as Administrator of the USDA's Food Safety and Inspection Service (FSIS) and as Deputy Commissioner for Policy at the FDA. He was a member of the National Academy of Sciences (NAS) committee that developed the 2002 report *Animal Biotechnology: Science-Based Concerns*, and he spoke to workshop participants about that committee's findings. His comments are paraphrased below.

The NAS report *Animal Biotechnology: Science-Based Concerns* is now about two-and-a-half years old. It was the product of a group effort, as all NAS reports are. It was a group of scientists primarily, though the committee included two nonscientists. (I was one of them.) This membership reflected the fact that the science issues and the social and policy issues are essentially inseparable. I will talk first about the purpose of the report, then give a synopsis of the risk issues identified, and then discuss the policy and institutional issues specified in the report.

This report was an effort by the FDA to get ahead of a set of issues, and the agency deserves credit for asking for the report from the NAS and for underwriting the process. The committee was specifically charged with identifying and prioritizing science-based concerns relating to animal biotechnology. The committee did not make recommendations. When we started, in the fall of 2001, the FDA was in the process of considering the safety of genetically modified (GM) salmon and milk from cloned dairy cows, so those cases provided some framework and context.

The committee first had to grapple with how to approach risk assessment regarding the products of animal biotechnology. The two major categories of risk were food safety and environment. We found that the traditional framework of food safety assessment can be used to consider the safety of food from GM animals. As with any food, you have to ask: Are we introducing something into the food supply that is hazardous? That is a common food safety question, and it parallels the kinds of questions asked about GM plants. The basic framework for analysis is thus traditional. For GM animals, the data needed to answer the question are not so traditional, since you have to look at biological expression products. But the initial question is, "What expression products produced as a result of the genetic modification are likely to remain in food?"

The environmental risk side was far more difficult. We are talking about ecological risk assessment in elaborate natural systems. You have to ask: Does the introduction of a changed organism change the ecological system? It's a complex question. It's challenging to know how to assess environmental risk, with all its attendant uncertainties. "Uncertainty" became a bit of a theme in this part of the report.

In order to prioritize the risk concerns in the report, the committee used its best judgment regarding what is known about a potential change. We didn't use a rigorous, data-driven approach to prioritizing concerns. But we gave it our best shot.

So, let's look at the risk issues identified in the report. First we'll look at food safety. (See box below.) The overall concern level for food safety was determined to be low to moderate, mostly because we have a familiar framework for looking at food safety hazards, and we have enormous expertise and a good ability to define potential hazards. The report did mention three specific food safety concerns. The first is allergenicity. This deserves to be at the top of the list because of concerns about the allergenicity of new proteins. There are lots of issues about how to anticipate allergenicity adequately. But it's not a new issue, and it's manageable. The second risk issue is bioactivity. If we put a functional protein like a growth hormone in an animal, can that affect the person who consumes food from that animal? This is a speculative question, but one that needs to be addressed. The third issue is the toxicity of unintended expression products. This is not of particularly great concern in regard to GM animals intended for the food supply, but it needs to be thought about and anticipated in a risk assessment.

Because of the pending review of milk from cloned dairy cows, the committee did look at that issue a bit. We felt that, based on our understanding of the technology, there wasn't a reason to be greatly concerned. But it does depend on the technique used to produce the animal. And there needs to be some confirmatory data. It's not enough to say that we have confidence that the risk is low. It needs to be proven that the nutritional profile does not change and that no unintended and potentially harmful expression products appear.

The environmental concerns are more difficult to sum up. They are far more unpredictable and complicated. But the committee catalogued the possibilities. The focus was ecological risk. To assess ecological risk, you first have to look at the possibility that a transgenic animal will enter the environment. This will differ based on the animal, of course. The probability is higher for a fish than a cow. The second factor affecting risk is, will it become established in the environment? And finally, will it in fact disrupt the receiving community? In other words, will it interact with and affect the success of other animals in a detrimental way? That was the starting point for the analysis. We said that the potential for risk was affected by the animal's ability to escape, disperse, and

#### FOOD SAFETY CONCERNS

- Overall concern level: Low to moderate
- Range of issues
  - Allergenicity – potential hazard with any novel protein
  - Bioactivity – if performance-enhancing proteins enter food
- Toxicity – of unintended expression products
- Milk from cloned dairy cows – concern low but confirmatory data needed

become feral; the nature of the new trait (its fitness and adaptability); and the nature of the receiving community itself (i.e., whether it is stable, or liable to be upset by a new introduction).

The report contains a list of possible adverse impacts to the environment from GM animals. (See box below.) For example, a GM animal could competitively displace other animals; the ecological balance could be disrupted; the mating of a transgenic animal and a nontransgenic animal might create a new animal with some different level of fitness; and the introduction of sterile animals could disrupt the reproduction of a naturally occurring group of animals. Clearly, environmental risk was identified as the greatest concern, largely because of the complexity and level of uncertainty. How do we assess ahead of time these potential ecological effects? Do we really have the models and data needed to assess environmental risk?

A third area of potential concern—in addition to food safety and environmental concerns—is animal health and welfare. (See box on the following page.) Everyone recognized that this needs to be addressed, but it isn't easily addressable. Some of the potential problems are as follows. There is a history of "large offspring syndrome" among transgenic animals. This can have damaging effects on the mother during delivery and can affect the survival of the offspring. There have also been physical abnormalities in transgenic offspring due to unintended mutations or uncontrolled gene expression. These can result in pain, suffering, and/or disability for the resulting animals. We also recognized, however, that the technology has potential benefits for animals, including increased disease resistance and the ability to reduce pain and suffering in other ways.

So, those are the technical issues raised by the committee. But the committee felt it was impossible to look at those issues and not also look at policy and institutional issues.

Among the policy and institutional issues discussed by the committee was scientific uncertainty. The report mentioned three levels of uncertainty: (1) statistical uncertainty (in which you have a clear model for understanding risk, but not ample data), (2) model uncertainty (in which it's not clear if you have the right model for assessing risk—for example, do we understand enough about ecological systems to assess the ecological risk of an introduced animal?), and (3) fundamental uncertainty (in which you don't know what you don't know).

## ENVIRONMENTAL CONCERNS

Potential harms include:

- ▶ Altering the ecologic balance regarding feed sources and predators
- ▶ Introducing transgenes that alter the fitness of existing populations
- ▶ Disrupting reproduction patterns and success

Concern high but uncertainty pervasive as to:

- ▶ Actual likelihood of harm: How real are the hazards?
- ▶ Models and data required to assess risk: How do we determine the magnitude of the risk prior to introduction?

The point of looking at policy and social issues was not to say that societal concerns should affect scientific decisions, but societal concerns will (and should) affect scientific processes.

► Michael Taylor

The technology is potentially sufficiently novel that we may miss altogether some potential effects. The committee felt this uncertainty will affect the scientific processes used to evaluate the technologies. If there is model uncertainty, for example, then we need some way to get scientists together to discuss the models and develop some consensus around them. It's not fair to leave the agencies by themselves to figure this out, since these are such new scientific issues.

The uncertainties will play into policy issues too. For example, what do we mean by "safe" if there's a high level of uncertainty? How do we manage uncertainty in determining safety? The committee looked at the existing policy context for making these decisions. The food safety standards seem clear, in the view of the committee. But the environmental safety standards are unclear. What is "safety" regarding transgenic salmon, for example? There is no safety standard there.

Regarding institutional roles and capacities, a potentially large number of agencies have roles in these issues. These may include the National Marine Fisheries Service, the Army Corps of Engineers, the USDA, EPA, FDA, and state agencies. A lot of questions exist about the proper roles of each of these agencies. In particular, there seem to be limits to the FDA's legal authority to oversee environmental issues. Also, coordination among the agencies needs to be bolstered.

The point of looking at policy and social issues was not to say that societal concerns should affect scientific decisions. But societal concerns will (and should) affect scientific processes. For example, how do you bring the scientific community broadly into regulatory decision-making? Given the range of issues involved, particularly on the environmental front, the agencies need to define the boundaries of what they will consider. If the FDA cannot have publicly acceptable boundaries regarding its decision-making, then that will affect credibility. The committee's view is that other forums need to be created to deal with social concerns, so the regulatory agencies can deal with the science. ◀

#### ANIMAL HEALTH AND WELFARE

- Large offspring syndrome and other reproductive problems, including early death of offspring
- Physical abnormalities of offspring due to unintended mutations or uncontrolled gene expression
- Potential for animal welfare *benefits* by increasing disease resistance and reducing the pain and suffering of food animals

IN THE BRIEF QUESTION AND ANSWER SESSION THAT FOLLOWED,

one person noted that transgenic animals would likely be food sources for bacteria, flies, and insects, and that they also produce manure. He wondered if the committee considered environmental risks relating to those factors. Bill Muir, a workshop participant who was on the NAS committee, said those issues were discussed, and it was decided that they would be handled in a risk assessment for a transgenic animal in the same way they would be handled in a risk assessment for any other animal.

Another participant asked about a statement on Mr. Taylor's last slide, which said, "Social concerns should not affect scientific decisions." She asked what he meant by "scientific decisions." Mr. Taylor said that he was referring to regulatory decision-making at the FDA. The FDA's science-based regulatory decisions, he said, are not a discovery process. They involve applying a set of data to a standard and making a decision about whether or not the standard is met, based on the data. So one objective should be, he said, to find a way to maintain the integrity of the risk assessment and not have social concerns affect the agency's scientific decision-making.

► HOLLY WHEELER  
*STATUTORY AUTHORITIES OF THE U.S.  
DEPARTMENT OF THE INTERIOR AND THEIR  
POTENTIAL RELEVANCE TO GE ANIMALS*

HOLLY WHEELER is an attorney with the U.S. Department of the Interior (DOI). She spoke about the statutory authorities of the DOI that may be relevant to transgenic animals. Her paraphrased comments are below.

I am currently an attorney with the Department of the Interior. Please be aware that, as a representative of the federal government, my ability to share my personal opinions on policy issues is limited.

The DOI contains a number of agencies, including the Fish and Wildlife Service (FWS), the National Park Service, the Bureau of Reclamation, the Bureau of Indian Affairs, the U.S. Geological Survey, the Office of Surface Mining, the Minerals Management Service, and the Bureau of Land Management (BLM). I'm an attorney for the FWS, and so I will focus mostly on that agency's authorities, which deal mostly with conservation law. I will touch on the authorities that affect other agencies as appropriate.

Within the DOI, there are no authorities I know of that deal specifically with GM animals. As a general conservation and land management department, the DOI implements two types of laws: (1) regulatory authorities that govern the conservation of fish and wildlife, and (2) land management authorities. The agencies I mentioned manage, all told, a large chunk of federal land under U.S. jurisdiction. Another fact to keep in mind is that the FWS and other DOI agencies do not regulate livestock or domestic animals. We regulate plants and wildlife—though not all of them. The states have primary jurisdiction over numerous species of wildlife. White-tailed deer, for instance, unless on federal land, are under state jurisdiction. That is the case for many wild animals, unless authority is transferred to the federal government in part or in whole.

So, I'll first give you an overview of the primary regulatory authorities implemented by the FWS. Let's discuss the Lacey Act first. Three laws, each dealing with separate legal issues, are all called the Lacey Act, so it's very confusing. I'll talk about two of them today. The first part that we call the Lacey Act is the "injurious species" aspect. (See box on the following page.) This part is very old; it was enacted in 1900, when issues relating to invasive species were coming to the fore. This Lacey Act prohibits the interstate transport and importation of injurious wildlife species, including wild mammals, wild birds, fish, amphibians, reptiles, mollusks, and crustaceans. It doesn't extend to invertebrates other than mollusks and crustaceans. The animals must be injurious to humans, agriculture, horticulture, forestry, wildlife, or the wildlife resources of the United States. So, to fall under this part of the Lacey Act and be listed as "injurious" by the FWS, an animal must fit into one of the designated categories of species and be injurious to one of those specific interests. The FWS can authorize, by permit, the importation or interstate transportation of an injurious species for zoological, educational, medical, or scientific purposes.

So, would GM wildlife be included under this Lacey Act? Could the FWS list a transgenic animal as "injurious"? We are considering these questions within the agency right now. This part of the Lacey Act has not been amended significantly since 1960, so it certainly predates GM animals. In my view, however, strong arguments could be made that you could list such a species as "injurious" under this law if it met all requirements. Nothing in the law or in the legislative history indicates that Congress only had naturally occurring forms of these species in mind. Of course, genetic modification could work in one of two ways. It could either create something new that is injurious, that wasn't before, or it could remove the injurious traits of a species. In any case, it's an interesting law that is difficult to assess, because it was developed so long before current scientific advances.

The second part of the Lacey Act I'll talk about is commonly called the Lacey Act Amendments of 1981. (See box below.) The Lacey Act Amendments of 1981 make it a federal violation to, among other things, transport wildlife across state lines that was taken, possessed, transported, or sold in violation of a state law. For example, if someone possesses wildlife in violation of a state law, and then they move that specimen across state lines, it becomes a violation of this federal law. "Fish and wildlife" under this law includes all invertebrates and vertebrates, alive or dead. I'm not aware if there's ever been a violation of this law involving a transgenic species.

The third law I'll discuss is the Endangered Species Act (ESA). Some aspects of the ESA could affect transgenic animals. It is administered jointly between the DOI and the Department of Commerce. Fish, wildlife, or plants that are determined to be threatened or endangered are put on a list. The FWS has jurisdiction over terrestrial and freshwater species; the Department of Commerce's National Oceanic and Atmospheric Administration (NOAA) has jurisdiction over marine species. By statute, an insect species that has been determined to be a "pest" cannot be listed as endangered.

The part of the ESA that is most relevant here is the consultation requirement in Section 7. Under Section 7, any federal agency must consult with the FWS or NOAA if that agency is going to take any action that may affect a species (or critical habitat for a species) that is listed under the ESA as threatened or endangered. "Action" is defined broadly to include the promulgation of regulations, the issuance of permits or licenses, or other any action that directly or indirectly modifies land, water, or air. Under Section 7, the two agencies

#### THE LACEY ACT

Prohibits the interstate transport and importation of injurious wildlife species, including wild mammals, wild birds, fish, amphibians, reptiles, mollusks, and crustaceans.

#### THE LACEY ACT AMENDMENTS OF 1981

Make it a federal violation to transport wildlife across state lines that was taken, possessed, transported, or sold in violation of a state law.

Importers and exporters have to file declarations, import and export through designated ports, and meet other requirements. Transgenic wildlife would be included under these requirements if they meet the criteria under the law.

► Holly Wheeler

consult, and the consultation culminates in a biological opinion. The opinion may include an "incidental take" statement. That's a liability shield for that agency in case they "take" a listed plant or animal in the course of conducting the action. A biological opinion also includes measures to minimize impacts to the species. I know of only one Section 7 case involving a transgenic species. It involved a nonprofit environmental organization suing the EPA, alleging failure to consult under the ESA regarding transgenic plant pesticide products.

Section 9 of the ESA is also relevant. Section 9 prohibits the "taking" of any listed species, unless that taking has been authorized. Any importer or exporter of fish or wildlife also has to be licensed under Section 9. This is true for importers and exporters of all species (with a few exceptions), not just species listed as threatened or endangered. Importers and exporters have to file declarations, import and export through designated ports, and meet other requirements. Transgenic wildlife would be included under these requirements if they meet the criteria under the law.

I want to elaborate here on the concept of "take." Several laws prohibit the "taking" of protected wildlife. The ESA is one of them, but the Marine Mammal Protection Act and the Migratory Bird Treaty Act also have such provisions. "Take" includes lethal take (killing), but it also may include "harassment" or "harm." "Harm" under the ESA has a habitat component; it includes significant habitat modification that actually kills or injures listed fish or wildlife. Also, the prohibition against take includes directed take (like shooting a listed species), but it also includes incidental take—accidentally or unintentionally causing the take of a protected species. Those laws then have a system to get authorization if you think there might be a problem. The definition of "persons" who can be held liable under these laws is also important. "Person" can be a corporation or partnership, or a government agency, in addition to an individual person.

Another law I will touch on is the Nonindigenous Aquatic Nuisance Prevention and Control Act of 1990. This law deals with ballast water exchange and the unintentional introduction of invasive species. I'm not sure how directly relevant it is to transgenic animals. But it is relevant to invasive aquatic species, like zebra mussels. The Aquatic Nuisance Species Task Force, which is set up under this law and is jointly chaired by the FWS and NOAA, addresses unintentional introductions and develops control and monitoring programs for problem species.

I want to mention briefly international wildlife laws. The U.S. is not a party to the Convention on Biological Diversity (CBD), so we are not held to its provisions. But, it has articles on access to genetic resources and access to and transfer of technology, including genetic resources. This clearly has implications for genetic modification. We are a party to CITES, the Convention on International Trade in Endangered Species of Wild Fauna and Flora. CITES, which has 168 parties to it, is the major international treaty regulating trade in species that are threatened by trade. It regulates import and export through a system of permits. It is similar to the ESA in that it doesn't cover all species. Countries meet every two or three years and vote on which species will go on the CITES lists. The countries try to work by consensus. CITES has never

addressed transgenic animals specifically, but countries have started to raise invasive species and genetics issues. The parties to CITES have passed three resolutions that are relevant here. One calls on all parties to consider the problems of invasive species when developing national legislation regarding trade in live animals and plants. Also, a couple of resolutions call for synergy between CITES and the CBD. These are very broad, and no one knows what they will mean in practice. But it's clearly a movement we'll be hearing more about in the future.

Finally, I'll talk about the DOI's land management authorities. The issue of the effects of transgenic animals could arise if they are released on federal lands either intentionally or unintentionally. The legal authority governing the national wildlife refuges is the National Wildlife Refuge System Improvement Act. Under FWS regulations, anyone who wants to collect plants or animals from (or release plants or animals onto) refuges is prohibited from doing so unless authorized by permit. The National Park Service has its Organic Act, a broad law that sets standards for the management of national parks. They have programs for dealing with invasive species. Also, notably, their 2001 management policy specifically addresses the issue of bioengineered products. The policy states that an application for the release of any bio-control agent or bioengineered product related to pest management activities must be reviewed by a designated Integrated Pest Management specialist in accordance with a director's order. Finally, the BLM is governed by the Federal Land Policy and Management Act, which is mostly a planning authority for the management of the BLM's vast land holdings in the West. There are no BLM regulations specific to transgenic animals. ◀

#### IN THE QUESTION AND ANSWER PERIOD THAT FOLLOWED, ONE

participant noted that, even though the U.S. is not party to the Convention on Biological Diversity, the Lacey Act federalizes crimes that are committed under other jurisdictions. Does that include international law? he asked. In other words, could Americans be held to comply with the CBD via the Lacey Act, even though we are not a party to the CBD? Ms. Wheeler explained that the CBD is different than, say, CITES. CITES has specific, detailed requirements for exporting and importing species. The CBD is much more general; it contains policy statements rather than details. Countries are supposed to adopt those policy concepts into their own national legislation. So one country may have or may develop domestic legislation based on the CBD that regulates, for example, sale of a species. If someone in the U.S. imports that species, which was sold in violation of the country's domestic law, that would be a violation of the Lacey Act. So, the Lacey Act would not come into play if something were just a violation of the CBD in general, but it does come into play if an action constitutes a violation of another country's domestic law regulating take, possession, transportation, or sale. Ms. Wheeler added, however, that it can be difficult for the U.S. government to prove a violation of foreign law.

Another workshop participant asked for clarification regarding how the FWS differentiates between domestic and wild species (since the agency does not regulate domestic animals). At what point do cultured catfish become domestic catfish? he asked. Also, zebra fish have been in captivity for 100 years—are they considered domestic or wild? When does something become “domesticated”? Ms. Wheeler said she could not give precise definitions on the spot. She noted, however, that the agency’s interpretation is that simply removing something from the wild, even for multiple generations, does not make it domesticated. Zoo animals, propagated in captivity, are not considered livestock or domestic animals. So, Ms. Wheeler said, just holding it in captivity does not change its status as wildlife.

One workshop participant said that massive traffic in transgenic invertebrates is already taking place. He wondered if the FWS was concerned about that. Ms. Wheeler she was not the best person to answer that question, but that other FWS colleagues would have an answer. Ms. Wheeler did note that the injurious species portion of the Lacey Act does not include invertebrates except for mollusks and crustaceans. However, if a state has prohibited the taking, possession, transportation, or sale of an invertebrate and then someone moves it across state lines, the Lacey Act Amendments of 1981 would apply. Under the ESA, if someone is working with a transgenic invertebrate, and a federal agency has to approve it or license it, and the agency’s action may affect an endangered or threatened species, then the agency should consult with the FWS.

A participant then asked Ms. Wheeler to describe the “citizen suit” provisions of the ESA. Most lawsuits against the federal government, Ms. Wheeler explained, fall under the Administrative Procedure Act. That law puts various limits on citizens’ ability to sue federal agencies. The ESA has a citizen suit provision that allows citizens to bring lawsuits alleging violations of the ESA, including lawsuits against federal agencies. If someone is causing a take, Ms. Wheeler said, under most federal laws the federal government is the appropriate party to bring an enforcement action. But under the ESA a private person can sue someone directly for causing a take. An environmental group, for example, could sue a land developer or a timber company for an alleged take without the appropriate authorization. The federal agency does not have to be a party to the case.

This participant also asked if the FWS has done any consultations on transgenic fish. Ms. Wheeler said she thought not, but was not sure. The closest she knew of, she said, was a consultation on the effect of nonnative salmon in aquaculture on Atlantic salmon. The FWS was aware at the time, Ms. Wheeler said, of the possible future use of transgenic salmon in aquaculture, but that issue was not specifically a part of that consultation. Another participant clarified that, in that consultation, the Army Corps proposed prohibiting transgenic salmon from being used in that case, because they wanted the opportunity to look at transgenics separately.

► THOMAS BUNDY  
*STATUTORY AUTHORITIES OF THE U.S.  
DEPARTMENT OF AGRICULTURE AND THEIR  
POTENTIAL RELEVANCE TO GE ANIMALS*

**TOM BUNDY** formerly served as Deputy Assistant General Counsel at the U.S. Department of Agriculture. He talked to workshop participants about the USDA authorities that may be applicable to the regulation of transgenic animals. His paraphrased remarks are as follows.

In the mid-1980s, a House of Representatives oversight committee asked the USDA to consolidate its quarantine authorities. Nothing really gained traction in the animal arena until the plant industry got behind the Plant Protection Act (PPA). Then there was a big push to get something similar on the animals side. The result was the Animal Health Protection Act (AHPA), which ultimately passed in 2002. (See box at right.) The AHPA is in some ways similar to the PPA, but in some ways different. The scheme of regulation under the PPA is not automatically transferable to the animals side.

It took two years (from 2000 to 2002) to push the AHPA through the legislative process, in part because industry was not unanimous in support of it. There's little legislative history behind the AHPA regarding the intent of Congress. So, their intent must be figured out from the law itself, which is not easy in many respects. The AHPA is a consolidation of a hodgepodge of animal quarantine laws. There is broad authority under the AHPA to regulate animals, articles, means of conveyance, and anything else that might transmit diseases or pests of livestock. If the Secretary can do something under the old quarantine laws, he can do it under the AHPA. But he can do more as well. The purpose of the AHPA is to prevent the introduction and dissemination of diseases and pests of livestock.

The Secretary takes action under the AHPA with regard to the importation and interstate movement of diseases and pests of livestock. The law relies on states to take action within the states. The Secretary has three ways to regulate: General authority, emergency authority, and extraordinary emergency authority. The use of one type of authority does not preclude the use of the others. General authority can be used at any time. The Secretary declares an extraordinary emergency when he decides that a state is not taking sufficient action to

**ANIMAL HEALTH PROTECTION ACT**

- Passed in 2002
- Modeled after the Plant Protection Act
- Consolidation of animal quarantine laws
- Used to regulate the importation and interstate movement of diseases and pests of livestock

prevent the dissemination of a livestock disease or pest. This authority can be brought to bear against transgenic animals in the same manner as for other livestock. Generally it would apply to post-market and post-release activities, though parts are also applicable to pre-market and pre-release activities.

Under the AHPA, the Secretary has general authority to hold, seize, quarantine, treat, destroy, dispose of, and take other remedial measures with regard to almost anything that may spread a livestock disease or pest. He has the authority to take samples from animals that are moving interstate or into the United States from another country, and to hold those animals until the tests come back. He has specific authority to draw blood and do testing at points of concentration like slaughterhouses. If the Secretary is looking for one thing and happens to find something else of concern to another agency, he can refer it to that agency.

Action can be taken with regard to animals, their progeny, articles, and/or means of conveyance coming from a foreign country or moving interstate. The Secretary can take action when he has reason to believe that the animal, article, or means of conveyance may have carried or may have been affected with or exposed to a disease or pest at the time of movement, or if the animal was moved in violation of the AHPA, its regulations, or an order of the Secretary. As an example, a herd of sheep in Vermont were suspected of being exposed to bovine spongiform encephalopathy (BSE) in England. The Secretary could take authority under the old quarantine laws against the sheep that had come from England, but at that time the Secretary had no authority to take action regarding their progeny. Now, under the AHPA, he could take action regarding the progeny as well.

When the Secretary doesn't have the authority to use the AHPA's general authority, he can cooperate with a state, another federal agency, or an individual to take action. In cooperating with a state, the state has to have the authority to take the required action. In this way, the Secretary brings state law to bear to abate the risk. In cooperating with individuals, the Secretary doesn't have to require the destruction of the animal; he can work out a plan with the owner of the animal. He may also choose to put animals under quarantine. The Secretary can quarantine a state or a portion of a state. As a general rule, he will quarantine a whole state, not just a portion of a state, unless the state agency agrees to prevent movement within the state. (The federal government can't prohibit movement within a state—only across state lines.) A quarantine could go down to the level of one farm or even one field. There's no limit as to size.

Another type of quarantine is one regarding a federal program for movement of animals. The USDA may have a nationwide program of disease eradication for a particular disease, and in furtherance of that program, the Secretary could require that certain things be done before an animal is moved across a state line. This creates a uniform national standard. Under a quarantine, the Secretary can prevent interstate movement unless the animals, articles, or means of conveyance have been identified, inspected, tested, and treated.

Regarding the identification of animals, there are different types of identification for different purposes. In the brucellosis program, for example, they use ear tags. Also, the Secretary sometimes requires identification for the purpose of aiding other agencies. In the residue traceback program for the Food Safety and Inspection Service, the USDA's Animal and Plant Health Inspection Service (APHIS) required the identification of swine at the earliest concentration point, or else it couldn't move across a state line. This is an expansive use of identification authority. In that case it encouraged the identification of a large number of swine.

If a state is unable or unwilling to take action to prevent the dissemination of a disease or pest of livestock, the Secretary can declare an extraordinary emergency. To do this, he must find that the disease actually exists and threatens U.S. livestock. (Under general authority, the standard is "has reason to believe" such a disease or pest exists.) He also must show that adequate measures are not being taken by the state, notify the governor or other appropriate official in the state, and publish his findings and their basis in the *Federal Register*.

When the Secretary declares an extraordinary emergency, he can then enforce a quarantine within a state. He can also order the disposal of the animals or other remedial action. If the owner doesn't carry out the ordered action, he can go to court to enforce it. Or, if going to court would take too long, the Secretary could have the USDA take the action itself. If the Secretary must resort to that, because the owner did not follow the original order, then the Secretary can recover the cost of the action from the owner.

Regarding the issue of compensation, the Secretary is required to pay fair market value for animals, articles, or products that are required to be destroyed (minus compensation received from any other source). There is no compensation for animals moved in violation of the AHPA or any regulation or order of the Secretary.

Compensation for loss is one area where the AHPA and PPA differ. Under the PPA, the Secretary is not authorized to pay compensation unless an extraordinary emergency is declared and destruction is ordered. Also, under the PPA, the Secretary can compensate for "economic losses." That's more than the fair market value. Under the AHPA, the Secretary is required to pay for animals destroyed, but only the fair market value as determined by the Secretary. It has often been debated what the fair market value is of a diseased animal. Essentially it should be zero. But the department has always paid the fair market value of a healthy, live animal, in order to get the cooperation of industry.

Emergency authority, the "middle step" in the AHPA, doesn't give the Secretary authority to do anything greater than under general authority. But it gives him the ability to immediately access funds to take a quarantine action without having to go to Congress. This is important in disease eradication. It could otherwise take too much time to get money from Congress, especially if they are in recess. So, under an emergency, the Secretary can transfer money within the department for disease eradication and control. Generally the Secretary takes

If a state is unable or unwilling to take action to prevent the dissemination of a disease or pest of livestock, the Secretary can declare an extraordinary emergency. To do this, he must find that the disease actually exists and threatens U.S. livestock.

► Thomas Bundy

money from the Commodity Credit Corporation (CCC) and gives it to APHIS to handle the problem. But the money doesn't have to come from the CCC and doesn't have to go to APHIS.

Which transgenic animals could be covered by the AHPA? (See box below.) First, animals that were genetically altered using a livestock disease or pest. On the plant side, a lot of plants were altered using a plant pest or disease. The regulations could be similar for the animal side. If the donor, recipient, or vector is a pest, the resulting animal would be a pest. But not many transgenic animals are created that way. An animal could also be covered by this law if "knockout" or silencing genes were used via bioengineering to make an animal more resistant to or more susceptible to a livestock disease or pest. These animals could be covered even if the intent was not to change their resistance to disease. It would also be possible to analyze the manner of creation of a GM animal, and develop a theory that certain kinds of animals could be covered under the AHPA. Finally, it would also be possible to analyze the alterations being made, and to develop a theory to cover such livestock (e.g., if you have a herd of cloned animals, they may be more susceptible to a disease than regular animals). Further analysis of how the animals are being altered could yield different areas of regulation under the AHPA.

Let's look at basic terms under the AHPA and theorize how they might be applied to regulate transgenic animals. Regarding "livestock:" Under the animal quarantine laws, all traditional forms of livestock were covered, except for poultry in some cases. Under the AHPA, "livestock" is defined as "all farm-raised animals." "Farm" is not defined in the law, however. The Secretary thus has broad discretion as to what constitutes a farm. What about domesticated rabbits or farm-raised fin fish? The Secretary has acted in both cases under the animal quarantine laws, and the AHPA is at least as broad. So, I think the definition of livestock in the AHPA, while possibly not inclusive of all animals, is quite broad. There is no legislative history to work from, however, to determine what Congress intended.

Regarding the term "disease:" The definition in the bill that was originally introduced by Congress defined "disease" as "any infectious or noninfectious disease or condition affecting the health of livestock." Under the old animal quarantine laws, the disease had to be communicable, but not in this bill. The bill's definition of disease also went on to say "any condition detrimental to the production of livestock." When the law was finally passed, however, that

#### WHICH TRANSGENIC ANIMALS COULD BE COVERED?

- Animals altered with a livestock disease or pest
- Animals altered with knockout or silencing genes that render them more susceptible or resistant to a livestock disease or pest
- APHIS could also analyze the manner of creation or alterations to be made to determine another "hook."

definition of disease was nowhere to be found. This definition was inserted instead: "The meaning given the term by the Secretary." There was no indication what that meaning should be. I would think it might be best for the Secretary to look at a dictionary definition. One such definition is: "Any deviation from the healthy or normal condition of any of the functions or tissues of the body." There is not yet a proposed rule that sets forth a definition of disease. Undoubtedly they are discussing it now within the agency.

"Pest" is defined in the law as a long list of traditional pests of livestock that can directly or indirectly injure, cause damage to, or cause disease in livestock. It includes the term "vector." A transgenic animal that is more susceptible to disease could be a disease vector (i.e., could spread the disease). So, if the animal could spread the disease, it is a live pest of livestock. The definition also includes any organism similar to or allied with any of the pests defined.

In the bill that was originally introduced by Congress, one of the pests listed was "animal." Under the PPA, also, an animal can be a plant pest. When the final AHPA passed, however, "animal" was missing. There's no legislative history as to why it was taken out. So, I don't know what that means in the final interpretation.

"Release into the environment" is also mentioned in the law. In the AHPA, as in the PPA, the definition of "move" includes "release into the environment." To violate this provision in the AHPA, there will have to be release into the environment in interstate commerce. I can see how pollen going across a state line could be considered a release across state lines. But what does that mean for animals? It's not clear. Also, what if a wild animal escapes from an enclosure? That could be a release into the environment, but is it interstate commerce? If the Secretary declares an extraordinary emergency, then that could involve a much smaller area than under his general quarantine authority. If it is an accidental release, and not intentional, it is still a release into the environment.

How does the Secretary enforce the law? He can send a "knowing violation" to the Department of Justice (DOJ) and they can criminally prosecute the case. But the DOJ doesn't have the money or attorneys to prosecute every case. So it is often difficult to get enforcement of those cases. But the Secretary can also enforce violations through civil penalties, which are determined before administrative law judges and can be appealed—first to the Secretary and then to the Federal Court of Appeals. Under civil penalty authority, a violation can result in up to a \$50,000 fine against an individual and up to \$250,000 for any other person (i.e., organization). Also, the Secretary has subpoena authority for any investigation. This could be used to investigate whether an animal was genetically altered.

Is there food safety authority under the AHPA? If it involves a zoonotic disease, yes; otherwise, no. A zoonotic disease is something that affects both animals and man, such as salmonella, tuberculosis, or BSE. Regarding the tracking of those animals, APHIS cooperates with other agencies to identify animals. There would be a quarantine on interstate movement, under which animals can't be

moved unless they meet certain conditions. This could include pre-market approval for certain animals. That could be a possible hook.

Regarding market disruption, the AHPA contains no direct authority that would allow the Secretary to take action. There would have to be some sort of theory as to why it would happen. If it affects production, it can be acted upon. But the agency would have to first need a reason to believe there is livestock disease or pest. ◀

#### IN THE QUESTION AND ANSWER SESSION THAT FOLLOWED, ONE

workshop participant asked Mr. Bundy if the Secretary has any way to encourage or require more research and development to be done to prevent the introduction and movement of animal diseases and pests into and within the United States, so that we can avoid eradicating those problems at significant taxpayer expense. Mr. Bundy replied that he was personally unaware of other USDA authorities concerning research on animal pests and diseases (that was another part of USDA), and he reiterated that the AHPA states that the Secretary must pay fair market value for everything he destroys. He can't not pay fair market value. He could say that the fair market value is lower than the industry thinks it is. And it's true, Mr. Bundy said, that the amounts can get very large. A large program of eradication, he added, would probably require additional appropriations from Congress, though if it were something serious, such as foot and mouth disease, the money would undoubtedly be forthcoming.

Another participant asked if any other statutes exist that give the USDA authority over transgenic animals. Mr. Bundy replied that no USDA statutes explicitly reference or provide authority regarding transgenic animals.

► FRED DEGNAN

*THE FDCA'S "NEW ANIMAL DRUG" RUBRIC*

FRED DEGNAN is a Partner with King & Spalding, LLP. He formerly served as Associate Chief Counsel at the FDA for both Foods and Veterinary Medicine. Mr. Degnan spoke to workshop participants about the FDCA's "new animal drug" rubric and the regulation of transgenic animals. His paraphrased comments are as follows.

In 1977, I was assigned to do work for what was then called the Bureau of Veterinary Medicine (now the Center for Veterinary Medicine) in the Food and Drug Administration. "How quaint," I thought, "drugs for dogs and cats!" I quickly realized that this office was at the forefront of the FDA's scientific thought and policy decision-making. For example, the first federal efforts in quantitative carcinogenic risk assessment of substances in food came in the context of the animal drug rubric of the Food, Drug, and Cosmetic Act. Simply put, the animal drug provisions have been interpreted broadly, in the interest of public health. This has led to a number of anomalous applications of the statute. The notion that a gene construct can be an animal drug is one of those applications. One of the first legal cases I argued on behalf of the FDA concerned an animal euthanasia agent. It was a combination of two drugs. Veterinarians were concerned that the product would actually take longer to kill an animal than the recognized single-ingredient euthanasia agent on the market. To take action against the product, we had to prove that it was not "generally recognized" as "safe" and "effective." The anomaly? We had to consider in detail whether a euthanasia drug was "safe!" We looked at the statute creatively, and said, in this context, "safe" really means painless and humane. We ultimately brought the case and won, and the product was withdrawn from the market.

With that as preamble and context, let's begin with preliminary observations regarding how the "new animal drug" rubric of the FDCA applies to biotechnology. The FDA interprets its statutory authority as broadly and efficiently as possible. The Supreme Court has said this is OK; the court has affirmed that the FDCA has to be applied in a manner to effectuate its purposes. There is wonderful language from a 1943 Supreme Court case: The FDCA "is not merely a collection of words, but rather a working instrument of government, an instrument that should be interpreted to touch all phases of people's lives, people who are beyond self-protection." In sum, well-established agency principles governing food safety apply to food products of biotechnology. Similarly, in the context of both animal and human drugs, the fundamental statutory assumption that all drugs are inherently risky leads to a series of systems designed to identify the nature and extent of the risks and to balance those risks in the context of the therapeutic benefits conveyed.

One of the anchors of the FDA's approach to regulating any product under the FDCA is that changing the statute creates its own risks, takes time, and sacrifices expertise to political pressures. So, there is a bias within the FDA toward resolving issues under existing statutory authority, and, in the process, toward being creative, as need be.

In final arguments, we pointed out that we had proved that there was a genuine dispute among qualified experts on the issue of safety. The issue wasn't the number of experts, it was whether a true scientific dispute existed. The court agreed.

► Fred Degnan

So, let's start with the basics. Under the FDCA, a substance is an "animal drug" if it is intended to cure, mitigate, treat, or prevent disease in an animal or it is not food and is intended to affect the structure or function of the body of an animal.

If a substance is an animal drug it must by law go through pre-market clearance, unless it is "generally recognized as safe" (GRAS) and "generally recognized as effective" (GRAE). GRAS and GRAE status are only granted when there are adequate publicly available data and information supporting expert recognition. I'll give you another court example. I was arguing a food additive case in the 1980s. It was a five-day trial. We had two toxicologists arguing that the additive was not GRAS. The opposing side had 20 experts arguing that it was GRAS. In final arguments, we pointed out that we had proved that there was a genuine dispute among qualified experts on the issue of safety. The issue wasn't the number of experts, it was whether a true scientific dispute existed. The court agreed. Also, even if there isn't a dispute, for there to be a finding of GRAS, there must be a body of convincing scientific data like that which would support an approval in the first place. These data also have to be publicly available. All three points have to be met. So, GRAS is in some ways a higher standard than the FDA's "reasonable certainty of no harm" safety standard for food additives and the safety standard for new animal drugs. As a result, in the veterinary area, more products are shunted into the pre-approval system than the GRAS system—i.e., most animal drugs are "new animal drugs" and subject to pre-market approval.

The fundamental focus of the new animal drug rubric is threefold: Is the new animal drug safe for the animal? Is the new animal drug effective—does it cure, treat, or prevent disease in the animal or does it affect the animal's structure as intended? And, if the drug is for a food-producing animal, is the resulting food safe for you and me to eat? To answer the foregoing questions, over the last 50 years the FDA has developed a robust, data-based process of regulatory inquiry and evaluation. It starts at the earliest stages of clinical testing in animals and includes comprehensive data collection with regard to the safety and effectiveness of the drug and the safety of residues of the drug in meat, milk, and eggs. It also includes layers of expert agency review and analysis, mandatory post-market reporting, facility inspection, and the potential for post-market control and surveillance.

Use of a new animal drug without FDA approval is a per se violation of the law. Marketing the animals themselves or products derived from them would violate the law. The manufacturers and users of the unlawful drug could be enjoined or prosecuted for marketing or using the drug.

Now I'll talk about the new animal drug application (NADA) process and transgenic animals. (See box on the following page.) The NADA process is not a perfect conceptual fit with transgenic animals. The framers of the FDCA in 1968 obviously never intended this section of the act to deal with these types of genetic transfers. That doesn't mean, however, that it is inappropriate to apply the new drug rubric in an effort to regulate such transfers. Of course, questions relating to process and governing criteria remain unanswered. And the rubric

does not involve a transparent system. In fact, in many ways it's a closed system. For example, even the identity of an investigational new animal drug (INAD) application and of an NADA is privileged; neither can be disclosed by anyone but the sponsor.

The application of the law to transgenic animals results in some "Byzantine" situations, as the Pew Initiative report, "Issues in the Regulation of GE Plants and Animals," says. Clearly some mental gymnastics are required to make the factual situations relating to transgenic animals fall within the FDCA framework. But, it's fair to say that the act offers an opportunity for comprehensive regulation and for assuring safety for the animal and for us eating products from the animal. Also, the act provides an opportunity for coordination between the FDA's Center for Veterinary Medicine (CVM), which takes the lead in implementing the law, and the FDA's Center for Drug Evaluation and Research (CDER) and Center for Biologics Evaluation and Research (CBER), regarding products that are not intended for food use but that involve plants or animals for use in the production of drugs.

Under the act, the introduced genetic constructs are considered "drugs" if they are not food and they are intended to affect the structure or function of the animals. The animals themselves are not considered drugs. In the case of the transgenic salmon that contains a growth hormone, the construct is clearly not food, and it affects the structure or function of the salmon. So, that's a fit within the literal language of the act's definition of "drug." The genetic construct could also meet the "drug" definition if it was meant to cure, treat, prevent, or mitigate a disease. If that construct is not GRAS or GRAE, then it is a new animal drug and has to go through pre-market approval. Could we make a presumption of GRAS here, as with plants? Probably not. It's a more difficult case to make because the construct would have to be GRAE, not just GRAS. We don't know as much about transgenic animals—about the effects of genetic transfers in animals. They are less well understood. As a result, such a presumption would be very unlikely.

Under the statute, a sponsor submits an INAD application in order to ship a new animal drug for clinical testing in animals. A sponsor can ship the drug only if it has an INAD authorizing shipment and if the drug is labeled for investigational use. The sponsor conducts research under the INAD. Section 511 of the FDCA, which governs the INAD process, has extensive regulations. It includes numerous opportunities for discussion between the sponsor and the CVM. The sponsor

## THE NADA APPROVAL PROCESS AND TRANSGENIC ANIMALS

The NADA paradigm and transgenic animals are not a perfect fit conceptually:

- Clearly not contemplated by the framers of the FDCA
- Questions re: process and governing criteria remain unanswered – thus, not fully transparent

But it offers, in large part:

- An opportunity for comprehensive regulation
- An opportunity for coordination with CDER and CBER

submits a product development plan. The sponsor develops, and the agency reviews, the study protocols. There is an opportunity for pre-submission review and conference. And the edible products of "treated" animals may be authorized for food use. There's also an opportunity for the FDA to inspect the facility where research is being conducted and to have access to records.

So, does the INAD process work for transgenics? (See box below.) I think so: the INAD rubric is a logical entry into the FDA's regulatory system for transgenic animals. It provides a foundation for the next steps, regardless of what kind of transgenic animal we are dealing with. For food animals, it's a mechanism for achieving a full NADA approval. For other animals, it provides the groundwork information for CDER and CBER to evaluate the new drug (i.e., for animals that produce human biologics or drugs).

Currently, though, some issues relating to the INAD process remain unresolved. The INAD process suffers, in my view, from a lack of a published road map, with mileposts, outlining how it will be applied with transgenic animals. We don't know exactly what the process is. We don't know what testing needs to be conducted or what information needs to be filed. We don't know the nature of the review for different types of applications. We don't know how CVM will coordinate its efforts with those of CBER and CDER. We also have no idea of the cost of compliance, since we don't know what the process is.

The statutory data requirements for approval of an NADA remain demanding. There must be "substantial evidence" of effectiveness (consisting of one or more adequate and well-controlled investigations) and "adequate tests by all methods reasonable applicable" showing that the drug is "safe" for use under its intended conditions of use. Substantial evidence of effectiveness has to be shown by studies in the target species and in the real-life conditions of field investigations.

"Adequate tests" have traditionally included human food safety studies focusing on total metabolism, comparative metabolism, and residue depletion. Human food safety studies must include a traditional toxicology profile, including mutagenicity, 90-day-feeding studies, effects on reproductive systems, teratology, user safety, and resistance. The point: This is a very comprehensive rubric for evaluating safety and effectiveness.

We can look at how these standards were applied in the case of recombinant bovine somatotropin (rBST). In the mid-1990s, Monsanto succeeded in getting

#### THE INAD PROCESS: DOES IT WORK FOR TRANSGENICS?

Logical entry into the regulatory system

Provides foundation for next steps:

- Full NADA (e.g., for growth-promotion drugs)
- Dealings with CBER, CDER (e.g., for production of human biologics or drugs)

rBST approved as a new drug for increasing milk production in cows. The use of the product raised a food safety question. Resolution of that question involved a novel approach to demonstrating the safety of milk from cows receiving the drug. The path the FDA pursued was as follows: The FDA developed a guidance for "toxicological testing" focused on the potential exposure of people to residues and the possible related biological effects. A determination of the potential oral activity of "active proteins" in laboratory animals was required. If the compound was determined to be orally active, the toxicological focus was on the results of exaggerated-dose laboratory animal studies with the active ingredient. The agency will, undoubtedly, continue to use this or a similar path for transgenic animals.

Regarding target animal safety, the FDA looks at the cumulative effect of the drug—at tolerance, reproductive repercussions, animal class (young, old, etc.). There's not as much focus on the individual as on the health of the herd overall.

Some legal issues exist with regard to environmental safety. The FDA focuses on its inherent safety authority under the NADA rubric to evaluate environmental impacts. It looks at hazards to humans arising during the manufacture of the drug, such as emissions; hazards to humans associated with administering the drug to the animals; and hazards to humans and animals from the use and disposal of the drug. The FDCA doesn't specifically empower the FDA to look at environmental effects, but it does define "safe" as affecting the health of man or animal. The agency relies on this authority to evaluate environmental impacts.

In the context of environmental assessment, the FDA has stated that it has broad authority to require information on environmental impacts. In the context of a new animal drug application, the practical bottom line is that if the agency wants information about environmental impacts, the sponsor will provide it—whether required "by law" or not. The agency has said that, under the FDCA, it may require environmental safety instructions on product labels; impose conditions to ensure the mitigation of environmental impact; and refuse to approve a product in the face of unmitigatable environmental impacts that adversely affect the health of humans or animals. To this end, prior to approving rBST, the CVM considered: the viability of the organisms in an aquatic microcosm; gene transfer from the organism to indigenous organisms; potential accidental exposure at production facilities; worker exposure; dairy farmer exposure; potential environmental introductions into water and waste

Suffers from lack of established road map with mileposts:

- ▶ What, exactly, is the process?
  - ▶ What testing needs to be conducted and what information needs to be filed?
  - ▶ What is the nature of the review for different types of applications?
  - ▶ What is the coordination process for dealing with CBER, CDER?
  - ▶ Absence of road map hinders reliable estimation of cost of compliance
- Relies on agency/industry dialogue

systems; its potential impact on carbon dioxide emissions; and the possibility of a "used syringe" disposal problem. The FDA concluded that there was no need for concern in seven of those eight areas. Used syringes were a concern, however, and so "mitigations" were required. The upshot of the rBST experience is that the CVM can thoroughly address environmental risk and can require or recommend procedures to avoid hazards.

Of course, environmental risk assessment can be imprecise—particularly on issues where there is a lack of governing criteria. Ecological impact is difficult to assess. So, the NADA system, although comprehensive, is not perfect. Moreover, to the concern of many, the NADA rubric, as noted earlier, embodies a "closed" system—the public doesn't know what's happening until after a product is on the market. And, with respect to the FDA's ability to rule upon "environmental" safety issues, questions of legal authority exist.

No questions exist, however, with respect to the FDA's authority over manufacturing methods and controls. The sponsor must develop methods and controls to ensure consistent manufacturing, including stability data and related information.

Once a sponsor has addressed all of the above concerns (e.g., human food safety, target animal safety, effectiveness, environmental safety, etc.), the sponsor makes an NADA submission, which must include all data—favorable and unfavorable—relevant to the application.

The FDCA contains plenty of post-approval controls. Product experience reports must be submitted every six months, there's an adverse-event reporting system, inspections are conducted, and so forth. The FDA will occasionally impose post-market distribution controls as well, as with Clozaril and Accutane. One unique thing the FDA can do is request that a manufacturer do post-approval monitoring. It did this for Olestra and rBST.

I have developed a long list of administrative actions that I believe could enhance the FDA's existing authority. They include the following: Resolve regulatory questions; develop guidances and criteria governing the safety of food resulting from transgenic animals; develop guidances and criteria designed to assure that no unreasonable adverse impacts to the environment occur as a result of the development and marketing of transgenic animals (focus on the FDA's authority to impose environmental mitigations and the types of mitigations appropriate in given circumstances); develop a specific transgenic animal enforcement/inspection program beginning with the INAD process and including commercialization; update existing relevant regulations and policies regarding clinical investigation, Good Manufacturing Practice controls, and so forth, to specifically apply to transgenic animal development and production; consider mechanisms for informally and formally enhancing the coordinated decision-making among the federal agencies possessing authority and expertise regarding issues related to investigational use, pre-market review, and post-market enforcement related to transgenic animals; and develop guidances and criteria pertaining to the interplay between CVM and CDER/CBER.

In closing, I believe transparency would be enhanced by guidance on criteria for testing and criteria for the various evaluations the FDA will perform. The pace of decision-making would be improved if review procedures and data collection requirements were laid out better. We need a better understanding of when enough data is enough. Moreover, the agencies need to resolve issues of regulatory clarity and coordination. On economic issues, the cost of innovation is not the FDA's problem. Cost of data collection is an industry problem. Resources are a problem—the FDA simply needs more resources to do its job in this important area.

One final thought: Rigorous regimes have a far greater potential to foster innovation and technology than less rigorous regimes. They eliminate the temptation to take the easy road. They demand precision. The NADA rubric is such a regime. ◀

#### IN THE QUESTION AND ANSWER PERIOD THAT FOLLOWED MR. DEGNAN'S

presentation, several participants commented that they remain unconvinced that the new animal drug provisions are the most effective means for regulating transgenic animals, since the law has to be “stretched” to fit and concerns regarding the lack of both transparency and a clear standard for environmental review. Mr. Degnan said he has heard those concerns, but still believes that transgenic animals can and do fit within the law because the inserted genetic construct affects the “structure or function” of the animal. Another participant said the take-away message he heard was the need for specific guidance from the agency on the application of the law to transgenic animals.

Much of the discussion served to clarify the limits on transparency and public participation that govern the FDA under the FDCA. One workshop participant, for example, asked if the FDA would allow for public comment periods on specific products from transgenic animals before the agency approves them. A participant from the FDA said that, in general, the agency is always interested in hearing the opinions of stakeholders, but that the new animal drug provisions of the FDCA prohibit the FDA from releasing information that is under pre-market review. Public comment may be sought, however, if the agency drafts a new guidance document or overall statement of policy regarding how it will regulate transgenic animals under the FDCA.

Another participant asked about the apparent conflict between the FDCA's confidentiality provisions and the public participation requirements of the National Environmental Policy Act (NEPA). If an environmental impact statement (EIS) were conducted on a transgenic animal, she asked, would that process be public? Mr. Degnan said he was not sure. In the case of an environmental assessment (EA), another participant said, public comment is not required, so the EA would just be released when and if the transgenic animal is approved for commercialization.

A participant who is a biotech developer said the FDCA's confidentiality provisions protect valuable trade secrets, which is essential given the competitive nature of the pharmaceutical and biotech industries. We could bring things to a screeching halt, and even undercut the development of human drugs, he said, if we dismantle these protections. That said, he added that perhaps a category could be created for transgenic animals that falls somewhere between the open GRAS process and the highly confidential INAD/NADA process. Finally, he noted that a robust comment period on a proposed FDA guidance document would go a long way toward getting all concerns on the table and enabling a clear understanding of and ability to influence areas where the FDA needs work, especially regarding environmental issues.

Another biotech developer said that the issue of data collection—and of determining when enough data has been collected—is in his mind the most important unresolved issue.

► LAWRENCE CULLEEN  
*STATUTORY AUTHORITIES OF THE  
ENVIRONMENTAL PROTECTION AGENCY  
AND THEIR POTENTIAL RELEVANCE TO GE  
ANIMALS*

LARRY CULLEEN, an attorney in Arnold & Porter's environmental practice group, spoke about the Environmental Protection Agency's authorities regarding transgenic animals. Mr. Culleen formerly served as chief of the EPA's New Chemicals Branch. His presentation is paraphrased below.

The basic question I will cover is, What authorities are available to the EPA to regulate bioengineered animals? To be clear, I'm defining "regulate" to mean pre-market review and approval and post-market control. By "bioengineered" I mean transgenic animals, but not cloned animals. Also, "animals" refers to whole animals, not simply the inserted transgenic material.

Of the potential pre-market authorities, I'll talk first about the Toxic Substances Control Act (TSCA). (See box below.) TSCA was enacted in 1976 and regulates "chemical substances" (defined as "any organic or inorganic substance of a particular molecular identity including any combination of such substances resulting in whole or in part from a chemical reaction or occurring in nature"), excluding foods, drugs, cosmetics, pesticides, and tobacco. "New chemical substances" are those not on the EPA's Inventory of Chemical Substances. The Inventory was created through a public process lasting over two years, from 1977 to 1979. Chemical substances produced commercially at that time were listed. Anything that was not listed during that time is defined as "new." New chemicals are subject to pre-manufacture notification. Note that this process is pre-manufacture, not pre-market. Thus, before any creation of the new substance, the manufacturer has to notify the EPA 90 days in advance. There are some exemptions from notification (including certain R&D activities). Note that "manufacture" includes import. Mailing a package across national boundaries is import.

Also, note that pre-manufacture notification authority is not a pre-market testing requirement. It's just a notification requirement. The manufacturer has to provide the EPA with available information regarding health and environ-

#### TSCA

- "EPA has consistently applied [the] definition [of chemical substances] to life forms..."
- "Plants and animals could also be chemical substances under TSCA."
- However, "...as a matter of policy, EPA has limited the [TSCA biotechnology] rulemaking to microorganisms..."

59 Federal Register 45526, 45527 (Sept. 1, 1994)

mental effects, but they don't have to test to demonstrate safety or efficacy. They just give the information they have to the agency. Thus, the agency sometimes has to make decisions with no data at all. The EPA can invoke certain provisions of TSCA to compel manufacturers to test a chemical; however, generally the agency must make one of two determinations: (1) that the material in the notification may present an unreasonable risk to human health or environment, or (2) that the material will be used in a way that there is substantial or significant human exposure or environmental release. If the EPA makes either of those findings, which are really a reasonably low threshold, then the agency can see data and regulate through the pre-market phase pending the development of those data. In any case, notification must be done before any commercial purpose is pursued. Virtually every undertaking is considered a commercial purpose. Research and development activities can be exempt, but the exemption is very limited.

The EPA has consistently stated that the definition of chemical substances may be applicable to certain life forms. The agency has said that "plants and animals could also be chemical substances under TSCA." As a matter of policy, though, the EPA limited its TSCA biotechnology rulemaking to "microorganisms."

The Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) is also a registration law. It contains pre-market review authority for pesticides. "Pests" are defined in the act and in regulations. In certain instances, the EPA has excluded certain things; for example, biological control agents are not covered, because other agencies cover them. I read this to mean that if you engineer an organism that preys upon a pest you wouldn't need EPA approval under FIFRA. That's a regulatory interpretation of longstanding, though it could be changed. FIFRA excludes microorganisms when they are found within any living animal, as well as animal drugs, from the definition of pest. I'm inclined to say that under FIFRA the EPA is not seeking to require approval of animals that are bioengineered for pest control purposes. So, FIFRA is unlikely to be used to regulate transgenic animals at this point in time.

Let's look a little more closely at TSCA again, however. The current regulations are at 40 CFR Part 725—this is the Microbial Commercial Activity Notice (MCAN) rule. I know we are here to talk about animals, but the hook here is the transgenic construct itself. When assessing the risk, the agency does a full assessment with respect to all aspects of the genetic change. The animal is along for the ride, but the agency looks at the effects of the change on the animal. This includes assessing the opportunity for, and impact of, failures of "containment" and inadvertent genetic "creep."

Under these requirements, the agency doesn't require pre-manufacture testing. It has published a "points to consider" document to indicate the kinds of data the agency would like to receive. But there's a concern that there is a thinness of data in any pre-manufacture notice. It can take as many as 180 days for the agency to consider a pre-manufacture notification. (Ninety days are provided under the statute, and the EPA has the authority to extend the review for

another 90 days.) But the agency has to serve an order 45 days before the close of the review period if it wants to stop or otherwise regulate the manufacture. So, it can be challenging undertaking. It's a bit of a fire drill at the agency every time.

TSCA contains a number of post-market authorities. Section 4 allows the agency to require, by rulemaking, that manufacturers test a substance for particular health or environmental effects. Such requirements have broad applicability industrywide—that's why it's done via rulemaking. Agency rulemakings are traditionally targeted in nature—they will say what tests must be performed, what protocols should be used, and so forth.

Under Section 5, the orders that can be issued if a decision is made to regulate a substance are pertinent solely to the submitter of a pre-manufacture notification. They are specific to the submitter and are not broadly applicable. This is problematic for the EPA. New microorganisms are those not on the Inventory. When an organism goes through the notification process, it is added to the Inventory. Thus, other companies who subsequently manufacture the material don't have to notify the agency, because it's already on the list. To rectify this situation, the EPA typically also issues a significant new use rule (SNUR), so as to "level the playing field," to impose the same requirements on the industry generally. A SNUR requires companies that are making the same substance as the original submitter to notify the agency as well.

Section 6 is a rulemaking authority that the EPA rarely implements for the purposes of regulating an unreasonable risk. The standard is "will not present an unreasonable risk." EPA is hesitant to use this authority because of a lack of success in litigation over these rules. Section 7 enables the agency to act in the case of an imminent hazard. This authority has not been used in the nearly 30 years since TSCA was enacted. Section 8 concerns information gathering. It enables the EPA to either conduct rulemaking through the calling in of data, or require the reporting of information concerning adverse effects. Under Section 9, the agency has the authority to refer to other agencies issues they think are better handled by those agencies.

Another post-market authority is Section 6 of FIFRA, which is a cancellation authority. Also, people have done voluntary recalls.

To be subject to TSCA, intent is a critical issue. Section 3 excludes foods, drugs, cosmetics, pesticides, and so forth. If an animal were changed through transgenic methods such that its behavior or lifecycle were effected, that transformation event might be an animal drug; if so, it would fall outside the scope of TSCA. However, the EPA has said there are possibly dual-use chemicals—substances that might have both drug and chemical purposes. In those cases the EPA would regulate it in addition to the FDA. Also, the EPA has said that TSCA will serve as a "safety net," to capture any product of biotechnology that isn't covered by other laws. I think that's reasonably undisputed. So, if you can't demonstrate that a modification was developed strictly for a drug purpose, then it's possibly subject to TSCA as well.

However, the EPA has said there are possibly dual-use chemicals—substances that might have both drug and chemical purposes. In those cases the EPA would regulate it in addition to the FDA.

► Lawrence Culleen

Because tropical aquarium fish are not used for food purposes, they pose no threat to the food supply. ...[T]he FDA finds no reason to regulate these particular fish.

► FDA statement December 9, 2003

The GloFish™ provides an interesting case example. (See box below and on following page.) People have always said that TSCA is the gap-filling law, expected to be used where other substances fall through the cracks, especially with regard to environmental risks. The GloFish is a bioengineered zebra fish that is bioluminescent. Its original purpose was as a biomarker to indicate certain pollutants. But some fish were created that switch "on" but not "off"—these were proposed to be sold as companion animals. I'm assuming they were imported. So, the argument could be made that the GloFish would fall under TSCA. The FDA put out a statement saying, "Because tropical aquarium fish are not used for food purposes, they pose no threat to the food supply. ...[T]he FDA finds no reason to regulate these particular fish." The notice didn't say whether or not the agency considered the GloFish to be animal drugs. It just said the fish were not food. You could argue that if the fish were not food, by inference they might fall under TSCA. Litigation is pending at the FDA on this point. So, we have a fish that's not a food and not a pesticide. It contains intergeneric material. Clearly there's a commercial use of the fish as a companion animal. So, the GloFish seems to me to fit under TSCA, assuming it is imported.

But the EPA didn't assert jurisdiction. Why? I don't know. Did they lack authority? Maybe so, if it's definitive that any modification of the animal makes it an animal drug, per se. But the FDA's statement did not address that. So, was it a lack of interest on the EPA's part? A lack of risk? The FDA said there was no perceived risk, but for TSCA purposes risk is not a barometer for jurisdiction. What could happen next? Section 21 of TSCA authorizes private persons to ask the agency to conduct a rulemaking on a particular product, so that's one possibility. Even if the EPA has jurisdiction, it seems unlikely that the EPA would bring an enforcement action against the company alleging a TSCA violation.

So, who else has a stake in the GloFish situation? It seems to me that the Consumer Product Safety Commission might be interested. They have no exclusion for animals. I can't speak for the other federal authorities. State authorities also might be pertinent. The California Fish and Game Commission has stepped in to stop the distribution of the GloFish in California.

What could be next? If the barometer is therapeutic claims, then all kinds of modifications to animals could fall under the scope of TSCA—for example, animals modified to harvest crops; wildlife that resist the adverse effects of oil spills; and/or heartier bees that pollinate over greater distances. ◀

#### INTERESTING CASE STUDY – GLOFISH™

- Zebra fish (*Danio rerio*), native to the Ganges River in India, are normally striped black and gray and are commonplace both in labs and as pets.
- Scientists at the National University of Singapore altered the fish using the gene for red fluorescent protein from sea anemones and coral.
- GloFish now come from stable lines bred from the original experimental animals.

#### A QUESTION AND ANSWER DISCUSSION FOLLOWED MR. CULLEEN'S

presentation. First, it was noted that “technically” the EPA regulates the Bt toxin inserted into corn, not the corn itself. Also it was explained that the EPA, using TSCA authority, issued a rule regarding a GE rhizobial bacteria.

The remainder of the discussion focused mainly around the GloFish. One person suggested that the FDA’s statement about the GloFish could have been more artfully crafted, to make clear whether it presumed the fish was a “new animal drug,” and, as such, should not be regulated under TSCA. Mr. Degnan said it appears the fish clearly would meet the “new animal drug” definition, since the introduced genetic construct changes the structure or function of the fish. Another person noted that the FDA didn’t ignore the issue or do nothing; it simply decided for a variety of reasons (including that the fish will not be used for food and is not viable in U.S. waters) that regulation was not warranted. Another participant said that if the FDA is going to regulate GE animals because the gene construct is a new animal drug, that would appear to include all GE animals. Only in cases like the GloFish where the agency decides not to regulate, or where the EPA decides that a genetic construct is a “dual use” chemical, could the EPA regulate the animal under TSCA.

#### SO LET'S TAKE A LOOK AT THAT AGAIN...

- Not a food, not a pesticide
- Intergeneric material?
- Commercial use?
  - Companion animals
  - “bioindicators” for pollutants
- Manufacture? (importation)

#### WHY DID EPA NOT STEP IN?

- Lack of authority?
- Lack of interest?
- “Risk” does not determine jurisdiction
- TSCA and 21 Petition?
- Enforcement Action?

➤ JAMES MACDONALD, PH.D.  
*OVERVIEW OF THE U.S. MARKETING  
STRUCTURE FOR LIVESTOCK*

JAMES MACDONALD is Director of the Agriculture Structure Branch of the USDA's Economic Research Service. He spoke to participants on the second day of the March workshop about the structure of the meat, poultry, and dairy industries. His paraphrased comments are as follows.

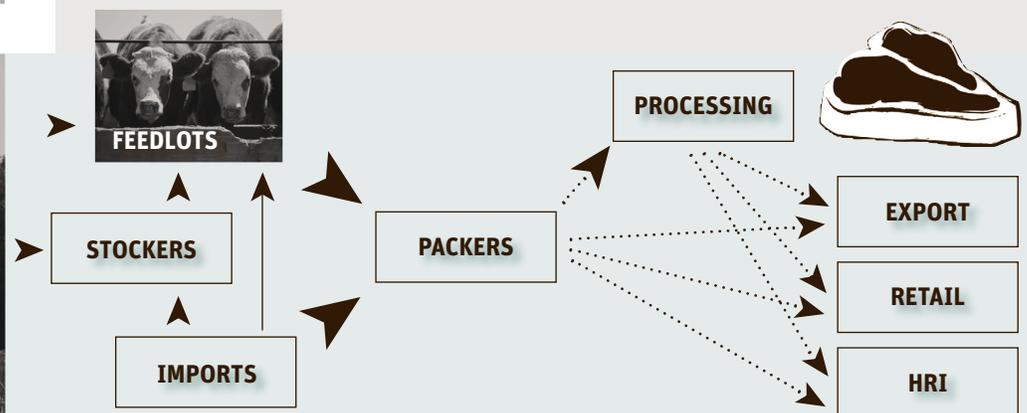
My talk today will be about how the agriculture industries are organized. I'll first discuss how production is organized by commodity (beef, dairy, poultry, and hogs); then review common developments in processing; then finally mention several critical issues regarding new technologies.

I've put together a few slides showing how the supply chains are organized. First let's look at the beef supply chain. (See figure below.) The boxes on the left are cow-calf operations, stockers, and feedlots. Cows move from cow-calf operations, sometimes to stockers, then to feedlots. They then move out of feedlots to meatpackers. After meatpackers, the meat could go to processing plants (where it's made into sausage, hamburger, or other processed foods), or to export, retail outlets, or the hotel and restaurant industry.

Cow-calf production is extraordinarily diverse. There are about 100 breeds and breed combinations, most of which are tied to forage types and weather conditions. Cow-calf operations are generally grass- or grazing-based and are located all over the U.S. They are largely independent businesses. Some voluntary marketing efforts do exist, such as "Certified Angus Beef." There is a strong seasonal component, as two-thirds of calves are born in February, March, and April. There are wide differences in how calves get fed and treated in these operations. Calves are usually raised in these operations until weaning (3-5 months).

There are only about 5,000 cow-calf operations with more than 500 cows, but these larger operations account for 14% of the total inventory in the U.S. There are about 630,000 operations with 1-49 head. They account for 29% of the total inventory. The USDA says there are 2 million farms in the U.S., total.

THE BEEF  
SUPPLY CHAIN



(Any operation that produces \$1,000 per year counts as a farm, so it's a pretty low threshold. Half the operations counted as farms bring in less than \$10,000 per year.) About 800,000 of the 2 million farms in the U.S. have cow-calf operations.

Cow-calf operations are spread all over the United States. There's a dense concentration down the center of the country, but also a lot of operations out West, in Florida, and the East as well.

Stocker production is the second stage of beef production. Many animals move from cow-calf operations to stocker operations. These are also grass-based, and they specialize in animal growth and health for weaned animals. At these sites, calves add 200-400 pounds over 3-8 months. Stocker operations have a strong seasonal component, and also a marketing component in that they aggregate and classify like kinds of animals. Their purpose is to upgrade the quality of the animals they receive.

Feedlot production is the third stage, and it is much different than the previous two. In feedlots, animals are confined outdoors in pens, and they are fed purchased feed, such as corn and soy beans. There is a lot of custom feeding. Many feedlot operators feed other people's cows on a contract basis, though some own their own cows. Feedlots are typically owned by large corporations or very large family businesses.

Production is concentrated in the largest feedlots. (See table below.) The largest feedlots have 90,000-100,000 head of cattle. Increasingly, production has shifted to the largest operations. One firm likely owns 3-10 feedlots. Thirty to forty firms own the largest feedlots. Many small feedlot operations still exist, but they account for only 15% of all marketings. The densest geographic concentration of feedlots is in the Plains states, from North Texas up through to Nebraska. That's where the big feedlots, slaughterhouses, and packing plants are.

Another trend I should mention is the tighter coordination in animals coming out of feedlots. In cow-calf farms, operators typically sell the cattle in "spot" markets. Increasingly with fed cattle, the cattle are moving under long-term contracts between feedlots and packers. So, the industry is shifting toward greater coordination and contracting, though it's still less coordinated than the rest of the livestock sector.

PRODUCTION  
CONCENTRATION  
IN LARGE BEEF  
LOTS

LOT SIZE (CAPACITY)	# OF OPERATIONS	% OF 2004 MARKETINGS
< 1,000 head	88,000	14.7
1,000-15,999	1,912	24.8
16,000-31,999	140	17.9
32,000-49,999	70	16.8
50,000+	54	25.7

In milk production, dramatic changes are taking place right now. Farmer cooperatives and marketing contracts are still important (and distinctive to dairy). But recent trends include a dramatic decline in the number of small operations, a sharp growth in nontraditional areas, and sharply increasing per-cow productivity, especially in larger operations.

In the milk sector, dairy operators must make a series of key choices. The first is what the animals will eat: purchased feed, home-grown feed, or grass. The largest operations use more purchased feed. There is a small but growing area in traditional grazing. And the middle part of the sector uses home-grown feed. That's probably declining these days, however.

Dairy is different from beef in that there is breed specialization. The Holstein is the main breed in 94% of dairy operations. The use of rBST is strongly associated with big operations.

As this slide shows, dairy farms have a complex array of outputs. (See figure below.) On the left side we have cull cows. Once a cow's milk production starts to decrease, she is culled and sent to a meatpacker. The second output is dairy calves. Some female calves are kept on the farm as replacement cows; others are sold to other dairy farms. The male calves, of course, go off-farm and eventually end up at the meatpackers. Other outputs include milk flowing to processors for milk and cheese. Milk is made into a variety of products, and that variety is increasing.

Cows' milk is 1/8th solids and 7/8ths water. The solids include fat, protein, lactose, and minerals. The components can be used to make many products, and can be marketed and transported over long distances. Fluid milk has long been declining in importance. Farmers' cooperatives market most cows' milk—about 80%. The milk goes to milk and product processing plants.

From 1992 to 2002, the number of dairy farms in the U.S. decreased by 40%, but the average size of each farm increased markedly. Between 1997 and 2002—just a five-year period—the number of small dairies (with fewer than 50 cows) declined by about a third. They are going out fast. What we now call medium-sized farms (with 50–199 cows, which used to be considered large commercial operations) decreased by 20% in those five years. Large-scale operations have grown just slightly during this time period. The real increases have been in industrial-scale operations, which have more than 500 cows and in fact often have 5,000–10,000 cows at one site.

## FLOWS OF DAIRY FARM OUTPUTS



The traditional area of highest dairy production is the crescent-shaped region from New England through Ohio and Indiana and up into Minnesota, in addition to California. Wisconsin and California are currently the leading milk-producing states. Recently, however, production has been shifting to Idaho, New Mexico, and the Central Valley of California. Lots of producers have moved away from Southern California, where the land prices have increased so much that the farmers have sold out. Some of these same farmers have moved to Indiana, where industrial-scale production has been increasing.

Milk cow productivity has increased sharply. There has been an increase of 20% in milk coming out of each cow in from 1993 to 2002. That alone makes for fewer cows and fewer dairy farms. Milk production costs decline with the size of the operation. There are substantial economies of scale. Big operations have lower costs per cow, in both operating costs and ownership costs.

Now let's switch to the hog industry, where dramatic changes have taken place in the last 15 years. The traditional way to raise hogs was "farrow to feed"—that is, farmers raised piglets until they were large enough to sell to market. The typical farmer had between a few hundred and 1,500 pigs. The hogs were shipped to a packer through spot market sales. And hog farms tended to be quite diversified.

Contemporary hog operations are much more specialized and involve more contractual relationships. The industry is evolving as we speak, actually. Three types of operations now exist: nurseries (for piglets), feeder operations (for weaned pigs), and finishing operations (for "filling out" pigs before they are sent to slaughter). Typically, the farmer doesn't own the hogs anymore. An "integrator" provides the pigs, the feed, and the veterinary services. The integrator is not necessarily a packer, as in the poultry industry. The integrator contracts for the genetics, hires the growers, and contracts for the meatpackers. Thus the business is more tightly coordinated than it was 15 years ago. The integrator coordinates everything via contract. After going to a packer, the pork goes on to various processors.

Small hog farms are going out of business. In the ten-year period from 1992 to 2002, the number of small hog farms (those with less than 500 head) decreased by 65%, and medium-sized farms (500-2,000 head) decreased by 50%. At the same time, large farms (2,000-5,000 head) increased by 45% and industrial-scale farms (5,000+) increased 165%. So, production is shifting dramatically.

The areas with the most hog production are North Carolina, Iowa, and southern Minnesota. There are some operations spread out around the country, but those are mostly left-over small farms. The decreases in small and medium-sized farms have occurred all over the Midwest, mostly. Some new areas for industrial-scale hog production have opened up in Utah and western Oklahoma.

The shift to large-scale operations is taking place primarily due to the substantial economies of scale in and higher productivity of large confinement operations. Large producers have much lower costs per hog. We think the productivity improvements have to do with the nature of the genetics and control over the genetics.

Now let's turn to poultry. This is where tighter networks started. The poultry industry is organized much like new hog production. The poultry farmers are growers, but they don't own the birds (unless the birds die!). The farmers grow broilers, roasters, and/or layers. The farmers provide capital, labor, and energy. In this industry, the integrators are usually processors. The integrators provide the chicks, feed, and services, and they operate the hatcheries and feed mills. Branded products are linked together by production contracts.

Poultry production is concentrated in networks throughout the Southeast and typically takes place in very large operations. The number of poultry farms has steadily decreased, while the number of birds per farm has increased. From 1992 to 2002, for instance, the total number of farms with layers and pullets decreased by 18%, while the number of layers and pullets per farm increased by 27%.

On the corporate side of the animal agriculture industry are processors and integrators. Developments in these areas include consolidation into bigger plants, which largely occurred in the 1980s and 1990s, and concentration into fewer firms. Tighter coordination is increasingly common, and spot or open markets are increasingly less common. Major issues in this area include competition, food safety, pollution, and farm autonomy. Farm autonomy is an issue because farmers generally really dislike being contractors, so lots of political battles take place over that.

Slaughterhouses and processing plants are much larger now than in the past. Plant size in the beef industry increased more than fourfold between 1980 and 2000. Cheese plants have sharply increased in size as well. Plants have gotten bigger for a number of reasons. New technology provides economies of scale. Deunionization, and the consequent disappearance of union wage premiums in large plants, reduced large-plant labor costs more than small-plant labor costs, and hence provided a further cost advantage to larger plants. And agricultural developments mean an assured supply of livestock. A big cattle packing plant needs 5,000 cattle each day. Because of developments on the feedlot side, meatpackers can have more assurance of a regular, steady flow of cattle. On the poultry side, hatcheries, feed mills, growers, and processors are all at the same site or nearby. So a steady flow of animals is assured. Transportation has improved as well. Assured livestock supplies and reduced transportation costs mean that large-scale plants will be more likely to fully utilize capacity, thus realizing their potential cost advantages over smaller plants.

So, large plants have serious cost advantages. An ERS study found that a slaughterhouse that handled 175,000 head of cattle per year would realize processing costs that were about 65% greater, per head, than costs at a plant handling 1.35 million head per year.

Some parts of the processing industry have become much more concentrated. In 1980, the top four processing firms in the beef industry slaughtered less

than 40% of all steers and heifers. In 2000, they slaughtered more than 80%. The top four hog processing firms slaughtered less than 40% of all hogs in 1980, but that figure grew to nearly 60% in 2000. The changes were similar but not as dramatic in the poultry industry. I know of no industry that has concentrated as much, as fast, as meat processing. Concentration has taken place because of increased plant sizes and differences in demand growth.

Let's look for a moment at animal slaughter trends. The peak year for cattle slaughter was 1977; slaughter numbers fell after that time as U.S. beef demand fell sharply, and still have never exceeded the 1977 numbers. Hog slaughter grew only slightly between 1980 and 2000. By contrast, chicken slaughter numbers doubled over that period, as demand increased sharply. With increasing chicken slaughter volumes, the industry could easily handle increased plant sizes with little increase in concentration. In contrast, shifts to much larger cattle slaughter plants, in the face of no real increases in aggregate slaughter, could only be accommodated with a sharp decline in plant numbers and a large increase in concentration.

Finally, I'll talk briefly about critical issues for new technologies. The one million existing beef and dairy producers are widely dispersed and have significant political power. Their perceptions matter. The last Farm Bill, for example, contained a proposal to ban packers' control of the livestock industry. It would have meant banning some types of contracting. That proposal passed the Senate but not the House. I believe that every Mountain State Republican voted in favor of the bill. Also striking was that many Democratic Senators from hog states did not vote for it, because the small-scale producers who would have supported the ban just don't exist anymore.

What's important to think about is what leaves the farm. The poultry and hog industries are moving toward more specialized operations. Farmers in these industries now only do a few things. They are not as diverse as they used to be. In the dairy and beef industries, however, lots of different products still leave the farm. Also, transportation matters, especially in poultry. What you build is a network of processing plants linked to farm plants. The organization of the whole network starts to matter.

So, what do you want farmers to do? The changes we've seen have led to different functions for farmers. One issue is going to be what functions the farmers are going to carry out. If identity preservation is important, what do the farmers have to do to achieve that? Also, what's the product market? What are consumers' perceptions? How is identity preserved? How is it assured to consumers? Those questions are going to be important.

If you want further information on the industries I've discussed today, please see the following four web sites: [www.ers.usda.gov/Briefing/Cattle/](http://www.ers.usda.gov/Briefing/Cattle/), [www.ers.usda.gov/Briefing/Dairy/](http://www.ers.usda.gov/Briefing/Dairy/), [www.ers.usda.gov/Briefing/Hogs/](http://www.ers.usda.gov/Briefing/Hogs/), and [www.ers.usda.gov/Briefing/Poultry/](http://www.ers.usda.gov/Briefing/Poultry/). ◀

With increasing chicken slaughter volumes, the industry could easily handle increased plant sizes with little increase in concentration. In contrast, shifts to much larger cattle slaughter plants, in the face of no real increases in aggregate slaughter, could only be accommodated with a sharp decline in plant numbers and a large increase in concentration.

▶ James MacDonald

A QUESTION AND ANSWER PERIOD FOLLOWED MR. MACDONALD'S presentation. The first questioner wanted to know how cattle are segregated and tracked for products such as Certified Angus Beef. Mr. MacDonald said that tracking in the beef sector is fairly difficult, because the industry is loosely integrated. Tracking is being done in Europe, however, which proves it can be done. (The beef industry is much smaller in Europe, however.) MacDonald said the Angus Beef association gives farmers information about how to produce better-quality animals, so they can get more money for the carcass at slaughter. But he didn't know exactly how those animals were tracked throughout the process.

Will Pape, who gave a presentation later in the day about tracking and identification, provided some input. Mr. Pape said that his company recently completed a study of 15,000 head of cattle. The study showed that, in their lifetimes, these animals had each spent at least 12 hours in at least 12 states. He said cattle often have 10 to 12 owners before they show up on someone's kitchen table, and virtually no information is "connected" to those animals regarding where they have been. Mr. Pape also pointed out that animal agriculture is in many ways a closed system. That is, livestock byproducts such as "protein blocks" are taken from meatpacking plants and used in the manufacture of animal feed.

One workshop participant said that the recent BSE case in the U.S. pointed to the lack of effective tracking mechanisms. Approximately 400 calves were slaughtered in that case as a precaution, he said, because they could not track down the one sick calf. This participant also asked Mr. MacDonald what he envisioned regarding a national livestock ID system. MacDonald said he suspects the future will bring greater contracting and coordination, which will lead to better tracking and also more industrialization. Another participant said that the FSIS and APHIS are working on ID systems, and they expect to have one available this summer. The industry is also working to develop a tracking system.

Moving to another topic, one participant said that MacDonald presented "a pretty depressing picture" regarding the disappearance of small farms and its effect on animal welfare. She asked how MacDonald thought the introduction of GE animals and animal clones would affect the concentration of the animal agriculture industry. Mr. MacDonald said it depends whether biotech is used to deliver a specialized end product, or if it is ultimately just another means for producing meat and dairy. If the latter, he said, we'll increasingly see a more industrialized business.

Another participant pointed out that 99% of all dairy operations are family owned, which is very different than in the poultry and hog industry. MacDonald agreed, though he said these family-owned businesses may still be very large (e.g., \$1 million in annual sales).

The issue of environmental law and tort law then came up. One person noted that large-scale hog farms are being challenged in court due to air and water pollution problems. Mr. MacDonald agreed, and noted that state environmental laws and policies have a significant effect on the siting of hog farms. Small changes in hog-producing costs in North Carolina, for example, (due to tighter environmental laws and policies), would shift more hog production to Iowa. He also said the enforcement of environmental laws could lead to an increase in smaller hog operations, and/or to the siting of operations in areas of low population density, such as Utah.

This participant also asked whether high gas prices could create diseconomies of scale for large producers. She noted that farmers growing poultry are finding natural gas prices to be a problem. MacDonald said that a typical broiler grower gets a fee that equals 10-20% of the value of the bird, and energy is a small part of their costs (and thus an even smaller part of total costs of production). There's no evidence that energy cost shares are substantially higher on larger operations, and so there's little to suggest that gas price increases will cause diseconomies of scale for large producers. In any case, integrators continue to find growers, suggesting that energy price increases aren't causing growers to shut down.

The final question was about exports. One participant asked MacDonald to describe the trends in the export of meat and poultry. Trade in meat products has grown steadily, said Mr. MacDonald, though it's not a dominant part of production; it accounts for about 10%. But, he added, it is currently a major focus of product development. The question has been how to develop products for overseas markets and extend shelf-life. It's also an increasing area of trade battles, he said—even more important than grain disputes.

## ► CARI WOLFE TRACKING, ENSURING, AND DELIVERING SPECIFIC DAIRY GENETICS

CARI WOLFE is Director of Research and Genetic Program Development at the American Jersey Cattle Association. She spoke to workshop participants about tracking, ensuring, and delivering specific dairy genetics. Her comments are paraphrased below.

There are 9 million dairy cows in the U.S. Of those, 91% are Holstein. Of those 91%, the Holstein Association has registered about 1.6 million, or 20% of the total. Of the registered ones, 100 are cloned animals. None of the dairy cattle associations are working with transgenic animals right now—only cloned ones. Clones are recorded in the databases with the name suffix "ETN."

Of the total 9 million dairy cows, 4% are Jerseys. (See box below.) Jerseys are the only part of the dairy population that is growing—largely in response to economic signals, driven by an increased demand for cheese. The American Jersey Cattle Association (AJCA) works with a high percentage of Jersey cattle. Upwards of 50%, or 175,000, are registered with us. Of those, we've recorded nearly 21,000 embryo transfer calves. Since January 1, 2004, we've registered 1,450 of those. So that's a small portion. We've also registered 20 clones and one daughter of a clone.

At the AJCA, our primary function is animal identification. We require permanent identification of registered cattle in the form of an ear tattoo, or a tamper-proof tag, or both. A National Animal Identification System is in development. A radio frequency identification (RFID) system is also in development. In that system, little button tags will carry transponders as permanent identification.

We maintain a large database of registered animals; we have 5 million records in our database at present. The information is submitted by farmers and producers. We have 2,300 members and provide services to 3,000 Jersey dairy farms, all of which are family owned. About 50% of the information we receive from farmers comes to us electronically. It's a sophisticated group of producers. We have a diverse group of customers. We have verification standards in-house as well as with the USDA's Animal Improvement Programs Laboratory, so that our records can be used in genetic evaluations.

### NINE MILLION DAIRY COWS IN U.S.

4% Jersey

► 50% or 175,000 registered

► 20,675 Embryo Transfer calves; 1,450 since  
1/1/04

► 20 registered clones

► One registered daughter of a clone

One way we ensure the integrity of the records is through DNA parentage verification. We do random verification testing; 1 in 500 are tested. All donor dams used in embryo transfer are verified and one in 10 of the female embryo transfer calves are verified. We find that 90% or so of the DNA matches are correct as submitted. So, there's still some human error in there. All bulls that enter artificial insemination are also required to have DNA parentage verification.

Another method of verification is that each dairy cow has a transponder that notes when she comes in for milking and milk weights. This is production-record verification. Data collection ratings include a combination of the number of test days, the frequency of test days, and component sampling. All of that information is compiled. If it's not done via computer recordings, the farmers collect samples manually.

The documentation we keep on each animal shows a performance pedigree. It lists a traceable ID, ear tag numbers, birthdate, what herd the animal was tested in, phenotypic information, genotypic information, how much milk she produced, how many sires, who her parents were, and so forth. That's the cornerstone of our business.

More than \$10 million is being spent on Jersey genetics. We do live auctions and internet auctions. All of that combines to make an international and national impact. The U.S. genetics of all breeds have a major impact around the world.

Looking to the future, genomic research will continue to be a priority for us. Jerseys have unique qualities. A national organization has been established specifically for marketing milk. You can make more cheese from the milk of Jerseys than from other cows. Regarding "biopharm" animals, we think there may be unique qualities of Jersey cows that could be useful. With regard to the development of human biologics, we know that animal biotech is the future. We are supportive of that.

What do we need? We need consumer education. Cloning and transgenics are two very separate issues. Consumers are confused about that. Those two activities and issues need to be handled separately. We also need to deal with the "yuck" factor. People get nervous about it. We want consumer acceptance of that glass of milk. And we need sensible regulation. ◀

What do we need? We need consumer education. Cloning and transgenics are two very separate issues. Consumers are confused about that.

► Cari Wolfe

A Q&A SESSION FOLLOWED MS. WOLFE'S PRESENTATION. THE FIRST questioner asked about the market for transgenic animals and animal clones. Ms. Wolfe said she expects that these technologies will be most useful in specialized situations, such as cloning bulls that are considered "genetic giants" but that can no longer produce semen. Right now, she said, cloned cows can bring up to \$80,000 at public auction. The market for cloned and transgenic cows will certainly be affected by the regulatory system governing those animals, she added.

In response to another question, Ms. Wolfe said that assisted reproduction is used at about the same rates in Holsteins as in Jerseys. She added that the value of Jersey milk is greatest in products in which the solids must be recovered, as in cheese-making. Holstein milk yields 10 lbs. of solids for every 100 lbs. of milk, while Jersey milk yields 12 lbs. of solids for every 100 lbs. of milk.

Asked if the AJCA is funding research into biopharm animals and the production of human biologics, Ms. Wolfe said they have provided some seed money for research in those areas, but they do not have the funds to do more at this time. They would love to put more money toward that type of work, she said, but it is very costly.

Finally, a workshop participant asked Ms. Wolfe how the AJCA is ensuring that their breed structure remains strong and that the gene pool is not narrowed via cloning. Ms. Wolfe said that she is the key in-house person in charge of inbreeding management, and that the organization is also advised by an array of experts. She said that cloning is not being adapted fast enough right now to present a problem, but that they will continue to monitor it carefully.

► JAMES RIDDLE  
*MARKETING OF ORGANIC BEEF AND DAIRY  
PRODUCTS*

JIM RIDDLE is the founder of Organic Independents, a consultancy and inspection service. He also serves at present as Chairman of the USDA's Organic Standards Board. Mr. Riddle spoke to the group about the regulatory requirements for marketing certified organic livestock. His remarks are paraphrased below.

I'm going to talk today about the USDA's regulations governing organic agriculture, and how they relate to the marketing of certified organic livestock. I want to note, first, that the web site of the national organic program is [www.ams.usda.gov/nop](http://www.ams.usda.gov/nop).

The USDA has a single legal regulatory definition of organic production, as follows: "A production system that is managed in accordance with the Act and regulations in this part to respond to site-specific conditions by integrating cultural, biological, and mechanical practices that foster cycling of resources, promote ecological balance, and conserve biodiversity." All operations that are certified under the regulation must operate in accordance with that definition.

I'm just going to focus on organic livestock today. Every organic operation must file an organic livestock plan before being certified. The plan must be approved or accredited by one of 97 authorized certification agencies. Half of these agencies are domestic, half are foreign. They must be competent and free from conflict of interest. Then the operations must follow their own plan. They must monitor their management practices and implement physical barriers as needed to prevent commingling and contamination. They might need buffer zones, for example. The land itself must be free of prohibited materials for three years prior to harvest in order to produce organic feed. It's a long transition process for the land. Also, recordkeeping is mandatory.

The livestock plan must contain information regarding the livestock requested for certification, including sources, living conditions, livestock feed and feed supplements, pasture water, a livestock health management plan, a recordkeeping plan, a handling for slaughter plan, a milk handling plan, and an egg handling and packing plan. All slaughter animals must be managed organically from the last third of gestation (i.e., the mothers must be managed organically

#### LIVING CONDITIONS

All animals must have access to shade, shelter, exercise areas, fresh air and direct sunlight suitable to species, stage of production, climate and environment.

Dairy animals must be organic for one year prior to selling their milk as organic. The entire herd can be converted by feeding it 80% organic feed for nine months, then 100% organic feed for three months. (That transition rule is being contested in court.) Once a herd is converted to organic, it cannot be rotated between organic and nonorganic production. It's either in or out.

► James Riddle

for at least the last third of the fetuses' lives). Poultry can be sourced from any hatchery but must be under organic management from the second day of life.

Dairy animals must be organic for one year prior to selling their milk as organic. The entire herd can be converted by feeding it 80% organic feed for nine months, then 100% organic feed for three months. (That transition rule is being contested in court.) Once a herd is converted to organic, it cannot be rotated between organic and nonorganic production. It's either in or out. The livestock feed must be 100% organic—that includes pasture and grains. And there must be records of that. Prohibited feed ingredients include plastic pellets for roughage, feed formulas containing urea or manure, and animal slaughter byproducts. (In Britain, organically raised animals never contracted BSE, because of the latter restriction.)

Regarding livestock feed and supplements, trace vitamin and mineral supplements approved by the FDA and the Association of American Feed Control Officials are allowed. Synthetic methionine is allowed until October 21, 2005, although the National Organic Standards Board (NOSB), of which I am chair, is recommending to extend that. (Note that, under the law, the 15-member NOSB has the unique authority of reviewing substances to be placed on a national list, and the Secretary of the USDA can only change the list with the two-thirds approval of the board.) Milk replacers are allowed, but antibiotics and rBST are not. Drugs, including growth hormones, cannot be used to promote growth.

Preventative health care practices are very important. These include appropriate selection of species that are suitable to site-specific conditions and resistant to prevalent diseases and parasites. There is aggressive culling of herds intended for organic production to get the problems out of the breeding lines. There is also aggressive breeding. Nutritional feed rationing is important too. We've observed that, once a dairy herd converts to organic, veterinary bills drop to maintenance levels. There are tremendous improvements in the health of the animals. Organic producers are required to establish appropriate housing, pasture conditions, and sanitation practices to minimize the occurrence and spread of diseases and parasites.

Physical alterations to the animals are allowed if done to promote animal welfare and in a manner to minimize stress and pain. Tail docking is not allowed, since it is not done to promote the animals' welfare.

Examples of allowed synthetics include vaccines, but not GE vaccines. This is the only area in the regulations where there is an open door for GMOs; the board could approve them. Other allowed synthetics include electrolytes (without antibiotics), glycerin/iodine in teat dips, mineral oil (as a lubricant only), oxytocin for therapeutic application only (and there's interest in re-reviewing this one), and vitamins that are FDA-approved.

Parasiticides are prohibited for slaughter stock. Ivermectin is on the list and can be used for emergency treatment only for breeder stock prior to the last third of gestation, and for dairy stock 90 days prior to milking. Antibiotics are prohibited. However, the farmer must not withhold treatment of an animal in

order to preserve an animal's organic status. They must treat the animal if a veterinarian recommends they do so in order to save the animal's life. Then the animal is just not used as organic. This does happen, but it is fairly rare.

All organically raised animals must have access to shade, shelter, exercise areas, fresh air, and direct sunlight suitable to the species, stage of production, climate, and environment. The rule about access to the outdoors is a bone of contention in the poultry industry. Ruminants must have access to pasture. There has been some controversy about that, because some big confinement dairies have been certified organic even though they have very little pasture available. The Board is making the rules on this clearer. Pastures must have buffers if they border land on which pesticides, synthetic fertilizers, genetically modified crops, or other prohibited substances are used.

Appropriate clean, dry bedding is required. If bedding is consumed, then it must be organic. Living conditions must accommodate the health and natural behavior of the animals and allow for natural maintenance, comfort behaviors, and the opportunity to exercise. The living conditions must reduce stress and the potential for injury. Shelter must allow for temperature level, ventilation, and air circulation suitable for the species.

Temporary confinement is allowed under certain conditions, such as inclement weather, an animal's stage of life (babies, or a final finishing phase for organic beef), and conditions that jeopardize the health, safety, or well-being of the animal. Also, confinement is allowed if it's too wet and there's a risk to soil or water quality.

Manure must be managed to prevent the contamination of crops, water, and soil. So, manure is generally composted, and you won't see much winter spreading on frozen ground.

The records kept must identify all animals, preserve the identity of animals and products, disclose activities, be auditable, demonstrate compliance with the regulation, and be maintained for five years. The types of records required include breeding and birth records, source of purchased animals, source of purchased breeding/bred animals, proof of purchase prior to the last third of gestation, date of birth of calves, proof of organic certification, proof of purchased certified organic feed, health care products used, production and sales, and animal ID number and lot number when selling. The grower must maintain records through slaughter and processing .

Some methods of production are prohibited as "excluded methods." The regulation states that excluded methods are: "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 (including gene deletion, gene doubling, introducing a foreign gene, and changing the positions of genes when achieved by recombinant DNA technology.) Such methods do not include the use of traditional breeding, conjugation,

fermentation, hybridization, in vitro fertilization, or tissue culture." That definition was developed originally for plants. We may need input regarding its appropriateness for animals.

Next I want to talk about concerns of my own (not my organization's) regarding GM and cloned animals. (See box below.) First, I'm concerned about the containment of transgenic organisms, and also about proper labeling and consumer right-to-know. On the plant side, the technology was rushed. You have to have something people want to buy. It has to be based on true science. When there is a product that has appeal, then there will be consumer adoption. The identification and traceability of products and byproducts is also a concern. I'm concerned about GM materials getting into an organic product. The only way to prevent that is with proper ID and traceability. I am also concerned about unanticipated effects, including environmental, health, economic, and societal effects. I'm glad we are thinking these issues through in advance in meetings like this. Also, I personally have problems with the patenting of life forms. Ethically, I find that questionable.

There are also concerns regarding the treatment of animals. For example, Canada chose to reject Monsanto's application for rBST because of health impacts on the animals. The U.S. looked at the food safety effects (for humans) but not at the health effects on animals. When you read the label, you can clearly see that the drug causes lower life expectancy and all kinds of problems for the animals. Those types of issues must be taken into consideration with this technology. I also have concerns about the use of public resources for private gain. A lot of public money is being invested in technologies that are going to be patented by and benefit private companies. The use of public dollars should be for the public good. ◀

IN THE QUESTION AND ANSWER PERIOD THAT FOLLOWED MR. RIDDLE'S presentation, much of the discussion focused on clarifying whether transgenic animals and/or animal clones could potentially be certified as organic. The first questioner noted that transgenic animals would likely not be allowed to carry the organic label, because they were created using a specifically excluded method. But he asked whether the progeny of transgenic animals could potentially be certified as organic.

#### ORGANIC CONCERNS – GM & CLONED ANIMALS

- Containment of transgenic organisms
- Proper labeling – Consumer right-to-know
- Identification and traceability of products and byproducts
- Unanticipated effects – Environmental, health, economic, societal
- Not “substantially equivalent” or GRAS
- Patenting of life forms
- Ethical treatment of animals
- Use of public resources for private gain

Mr. Riddle said he thought the progeny probably would not qualify, since it is indirectly the product of an excluded method, but that the NOSB would have to review this issue and decide.

Another person asked whether animal clones could be certified organic. Mr. Riddle said he felt animal clones would not be allowed, because the cloning process uses artificial hormones. One participant noted that cloning does not require the use of such hormones, but even if they are not used, the process of cell fusion would probably exclude cloning from being considered organic. He then pointed out, however, that an animal only has to be organic for the last third of gestation. So, does it really matter how the animal was created at the outset? Mr. Riddle said that clearly clarity is needed on this question, but it is not on the table at the NOSB at the moment.

Mr. Riddle said the debate regarding biotechnology at the NOSB at present is focused on the adventitious presence of GE crops in organic crops. The use of GE seed is clearly prohibited, he said, but not the adventitious presence of it. Mr. Riddle explained that if GE material were found in a crop, the crop cannot be sold as organic, but the farmer does not lose his organic certification if it happened through no fault of his own. The NOSB has set tolerances for pesticide residues, but not yet for GE material.

Another participant asked how the auditing process works. Mr. Riddle explained that the audit is typically a five-hour process, conducted at least annually, during which both crops and livestock must be observed. Guided by a standardized audit checklist, the audit involves a physical inspection of all fields, borders, equipment, storage, and inputs, as well a review of the records. It also looks at the living conditions of the animals. The audit report then goes to the certification agency. The inspector never makes a decision; he or she just makes observations and conducts an exit interview. The certification agency makes any decisions that need to be made.

Finally, one participant responded to Mr. Riddle's concern about the use of public research funds for private gain. The participant said that, when publicly funded research is conducted, private funds are also often used, but the intellectual property ends up being owned by the university. The companies then get first right of refusal to buy it. This is the best way to be sure the technology is scrutinized in a public fashion, he said. Mr. Riddle said the primary concern behind his comment was simply that he wants to see more public dollars spent in the organic sector. Of the USDA's \$82 billion budget last year, he said, less than \$12 million was spent on organic, even though it's the fastest-growing sector of the food industry.

## ► WILLIAM PAPE LIVESTOCK MARKETING AND TRACKING

WILL PAPE is a rancher and the CEO of AgInfoLink Global, Inc., a company that designs and develops secure traceability tools for the world's food supply. Mr. Pape's presentation covered livestock marketing and traceability issues. His paraphrased comments are as follows.

I'm going to talk today about animal traceability. AgInfoLink has been involved in traceability since 1997. We are providing the link in the chain.

When we talk about traceability, we need to be clear about the true state of the art. In the beef industry in the U.S., fewer than 2% of beef cattle are tracked from birth all the way through slaughter. And that estimate may be on the high side. We helped to audit the United Kingdom's traceability system, which is a paper passport system. We found that 65% of the records were wrong. And the whole program is very expensive—approximately \$60 per head. So, they spent a lot of money, and the program is not very accurate. But everyone feels good about having some kind of system. I find that a little depressing.

There are some bright spots on the horizon. Traceability provides significant opportunities for both producers and food processors. It's not just a "stick"—it can be a "carrot." It has to do with regulation and profit opportunity. It can also help address issues of food safety and food security.

Who is AgInfoLink? We were founded in 1997. We're a private company that works in the U.S., Mexico, Brazil, Australia, and Canada. The U.S. trails the rest of the world on these issues. Our company's founders are experienced in the livestock industry, technology, and the credit card network industry.

What is "traceability"? We define it for each discrete "production unit," which could be an individual animal or a specific lot of animals. These units of production are discrete and don't commingle and don't change. These production units move around, obviously. When you have "license plates" on every animal, you find that they can travel several lots away from where you put them. For each unit, we look at how to collect relevant attribute information. The attributes of the unit of production are important from a commercial perspective. We are talking about tracking across more than one segment of production, and across product transformations (i.e., from wheat to flour to dough to bread).

What we are trying to do is put together the same kind of system for grocery and retail that we did for credit cards. A credit card could be issued by one of many banks, but there's one card reader and it's the same everywhere. We want to do same thing in this industry. AgInfoLink's PonyExpress, for example, is a "digital backbone" that can create a single point of entry for retail outlets and government agencies for the purpose of providing traceback, source verification, product compliance, and profit enhancement for food and food safety.

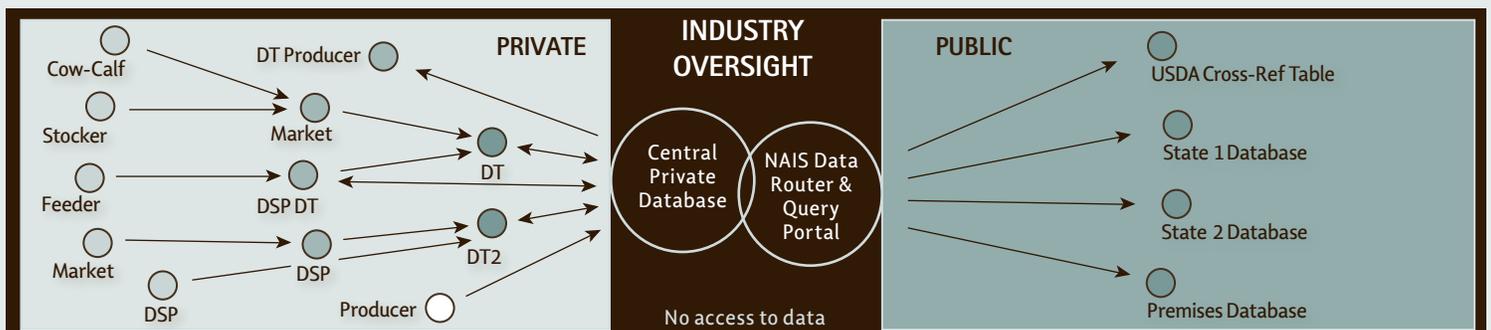
Traceability has two facets. There's compliance traceability, which you may want to do because of food safety requirements, food security record keeping, organic status verification, environmental requirements, protection from foreign diseases, and so forth. But there's also value traceability. This is traceability that's good for business. This is traceability that can yield improved consistency, higher yields, lower costs per unit of production, logistical savings (corridor management), justification of brand claims (e.g., attribute A delivers result Y), and lower-cost new products.

Let's go back to compliance traceability and look at the current regulatory snapshot. People in the U.S. began in the mid-1990s to discuss traceability seriously. A group was formed called the U.S. Animal Identification Project (USAIP). It included representatives from government and business. The USAIP called for a single, central federal data system that is palatable to the producer communities. A number of producer groups created review committees that said they want to administer the program jointly as well.

This diagram (below) represents the current thinking. (The diagram was part of a presentation that was put before the National Cattlemen's Beef Association (NCBA) at the annual convention in February. It was approved by the membership, and the NCBA is now working with other producer associations to get support for the concept.) The concept has a private part and a public part. It involves industry oversight via an advisory board with industry and government members, similar to what's been done in the organic movement. The advisory board would issue contracts for a central private database into which information would flow on animal ownership and animal movement. The only information that would flow into the public realm would be on individual animals that are under surveillance or investigation. The benefit of this is that the vast majority of producer information would be kept private, until it's needed.

So, how can we be sure we'll get the information we need when we need it? Well, we did that in the credit card industry. Your credit card data resides at the bank that issued you the card, not at VISA or MasterCard themselves. But VISA and MasterCard have the ability to pull information from the banks when it's needed. If we follow this model in the animal agriculture industry, the information that needs to remain private would remain private, and the information that needs to be obtained can be obtained. So, we have the capability to do this today. This isn't rocket science.

CURRENT  
REGULATORY  
SNAPSHOT



What's important is that producers would have multiple ways to access the National Animal Identification System. That network then speaks to a central database. That's all on the private side. Again, this is industry's idea on how such a system should work. Where this dialogue goes, nobody yet knows. The USDA has funded a number of pilot projects that began this fall, and we are moving toward premises identification systems (37 states have them now). This is a solidly public system, and nobody disagrees with that. What needs to be fleshed out now is how the data actually move in the system.

So, that's the compliance side. Let's talk now about the state of the art in value traceability. How does traceability deliver value? It could provide less variability in certain key attributes. In most of agriculture today, there is more variability within a group than between groups. For example, if I have two groups of 250 head of cattle, there may be \$10 per head difference between the two groups, on average. Within a single group, however, I could have a \$300-\$500 range of difference in price between the individuals. That's really important. Understanding which attributes are best used for which processes is important. So, we want to trace those animals that have the most desirable attributes across transformations and across different owners. For example, with those 12 different owners that your hamburger had before you ate it, not a single person provided any information of substance to the next person involved. There is simply no information flowing from one owner of an animal to the next owner. If you go back to the BSE case that arose on December 23 in Washington, we were only able to find 29 of the 72 cohorts of that animal. That was a dairy cow with a Canadian ID tag on it, thank goodness. The fact that we even found 29 surprises me, though it did take six months. So, systems until now haven't allowed us to view identity preservation across companies. But they do now. We've been doing this since 1998.

What's needed for a complete system? (See box below.) Three things are important. First, you need a unique identifier—a radio frequency ID (RFID) tag, a barcode tag, or a biometric identifier (e.g., a retinal scan). There are lots of possibilities, but we think we've identified the best one. We've identified a low-frequency RFID tag that works best. Second, you need a database managed by individual units of production, including herd management software, flour mill management software, and the ability to integrate traceability into existing ERP systems. And third, you need a network to connect the local databases

#### WHAT'S NEEDED FOR A COMPLETE SYSTEM?

Unique identifier: tag (RFID, barcode, etc.) biometric, etc.

Local database managed by individual units of production

- Herd management software
- Flour mill management software
- Integrating traceability into existing ERP system(s)

Network to connect local databases

- Interface to existing systems
- Across different owners
- Across transformations
- Across different segments of production

across enterprises. The network has to interface with existing systems, across different owners, across transformations, and across different segments of production. This network is AgInfoLink's core focus.

AgInfoLink's solution components include a data capture system, a way to securely share this information, a database system that will issue reports, web exposure, and a way to link these networks. In the food and agriculture industry, people are very proprietary about their data. They don't even want their data to be on the same computer as somebody else's data. To address that level of concern, you have to create systems that are separate networks that can loosely talk to one another.

Let's look at specific data collection devices. With the large number of small producers, you have to start pretty simple. The most basic technology in our system is a #2 pencil. We start there and work up. In Brazil, for example, we're using a system that includes an RFID device, a visual tag, and a form (a CattleCard™) for each calf, which is filled out by hand and sent in the mail to register the animal.

You can get more complex from there by having "readers" (wands) that read RFID devices. (Ours is called BeefLink™.) They connect wirelessly to a computer database for instant history checking and decision-making. With all these RFID devices, of course, you often have to deal with retagging for the 1% or so animals that aren't tagged properly the first time or lose their tag. Also, with the reader you have to be physically close to read the tags. If you have a group of animals moving down a chute, you have to be careful to read them all.

We also want to make sure we don't turn cowpunchers into keypunchers. Most of the folks we deal with don't want to do data entry via a computer keyboard. So, we also have a product that has "work cards" with an embedded RFID device. The work card might list, for example, "bull," "cow," and "steer." All you have to do is point to the animal's RFID ear tag with the reader and then point to the appropriate word on the card. The device will then talk back to you so you can verify that you've entered the right information.

The technology also exists such that we can set up databases, stored in a hand-held computer (or PDA, personal digital assistant), to track which animals have received particular vaccines. You read the animal's tag, communicate with the PDA, it responds back with voice information saying what needs to be done to the animal, then you do it and update the database right there. It communicates information via Bluetooth technology to a pocket PC. This is a huge time and cost savings. We found that 2,500-head dairies were able to go through a complete herd using this technology in about 30 minutes with one or two people, as opposed to five or six hours with three or four people using old methods. You can also take this to the packing plant—you can take identity all the way out to the cut-up animal after slaughter. We are doing that for a few customers.

So, who is going to pay for all this identification? Well, right now we can't export to Japan because of their concerns about BSE in our cattle. Because of this we are leaving \$150-180 per head across the national herd on the table.

In the food and agriculture industry, people are very proprietary about their data. They don't even want their data to be on the same computer as somebody else's data. To address that level of concern, you have to create systems that are separate networks that can loosely talk to one another.

► William Pape

That's the money we're losing because we can't export to Japan. The Japanese want birth records. We tried some other kinds of analysis, and they've more or less rejected that. So, these RFID systems might cost you \$6 per head, but you might get back \$180 from the ability to sell to the Japanese. Also, the outcome of all these systems are reports. This allows a producer to compare one lot of cattle to all he's ever produced, and compare them to the cattle of all his neighbors. The average herd size in our program is 19 head. On average we've brought back \$50-75 per head to each person. And it's only a \$5-6 per head investment. ◀

FOLLOWING THE PRESENTATION, ONE PARTICIPANT ASKED MR. PAPE to clarify the cost of the RFID tags. He said that existing RFID technologies, in commercial volume, wholesale in the range of \$1.75-\$2.25 each. He also noted that RFID technology is not monolithic; there are high-frequency and low-frequency RFID tags. AgInfoLink, he said, advocates the low-frequency models, because they can be read through biological material (e.g., a cow's ear or head). The high-frequency ones, which are cheaper and smaller, cannot be read through an ear or a head. Mr. Pape said he thinks the low-frequency tags will eventually get into the sub-dollar level. The high-frequency tags will likely get down to pennies each, he added, but they just are not as useful.

Another participant asked Jim Riddle if he felt Mr. Pape's traceability systems would be helpful in tracking organic livestock and keeping organic and nonorganic segregated. Mr. Riddle said that if the system is developed as Pape described, has clear containment and traceability aspects, and is compatible with models that the organic sector has developed, it could work well. Mr. Pape noted that genetic engineering is just one attribute they would be looking to track. If consumers can associate a label with a true set of facts, he said, then they can make the decisions they need to make.

► STEVEN TANNER  
*TRANSGENIC TRAITS IN GRAINS: MEETING  
THE CHALLENGE*

STEVE TANNER is the Director of the Technical Services Division at the USDA's Grain Inspection, Packers, and Stockyards Administration (GIPSA). He spoke about lessons the livestock industry could learn from the grain industry regarding traceability. Mr. Tanner's paraphrased remarks are as follows.

If the livestock industry can learn some lessons from the grain business, you might be able to anticipate and solve problems ahead of time. The grain industry has been through the first generation of biotech products. There were challenges, and there still are. Don't underestimate it. The industry is still working on segregation and identification and knowing the contents of the end products. The less testing required, the better. It will be more efficient and won't cost as much. Testing can add huge costs when shipping grain out of the U.S. I'm going to focus on the export market, as that's where it is most relevant to the grain industry.

I'm with the USDA's Grain Inspection, Packers, and Stockyards Administration. We provide and maintain grain standards. We also provide research to improve new test technologies, and we provide third-party official testing services and mandatory grain testing for export. I'll talk first about regulatory and technical issues relating to biotechnology, then testing technologies (protein- and DNA-based), and then lessons learned.

The U.S. continues to approve new "events" (i.e., new types of GE grain). Approvals lag in other countries. Approximately 50% of our grain is exported. Grain is a fungible commodity. Our grain infrastructure limits the ability to segregate grain. To do so is very expensive. More segregation is beginning to occur, due to the demand for different quality grains throughout the world. The U.S. has voluntary labeling; numerous other countries have mandatory labeling. "Adventitious presence" is not defined. And it's always a concern. Other countries can reject large quantities of grain if they find a small amount of GE grain in a shipment, and they don't want it.

To test a shipment for the presence of GM grain, you must consider protein expression variability and the stacking of traits. There are no internationally recognized standard methods and limited reference materials for analyzing grain. The meat industry should start now to determine how such testing will be performed! There are credible, valid methods, but little agreement on which to use. The expression of analytical results is inconsistent. Every testing laboratory has different procedures. It's very confusing.

Protein-based testing detects the protein expression products that result from a genetic transformation. DNA-based testing detects the specific sequence of nucleotides associated with a genetic transformation.

What we need are protein-based tests that are accurate, reliable, rapid, low cost, rugged, and easy to use. Such tests would help industry meet regulations and contractual requirements, manage risks, and verify identity preservation programs.

► Steven Tanner

At GIPSA, we formally asked industry how we could help to facilitate the grain markets with the presence of biotech grain. Ultimately, we developed a performance verification program for protein-based tests. There are two kinds of protein-based tests: Enzyme-linked immunosorbent assay technology and lateral flow strip technology. GIPSA has a formal relationship with the life sciences companies such as Dow and Monsanto. They give us detailed information on the types of GE grains in commercial production, and we use that information to verify privately manufactured test kits. We've found that approximately 20% of the test kits fail the initial evaluation by GIPSA scientists. Numerous kits have been verified, and a listing can be found on the USDA GIPSA website.

Protein-based testing is a rapid, inexpensive, and relatively simple technology; requires minimal training; and can be performed in nonlaboratory conditions. On the negative side, lateral flow technology is qualitative, not quantitative (it shows whether a protein is there, but can't detect how much is there); it's non-specific (it can't reveal which Bt protein, for example, is present); it can only identify single events (no stacked genes); and there are no test kits that can identify everything in commercial production.

Another challenge is protein expression and concentration. For example, StarLink is almost totally expunged from the U.S. grain market system, though we still require the milling industry to test every load of corn prior to milling. If I grow some StarLink corn in North Carolina and some in North Dakota, I might find a 5X change in the protein in the kernels because of the different environmental conditions in those two locations.

This makes it very difficult to determine the percent of the GE material in a load by weight. It's almost impossible. Yet the regulations for labeling in many other countries require a determination of percent of the GE grain by weight.

What we need are protein-based tests that are accurate, reliable, rapid, low cost, rugged, and easy to use. Such tests would help industry meet regulations and contractual requirements, manage risks, and verify identity preservation programs.

There are two kinds of DNA-based tests, also known as polymerase chain reaction (PCR) tests. Conventional PCR tests are used for qualitative analysis. Real-time PCR can be used for qualitative and quantitative analyses. The advantages of DNA-based testing are that it's sensitive and specific, may detect all events, includes the determination of quantity, and has many standardized methods. The disadvantages: It's expensive, requires hours to days to complete (and thus can hold up shipments), must be done in a controlled laboratory environment, and requires highly trained staff and expensive equipment, and many current methods are proprietary.

In DNA-based testing, the units can be in percent weight or percent DNA. There is no internationally recognized reference material. Also, it's not possible to distinguish between single events and stacked events. Sometimes stacked events aren't approved in other countries, while the single events might be. Given

these challenges, and the challenges of protein-based testing, I believe that production agriculture should attempt to market its products on the basis of preserving product identity.

GIPSA has developed a proficiency program for testing laboratories. It's a way to help labs get a handle on how well they are performing. It's a voluntary program. To meet the grain industry's needs, the proficiency program was designed to determine if laboratories are reliable and accurate in the detection of all events and in agreement among themselves. The proficiency program is a risk management tool for the grain and food industry. It helps labs identify areas of concern; improves the reliability and accuracy of testing on a global basis; and identifies labs that can provide accurate and reliable results. The laboratories are listed on our web site. Early on, many labs performed poorly. Those have dropped out of the program, which is what needed to occur. We now have 110 participants in the proficiency program worldwide.

This relative measurement variability slide shows essentially that testing is still not reliable. (See figure below.) The section on the left is what we would normally expect—that's the coefficient of variation (CV) that is predicted given different percentages of the analyte. The section on the right shows real-life data based on what labs have submitted to us. When we used a highly controlled ground sample of .1%, the CV range came out to be 57-147%. Consistency in testing is one of the most important things. Even as you go higher in parts per million, there are large CV ranges. So, the fact is that only five to ten labs in the world can perform very well.

Observations from our proficiency program are as follows. Qualitative detections of GM material are correct for more than 90% of the results. False positives and negatives are less than 10%. A lab's performance appears to improve over time. With the quantitative samples, the observed results are generally consistent with fortification levels, and the CVs trend downward as fortification levels increase.

Overall, a synergistic approach to the application of detection methods for biotechnology-derived products is necessary. No single method can detect all events. No single method exists for the quantitation of all events. But both DNA-based and protein-based methods have appropriate applications.

#### RELATIVE MEASUREMENT VARIABILITY

ANALYTE		CV*	DNA-BASED		CV RANGE**
1 ppb (0.0000001%)		45%	0.1% (1,000 ppm)		57-147%
1 ppm (0.0001%)		16%	0.5% (5,000 ppm)		30-74%
	1%	4%	1.5% (15,000 ppm)		27-62%
			3.0% (30,000 ppm)		23-40%

\*Horwitz predicted values

\*\*Actual Proficiency Program values (% by wt)

We at GIPSA are working in partnership with life science companies to improve testing. We have an agreement with the National Institute of Standards and Technology (NIST) on research, reference materials, and methods, and we are performing research with NIST and others on DNA isolation procedures. We are actively participating with various international organizations as well.

The lessons we have learned are as follows. Standard terminology for the expression of results is needed. We need viable and internationally accepted testing methods in the public domain. Reference materials are needed. We need to maintain our professional relationships with life science organizations. And proficiency-type programs are valuable to laboratories. ◀

IN THE QUESTION AND ANSWER PERIOD, ONE PARTICIPANT ASKED IF tests exist that could detect if an animal is a cloned or transgenic animal, or if milk is from a cloned animal. Another participant with knowledge of the subject said you could only test for clones if you had the parent animal and you did tests to show that they were genetically identical. Likewise, you could only identify that an animal is transgenic if you knew the DNA sequence that was inserted and you tested specifically for that. Another participant said that the new animal drug provisions of the FDCA require developers to come up with a determinative method for identifying “drug residues” (i.e., the transgene, in this case) in food. So it’s required that the DNA sequence be known and testable.

Another participant asked which agency is going to be defining and regulating adventitious presence, including determining liability when unwanted GM seed is found in a field or shipment. It was noted that the White House Office of Science and Technology Policy was working with the USDA, FDA, and EPA and was aware of the complex international issues associated with the issue of adventitious presence. Tom Bundy, who spoke earlier, said APHIS was in the process of looking at the issue. He noted that it presents some difficult legal issues, because no law instructs or specifically allows APHIS to set levels for the adventitious presence of GM crops in traditional crops. Another participant noted that the issue of adventitious presence is typically viewed as separate from the issue of commingling, and that the OSTP stated in 2002 that they were going to work on the adventitious presence issue.

► MICHAEL RODEMEYER AND  
THOMAS BUNDY  
*SHORT OVERVIEW OF THE NATIONAL  
ENVIRONMENTAL POLICY ACT*

At the request of workshop participants, MICHAEL RODEMEYER of the Pew Initiative and TOM BUNDY, formerly with USDA's Office of the General Counsel, gave a short presentation about the National Environmental Policy Act (NEPA). Mr. Rodemeyer went first; his paraphrased comments are summarized below.

NEPA is one of the oldest environmental statutes. The Council on Environmental Quality in the White House is responsible for implementing NEPA. It's a procedural statute that applies to federal agencies. The CEQ issues regulations to implement NEPA, plus individual agencies issue their own regulations as well. The EPA doesn't technically fall under NEPA; it is assumed that they are carrying out the intent of NEPA in all their activities.

NEPA applies to major federal actions significantly affecting the quality of the human environment. If an agency is going to undertake an action that will affect the environment, they must respond to NEPA in one of three ways.

1. Declare a categorical exclusion.
2. Conduct an environmental assessment to determine if the action will have a significant effect on the environment. In order to move forward without conducting a more detailed environmental impact statement, the agency in an EA must reach a finding of no significant impact (FONSI). The agency can outline mitigations they will take in order to get to a FONSI. Usually, a 30-day public comment period is provided on a draft EA.
3. Conduct an environmental impact statement. If the agency can't make a FONSI, then they do an EIS. An EIS is a detailed statement of impacts and possible alternative actions. It is submitted for public comment. A final EIS is issued before a decision is made.

NEPA is a process law. There's no substantive restriction on what actions the agencies can or cannot take. Agencies are not required by this law to choose the least-harmful option. The law doesn't provide any new authority to make decisions about environmental impacts. You can't make a decision on a permit based on NEPA requirements. It has no environmental decision standard in it, unlike TSCA or FIFRA. NEPA has been subject to extended litigation over the years. People can sue to force procedural delays.

The EPA doesn't technically fall under NEPA; it is assumed that they are carrying out the intent of NEPA in all their activities.

► Michael Rodemeyer

The presentation continued with Tom Bundy's remarks, which are paraphrased below.

My examples are from my APHIS background. NEPA only sets up minimum standards for public participation. Sometimes agencies go beyond those minimums. Sometimes they put out draft EAs for public comment, even though they are not required to do so. For a notice of petition for deregulation at APHIS, for example, they will prepare a draft EA and put it out for public comment.

APHIS puts out many EAs and very few EISs. EISs are very time consuming and cost a lot of money. At APHIS, an EIS took a minimum of two years to complete. So, there's a big push to try to simply mitigate any identified impacts, so the agency can issue a FONSI.

Under the regulations, one of the most important parts is the "categorical exclusion." If you can set up a broad categorical exclusion for a particular type of action, you don't even have to do EAs. So agencies try to make these as broad as possible. They do an EA on a regulation itself, for example; then, any individual agency action conducted in compliance with that regulation is automatically exempt from requiring an EA. The agency does have to at least look to see if the action fits in the categorical exclusion. If they don't look at it, they are in violation of NEPA. That has happened before.

One of the purposes for litigation under NEPA is to slow down a decision-making process and stop something altogether that may be time-sensitive. Lawsuits usually concern lack of sufficient detail regarding environmental effects, or lack of sufficiently detailed alternatives. If those bringing the lawsuit win, they agency has to conduct another EIS.

#### IN THE SHORT DISCUSSION THAT FOLLOWED, ONE PARTICIPANT

pointed out that agencies can work together on EAs or EISs where appropriate, with one agency designated the lead. Another person said that, in the case of new animal drugs, the sponsor (the company) conducts the EA, to save the agency time and money. Mr. Bundy said that, yes, applicants to any agency can speed up the process and help agencies with resource problems by conducting the EAs or EISs and submitting them to the agencies for approval. The agency then has to adopt the EA or EIS as their own, however. And if any litigation ensues, the agency is fully liable for the contents of the document and its actions as a result of it. Finally, another participant pointed out that NEPA is concerned with the "human environment," not just the natural environment, so a lot of the issues discussed in this meeting relating to the approval of new animal drugs would have to be assessed under NEPA.

## SECTION 3

# DISCUSSIONS

THIS SECTION CONTAINS HIGHLIGHTS OF PARTICIPANTS' DISCUSSIONS IN THE MARCH AND MAY WORKSHOPS. These conversations took place in both full plenary and small work group settings. Participants did not seek consensus, so this section simply characterizes the range of ideas and viewpoints that were raised.

The discussions are organized into ten categories of issues. The first category summarizes participants' thoughts regarding the attributes and components of a theoretical, ideal regulatory system. Most of the remaining categories relate, in some degree, to the FDA's application of the "new animal drug" rubric to the regulation of GE animals. These categories address: using the (New Animal Drug Application (NADA) v. amending the law; the need for a clear road map; how the system works today; transparency; public participation; the regulation of environmental risk; consumer choice/labeling; animal welfare; and additional issues of concern.

The FDCA's new animal drug provisions were discussed in detail in Fred Degan's presentation, summarized earlier. As a reminder, researchers seeking to develop a marketable product from a transgenic animal generally first establish with the FDA an "investigational new animal drug" file, or INAD, and then conduct research under the INAD's requirements. Once they develop a product they would like to market, they submit to the FDA a "new animal drug application," or NADA, under which the agency then reviews the product for safety and efficacy. The current INAD/NADA regulations were written for conventional new animal drugs, but they are being used for GE animals because the introduced genetic construct can be said to meet the definition of "animal drug" in the law, since it changes the "structure or function" of the animal.

It should be noted that participants seemed to agree, overall, that the INAD/NADA system is rigorous and risk-based and appropriately requires products to undergo an in-depth pre-market review. Few (if any) concerns were raised in the workshops regarding the FDA's ability to adequately assess the safety of food from GE animals or the safety and efficacy of drugs or biologics derived from those animals, as long as the agency is given adequate staff and resources to conduct its work.

## ATTRIBUTES AND COMPONENTS OF AN IDEAL REGULATORY SYSTEM

In both workshops, participants spent time discussing their vision of an ideal regulatory system for governing GE animals and the products derived from those animals. The overarching goals of an optimal

system, many participants said, should be to protect the safety of humans, the environment, and animals. Participants brainstormed a number of attributes that they felt an ideal regulatory system should have, in order to achieve these goals. These attributes are summarized below in alphabetical order. *Participants did not seek consensus on this list of attributes, so it is likely that individual participants would disagree with the inclusion of one or more of the attributes and/or with how they are defined here.*

- **Adaptive:** The regulatory system should be capable of both adjusting its processes and decisions in response to changes in the knowledge base, and adapting to address new products.
- **Comprehensive:** The regulatory system should address all the aspects of product research, development, commercialization, and production that are needed to ensure the goals of the system. It should also have adequate authority and resources to achieve its goals, including enforcement authority. The system must be able to cover all products of animal biotechnology.
- **Credible:** The regulatory system should be accountable to the public and should be perceived as trustworthy. The integrity of the system must not be compromised by conflict-of-interest or “revolving door” concerns.
- **Effective:** The regulatory system should be able to meet its goals of protecting human, environmental, and animal safety. Also, agencies should coordinate their mandates effectively.
- **Efficient:** The regulatory system should be cost-effective; it should achieve its regulatory goals in a manner that minimizes the time and resources expended by all parties.
- **Fair:** Products that present similar risks should be treated by the regulatory system in a similar manner.
- **Participatory:** The regulatory system should provide opportunities for public input on (1) the processes, standards, and means by which the regulatory system will make decisions, and (2) specific transgene-animal combinations being reviewed.
- **Predictable:** Agency policies and procedures should be consistently applied, such that developers and the public can understand in advance what will take place in a review process and can assess the time, resources, and information required.
- **Proportionate:** Products should be regulated on the basis of their risks to human, environmental, and animal safety. The regulatory burdens imposed on product sponsors (e.g., in the review process and in terms of data and risk mitigation measures required) should not exceed those necessary to assess and manage the specific risks of a product.

- **Rigorous:** The regulatory system should collect enough data to enable it to conduct an objective, thorough, and sound analysis of all reasonably foreseeable risks and risk-reduction options.
- **Risk-Based:** The regulatory system should address those risks to human health, animal health, and the environment that are determined by a scientific risk assessment to exceed legally allowable levels. Also, the system should use risk assessment as a basis of action for managing identified risks, and risk management should be commensurate with the identified risks. Risks for which information is incomplete or uncertain should be regulated in accordance with requirements set out in relevant laws (e.g., the “reasonable certainty of no harm” standard in FIFRA).
- **Transparent:** The data, information, process, and standards by which the regulatory system makes decisions about products should be clear, comprehensible, and publicly available. Also, the regulatory system should provide adequate information about products to enable the public to make informed decisions in the marketplace.

Participants noted that some of these attributes are “the enemy of each other.” That is, tensions may exist between them that need to be balanced. For example, “participatory” and “efficient” may conflict in practice. Public participation could increase the time and cost of a regulatory decision-making process, making it less cost-effective. Also, “adaptive” and “predictable” could be in tension with each other. A regulatory system that is designed to change quickly to react to new products, data, or scientific understanding may not provide the predictability some people seek. In general, however, participants seemed to believe that a regulatory system could be designed that could balance most of these attributes effectively.

Participants also spent some time discussing specific components of an optimal regulatory system. *Again, they did not seek consensus on these components, but simply brainstormed ideas.* Among them were that an ideal regulatory system ought to include:

- Public input on the development of the regulatory review process itself
- Two sets of clear guidelines describing the regulatory process—one written for the lay public and another, more detailed, for product developers
- A mandatory pre-market approval process for all products of animal biotechnology, with an affirmative finding of safety by a government agency
- A single-door approach, in which an applicant could go to one office or agency and be guided through the regulatory process from there

Participants noted that some of these attributes are “the enemy of each other.” That is, tensions may exist between them that need to be balanced. For example, “participatory” and “efficient” may conflict in practice. Public participation could increase the time and cost of a regulatory decision-making process, making it less cost-effective.

"Although [the INAD/NADA system] is not intuitive," said one participant at the workshops, "it provides one very powerful and comprehensive regulatory path. It is not without difficulties and places for improvement. But it can meet its intended goals."

- Data submission commensurate with the perceived risk of the product
- An iterative process of decision-making, with deadlines at each stage
- A formal call for public comment on each product, before a decision is made
- Procedures for the post-market surveillance of products
- Regulations that eventually sunset, as sufficient experience is gained with the products of animal biotechnology

## USING THE NADA V. AMENDING THE LAW

A few workshop participants argued strongly that the FDCA should be amended to more clearly cover transgenic animals and to resolve concerns regarding the lack of an environmental standard and the lack of transparency in the approval process. "The NADA falls desperately short regarding environmental safety and transparency," said one participant. "And if you have to start out by explaining that a transgenic animal is a 'new animal drug,' you've taken on quite a burden in getting people to support this. The FDCA can be amended. It is not the Ten Commandments. A change in the law would improve the public's confidence in the law and the technology."

Supporters of the use of the INAD and NADA for regulating transgenic animals admitted that it requires some "mental gymnastics" to think about regulating a living animal under a rubric that was designed to regulate pharmaceuticals. Nonetheless, they said, the approach can effectively protect human and animal health and the environment. "Although [the INAD/NADA system] is not intuitive," said one participant at the workshops, "it provides one very powerful and comprehensive regulatory path. It is not without difficulties and places for improvement. But it can meet its intended goals." One participant said she felt it unlikely that Congress could come up with a better system. A technology developer put his support for the NADA system even more bluntly: "The train has left the station for us," he said. "The NADA is the route we are taking."

## THE NEED FOR A CLEAR ROAD MAP

During both workshops, participants repeatedly voiced the need for more clarity regarding the regulatory system governing transgenic animals. Specifically, participants called on the federal government to publicly clarify which agencies and statutory authorities, in addition to the FDA and its FDCA, will be involved in regulating the animal biotechnology industry. The uncertainty surrounding agency jurisdiction,

it was said, is of particular concern to technology developers, who need a better sense of which agencies must review the products of animal biotechnology before they go to market.

Equally needed, participants said, is greater clarity regarding exactly how the FDA will apply the INAD and NADA processes to GE animals. Participants expressed an interest in having documents—be they new regulations, guidances, policy statements, or some combination of the three—that specifically set forth the mandatory pre-market approval process that will be applied to transgenic animals under the FDCA. Such documents would provide clarity for technology developers and some level of assurance for consumer and environmental advocates that the system is robust and effective. Many participants also said that the public should have an opportunity to provide input and comment on such documents before they are finalized.

In response to these comments, a workshop participant who is an FDA official said that the desire for clarity was coming through “loud and clear.” This individual said that the FDA and other agencies have been working at the highest levels for at least two years to determine how to implement the Coordinated Framework to regulate transgenic animals and the products derived from them. U.S. government representatives were assessing, among other things, where their authorities complement and overlap. The participant added that it was difficult to predict when these jurisdictional issues will be resolved.

FDA representatives at the meeting also stated that the agency is currently reviewing GE animals under the paradigm laid out in the OSTP-CEQ case studies (i.e., the new animal drug provisions of the FDCA), to ensure that no products derived from GE animals enter the food supply without regulatory scrutiny. The 2003 letter from the FDA to university researchers, which is posted on the agency’s web site, states that “research involving genetic engineering in animal species commonly used for food...may require an investigational new animal drug exemption (INAD) or another type of regulatory approval from the Center for Veterinary Medicine.” The FDA officials added that the agency’s primary concern at present is that animals covered by the provisions include the putative transgenic animals, surrogate animals that are carrying transgenic animals in the womb, and co-gestated animals. These ancillary animals are considered investigational and cannot be released into the food supply without explicit approval from the FDA. “We appreciate that people really want guidance” on how the NADA process will work, one of the officials said in closing. “We believe that the guidance process will be transparent. Under 21 CFR 10.115, the FDA’s regulations on good guidance practice would require any draft guidances on this topic to be made available for public comment.”

It became clear in later discussions that at least one GE animal is undergoing the NADA review process at present. One participant expressed concern that, considering the time it will likely take for agencies to publish new regulations or guidance governing GM

animals, it might be possible that products from that animal may be approved by the FDA for human consumption before any overarching guidance document or regulation governing GE animals is proposed. This participant expressed hope that the public would be given the opportunity to comment on the overarching regulatory framework for GE animals prior to any such animals being allowed on the market.

## HOW THE SYSTEM WORKS TODAY

At various times during the two workshops, participants asked the FDA officials clarifying questions about how the INAD and NADA processes are functioning at present in the context of GE animals. A wide array of points were addressed.

For example, one participant asked when, in the course of basic research, an INAD application should be filed. An FDA official responded that an INAD application should be submitted “when you have that ‘aha’ moment and you identify a product you want to develop.”

Participants also asked about containment requirements for GE animals in the INAD stage. The FDA officials said they require researchers to provide detailed information about proposed containment practices and the opportunity for escape or release. Containment requirements are then determined on an individual basis, they said, since the issues differ depending on the animal and the facility involved. With hogs, for example, double fencing might be required.

In response to a question about the disposal of GE animals in the INAD phase, an FDA official responded that such animals cannot be rendered without explicit authority from the FDA. Part of the INAD process is determining appropriate disposal procedures, which generally means incineration only. The official added that “it is unlawful to introduce an investigational animal into food or feed without positive affirmation from the agency for a specific set of animals under a specific set of circumstances.”

One biotech developer noted that researchers are not interested in putting their animals into the food supply. “The company I worked with tracked their animals extremely carefully,” she said, “because each was of such high value. It wasn’t even considered to have even the non-transgenic animals or their milk go out into the food supply.”

On another topic, one FDA official confirmed that, if the NADA paradigm were to become long-term policy, GE animals would likely be regulated “by event,” as GE plants are. That is, each new transgene-animal combination would require an FDA approval before it or products derived from it could be commercialized.

Another FDA representative affirmed that GE animals that produce pharmaceuticals in their milk might be subject to multiple reviews

before final approval. One Center of the FDA could assess the effectiveness of the drug, while another Center would assess the food safety of meat and milk from the animal (if it is a species traditionally used for food and the producers wish to introduce food from those animals into the food supply). The pharmaceutical produced by the animal could be approved for use even if food from the animal were deemed unsafe, as long as containment and disposition requirements were met to ensure that the GE animals never make it into the food supply.

## TRANSPARENCY

The term *transparency* refers to information available to the public about a regulatory system and products going through that system before those products are approved for commercial use. The related issue of public participation (i.e., public input into the development of the system and into the product review process) is addressed subsequently.

As discussed in Fred Degnan's presentation, the FDCA requires the FDA to keep confidential all information about a new animal drug being regulated under an INAD or being reviewed under a NADA, until the drug or animal is approved by the agency for commercial use. The agency cannot reveal the names of drug developers or sponsors, the name or nature of the drug, or any details about how the review is conducted, until the drug is approved for marketing. Only if drug developers reveal information themselves can the FDA confirm that information in public. These confidentiality provisions were presumably enacted to protect confidential business information in the extremely competitive pharmaceutical industry.

Because the FDA is currently operating under the new animal drug provisions of the FDCA, the agency must likewise keep confidential all information about GE animals under review. This lack of transparency is of significant concern to many consumer and environmental advocates, who feel they have no way to assess the rigor of the regulatory review process or be made aware of the transgene-animal combinations being reviewed by the agency. "It is not acceptable for the government to do the public's business in private," said one consumer advocate. "The public at the least needs information about the factors the agency uses to make decisions on these kinds of products."

Several people noted that the lack of transparency seems to arouse the public's suspicion, rightly or wrongly, of the agency's activities. One participant said that the suspicion arises from the information imbalance that exists between the government and biotech companies, on the one hand, and the public, on the other. He compared it to the imbalance involved in used car sales. "The people who sell used cars have much more information about those cars than the potential buyers," he said. "It's thus rational to regard used cars suspiciously.

Likewise, the risk people associate with biotechnology comes from the concern that [the agency and the biotech companies] know something that [they] aren't telling the public. So, people see a product as risky not because it is, but because they know they don't have all of the information about it that the other parties do."

Some technology developers were clear in their support for the confidentiality provisions. "The protection of confidential business information and trade secrets is needed to encourage the development of drugs," said one participant. He later added: "One assumption some people are making is that greater transparency will enhance acceptance among the public [of the products of animal biotechnology]. That very well may not be true. It may scare the heck out of the public."

One way in which some information could potentially reach the public under the NADA paradigm for regulating GE animals is through the use of the Veterinary Medicine Advisory Committee (VMAC) at the FDA. The FDCA allows the agency to take specific questions about safety to public meetings of the VMAC. However, the questions asked are often fairly generic. "There's usually a particular question or two that we want to pose to the VMAC," said one FDA official, "so we release information on that specific question. Antibiotic resistance might be one example." Also, meetings in which more complete information is revealed to the committee are often closed to the public. This is accomplished legally by designating all the committee members as "special government employees," so they can be bound by the FDCA's confidentiality provisions and thus privy to the confidential information.

## PUBLIC PARTICIPATION

Closely related to the issue of transparency is that of public participation in the regulatory process. Workshop participants seemed to generally agree that the public ought to be able to comment on any regulations or guidelines the FDA develops regarding the specific process the agency will use to review GE animals. "We know the public has an interest in the overall process," said one FDA official present at the workshops. "As we move forward, there will be lots of opportunity for comment, and any rulemaking will be subject to public comment."

A number of workshop participants argued, however, that the public should also have the opportunity to comment on individual products before they receive approval from the FDA for commercialization. "Public participation can help to raise all the key issues—scientific and otherwise—in a review process," said one participant. "In a number of cases, [consumer advocates] have raised issues that risk assessments have not included." She mentioned a case in which a USDA risk assessment on *E. coli* in ground beef failed to consider a major cause of *E. coli* illness—that of cross-contamination in the home. "Their risk assessment had a false basis for finding 'no harm,'" she said, adding

that “industry and consumer groups can bring up issues that the agency may have forgotten are important.”

The confidentiality provisions in the FDCA clearly prohibit public comment on specific product approvals, however. “We could negotiate with sponsors about having open meetings on things,” said an FDA official, “but they would have to agree before we could say anything. That’s about all we could do prior to an approval, under the new animal drug provisions.”

One participant suggested a possible way around the legal restrictions. “What if there were a mandatory 120-day public comment period after the FDA has done its expert review and come to a conclusion?” he asked. “Then the FDA could put out considerable information about the product and take comment. After compiling the comments, they could take a second look at their decision under post-market authority and adverse-event reporting and amend it as needed.” One participant said the plausibility of such an approach would depend on how the agency’s lawyers interpreted the FDCA. “It’s possible it would require a regulation change,” said the participant, “but not necessarily a statute change.”

Consumer and environmental advocates did not favor this idea, however. “The public can participate when the review process is over?” one asked. “That’s not right. Once an agency has made an approval and issued an EA and a FONSI, they’ve made a public statement. It would be very difficult for them to back off at that point.”

## THE REGULATION OF ENVIRONMENTAL RISK

Some workshop participants at various times expressed concern that the FDA will not be able to adequately assess or mitigate the potential environmental or ecological risks posed by GE animals. The FDA did look at environment-related risks in its review process for rBST, and says it will do the same for GE animals. But the FDCA is a food and drug safety statute, not an environmental statute, and as such it contains no environmental standard that must be met. So it is unclear if a GE animal could ever be denied approval for commercialization, or removed from the marketplace, solely for environmental reasons. Other federal agencies implement laws with specific environmental standards, but it is as yet unclear how those agencies will be involved in the regulation of GE animals. Also, as Mike Taylor noted in his presentation, it is simply very difficult to assess the environmental risks that might be posed by some GE animals; the process involves a great deal of uncertainty.

Asked whether the FDA will look at environmental risks under the authority of the FDCA or of NEPA, an FDA official replied that it could

Also, as Mike Taylor noted in his presentation, it is simply very difficult to assess the environmental risks that might be posed by some GE animals; the process involves a great deal of uncertainty.

be “a little bit of both.” “Some of the issues are looked at under the safety provisions of the FDCA,” the official said, “while NEPA catches all the issues that aren’t otherwise caught.” NEPA is a procedural statute, however; it does not contain an environmental standard that must be met. NEPA also presents problems for the FDA, in that its public participation requirements directly conflict with the confidentiality requirements of the FDCA. The FDA official explained how this conflict has been handled during reviews of conventional drugs. “If we prepare an EA and it results in a FONSI, we release the EA at the time of the approval,” he said. “If we can’t reach a FONSI and need to prepare an EIS, then we have to work a deal with the petitioner to allow for an open public participation process and scoping. They don’t have much of a choice. Either the sponsor is willing for us to release information in the EIS process, or we can’t move forward with the application review.”

A biotech developer suggested one novel way to ensure that a product receives a complete and public environmental review by an environmental agency. He pointed out that the “structure and function” definition in the FDCA is based on the genetic construct and its expression products, which are genotypic attributes. Thus, he said, the FDA could release information on the phenotype of a GE animal under review, and an environmental agency could do an environmental risk assessment based on the phenotypic information. “The information that the company needs protected is in the genetic construct,” he said. “That’s what’s proprietary and protected. But there would be no need for restricting the phenotypic information. You could go through the NEPA process publicly using that information.” Workshop participants seemed to agree that this was a promising possibility.

It was also pointed out during the workshops that, at least for transgenic fish grown in ocean net pens, biotech developers will need to undergo an additional round of environmental assessment under the rules of the Army Corps of Engineers and the National Marine Fisheries Service, in order to get permits to grow the fish in net pens. “This is a rigorous public process,” said one participant. “It’s very contentious. It’s difficult to get a license for a pen.”

Finally, another participant suggested that the FDA do a full programmatic EIS on any new animal drug regulations that it develops for GE animals.

## CONSUMER CHOICE

The issue of consumer choice or labeling was discussed at several points during the workshops, and it became clear that participants held deeply diverging views on the subject. Some workshop participants argued strongly against the mandatory labeling of products derived from GE animals; others argued equally strongly in favor of it.

Those opposed to mandatory labeling said that it violates the government’s traditional focus on regulating products, not processes. If a

product of animal biotechnology has been scientifically proven by the FDA to be safe for human consumption and the environment and not materially different from like products produced via conventional means, they said, it is unfair and without scientific rationale to single out that product for labeling solely because of the process by which it was made. (For this reason, the government has not required the labeling of products derived from GE plants.) Others pointed out that the labeling of products produced via cloning, in particular, would be difficult. “Cloning of various sorts has been in use for 20 years,” said one industry representative. “How do you differentiate what’s going on now from what’s been going on for years?” In addition, one participant said that mandatory labeling was akin to implementing the “precautionary principle,” which is generally not applied in the typically science-based U.S. regulatory system.

Those in favor of mandatory labeling argued that labeling is a consumer “right-to-know” issue. They said that consumers need full information about products in the marketplace—including the processes used to make those products—not for food safety or scientific reasons, but so they can make choices in line with their personal ethics. “Most of us will not have much concern about the human safety of GM animals as food,” said one consumer advocate, “but you do have people who object on moral, ethical, and social grounds. You thus have to have public information via labeling so that consumers can opt in or out.” This participant said that the public clearly has more ethical concerns about GE animals than GE plants. Another participant concurred: “For a lot of people, the process is what matters here, not just the end product.”

Some participants expressed favor for voluntary, but not mandatory, labeling. This could include either voluntary “negative” labeling (e.g., “This product was not made from GM sources”) or voluntary “positive” labeling (e.g., “This product was made from GM sources”). Some biotech developers, in fact, said they would gladly label their products on a voluntary basis, because it will increase the value they can receive for the products. Other participants felt, however, that the FDA ought to require labeling in its regulations. They argued that food manufacturers and marketers would likely discourage any “positive” labeling, because it could alarm consumers who are skeptical of the technology. These participants said, too, that voluntary labeling would create a situation in which consumers have to pay more for the alternative (non-GM) products, which they believe is unjust.

## ANIMAL WELFARE

Another issue that came up on several occasions was that of the welfare of GE animals involved in biotechnology research and development and, in the future, those bred for commercial purposes. In its reviews of animal drugs under the FDCA, the FDA looks at the benefits and risks of the drug to the animal, including its effects on reproduction, toxicity,

“Most of us will not have much concern about the human safety of GM animals as food,” said one consumer advocate, “but you do have people who object on moral, ethical, and social grounds. You thus have to have public information via labeling so that consumers can opt in or out.”

and sometimes behavior. However, animal welfare is not part of the FDA's mandate, so it is unlikely that an application could ever be denied purely for animal welfare reasons. Several participants pointed out, for example, that rBST was denied approval in Canada for animal health and welfare reasons, but it was approved by the FDA.

An animal welfare advocate at the workshops said that she would like the regulatory system to give more weight to animal welfare. "The current system is not sufficient," she said. "In the process of creating transgenic animals and clones, there is suffering." She noted a recent effort by the USDA to create transgenic cows resistant to mastitis, an infection of the udder. "Of 330 attempts," she said, "only 8 calves were born and only 5 of those survived to adulthood, meaning a success rate, if one could call it that, of 1.5%." This participant said she would like to see regulatory agencies assess animal safety in all research on GE animals and all potential commercial production of GE animals, and then prohibit activities that "cost too much" in terms of animal suffering. "Animal biotechnology is a continuation of the problems with factory farm production methods," she said later. "It reveals a lack of concern for animal welfare and a preoccupation with increased production."

Other participants pointed out that, as required under the Animal Welfare Act (AWA), most research facilities have Institutional Animal Care and Use Committees (IACUCs), which review and comment on issues relating to the welfare of animals used in research. "Animal research is not a free-for-all," said one biotech developer. "There are stringent guidelines on the use of animals in research." Farm animals used for food and fiber research are exempt from the AWA, however, and thus are not technically subject to IACUC oversight. But one participant said, "My sense is that there is very little research being done today on agricultural animals that isn't reviewed by IACUCs." Another participant suggested that the FDA and/or USDA set policies and offer training courses to better enable all IACUCs to consider and address animal welfare issues.

In the end, a food industry representative acknowledged, "Consumers are now telling us how to raise animals, in a sense. And animal welfare will keep growing in importance. What was acceptable in the past is not today, and what is acceptable today will not be in the future."

## ADDITIONAL ISSUES OF CONCERN

Several other issues arose during the two workshops that do not fit neatly into the above categories. Among these were the preservation of genetic resources, intellectual property issues, and general ethical concerns about animal biotechnology.

One participant argued that animal biotechnology raised questions not just about the safety of specific processes, but about the preservation of germplasm and genetic resources that are of importance to the whole world. “Who’s keeping an eye on interbreeding and the health of a population of animals that we all depend on?” she asked. “Also, what if a transgenic dairy cow becomes the standard, and most dairy cows thus have a patent on them? What are the implications for herd management and on-farm breeding programs? No one is looking at the big picture.” She said the government should be taking a look at these issues. While others noted that these issues are the responsibility of breed groups, this participant said her concern is that those groups do not have the funding nor expertise to effectively deal with the potential problems that may arise.

This discussion merged into the consideration of issues relating to intellectual property protections. Nearly all researchers are protecting their biotechnology investments and intellectual property through the patent system, but some people are ethically opposed to the patenting of life forms and concerned about its impact on small farmers. One participant suggested that breed registries might be an alternative way to protect intellectual property. “There is a significant movement for an alternative system that would still allow some control of the intellectual property of specific varieties,” he said, “but would not involve such extensive use of the patent system.”

Finally, it was mentioned several times that some people hold concerns about animal biotechnology that are not scientific in nature, but ethical. These conversations harkened back to the first workshop in this series, held in January 2005, on ethical and moral considerations relating to animal biotechnology. “Some people think a transgene in a non-transgenic environment is by definition harmful,” said one participant. “They see it as genetic pollution. It’s like a beer can in the woods. It’s a harm, period.” He argued that these people cannot and should not take part in the regulatory system, because their concerns are unscientific. Several participants suggested that a separate forum or forums, such as an FDA advisory committee or another multistakeholder committee, should be set up to address the social and ethical issues relating to GE animals. “If you want acceptance of the products,” said one participant, “the government must address the ethical and social concerns that exist in the population. You can give the ‘science’ answer again and again, but it won’t be sufficient.”

## SECTION 4 CONCLUDING REMARKS

At the end of the May session, participants shared their thoughts about the overall value of the two workshops. Participants seemed to agree that the workshops met their goal of enabling joint learning and the sharing of information among diverse parties. The following is a sampling of participants' final comments:

"It's apparent that even though we don't have all the answers nor agree on everything, we've asked the right questions, and there's a lot of value in that."

"I appreciate that the people around the table are very willing to work and try to find solutions."

"It was so helpful for me to hear others' points of view."

"I've learned a lot in these sessions—and in the coffee breaks. This is a great cross-section of people. It's been a great experience for me."

"I think it was good for the regulators to see the diversity of the opinions that are out there. Maybe it can help them regulate the products even more effectively."

Finally, several participants urged the Pew Initiative to continue its efforts to foster learning and information exchange on issues—both scientific and ethical—relating to animal biotechnology. "We've just been cracking the egg here," concluded one participant, "and I'd like to see the soufflé rise!"

## APPENDIX A

# PRESENTERS' BIOGRAPHIES

### THOMAS E. BUNDY

Tom Bundy served as Deputy Assistant General Counsel at the U.S. Department of Agriculture from 1978 to 2002. In this role, he supervised the legal work of the Animal and Plant Health Inspection Service APHIS concerning the control and eradication of plant and animal diseases and pests. He reviewed APHIS documents for publication in the *Federal Register*, including the publication of the first regulations governing the interstate movement and release into the environment of GE plants under the Federal Plant Pest Act. Mr. Bundy was also significantly involved in reviewing and defending APHIS's compliance with environmental laws, including the National Environmental Policy Act, as well as in developing the USDA's position on the consolidation and updating of the plant and animal quarantine laws and representing the department's position to Congress with regard to the Plant Protection Act of 2000 and the Animal Health Protection Act of 2002. Mr. Bundy's career began in the USDA's Office of the General Counsel in 1970 as a trial attorney. He graduated from the Pennsylvania State University in 1967 and the University of Virginia School of Law in 1970. Now retired, Mr. Bundy currently does consulting work and volunteers at a local legal aid office.

### LAWRENCE E. CULLEEN

Larry Culleen is an attorney in Arnold & Porter's environmental practice group. Mr. Culleen's practice concentrates on administrative matters with federal agencies, including the Environmental Protection Agency, the Food and Drug Administration, and the Consumer Product Safety Commission. Prior to coming to the firm, Mr. Culleen served as the Chief of Staff to the Assistant Administrator of the EPA, where he was instrumental in policy development and execution for the Office of Prevention, Pesticides, and Toxic Substances. Mr. Culleen previously served as the Acting Director of the Registration Division in the EPA's Office of Pesticide Programs, and as the Chief of the EPA's New Chemicals Branch. He also directed the EPA's asbestos-in-schools loan and grant program. Mr. Culleen serves as an adjunct professor of environmental law at the George Washington University National Law Center. He received his B.A. and J.D. from George Washington University.

## FRED DEGNAN

Fred Degnan is a partner in King and Spalding's FDA practice group. Mr. Degnan specializes in food law and handles a wide array of food safety, good manufacturing practice, and labeling issues. He represents several large multinational food companies, a number of domestic food producers, and several international science-based nonprofit associations. Mr. Degnan also serves as General Counsel to the Food and Drug Law Institute. Prior to joining King and Spalding in 1988, Mr. Degnan served for 11 years at the FDA, as the agency's Associate Chief Counsel for Foods and as Associate Chief Counsel for Enforcement. He has published and lectured extensively on a wide array of FDA issues and is the author of the recent book *FDA's Creative Application of the Law: Not Merely a Collection of Words* (2000). Mr. Degnan received his undergraduate degree cum laude from the College of the Holy Cross and his law degree from Georgetown University.

## JAMES MACDONALD, PH.D.

Jim MacDonald is chief of the Agricultural Structure and Productivity Branch at the U.S. Department of Agriculture's Economic Research Service. In that position, he leads a program of data collection and analysis aimed at understanding changes in how farming in the U.S. is organized and how those changes affect farm performance and farm household incomes. Dr. MacDonald has published widely on the economics of pricing and competition, with a particular emphasis on the food sector. Dr. MacDonald received a bachelor's degree from Siena College and a Ph.D. in economics from the State University of New York at Buffalo. He has served on the faculties of Hamilton College, Rensselaer Polytechnic Institute, and the Ohio State University.

## WILLIAM R. PAPE

William Pape is the Chief Executive Officer and Chairman of AgInfoLink Global, Inc., an information-services company providing food traceability solutions. AgInfoLink works with food supply chain members to build data networks that track information on each production unit across company ownerships and product transformations. Mr. Pape is also a third-generation rancher, with ranches in Hawaii and New Mexico. From 1997 to 1999, Mr. Pape was a co-founder and Chairman of Hawaii Natural Meats, Inc., a niche meat marketing company. From 1982 to 1998, Mr. Pape was a co-founder, senior manager, and corporate officer of VeriFone, which

pioneered the electronic acquisition and transfer of credit card information and ultimately handled more than 65% of the world's daily credit card traffic. Before VeriFone, Mr. Pape was a General Partner at Innovative Software Applications, where he co-designed Spellguard, the first commercial spelling checker for personal computers. Mr. Pape holds an A.B. degree in Psychology from Stanford University and two advanced degrees from the University of Hawaii—an M.A. in Social Psychology and an M.A. in Communications.

## JAMES A. RIDDLE

Over the past 25 years, Jim Riddle has been an organic farmer, gardener, inspector, educator, policy analyst, author, and consumer. He was founding chair of the Independent Organic Inspectors Association (IOIA) and co-author of the IFOAM/IOIA International Organic Inspection Manual. He has trained hundreds of organic inspectors throughout the world. Mr. Riddle chairs the Minnesota Department of Agriculture's Organic Advisory Task Force, and was instrumental in the passage of Minnesota's landmark organic certification cost-share program. He also serves as chair of the National Organic Standards Board, which advises the USDA on organic agriculture policies and regulations. Mr. Riddle works part-time as an organic policy specialist for Rodale's newfarm.org. In 2003 and 2004, he served as Endowed Chair of Agricultural Systems at the University of Minnesota. Mr. Riddle holds degrees in biology and political science from Grinnell College.

## STEVEN N. TANNER

Steve Tanner has been Director of the Technical Services Division in the USDA's Grain Inspection, Packers, and Stockyards Administration since 1994. In this position, he develops, manages, and coordinates the agency's research, technical training, and analytical service functions to promote the accurate assessment of grain quality throughout the national grain market system. Mr. Tanner held the position of Deputy Director of this facility from 1993 to 1994, and he previously served as the staff assistant to the Administrator of GIPSA. In 1988, Mr. Tanner was appointed by the U.S. government to chair the Codex Alimentarius Commission's Committee on Cereals, Pulses, and Legumes. This committee is charged with developing grain and processed grain standards for world trade. Mr. Tanner began his career with the USDA in 1976 as a laboratory manager. He received a B.S. in chemistry in 1974 and an M.B.A. in 1988.

## MICHAEL R. TAYLOR

Mike Taylor is a Senior Fellow at Resources for the Future (RFF), a non-profit organization that conducts independent research on natural resource and environmental issues. Mr. Taylor's research focuses on U.S. policies affecting African agriculture, poverty, and hunger reduction, and food safety as a global public health concern. Prior to joining RFF in 2000, Mr. Taylor served in government, practiced law in Washington, and worked in private industry. He was Administrator of the USDA's Food Safety and Inspection Service from 1994 to 1996, Deputy Commissioner for Policy at the FDA from 1991 to 1994, and an FDA staff lawyer and Executive Assistant to the FDA Commissioner from 1976 to 1981. He practiced food and drug law as a partner at King and Spalding for ten years and served for sixteen months as Vice President for Public Policy at Monsanto. Mr. Taylor received his B.A. in political science from Davidson College and his law degree from the University of Virginia.

## HOLLY WHEELER

Holly Wheeler has been an attorney with the U.S. Department of the Interior's Office of the Solicitor since 1997. She works in the Branch of Fish and Wildlife, where she specializes in the Marine Mammal Protection Act, non-native invasive species issues, international wildlife law, and the Endangered Species Act. Previously, Ms. Wheeler served as a clerk for the Vermont Supreme Court and worked for state conservation agencies and nonprofit conservation organizations. She holds a bachelor's degree in fisheries and wildlife biology from the University of Missouri and a law degree from Vermont Law School.

## CARI W. WOLFE

Cari Wolfe is Director of Research and Genetic Programs at the American Jersey Cattle Association, where she has been a staff member since 1983. Ms. Wolfe is responsible for genetic development, and she administers the research grants program. Her educational background includes an M.S. in dairy cattle breeding from North Carolina State University and a B.S. in dairy science from Virginia Tech. Together with her husband Larry, who is a member of the AJCA's IT staff, and 15-year-old daughter Rebecca, Ms. Wolfe owns and breeds registered Jerseys housed at Shenandoah Jerseys in Maryland.

## APPENDIX B

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## APPENDIX D BIBLIOGRAPHY

Council on Environmental Quality and Office of Science and Technology Policy. (2001). *CEQ and OSTP assessment: Case studies of environmental regulations for biotechnology*. Washington, DC: OSTP. <http://www.ostp.gov/html/012201.html>.

Findinier, Isabelle. (2003). *Animal Biotechnologies: State of the Art, Risks and Perspectives*. Rome: Food and Agriculture Organization.

Institute of Medicine and National Research Council. (2004). *Safety of Genetically Engineered Foods: Approaches to Assessing Unintended Health Effects*. Washington, DC: National Academies Press.

National Research Council. (2005). *Biological Confinement of Genetically Engineered Organisms*. Washington, DC: National Academies Press.

National Research Council. (2002). *Animal Biotechnology: Science-Based Concerns* (Executive Summary). Washington, DC: National Academies Press.

Pew Initiative on Food and Biotechnology. (2004). Regulating genetically engineered animals. In *Issues in the Regulation of Genetically Engineered Plants and Animals*. Washington, DC: Pew Initiative on Food and Biotechnology.

———. (2003). *Future Fish: Issues in Science and Regulation of Transgenic Fish*. Washington, DC: Pew Initiative on Food and Biotechnology.

———. (2003). *The Stakeholder Forum on Agricultural Biotechnology: An Overview of the Process*. Washington, DC: Pew Initiative on Food and Biotechnology.

## APPENDIX E

# ABBREVIATIONS

AHPA	Animal Health Protection Act
AJCA	American Jersey Cattle Association
APHIS	Animal and Plant Health Inspection Service (USDA)
AWA	Animal Welfare Act
BLM	Bureau of Land Management (DOI)
BSE	bovine spongiform encephalopathy
CBD	Convention on Biological Diversity
CBER	Center for Biologics Evaluation and Research (FDA)
CCC	Commodity Credit Corporation (USDA)
CDER	Center for Drug Evaluation and Research (FDA)
CEQ	Council on Environmental Quality (The White House)
CFR	Code of Federal Regulations
CITES	Convention on International Trade in Endangered Species
CV	coefficient of variation
CVM	Center for Veterinary Medicine (FDA)
DNA	deoxyribonucleic acid
DOI	U.S. Department of the Interior
DOJ	U.S. Department of Justice
EA	environmental assessment
EIS	environmental impact statement
EPA	Environmental Protection Agency
ESA	Endangered Species Act
FDA	Food and Drug Administration (Dept. of Health and Human Services)
FDCA	Food, Drug, and Cosmetic Act
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
FONSI	finding of no significant impact

FSIS	Food Safety and Inspection Service (USDA)
FWS	Fish and Wildlife Service (DOI)
GE	genetically engineered
GIPSA	Grain Inspection, Packers, and Stockyards Administration (USDA)
GM	genetically modified
GRAE	generally recognized as effective
GRAS	generally recognized as safe
IACUC	Institutional Animal Care and Use Committee
INAD	investigational new animal drug
MCAN	microbial commercial activity notice
NADA	new animal drug application
NAS	National Academy of Sciences
NCBA	National Cattlemen's Beef Association
NEPA	National Environmental Policy Act
NIST	National Institute of Standards and Technology
NOAA	National Oceanic and Atmospheric Administration (Dept. of Commerce)
NOSB	National Organic Standards Board (USDA)
OSTP	Office of Science and Technology Policy (The White House)
PCR	polymerase chain reaction
PDA	personal digital assistant
PIFB	Pew Initiative on Food and Biotechnology
PPA	Plant Protection Act
rBST	recombinant bovine somatotropin
RFID	radio frequency identification
SNUR	significant new use rule
TSCA	Toxic Substances Control Act
USAIP	U.S. Animal Identification Project
USDA	U.S. Department of Agriculture
VMAC	Veterinary Medicine Advisory Committee