

BIOTECH IN THE BARNYARD:
IMPLICATIONS OF GENETICALLY ENGINEERED ANIMALS



INTRODUCTION:

Animal biotechnology now gives scientists new opportunities to utilize animals in providing vital services to humans. Scientists are developing transgenic animals—which incorporate genes from other organisms—with a variety of goals, including treating human disease, easing the shortage of organs for transplant patients, improving the efficiency of food production, and providing more nutritious foods.

At the same time, as pointed out in “Animal Biotechnology: Science-Based Concerns,” a report recently released by the National Research Council (NRC), both transgenic and cloned animals raise potential new concerns about food safety, animal welfare, human health, and the environment. A number of the conference presenters had participated in researching and writing the NRC report, and brought its conclusions as well as their own perceptions to the discussion.

A two-day multidisciplinary conference sponsored by the Pew Initiative on Food and Biotechnology provided an in-depth exploration of the potential benefits and risks of genetically engineered animals and a review of the current laws and regulatory policies that apply.

Biotech in the Barnyard brought together representatives of industry, academia, consumer groups, animal welfare groups and government agencies to share information and exchange views. The views that emerged from the conference are captured here to demonstrate the broad diversity of perspectives and to provide context for future dialogue on this very important issue. It should be noted that the exchanges among participants reflect only their opinions and not necessarily those of the sponsoring organization.



Michael Fernandez, Ph.D.
Director of Science
Pew Initiative on Food and Biotechnology



EXECUTIVE SUMMARY:

The Pew Initiative on Food and Biotechnology held three days of conferences in September 2002 in Dallas on animal biotechnology. Two days focused on transgenic animals and a one-day conference, cosponsored with the U.S. Food and Drug Administration's (FDA) Center for Veterinary Medicine (CVM), focused on animal cloning.

The event attracted over 100 participants from around the United States. Scientists, industry and government representatives, animal welfare advocates, consumer rights representatives and policy analysts were among those who attended. Speakers addressed the potential uses of genetically engineered animals, ethical and animal welfare considerations, human health and environmental concerns, the state of the technology and future trends, marketing issues, and regulation of transgenic and cloned animals.

On any given topic, several points of view were expressed. What emerged was a complex tapestry of concerns. Repeated calls were made to extend the dialogue on societal and ethical concerns and to clarify the legislation regarding genetically engineered and cloned animals. At the same time, representatives of industry expressed an urgency to resolve many of these issues or risk losing considerable resources already invested in developing new animal products.

A brief summary of several discussion topics reveals diverse points of view that will ultimately inform society's approach to these issues.

Fundamental ethical differences formed an undercurrent to the discourse. On the one hand, some researchers expressed an ethical imperative to develop genetically engineered animals that could help to improve human health and even save human life. The goals of developing safer blood products, affordable pharmaceuticals, and organs for human transplantation presented a compelling case for transgenic animals.

In addition, several scientists stressed that advances in genetic technology are overcoming the negative health impacts sometimes experienced by transgenic and cloned animals. At the same time, animal welfare advocates pointed out that the technology remains risky to animals used in research and may ultimately be used to further intensify animal agriculture, harming animal welfare on a large scale. In addition, some questioned the appropriateness of changing an animal's "genetic integrity."

Still others stressed the need to evaluate the technology on a case-by-case basis. Some suggested that the ethics of using transgenics depended on the outcome: modifying animals to help save human lives may be an ethically sound use, while engineering animals to increase food production or alter food qualities may not be.



Many expressed concern that the debate over transgenic and cloned animals could become a proxy for discussion of problems in agriculture generally, short-changing full consideration of the technology and its potential benefits.

Participants also considered a range of human health and environmental issues. They presented various scenarios in which transgenic and/or cloned animals could lead to undesired outcomes. For instance, transgenic animals created with the use of viral vectors could, in theory, give rise to novel viruses that create new epidemics. Speakers identified the principal environmental concern as the possibility that transgenic animals could escape and disrupt ecosystems, possibly driving other species to extinction.

Panelists described almost all potential negative outcomes, however, as improbable. They stressed ways to mitigate or avoid problems through changes in technology and the regulatory process.

But not everyone agreed that the risks could be so easily dismissed. Consumer advocates said that the time is now to conduct a thorough public education campaign and societal debate, addressing the basic question of whether the technology is even necessary.

If one accepts the appropriateness of transgenic and cloned animals, several additional questions arise: How should they be treated and viewed? How should they be regulated?

Throughout the deliberations, participants largely agreed on the need to review, and possibly reform, federal legislation. In particular, people were concerned that the FDA have the authority and expertise it needs to address novel scientific issues raised by this topic. People expressed particular concern about the FDA's ability to address broad ecological impacts of the technology. Another widely expressed view was the need to increase the transparency of the regulatory process. For some, this was a pre-requisite to consumer acceptance of the technology.

Finally, another recurring theme was the need for society to develop clear avenues to address the complex social and ethical questions raised by the genetic engineering and cloning of animals. Nearly all felt that such consideration was beyond the scope of regulatory agencies, and that expectations to the contrary could jeopardize the integrity of the scientific and regulatory reviews for which they are responsible.



CONFERENCE AGENDA:

SEPTEMBER 24-25, 2002 / DALLAS, TX

Panel 1: Animal Matters: Social, Ethical, and Animal Welfare Considerations

How the technology fits into the context of public views on animals

Transgenic Animals: Present Status of Technology and Future Applications

William Velander, Virginia Polytechnic Institute and State University

Social Values and the Bioengineering of Animals

Gary Comstock, North Carolina State University

Animal Welfare Issues

Joy Mench, University of California-Davis

Panel 2: Beyond the Barn: Ecological and Human Health Considerations

Potential impacts of transgenic animals on the environment and humans

Ecological Risk

William Muir, Purdue University

Food Safety

James Murray, University of California-Davis

Human Health and Safety

John Coffin, Tufts University



Panel 3: To Market, to Market: Marketing Issues for Transgenic Animals

Factors that influence the marketplace for products of transgenic animals

Economics and Marketing of Transgenic Animals

Cecil Forsberg, University of Guelph, Ontario

Consumer Perspectives

Jean Halloran, Consumers Union

Future Outlook of Animal Genetic Modification

Lawrence Schook, Pyxis Genomics, Inc.

Panel 4: Institutional and Legal Background

An analysis of the laws and regulations governing the use of transgenic animals in the U.S.

Overview of Laws and Authorities

Fred Degnan, King and Spalding, LLP

Strengths and Weaknesses of Current Laws

Michael Taylor, Resources for the Future

International Organizations and Policy Affecting Animal Biotechnology and Trade in Future Products

Lonzell (Bud) Locklear, U.S. State Department, Ottawa

PANEL ONE:

ANIMAL MATTERS: SOCIAL, ETHICAL AND ANIMAL WELFARE CONSIDERATIONS

“BREATH TAKING OPPORTUNITIES DISGUISED AS INSOLUBLE PROBLEMS”

Neal First, a professor of reproductive biology and animal biotechnology at the University of Wisconsin, reviewed the history of transgenic technology, and its many actual and potential applications.

The technology had its start in 1981, when scientists first microinjected DNA into the oocytes of mice. Since then, “Transgenic mice have become the work horse of animal biology,” First said. Scientists have used these animals to do everything from identifying genes linked to specific diseases to revealing developmental pathways.

Over the ensuing years, scientists developed a range of transgenic technologies. They used viral vectors to create transgenic animals in 1985, and, by 1988, cattle, rabbits, sheep and pigs had joined the transgenic barn.

Today, transgenic technology offers a number of potential commercial and medical applications. Biotech firms are developing transgenic animals to: provide organs for human transplantation, provide proteins for pharmaceutical and industrial production, limit environmental harm from agricultural practices, and improve production traits such as disease resistance.

First pointed out that the power of transgenics is such that if Brazil were to develop cows resistant to hoof and mouth disease, “...it would probably put the U.S. out of the world beef market.”

He stressed that the potential benefits of transgenic animals to humans and society are great. In particular, he pointed to the use of transgenic animals to produce blood proteins, pharmaceuticals and vaccine components in their milk. According to First, blood products produced through transgenics would be much safer than current blood transfusions from human donors: “Products of transgenic animals impose less threat to human health than older products now in use. That’s the case with blood products,” he said, pointing out that tainted blood transfusions have been responsible for spreading diseases such as leukemia and HIV/AIDS.

Industrial uses are also on the way. For example, one company is producing spider silk in the milk of transgenic goats. “It is the finest fiber man knows and the strongest,” First said. It is so strong, in fact, that the military is proposing to use it in body armor.



POTENTIAL COMMERCIAL APPLICATIONS OF TRANSGENIC ANIMALS

1. PRODUCTION OF NEW PRODUCTS IN MILK
 - Pharmaceuticals
 - Blood proteins
 - Antigens for vaccine production
 - New food products
2. XENOTRANSPLANT ORGANS WITHOUT HUMAN REJECTION
3. FOOD PRODUCTION ANIMALS IMPROVED IN PRODUCTION TRAITS
 - Disease resistance
 - Environmental adaptation
 - Environmental contamination

Source: Adapted from a slide prepared by Neal First, University of Wisconsin.

PIGS WITH A PURPOSE

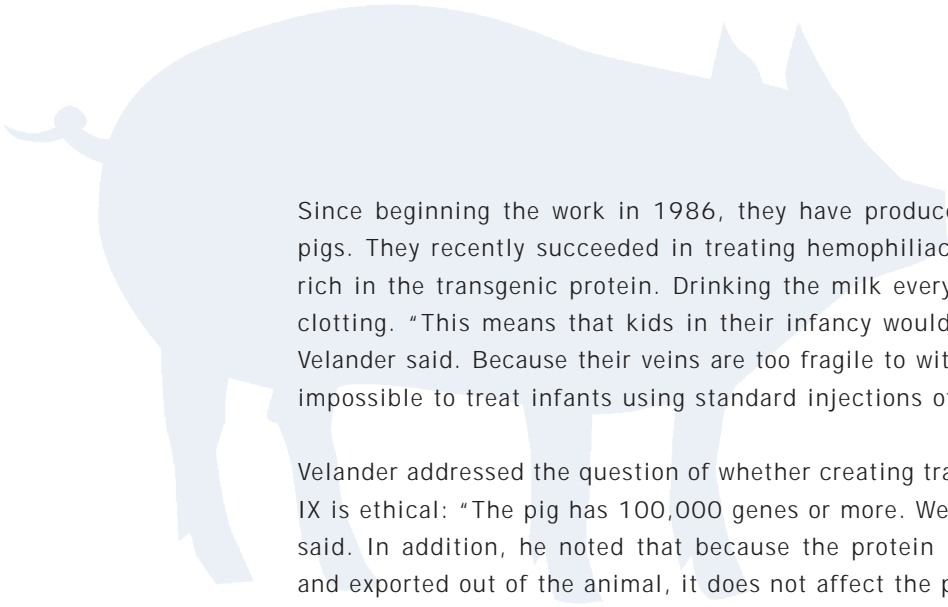
Dr. William Velander, of the Virginia Polytechnic Institute and State University, discussed his efforts to treat hemophilia using transgenic pigs as “self-replicating bioreactors” to produce a critical blood clotting protein called Factor IX.

Because hemophiliacs lack Factor IX and similar proteins, they suffer from excessive bleeding. Uncontrolled internal bleeding can cause pain, swelling, and permanent damage to joints and muscles. “If you are a hemophiliac and live in a poor country, you probably will not live to see your 20th birthday,” Velander said. “You will have a horrendous life beginning at birth, with the last years of your life confined to a wheelchair with all of your joints destroyed by bleeding processes.”

While the missing blood-clotting protein can be produced in mechanical bioreactors, the cost of this standard treatment—\$100,000 to \$200,000 a year per patient—is beyond the reach of the vast majority of hemophiliacs worldwide.

Velander’s group has developed a transgenic pig able to produce factor IX, a structurally complex blood clotting protein that causes one form of Hemophilia. The pigs produce the factor in their mammary glands at a productivity level 250-1000 fold higher than mechanical reactors. This high concentration makes the protein easy to purify.





Since beginning the work in 1986, they have produced four generations of transgenic pigs. They recently succeeded in treating hemophiliac mice through feeding them milk rich in the transgenic protein. Drinking the milk every other day restored normal blood clotting. "This means that kids in their infancy would have a good shot at treatment," Velander said. Because their veins are too fragile to withstand the needles, it is currently impossible to treat infants using standard injections of the existing drugs.

Velander addressed the question of whether creating transgenic pigs for producing Factor IX is ethical: "The pig has 100,000 genes or more. We've added only one new gene," he said. In addition, he noted that because the protein is produced only during lactation and exported out of the animal, it does not affect the pig's physiology. "These are happy and healthy pigs. It's a very suitable thing for them to dedicate their lives to giving milk to save [human] life," he said.

Velander additionally noted that just several hundred transgenic pigs could provide the whole world supply of Factor IX needed to treat hemophiliacs. "Compare this to the reality that 10,000 to 15,000 pigs are slaughtered every day for the dinner table," he concluded.



RECOMBINANT PROTEIN EXPRESSION SYSTEMS

	AMOUNT EXPRESSED	AVAILABILITY FOR PURIFICATION	POST-TRANSLATION MODIFICATIONS
BACTERIA	++++	++	+
YEAST	++++	+++	++
FUNGI	++++	+++	++
TRANSGENIC PLANTS	++++	++?	++
BACULOVIRUS	++++	+++	+++
MAMMALIAN CELLS	+	++++	++++
TRANSGENIC ANIMALS	++++	++++	++++

Source: Adapted from a slide prepared by William Velander, Virginia Polytechnic Institute and State University.

RESPECTING ANIMALS

What ethics should govern the treatment of transgenic farm animals? Gary Comstock, director of the Research Ethics Program at North Carolina State University addressed this question by asking how we respect animals, and by drawing lessons from intuitions about humans with mental capacities similar to animals.

“It’s not only trying to minimize pain and suffering that we care about as we live our lives, it’s also minimizing disrespect,” Comstock said. While it is relatively easy to understand what this means for humans, its meaning may be less obvious when applied to animals. Disrespect of humans is “failing to recognize them as subjects of their own life,” he said. “We respect the fact that even mentally disabled people have desires, things that matter to them.” Animals, however, do not have projects that give their lives meaning, so, “How would you measure disrespecting a pig?” he asked.

The key to respecting animals, he suggested, is respecting their right to satisfy their primary desires. In contrast, transgenic animals are often viewed as valuable production machines, much like sows in conventional agriculture. Comstock explained that in the case of sows in conventional agriculture, the only primary desires that are met are those that are “critical for meeting necessary efficiency goals of production.” Confined to cramped gestation crates, they are given no opportunity to follow their instincts to root or to nest. Yet, “They are entitled to satisfy those desires beyond the need to satisfy our production needs of those animals,” Comstock said.

He suggested that we should regard transgenic animals as beloved pets, which provide for sick humans and give us their lives in service, like “the old mare in the coral who carried thousands of children on her back.” Such animals we hold in high regard and care for even after their productive lives have ended.

“How would you measure disrespecting a pig? It sounds like a silly question, but I think actually it’s the most important question we can think about when we think about trying to sell products from transgenic animals to people.”



Gary Comstock North Carolina State University



WILL TRANSGENICS HELP OR HARM ANIMAL WELFARE?

Panelist Joy Mench, director of the Center for Animal Welfare at the University of California at Davis, reviewed the implications of extending transgenic technology into conventional agriculture, where she stated that there are no government-regulated animal welfare standards for animals on the farm.

Mench began by outlining basic principles to guide the treatment of animals:

- Animal pain and suffering should be minimized when possible;
- Animals should experience some quality of life within the context of our use of them;
- Animals deserve some kind of legal protection;
- If animals are going to experience pain and suffering, or if their quality of life will be diminished, they should only be used for important reasons.

With this in mind, she discussed the impacts of reproductive and gene insertion technologies used to produce transgenic animals.

Mench pointed out ways that gene insertion technologies can affect animal welfare. The primary method used to produce transgenic livestock is microinjection of DNA. Because there is no control over where the DNA inserts itself into the genome, microinjection can cause unintentional mutations that may result in deformities or unintentional expression of genes.

Many of the reproductive technologies used—such as super ovulation, in vitro fertilization, semen collection, and embryo collection—also have the potential to cause the animal pain and distress. For example, in vitro culture methods are associated with “large offspring syndrome” (LOS) in cows. LOS makes birth difficult and can cause a range of debilitating health problems in offspring. In addition, production of transgenic animals often involves repeated abortion if the fetus is found to be non-transgenic or the wrong sex.

But, Mench noted that almost all of these technologies are already used in conventional agriculture. “The production of transgenic animals by and large is not a special case,” she said. “It is a difference in degree and not in kind.” This, in itself then, raises questions about the acceptability of conventional reproductive technologies.

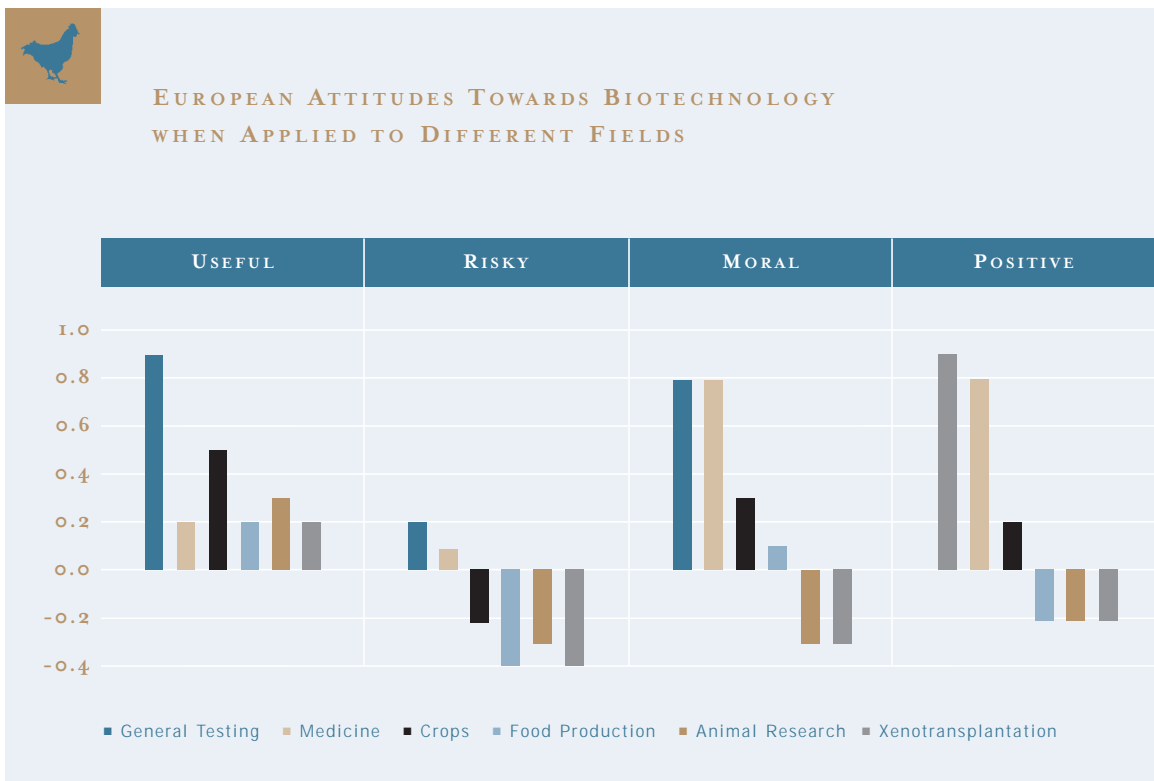
“We have managed, even through conventional selection techniques, to have very negative effects in some cases on the welfare of animals,” Mench said. She described the most serious animal welfare issues as disorders related to selection for high rates of production. She cited problems such as osteoporosis in laying hens, where because they produce so many eggs, their calcium goes into eggshell rather than into their own bones. Mastitis (an inflammation of the udder) and lameness in dairy cattle are both related to high rates of milk production, said Mench.



Mench suggested that when applied to conventional agriculture, transgenic technologies have the potential to do either harm or good. For instance, if scientists could breed hornless steer, ranchers could avoid the common and painful practice of surgical “dehorning.” On the other hand, modifying animals to be more disease resistant might lead to a further intensification of animal housing, causing more harm than good to their welfare.

Mench asked whether transgenic technologies should be used to better adapt animals to the crowded housing situations of conventional agriculture. “Should we use it to change docility or fearfulness or aggression or sociability or movement patterns in animals? That is, to adjust them to intensive agriculture practices?”

In summary, Mench urged that transgenic technology be considered against the whole background of the ethical acceptability of applying technologies to animals, whether they are biotechnologies, traditional selection techniques, or automation and intensification.



Source: Adapted from a slide prepared by Joy Mench, University of California, Davis.



DISCUSSION

Panelists and audience members grappled with the complex ethical issues raised by the presentations. Neal First asked the other panelists what animal welfare standard should be applied to transgenic animals. “What is the ‘normal’ you compare it with?” he asked.

Mench replied that conventional agriculture was not necessarily a good enough ethical standard. “We need to arrive, as much as we can, on a consensus about what constitutes appropriate treatment on farms, and what kinds of tradeoffs we are going to make for agronomic benefits,” she said. “We really haven’t had that discussion in this country, to any great extent.”

Comstock said, “There is a moral question about how we construct our society. I think we should be constructing it really differently at the moment.”

Marlene Halverson of the Animal Welfare Institute questioned Comstock about his statement that transgenic animals are “of the scientists own making,” and whether this changes our obligations to them. Comstock affirmed that it does put more responsibility on people to assure the welfare of the animals.

Bill Muir of Purdue University asked whether it is amoral to change the basic nature of an animal so that it no longer wants to carry out certain behaviors—such as pigs wanting to make nests or chickens wanting to dust bathe. He pointed out that people have already changed animal behavior through the process of domestication, selecting for behaviors that are appropriate to confined settings.

While acknowledging that domestication has changed animals, for example by increasing docility, Mench objected to genetically engineering a chicken so that it does not want to dust bathe. “It does not strike me as the best solution to the problem of how to gather chicken dust bathing material. I don’t have a logical reason, but it makes me uncomfortable as a solution,” she said.

Comstock objected to such a project because it would further reduce genetic diversity. “We don’t have any wild prairie chickens in Iowa anymore,” he said. “We are selecting how diverse God’s great creation is going to be according to our likes. This just pushes it more in a direction that is even less diverse.”

John Phillips, from the University of Guelph, expressed a popular sentiment when he said, “Until we get general animal production practices in order and make the public more easy with how animals are being raised for traditional consumer practices, transgenic approaches—however good they might be to cure world ills—will not be widely embraced.”

PANEL TWO:

BEYOND THE BARN: ECOLOGICAL AND HUMAN HEALTH CONSIDERATIONS

IF TRANSGENIC ANIMALS ESCAPE

William Muir, director of the High Definition Genomics Center at Purdue University, and a member of the committee that authored the NRC's Animal Biotechnology report, identified two principle environmental risk issues associated with transgenic animals: an invasion risk and an extinction risk.

In terms of both risks, Muir likened transgenic organisms to exotic species that invade new areas, disrupting ecosystems and displacing other species. As an example of such an exotic species, he pointed to the gypsy moth. It was introduced on the East Coast to increase silk production, got loose and is moving westward, causing extensive destruction to plant life as it goes.

Like an exotic species, Muir said that a transgenic escapee could pose an invasion risk if its new gene increased its ecological adaptation, allowing it to extend its range into different environments. For instance, if a freshwater catfish that was genetically engineered to tolerate saltwater escaped into the ocean, it could potentially displace species already there.

Transgenics in new environments could displace other species through increased competition for limited food, or through changing predator-prey relationships. Fish that are genetically modified to grow more quickly or larger than normal could displace other fish by eating larger prey that other species had previously relied upon. At the same time, the transgenics would less likely become prey themselves.

Escaped transgenic animals engineered in ways that remove natural biological barriers that limit their numbers could also displace other species. One example is a transgenic catfish that uses a moth gene to excrete its own antibiotic. No longer subject to diseases that formerly culled its numbers, the transgenic catfish could multiply, putting pressure on other species.


Finally, Muir explained the workings of "Trojan Genes." Based on this hypothesis, if an escaped transgenic animal introduces a maladapted new gene, one that lowers the net fitness of the animal, into wild populations through interbreeding, the end result could be the extinction of both the escaped transgenic population and its wild relatives.

Trojan genes give transgenic animals an initial advantage over wild relatives, but lower their long-term fitness. For instance, an escaped male transgenic fish engineered to grow larger than normal would enjoy an outstanding mating success, because female fish see large males as more "fit" than small males. Thus, he would rapidly spread the transgene through the wild population. "In this example, however, the large transgenic male also carries a maladapted gene, one which results in decreased offspring viability." Because he is successfully and rapidly spreading a maladapted gene, then, in the long run, both the transgenic fish population and the wild species that carries its gene may face extinction.

Muir said that not all transgenic species present the same ecological risks. Those that are highly mobile, able to escape captivity and that can easily return to a wild state would be more worrisome. Mice, insects, and fish, therefore, create the greatest concern. Chickens, cows and pigs have low mobility and are generally of lower concern, but pigs can readily return to the wild state.

Scientists can estimate the risk posed by a particular transgenic animal prior to release by analyzing the likelihood that it can spread into the environment. Muir described a new way to do this, called the net fitness component methodology. To assess risk, it evaluates six fitness components: juvenile viability, age of sexual maturity, mating success, male fertility, female fecundity, and adult viability.

Because this risk assessment methodology provides a rigorous scientific test that regulatory agencies can easily adopt, "I believe this will actually result in a greater acceptance of the technology because we know that we have sound scientific principles going into it. Even more importantly, we can debate those scientific principles," said Muir.



IMPACT OF THE TYPE OF SPECIES TRANSFORMED ON THE LEVEL OF RISK

SPECIES TRANSFORMED	DOES THE SPECIES HAVE:		
	MOBILITY	ABILITY TO RETURN TO A WILD STATE	ABILITY TO ESCAPE CAPTIVITY
MICE	HIGH	HIGH	HIGH
FISH	HIGH	HIGH	HIGH
INSECTS	HIGH	HIGH	HIGH
PIGS	LOW	HIGH	MODERATE
CHICKENS	LOW	LOW	LOW
COWS	LOW	LOW	LOW

Source: Adapted from a slide prepared by Bill Muir, Purdue University.



IS IT SAFE TO EAT?

How likely is it that transgenic animals would introduce new food allergens, toxins, or bioactive compounds such as hormones into our food?

James Murray, Vice Chairman of the College of Agriculture and Environmental Sciences at the University of California, Davis, addressed this question. He said that such introductions could come either through the transgene itself, or by activating other genes in the host animal.

The technology used to create the transgenic animals is one factor to consider. For example, microinjection—whereby the new gene is integrated at random spots in the genome—could, in theory, activate a host gene that produces a novel toxin or allergen, or even a prion-like element (similar to that responsible for “mad cow” disease).

However, Murray said that this risk is low. “I would say you are probably looking at a rare event. Something like two percent of the DNA in an organism actually codes for a gene. The remaining DNA is for non-coding material.” In addition, he said that the microinjected DNA would not only have to land in a gene, but also to “actually hit where it can activate the gene.”

Murray pointed out that the risk is lower still since most farm animals do not produce known toxins. However some animal products – including milk and shellfish – do contain known allergens.

The risk that the transgene itself could cause allergenicity or toxicity depends on whether its protein product is already part of the human diet. If so, the risk would be very small. “We used to consume more animal body parts than we consume today, but in fact, we are probably already eating—in some form or another—the proteins of most genes that are expressed,” Murray said.

If the transgene’s protein is not already part of the human diet, however, Murray said that it then must be carefully assessed beforehand to make sure it is not a potential allergen or toxin. That could be done either experimentally or by using databases to compare the protein structure to that of known allergens and toxins.

Another potential safety issue is leaky expression of the transgene. This is especially important for bioactive molecules such as hormones. For instance, if a transgene targeted for expression in the mammary gland were expressed in other animal tissues as well, this could both affect the physiology of the animal and the food safety of its meat. “Localization is an important issue,” Murray said. Similar problems could be caused if the hormone leaked out of the mammary gland into the animal’s blood circulation.

Murray said that both types of leakage are important to monitor and understand in evaluating the food safety of transgenic animals.

“I think it’s a different story in plants where you do have known toxin genes in a wide variety of plants. Certainly in the animals, or normal food animals, they don’t basically carry many toxin genes.”



James Murray University of California-Davis

THE RISK OF NEW DISEASES

Do transgenic animals pose a significant risk of infectious disease among humans? Not according to John Coffin, a retrovirologist and professor at the Tufts University School of Medicine. Coffin described several possible disease scenarios linked to transgenics, each one “highly improbable and requiring a number of improbable steps of a sort of increasing cumulative improbability.”

Coffin described the risks as technology-dependent and possible to mitigate or eliminate by changing the technology. He outlined several possible routes by which transgenic animals could cause infectious disease in humans.

For instance, antibiotic resistant genes used in some transgenic technologies could enter the environment and be taken up by other bacteria. Given the right chain of events, this could lead to an increase in antibiotic resistant pathogens. Coffin pointed out that one simple way to eliminate this possibility would be to stop the use of antibiotic resistant markers.

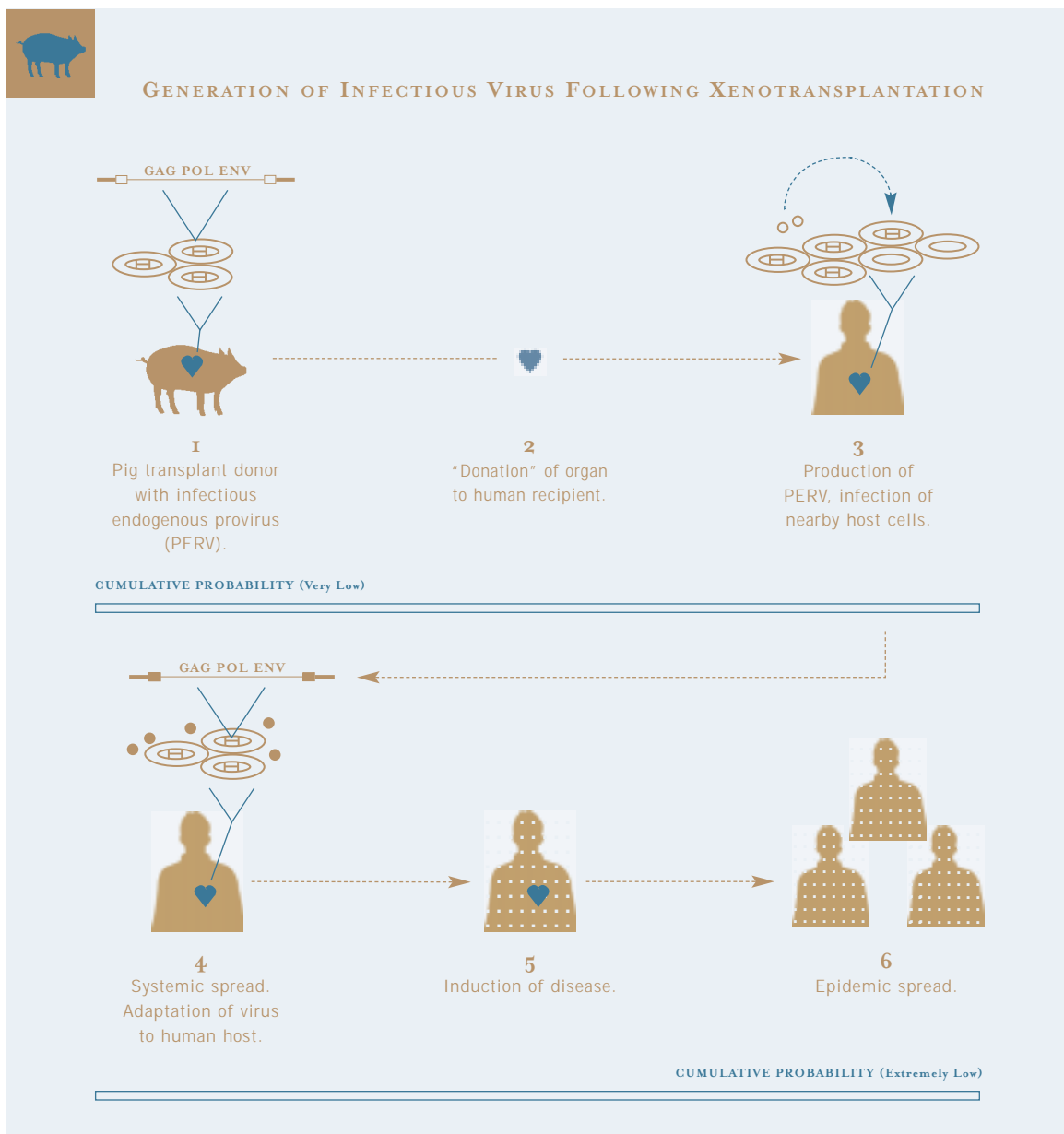
In another scenario, a retroviral vector used to deliver the transgene could recombine with a latent virus buried in the animal’s genome, or with another virus that infects the animal. This new recombinant virus could potentially spread into the food chain and then to humans. Coffin said that minimizing the transgene’s viral sequences would lessen this risk, while stopping the use of viral vectors would eliminate it.

Similarly, a retroviral vector, such as a murine leukemia virus, could recombine with a related virus, leading to “rescue” of the vector and the restoration of pathogenicity. He said the rescued virus, “could cause leukemia. It could cause immunodeficiency or any of the other diseases that retroviruses are famous for,” Coffin said. Again, Coffin emphasized that not using retroviral vectors would eliminate the risk.

Finally, a transplantation organ from a transgenic animal infected with an undetected animal virus could spread that virus to the human who receives the donor organ. The same genetic modification that would prevent rejection of the organ by the patient’s immune system could also destroy the patient’s immunity to the foreign virus. Once the organ was transplanted into the patient, the undetected virus could adapt itself to the new human host and cause infection. In a worse case scenario, the virus would not only infect the transplant recipient, but would also spread to others and cause a new disease epidemic.

Coffin said that scientists could minimize this risk by closely monitoring transplant recipients; they could eliminate it by breeding infectious animal viruses out of the animals—an extremely costly undertaking. Pigs, for example, harbor at least six such viruses, known as porcine endogenous retroviruses, or PERVs. The infectivity of PERVs is unknown.

Coffin concluded that all of the concerns related to infectious disease and transgenic animals “require a chain of events of very low cumulative probability but for which there are some experimental precedent.” He again stressed the changes in technology that would eliminate or mitigate these risks.



Source: Adapted from a slide prepared by John Coffin, Tufts University.

DISCUSSION

During the discussion, a number of audience members pursued the theme of mitigating the potential harmful effects of transgenic technologies.

Greg Jaffe from the Center for Science in the Public Interest (CSPI) asked whether transgenic animals could be designed to reduce ecological risk, possibly by applying so-called “terminator technology,” that knocks out genes important to reproduction.

“There is a way to use the technology itself to make it more safe,” Muir replied. For example, he suggested that scientists could combine two technologies to prevent escaped transgenic fish from reproducing with wild populations. The first would knock out the gene for estrogen production, making the fish sterile. The second genetic change would create triploids, which are normally infertile. “You then have a double safety mechanism where if it escaped one system you would have a backup,” Muir said.

Muir elaborated on ways to mitigate risk, reflecting on the typical course of development of new biotechnologies. “In the early history of these things, one takes what is available and uses it to make your animal, and only later one has to worry – after going through an enormous amount of effort and expense. ... I’m an advocate of very careful thinking about what it is that goes into the animal with these outcomes in mind at the end,” he said.

Patrice Jones, with United Poultry Concerns, questioned the whole approach of using technology to mitigate transgenic risks, rather than simply avoiding use of the technology all-together. For instance, regarding Murray’s efforts to use transgenics to create milk products that are lower in saturated fatty acids, she said, “The problems you are trying to solve are the human health problems that are associated with excessive consumption of saturated fatty acids, particularly in milk products.... The more parsimonious solution would be to simply get people to consume less milk and fewer dairy products.”

Jones said this goal could be met by the government reducing or eliminating dairy industry subsidies, which would lead to a reduction in the suffering of animals involved in transgenic research and in milk production.

Murray replied that people are not reducing intake of dairy products and saturated fat enough to make a difference in health. The technology, he said, could “give people the option to have what they want.”

Although all the panelists emphasized the low risk and relative safety of transgenic animals, not everyone agreed. Jean Halloran of the Consumers Union expressed little faith in the contention that threats to human safety appear to be low probability.

“There was a report from Harvard many years ago that concluded the probability of a nuclear power plant accident was so remote as to not consider it in setting policy.” Halloran warned against making a similar mistake with transgenic animals.

PANEL THREE:

MARKETING ISSUES FOR TRANSGENIC ANIMALS

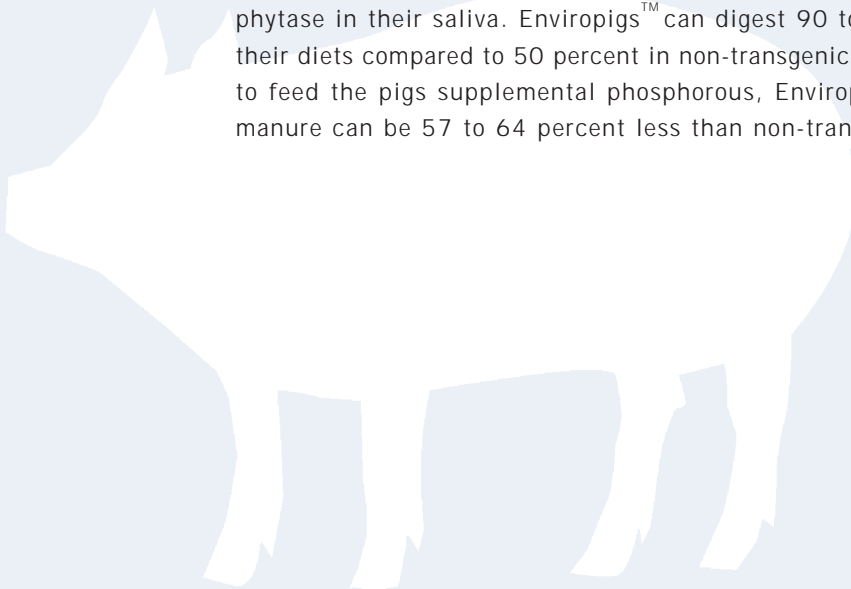
THE ENVIROPIG

Cecil Forsberg, a microbiologist at the University of Guelph in Ontario, Canada, presented the case of a transgenic pig that reduces environmental pollution from agricultural production practices.

Forsberg explained one of the environmental problems currently faced by the pork industry is the land application of pig manure as fertilizer. Because not all phosphorous in plant material is readily digestible and therefore, pig producers must add digestible phosphorous as supplements in their pig feed, pig manure usually contains high amounts of phosphorous. Repeated applications of manure to land can leave an excess of phosphorous in the soil, which, during heavy rain or irrigation events, may then run off into rivers and lakes, and eventually reach the coastal ocean. The abundance of phosphorous can cause massive algal blooms, which will kill other aquatic life.

Furthermore, the problem is expected to worsen, Forsberg said. "Over the next 50 years, there will be perhaps a 50 percent increase in the [human] population from six billion up to approximately nine billion." This will lead to an increase in food production and consumption, and, "There is expected to be a three-fold increase in pollution, particularly nitrogen and phosphorous, ...and a large portion of this will be related to manure production from food animals," he said.

To help solve this problem, Forsberg's group created the transgenic Enviropig™. It is better able to digest the phosphorous contained in cereal grains by utilizing an enzyme called phytase. Transferring a gene from bacteria, Forsberg's group was able to make pigs produce phytase in their saliva. Enviropigs™ can digest 90 to 100 percent of the phosphorous in their diets compared to 50 percent in non-transgenic pigs. Coupled with no longer needing to feed the pigs supplemental phosphorous, Enviropigs'™ phosphorous concentration in manure can be 57 to 64 percent less than non-transgenic pigs.



Nonetheless, the Enviropig™ remains a hard sell. It has competition in the marketplace: pig feed that contains the enzyme phytase also lowers phosphorous output in manure, although significantly less. Alternatively, farmers can buy cereal grains with reduced phosphorous. Ultimately, however, the Enviropig™ is more environmentally friendly than these alternatives, and may be more cost-effective, Forsberg said.

Many marketing hurdles lay ahead, according to Forsberg. These include meeting the requirements of the Canadian Environmental Protection Act, the Novel Foods Act, and legislation in importing countries, as well as gaining consumer acceptance. Given these obstacles, coupled with doubts about consumer acceptance of transgenic technology, it has been difficult to obtain the pre-commercialization financing needed. Researchers are currently seeking pork-breeding partners.



LAND BASE NECESSARY FOR SPREADING MANURE FROM TRANSGENIC AND NON-TRANSGENIC PIGS
(ASSUMPTIONS: 350 SOW FARROWING TO FINISH UNIT: 60% REDUCTION IN P).

PIGS	ACRES FOR SPREADING	% REDUCTION IN LAND FOR SPREADING
A. LOW EROSION POTENTIAL		
Non-Tg	377	—
Tg	251	33
B. HIGH EROSION POTENTIAL		
Non-Tg	857	—
Tg	325	62

NMAN2001 manure nutrient management computer simulation program (OMAF)
www.omafra.gov.on.ca/scripts/english/engineering/nman/default.asp

Non-Tg Non-Transgenic
Tg Transgenic

Source: Adapted from a slide prepared by Cecil Forsberg, University of Guelph, Ontario.

CONSUMER PERSPECTIVES ON MARKETING TRANSGENIC ANIMALS

Jean Halloran of the Consumers Union began by noting the divide between the views of scientists and industry on the one hand, and the public on the other.

“I’ve been struck by what seems to me to be a very big disconnect between the discussion that’s going on inside the academic community and the business world, and the kind of discussion going on in the outside world,” she said. “In fact, that discussion isn’t going on in the everyday world of consumers.”

While many scientists consider issues of transgenic animals resolved ten years ago, Halloran described a public unaware of the rapid development of transgenic animals. She predicted that once the public grows aware, it would question not only how, but also *whether* scientists should pursue research in transgenic farm animals.

From a consumer’s perspective, Halloran noted the special way that people think about animals. “We cannot generalize from our experience with plant biotechnology,” she said. “There’s no society for the prevention of cruelty to plants. The Endangered Species Act gets its support not from protecting plants, but animals, particularly large mammals,” she said.

Halloran anticipates a debate in which the public will raise many questions—about the ethics of using human genes in animals to produce biopharmaceuticals; about the fate of non-productive transgenic male offspring and of transgenic female animals when they come to the end of their useful lives.

“Should these animals be allowed to enter the food chain? If they are destroyed, how should their carcasses be disposed of?” she asked.

Furthermore, consumers need to be asked: “Do you want to eat a pig that has mouse genes in it?” she said. Although some responses to that question may be viewed as irrational, Halloran stressed that the marketplace is full of many irrational decisions, decisions about food consumption are hardly an exception.

If the “whether” question is answered affirmatively, Halloran said that the next question will be “How?” Should there be a system of pre-market safety review? Should transgenic food be labeled?

“We have mandatory labeling of orange juice as to whether it’s from concentrate or not. We have mandatory labeling of food if it’s been frozen or not. To say that those are important differences that consumers can have information about, and yet a product which contains genes from a species that it would never have in nature is not something worthy of consumer attention, or worthy of being a material fact, strikes some in the consumer field, at least, as a skewed interpretation of the law and intent of the Food, Drug and Cosmetic Act,” Halloran said.

On the contrary, Halloran said that many consumers desire, and should have the chance, to make personal choices about whether they want to buy transgenic animals—something she argues will only be possible through a mandatory labeling system.

In addition, Halloran raised concerns about the lack of a clear U.S. government policy to assure the food safety of transgenic animals. “We need a pre-market human safety review with an approval process at the end,” she said. “This is what consumers need to feel assured about the safety of genetically engineered animals.”

Finally, Halloran cautioned policy makers to pay attention to human nature, and the possibility that accidents will happen. She cited a recent case in which a plant technician took home some refrigerated meat that happened to come from an experimental transgenic animal. “People are not used to thinking about animals in these new ways, with these new uses,” she said.

Halloran urged the FDA to engage the public in discussion through putting a proposed policy out for public comment and holding open hearings to tackle both legal and ethical issues.

“We need a genuine dialogue on this issue, in all its complexity. Science and business cannot be afraid of democracy, including its occasional moments of lack of scientific rationality,” she concluded.

We need a genuine dialogue on this issue, in all its complexity. Science and business cannot be afraid of democracy, including its occasional moments of lack of scientific rationality.



Jean Halloran Consumers Union

TECHNOLOGY TRENDS

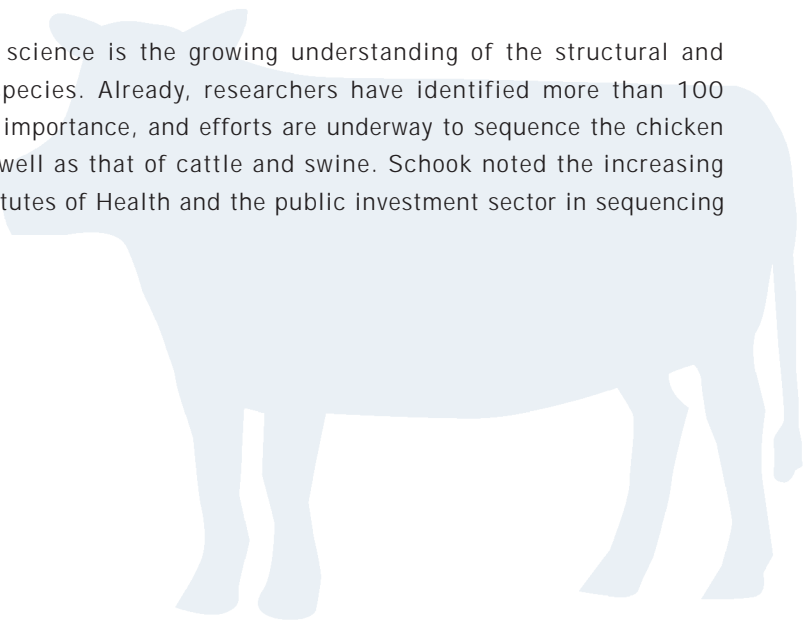
Lawrence Schook, President of Pyxis Genomics, Inc., a gene discovery company working in animal health, discussed how genomics will be able to solve many of the problems associated with transgenic animals. Genomics will be an important tool to address many of the health, safety, and ethical concerns that have consumers worried, he said.

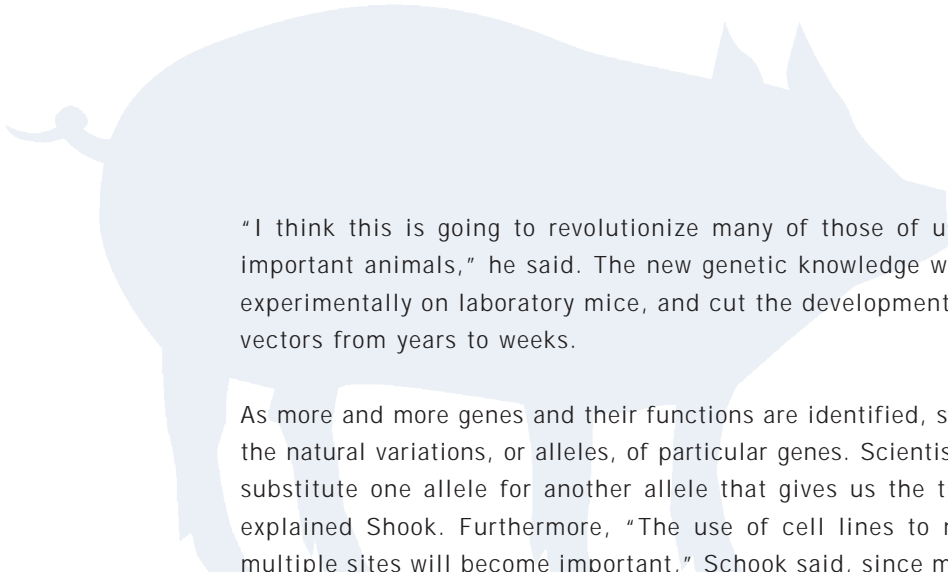
The advances will come from the new science of “recombineering” that should allow researchers to improve farm animal traits without creating transgenic animals, but rather by manipulating genes within a single species. Schook predicted that recombineering will make ethical concerns about mixing the genes of different species a moot point.

As an example of how recombineering will work, Schook explained that rather than relying on a growth gene from one species to promote more rapid growth in another, researchers will be able to identify the specific genes that control growth in the species of interest. Once these genes are sequenced, scientists will be able to make targeted genetic changes in cultured cell lines. Those cells could then be used to create clones of the animals.

In addition, innovative recombineering will allow the precise placement of genes, eliminating the accidental creation of mutations caused by microinjection. They will improve the “reprogramming” of a cell that must take place for the healthy development of a cloned embryo, solving related health issues for cloned animals.

Key to success of the new science is the growing understanding of the structural and regulatory genes within a species. Already, researchers have identified more than 100 genes that have agricultural importance, and efforts are underway to sequence the chicken and honeybee genomes, as well as that of cattle and swine. Schook noted the increasing interest in the National Institutes of Health and the public investment sector in sequencing new organisms.





“I think this is going to revolutionize many of those of us working with agriculturally important animals,” he said. The new genetic knowledge will overcome the need to rely experimentally on laboratory mice, and cut the developmental lead-time for creating new vectors from years to weeks.

As more and more genes and their functions are identified, so too will scientists recognize the natural variations, or alleles, of particular genes. Scientists should be able to “literally substitute one allele for another allele that gives us the traits that we’re looking for,” explained Shook. Furthermore, “The use of cell lines to make allelic substitutions in multiple sites will become important,” Shook said, since many important traits, such as growth and lactation, are controlled by more than one gene.

Schook predicted that recombineering would eliminate the need for antibiotic markers used in some transgenic technologies, thus eliminating risks related to the spread of antibiotic resistance. He concluded by saying that the new techniques combined with cloning will soon “out-perform natural breeding...the traditional boar stud or progeny testing will be replaced by the ability to do these kinds of studies in vitro and in the laboratory.”

“The question consumers have is whether the product they are buying is normal. I want to make sure that we’re using technology that produces normal outcomes, that meet consumers’ expectations of ‘normal.’”



Lawrence Schook Pyxis Genomics, Inc.

DISCUSSION

Because the challenge of marketing transgenic animals is intimately linked to questions of consumer acceptance, much of the discussion focused on factors that influence this acceptance, including ethical questions.

Kara Flynn, of the National Pork Producers Council, asked whether animals that result from recombineering rather than from transgenic technology would be more acceptable to consumers.

Schook replied that the key to acceptance is bringing an added value to consumers. "If you can demonstrate some consumer benefit, whether increased health, reduced fats or lean growth, I do believe that they will be acceptable to the consumer," he said. Until now, most genetically modified animals under development have been designed to bring benefit to the producer, rather than the consumer. The difficulty, however, lies in getting funding for consumer-oriented problems.

Greg Jaffe of CSPI questioned how researchers and producers were going to communicate to the public the environmental benefits of the EnviropigTM. To do so presents a "conflict of interest for the industry," he said, since, "generally, the people who are involved in the agricultural practices don't want to let the public know how bad for the environment those practices are."

Forsberg replied by saying, "It's a matter of how important the environment is to you, and how important it is to consumers. I think one would have to present it as environmentally friendly meat, and see if consumers would eat it."

Donald Coover, a veterinarian and owner of SEK Genetics, Inc., pointed out the similarities between clones made through molecular engineering and naturally born twins, which he described as "nature's somatic cell clones." He then turned the labeling question around, asking Halloran whether she would suggest that naturally occurring identical twins be labeled.

"No. And it's because I don't think that somatic cell clones are the same thing as identical twins," she replied, citing the animal welfare problems, such as Large Offspring Syndrome, seen with laboratory manipulations.

Tamiko Thomas, of the Humane Society of the United States, asked Halloran whether she thinks that consumers share “the assumption of biotechnology that it is proper to take animals, and to manipulate them in a manner as scientists see fit, and with impunity?”

Halloran said that the public holds a variety of views, and the main problem is the lack of public debate. “I think we’re going to regret it, if, as a country we adopt one point of view—which is to say that concerns don’t exist or don’t matter, or are unscientific, and just go forward.”

Alison Van Eenennaam, from the University of California-Davis Animal Science Department, asked whether Schook is suggesting that recombineering replace multi-species, transgenic technology. Schook replied that he is not against transgenic technology, but that the mapping of economically important traits in farm species means that research does not have to rely on multi-species constructs for progress.

Jim Murray from the University of California pointed out that the growing body of genetic information from a variety of species shows that most genes are held in common. “Most of the genes that are in fish are actually genes that we have, and what you’re really talking about are different alleles of the same gene.” This genomic knowledge can help predict which genes might be of more concern when used in transgenic animals.

Schook agreed, adding that the real issue regarding the safety of genetically engineered animals is not the precise genetic sequences used to create them, but the physiological outcome of those sequences. On a philosophical level, this raises the issue of what is “normal.”

“The question consumers have is whether the product they are buying is normal,” Schook said. “I want to make sure that we’re using technology that produces normal outcomes, that meet consumers’ expectations of ‘normal.’”

PANEL FOUR:

INSTITUTIONAL AND LEGAL BACKGROUND

REGULATION AT THE CROSSROADS

Fred Degnan, a partner in King & Spalding's FDA Practice Group and General Counsel to the Food and Drug Law Institution, noted that there are a number of federal statutes that come into play, and that none of them specifically addresses transgenic animals.

"The result is...federal regulation that has possible or apparent holes in the context of this particular technology," he said.

Degnan focused on the FDA, describing its authority over transgenics, which derives from control over the animal as a carrier of a drug. Most fundamentally, "drug" is defined as an article intended to affect the cure, mitigation, treatment, and prevention of disease. It is further defined by statute as any article, other than food, "*intended* to affect the structure or function of the body of man or other animals." This puts genetic materials, such as those designed to hasten an animal's growth, in the category of a "drug."

Within the FDA, the Center for Veterinary Medicine (CVM) holds the main regulatory authority for transgenics, through the New Animal Drug Application, or NADA. Under the statute, a drug is "new" if it is not already generally recognized by experts, based on scientific data, as safe and effective for its use. The statute offers "a very real opportunity for comprehensive regulation," Degnan said.

It establishes a pre-market approval process for new drugs that begins when companies file for an "Investigational New Animal Drug Exemption," or INAD. The process gives the CVM the authority to conduct inspections, monitor research and record-keeping, and assess animal welfare impacts. "Moreover, the agency can focus on harm—harm to the investigators, harm to the animal itself, harm to the environment if there's a potential for release—and the agency can institute a clinical hold on the INAD."

While the process was developed for and is well-suited to conventional drugs, it has possible shortcomings regarding transgenics, Degnan said. "Fundamental risk assessment problems" and lack of clarity on how to deal with uncertainties are two such shortcomings. For example, there is uncertainty regarding the criteria that FDA is going to follow and enforce in assuring human food safety.

Another possible shortcoming is the agency's authority and ability to assess environmental impact on people and animals. "FDA's authority under the act does not go to the greater environment and fundamental ecological concerns," Degnan said. "Can they look at a second generation affect, or a third generation affect? And then moreover, [do they have] authority to require studies on those possible impacts, how far does that authority reach?" he asked.

Degnan outlined a number of administrative actions needed to enhance the FDA's authority and improve transparency. Degnan recommended that FDA develop guidances and criteria governing the food safety and the environmental impact of transgenic animals. He also suggested that FDA establish a transgenic animal enforcement/inspection program, update existing relevant regulations and policies regarding clinical investigation and GMP controls, and consider mechanisms to improve interactions with other federal agencies that regulate transgenic animals.



KEY PLAYERS: FEDERAL REGULATION OF TRANSGENIC ANIMALS

- USDA:** Animal Plant Health Inspection Service (APHIS) (animal biologics; animal welfare)
- USDA:** Food Safety and Inspection Service (FSIS) (ante-mortem, slaughter, and post mortem inspection)
- FDA:** Center for Veterinary Medicine (CVM) (market entry requirements over animal "drugs")
- FDA:** Center for Drug Evaluation and Research (CDER); Center for Biologics Evaluation and Research (CBER) (market entry requirements over human drugs and biologics)
- FDA:** Center for Food Safety and Applied Nutrition (CFSAN) (milk, eggs, other edible products)
- NIH:** Office of Laboratory Animal Welfare (coordination of biomedical-related research)

Source: Adapted from a slide prepared by Fred Degnan, King and Spalding, LLP.

THE REGULATORY CONTEXT

Michael Taylor, a senior fellow at Resources for the Future, noted that society is just beginning a long process to figure out the best regulatory system for transgenics. In order to do so, however, “We need clarity about what we want the system to do and how we want it to do it,” he said.

He described the job of the regulatory system as ensuring food safety, protecting animal safety and welfare, anticipating and minimizing environmental risks, and engendering public confidence in regulatory decisions.

“The government has to focus on engendering public confidence in the integrity of its decisions, rather than becoming a support system for the technology itself,” he said.

Regarding how the system should work, Taylor stressed that, “Ensuring food safety...is the most fundamental expectation that the public has....The public won’t accept a food technology without assurance that it’s safe for their families.”

He outlined four requirements for the regulatory system:

- It needs the authority and the expertise to ask the right questions.
- It needs to be able to generate the right data.
- It needs scientifically sound processes that are by definition open to new information and to diverse points of view to evaluate that data.
- It needs a process that is publicly transparent and participatory. In addition, the process needs to place the burden of proof and the consequences of uncertainty on the sponsor of the technology.

Within this context, Taylor evaluated the FDA’s strengths and weaknesses regarding the regulation of transgenics.

He agreed that the FDA has the expertise to regulate food safety, and animal welfare, at least in relation to the health of the animal involved. He was skeptical, however, about the agency's ability to monitor "concerns about animal welfare that arguably go beyond the health impacts." Taylor noted that the lack of federal welfare standards for agricultural animals creates uncertainty about what animal standards the FDA should apply to transgenics.

Regarding environmental risks, Taylor said, "When you get beyond the barnyard and into the environmental and ecological affects that have to do with populations of animals or the whole ecological context in which certain animals exist, this is clearly beyond the authority of the FDA."

Taylor pointed out that the FDA has not had to deal with other disciplines that will be relevant to assessing ecological risk, such as marine ecology and evolutionary biology.

Both Degnan and Taylor agreed that the regulatory process lacks transparency. As an example, Degnan pointed out that the licensing process under INAD is totally privileged information. The public cannot know when an INAD has been filed, or for what product. Furthermore, "The private license process wasn't designed to answer some of the broad scientific questions and novel issues that are raised by the technology," Taylor said.

The lack of a transparent and participatory process leads to questions about the system's ability to engender public confidence. "There is a case for considering legislative reform," that would clarify FDA's authority to deal with broad environmental risks, and make the system more transparent, Taylor said.

"The weakness regarding FDA oversight of transgenic food safety issues is that the process is not transparent and participatory. It is a private license process between the sponsor and the agency."



Michael Taylor Resources for the Future

A WORLD OF REGULATIONS

Globally, a large number of national and multilateral organizations often hold conflicting policies on issues that affect transgenic animals, including policies on animal welfare, environmental impact, intellectual property rights, food safety, and labeling. Lonzell (Bud) Locklear, an economic specialist at the United States Embassy in Ottawa, Canada, began by describing examples of significant disputes in biotech products. For example:

- The European Union (EU) has imposed a moratorium on approvals of biotech applications. This has had a direct effect on the United States' biotech industry by factoring into decisions U.S. farmers make regarding the crops they intend to plant and their willingness to embrace new biotech applications.
- The lack of an internationally agreed upon standard for labeling biotech foods has led to a wide and often incompatible array of national labeling policies, which could possibly function as a barrier to trade.
- The European Union recognizes an overriding "precautionary principle" regarding transgenic animals; the US government approaches precaution as a flexible context-specific policy tool.

"What these three examples portray is that at this juncture, there is a certain lack of agreed-upon rules, which, in turn, is having significant impact on trade and biotech products," Locklear said. "Likewise, commerce and biotech animal products, whether for food, feed, medicinal purposes or what have you, will be affected by decisions taken and rules agreed to in international multi-lateral organizations."

Locklear pointed to additional contradictory actions and policies that have been implemented around the globe. While some countries take steps to curtail the development of transgenics, others take steps to encourage it. In the United Kingdom, for example, The Royal Society has recommended that the UK government fund research into the welfare implications of transgenic animals for agriculture. Similarly, The Royal Society of Canada recommends a moratorium on ocean pens for transgenic aquaculture.

On the other hand, in October 2001, President Bush met with leaders of the Asian Pacific Economic Cooperation organization to confirm their support for the development of biotechnology to help feed growing populations and its safe use based on sound science.

Internationally, the main organization involved with regulating transgenics is the World Trade Organization (WTO). The WTO describes itself as "the only global international organization dealing with the rules of trade between nations."

It has two major agreements that affect biotechnology. The Agreement on the Applications of Sanitary and Phytosanitary Measures sets out basic rules to ensure that a country's consumers are supplied with food that is safe to eat, while at the same time ensuring that regulations are not used as an excuse to protect domestic producers.

The second major WTO agreement, the Agreement on Technical Barriers to Trade, tries to ensure that regulations, standards, testing and certification procedures do not create unnecessary obstacles to trade.

In addition to these agreements, Locklear described an "alphabet soup" of organizations that affect issues of transgenic animals. (See table.)

He stressed that international law and policy are evolving with many players in the game. "As a consequence, there's not yet a comprehensive, well defined, globally agreed upon set of rules to manage commerce in biotech animals and animal products," Locklear said. However, he cautioned that international organizations and rules not only affect commerce, but also help define public perception and acceptance of the technology.



INTERNATIONAL ORGANIZATIONS SETTING RULES RELATED TO ANIMAL BIOTECHNOLOGY

WTO: World Trade Organization
TBT: Technical Barriers to Trade
SPS: Sanitary and Phytosanitary Measures

OIE: Office International des Epizooties

CODEX ALIMENTARIUS

ICH: International Conference on Harmonization

CBD: Convention on Biological Diversity

OECD: Organization for Economic Cooperation and Development

APEC: Asia Pacific Economic Cooperation

Source: Adapted from a slide prepared by Bud Locklear, U.S. State Department, Ottawa.

DISCUSSION

Audience members had varied views on the types of reforms that may be needed. Marlene Halverson of the Animal Welfare Institute and Greg Jaffe of CSPI both asked about post-approval monitoring processes. Halverson noted the lack of a post-approval monitoring process to deal with unforeseen impacts on animal welfare.

Jaffe's concern focused on the environment. "There isn't mandatory post-approval monitoring for these animals, especially in the environmental context," he said. He asked what could legally be done about the animals when they get out into the environment and cause a problem. "The FDA doesn't have authority under the new animal drug process to take back that new animal drug. I think that is a major weakness that needs to be fixed with new legislation," he said.

Taylor responded by saying that the problem is not so much the lack of legal authority, as the physical impossibility of taking back some things once they have been released into the environment. "This gets to the heart of the question of what degree of precaution is appropriate," and is one reason why it is fair to re-evaluate the current legislative approach to transgenics, Taylor said.

On the other hand, Degnan stressed that the law "doesn't put forth requirements for monitoring, because the notion is we're only going to approve it if it is safe." Nonetheless, he acknowledged that, "in the case with new drugs, clearly mistakes happen," he said. He also argued that the statute is flexible, and can require post-market monitoring, based on the fact that "safety is a time-dependent judgment."

Joe McGonigle of AQUA Bounty Farms, Inc., pointed to another level of FDA control over transgenic animals that had not yet been discussed – the product use label. He stressed that the FDA's legal authority to manage risks does not end with product approval, but extends into the marketplace where FDA can use the product label to impose specific restrictions and conditions on product use in order to minimize the kinds of risks that had been discussed. McGonigle explained that even after approving a product, FDA could "stack a whole series of restrictions on them that could make them either uneconomic, or completely environmentally benign."

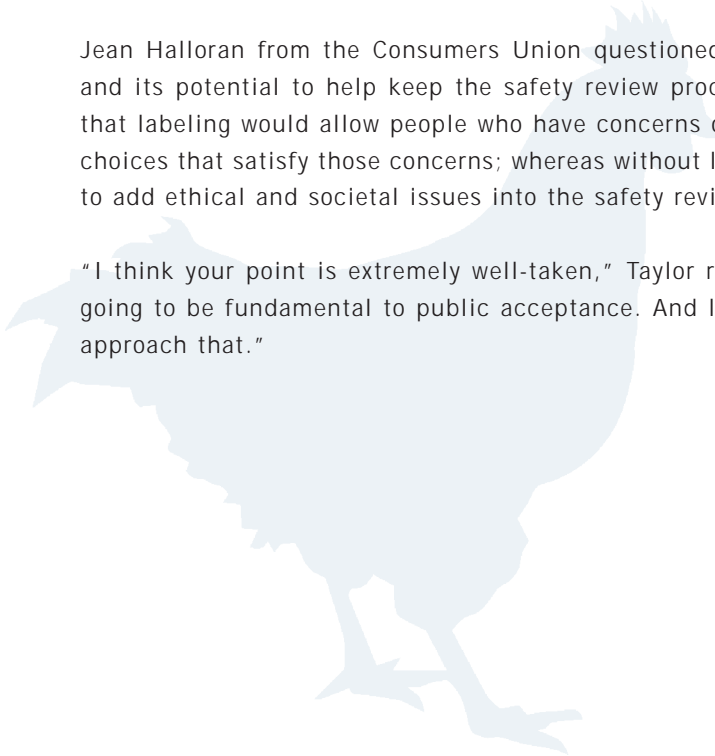
Laura Epstein, associate chief counsel for the FDA, asked if there are any downsides to transparency. “Particularly from industry’s perspective, is there any sense that transparency might, in any way, hinder the development of this technology, or is that not as much of a concern as it would be with more traditional drugs?”

Taylor suggested that requiring companies to disclose too much could come into conflict with protecting trade secrets, and thereby inhibit investment and development of the technology. Degnan pointed to a middle ground of focusing on transparent criteria and transparent methods of assessing the safety of technologies and food.

Highlighting the complexity of federal regulation, Robert Rose with the Animal Plant Health Inspection Service (APHIS) of the USDA pointed out that the Farm Bill of 2002 includes an Animal Health Protection Act, which has broader regulatory authority regarding animal welfare than any of the previous acts. Rose described it as a “risk assessment, permits and quarantine act” that covers transgenic animals and addresses their release into the environment. In addition, he said that APHIS recently formed a new division called the Biotechnology Regulatory Services, which includes transgenic plants and animals.

Jean Halloran from the Consumers Union questioned Taylor about his view of labeling and its potential to help keep the safety review process science based. She suggested that labeling would allow people who have concerns other than safety to make informed choices that satisfy those concerns; whereas without labeling, those consumers might try to add ethical and societal issues into the safety review process.

“I think your point is extremely well-taken,” Taylor replied. “The principle of choice is going to be fundamental to public acceptance. And labeling is the most obvious way to approach that.”



BREAKOUT:

PARTICIPANT VIEWS IN-DEPTH

At the conclusion of each day, workshop members participated in smaller group discussions for more in-depth exploration of the issues. These breakout sessions enabled people from across agriculture and biotechnology industries, and from government and non-government organizations to exchange views. It often facilitated face-to-face dialogue between proponents and opponents of transgenic technology. The concerns and questions raised in these sessions point toward ongoing areas of inquiry and work. A brief summary follows.

ENCOURAGING PUBLIC DEBATE

Many people stressed the need for more public involvement in the debate around this issue and for more public education. Some noted that science tends to be way out in front of public understanding. Encouraging this debate was widely perceived as a challenge: “How can we have a democratic resolution when there is not enough scientific literacy in the country for an informed debate?” one participant asked.

Others questioned how realistic it is to expect the public to be scientifically literate enough to make informed decisions on such technical issues. Alternatively, they stressed the importance of having trusted sources of information and decision-making institutions.

Many people made suggestions for avenues through which to increase public debate and discussion, including: presidential and multi-agency policy forums, state land grant universities increasing their public education efforts, improved science education in public schools, and an increased media role.

Others felt that the debate would be played out in the market through consumer decisions on whether or not to buy transgenic products. But that begged the question: how much information do consumers need for informed decision making in the market?

APPLYING ETHICS AND PROTECTING ANIMAL WELFARE

Participants noted that ethical issues, including the closely related topic of animal welfare, were present in all aspects of the first day’s panels and underpinned all arguments.

Participants discussed to what extent regulatory issues could be allowed to take ethics into account and whether and how ethical or social issues could be separated from scientific issues. Others noted that it is disturbing to expect the technology or regulatory agencies to solve ethical issues, and called for Congressional and White House attention to these issues.

Many felt that arguments on transgenics could become a proxy for discussion of problems in conventional agriculture and that it is important to distinguish between outstanding issues in conventional agriculture and those that flow directly from the biotechnology. Likewise, it is important to distinguish between animal welfare issues that exist in the research enterprise (which is highly regulated) versus in animal food production (which is largely unregulated).

CONSIDERING TRACEABILITY AND LABELING

Although many agreed that society needs a way of identifying transgenic animals in the population, questions were raised about how long traceability needs to be maintained as transgenic animals go through the breeding process—just through the second or third generation or in perpetuity?

One participant suggested that there may one day be a national identification system for livestock, perhaps in the form of a computerized mini-chip, that would allow people to know where the animals came from and whether they were genetically engineered.

Views differed widely on labeling, with some saying it is crucial to giving consumers the ability to make an informed choice in their purchases. Labeling, however, raises many questions: What would be its impact on agricultural production, particularly on producers? Would labeling be useful without widespread public education? How would consumers interpret the labels? Would labels be equally applicable to cloned and transgenic animals?

STRENGTHENING THE REGULATORY PROCESS AND TRANSPARENCY

Discussion ranged from general concerns about transparency, to specific regulatory issues, to questions of regulating “the process” or “the product.” One participant noted that current legislation would allow researchers to use selective breeding to make a four-legged chicken with no questions asked, while a four-legged chicken created through transgenic technology would trigger regulatory reviews.

Reflecting the concerns of an audience with strong industry representation, discussion about the regulatory process tended to be fairly specific. Many questions were left unanswered. For instance, people questioned what type of the genetic alteration should trigger the regulatory process.

Should recombineering, in which scientists use genes already within a species rather than making an inter-species construct, trigger the regulatory process? If the genetic modification merely alters the expression levels of a protein product rather than introducing a new gene, would this trigger the regulatory process?

Should there be different types of reviews for different types of modifications? For instance, should a transgenic animal made using a virus vector need a greater level of review than something made through intra-species gene shuffling?

Should the required level of transparency vary along with the product? Some thought that producing transgenic animals for food should require a higher level of transparency than creating transgenic animals for pharmaceutical production, in part because food production involves many more animals.

Participants were concerned with how to make the regulatory process more transparent. Some stressed the importance of allowing and incorporating public comment on draft guidelines.