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Biosafety, Ethics, and Regulation of Transgenic Animals

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1. Introduction

Transgenic animals—animals with genes added to their deoxyribonucleic acid (DNA) (either from organisms or eventually synthesized genes never before present in living organisms)—will no longer be limited by the gene pool of their parents. Such animals are slated to be created expressly to provide vital and novel benefits for human beings. These animals can have desirable characteristics or traits from virtually any gene pool and may also possess properties not present in nature or available through conventional breeding. They will be created for the production of new medical and pharmaceutical products and to enhance meat, dairy, and fiber production efficiency.

Transgenic animals such as antimalaria mosquitoes and cows that can produce desired pharmaceuticals in their milk have the potential to curtail or treat human diseases, respectively. It is likely that transgenic animals will also be created to produce tissues, living cells, and organs (with likely lower chance of immune rejection) as viable alternatives for transplant patients. Also, through cloning of herds of "elite transgenic livestock," animals can be engineered to provide more nutritious and efficiently produced foods, thus promising also to lower the cost of food for consumers. Other genetically modified animals such as the *Enviropig* of the University of Guelph in Canada may also help reduce agricultural waste and the number of animals needed for food and fiber production (for additional information, *see* refs. *1* and *2*). Similar animals may also serve to flush out agricultural pests, thus reducing the dependency on toxic pesticides.

Although animals with genomes that will be modified through manipulation of recombinant DNA, such as fish, sheep, cattle, pigs, goats, and insects, hold promise to improve our future, their existence also raises important ethical and public policy questions and concerns. Are products that have undergone genetic reconstitution safe? How are they substantially different from conventional products? What are the environmental impacts and risks of undesired gene transfer? Do transgenic animals present novel hazards? Will they create new pathways for animal disease to become hazardous to future generations of humans and animals? What are the ethical implications for the health and welfare of animals used in agricultural and biomedical research? How adequate are the national and international regulatory frameworks, respectively, and

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legal edifice in meeting the challenges raised by animal biotechnology? Is there international uniformity regarding standards and regulations? Are the government and intergovernmental agencies sufficiently prepared to respond to a biotechnological calamity should it happen? Are there sufficient guidelines to promote responsible research and application among private industries and researchers? Does the ability to modify mammals raise questions about the potential applications of genetic modification to human beings?

This chapter begins by providing an overview of some of the central concerns identified for the development of transgenic animals. Some have argued that those responding to the environmental risks and animal welfare and health issues should be paying greater attention to ethics and normative values, both in the process of risk assessment and management and in risk communication. Others have argued that there should be stricter regulation of biotechnology. Central issues in both the ethical and regulatory debates are reviewed. We conclude with a discussion of the role that working scientists should be expected to play in attending to these issues and the need to be attentive to public perception of environmental and animal welfare impacts from transgenic techniques. In limiting the focus of the discussion to transgenic animals developed for agricultural, industrial, and therapeutic applications, we do not consider issues associated with animals such as "knockout" mice altered solely for the purpose of studying gene functions.

2. Ethics, Public Policy, and the Regulation of Biotechnology

Generally, philosophical ethics is the study of a community's vision of how they ought to live responsibly and well. It concerns how individual and collective action should have an impact on others; which actions are morally permissible, impermissible, and insignificant; and embodies the values that a community sanctions as legitimate for promoting the good life. Philosophical ethics is an articulation and critical analysis of the norms, values, and framing assumptions that help determine the path a community should take and directs them on how to meet their responsibilities.

Central ingredients to living responsibly include having consideration of and respect for others, both human and nonhuman beings who matter from the moral viewpoint. Here, living responsibly enjoins recognizing vulnerability and dependency in others and promoting an environment of trust among members of the moral community. Living responsibly entails curbing specious profit-seeking behaviors and placing limits on institutions, practices, and technology that conspire against maintaining trust and respect for others. Finally, living responsibly also entails minimizing harms and maximizing benefits for all those with moral significance and encouraging equitable access to material goods that promote better quality of life. To ensure that an equitable distribution of the benefits and harms are shared among the members of the moral community in a trustworthy and respectful way, open communication between members is important so the interests of others as well as their values and concerns may be understood and considered in moral deliberations and during the formation of public policies. Thus, vibrant discussion and debate are central in establishing a community's shared vision of the ethical life.

A community's shared ethical vision is often mirrored by regulation and through public policy. Public policy is influenced by the moral arguments associated with the development of certain technologies and practices. Regulations and public policy con-

cerning the public good, the role and limits of government, and equitable distribution of goods also serve to promote the value assumptions and political consensus of a community's vision for living well and responsibly. However, public policy has a prescriptive dimension of its own and may serve to bind a community together despite the presence or absence of ethical consensus. When ethical consensus is absent or moral stalemates or division persist, regulation and public policy serve to establish, administer, and enforce practical compromises and political solutions that can be adopted by all constituents. When collective and univocal ethical judgments are present, regulation and public policy may serve as a positive guide to allow for effective and efficient actualization of these moral ends.

Animal biotechnology, although promising to improve quality of life, poses significant risks as well. Even if the prospects are exciting, mistakes have terrifying consequences. Not only can mistakes cause harm, but also the reaction to even minor mistakes can substantially undermine public support for biotechnology. Because the stakes are high if something goes awry, both the scientific community and the nonscientific public must come together to clarify their responsibilities to those who will be impacted by its applications, and to set limits so that what is potentially promising is not also inimical.

This idea of limits connotes some form of regulation. Animal biotechnology is regulated at three interlocking levels that affect research, product development, and use of and commerce in transgenic animals. *Institutional regulation* is conducted by the organizations themselves, although often according to legal mandates handed down from governmental authorities. *Governmental regulation* is conducted by specific agencies of local or national governments with specific areas of authority created by legislative or judicial actions. Finally, *international* organizations such as the World Trade Organization (WTO), the United Nations (UN), and certain multinational treaty and covenant bodies such as the North Atlantic Free Trade Association (NAFTA) have authority to coordinate and resolve conflicts that may arise as a result of diverse governmental regulatory regimes.

Institutional regulation represents the first line of regulation for animal biotechnology. Organizations (e.g., nonprofit scientific research institutes, hospitals, or universities) or for-profit private corporations have specific committees or institutional officers to establish internal policies for biosafety and animal use and oversee compliance with food safety and environmental or other regulations. Although these institutional regulatory bodies operate in accordance with minimum standards dictated by the legal requirements of local and national governments, most institutions conducting work with transgenic animals have adopted internal policies that exceed these minimums. For example, the US Department of Agriculture (USDA) requires organizations conducting animal research to establish provisions of internal oversight through an institutional animal care and use committee (IACUC). The IACUC has responsibility for ensuring that basic requirements of animal welfare are met, but the USDA specifically excludes birds, rats, mice, and farm animals from required oversight. Nevertheless, most US organizations conducting animal research have adopted internal regulations requiring IACUC supervision of these excluded species *(3–7)*.

Governmental regulation includes legal requirements enacted and enforced by local, regional, and national governments. The organization of governmental regulation var-

ies considerably from one country to the next, for example, with environmental regulations exclusively administered by local authorities in some instances, by national agencies in others, and by a combination of local, regional, and national authority in the majority of cases. In most countries, it is typical for different agencies to regulate food safety, environmental, animal welfare, and commercial activity, and in many countries, each subclass of regulatory action is subject to judicial review.

The authorizing legislation for each of these distinct regulatory activities specifies the scope and aims of the regulatory activity, and detailed discussion of regulatory activity is quite technical and varies considerably from one locale to another. However, there is a remarkable consistency in the general aims of regulatory authorities across the globe, and the discussion that ensues substantively addresses issues generally (but not in every case) subject to governmental or institutional regulation *(8–13)*.

Increasingly, however, governments are not the final authority for regulatory decision making because governments participate in international forums that harmonize regulatory activity. The Codex Alimentarius, for example, is a body within the Food and Agricultural Organization (FAO) of the UN that has long had the task of ensuring consistency among global standards for food identity and food safety. The WTO has undertaken review of national regulatory decisions on genetically engineered plants. The basis for this are components of the treaty that established WTO that are intended to limit the possibility that member states will erect spurious food safety or environmental regulations as *de facto* trade barriers. Similar actions within the WTO framework could certainly affect the fate of transgenic animals *(14)*.

The direction that animal biotechnology takes should be determined on the basis of ethics, that is, on the basis of a shared vision of how people ought to live, and on actions collectively sanctioned out of respect for the members of the moral community. Regulations represent the institutionalization of this vision. The definition of ethics provided here is consistent with a philosophical viewpoint that is sometimes stated by opposing the importance of ethics. Some commentators believe that regulations should be based solely on scientifically demonstrable risks and benefits to human beings and presume that the word *ethics* implies something more. But, the belief that regulations should be based solely on scientifically demonstrable risks and benefits is itself a vision of how communities should live, and as such it is an ethical viewpoint. Ethics should not be understood to indicate a single or dominant philosophical vision. The term *ethics* serves to call attention to the norms, goals, and shared assumptions that guide actions and policies and should include debate over differences in these norms, goals, and assumptions, which itself is a characteristic of a community's ethical life. As discussed here, the scientific community has a leadership role to play that entails deliberating with the public and relevant government agencies on the ethical and social implications and risks associated with animal biotechnology in advance before policy is formulated.

3. Ethics and Science-Based Concerns Associated With Animal Biotechnology

In August 2002, the National Research Council's (NRC) *ad hoc* committee on Agricultural Biotechnology, Health, and Environment published a report that identified central science-based risk issues associated with animal biotechnology and its products.

The committee determined risks in terms of criteria that assessed the immediacy and severity of impact of animal biotechnology and the rapid fluidity of technological change. The committee evaluated risk in terms of the nature of the technology, possible undesired and unanticipated effects of application and misapplication, novel ethical and social questions raised by animal biotechnology, and whether the various government agencies and the present-day statutory infrastructure and technological expertise were sufficiently ready to meet these challenges.

The committee applied these criteria to four major areas of concern associated with agricultural biotechnology and genetic modification of animals, including cloning. These areas are environmental concerns, animal welfare issues, food safety, and policy matters and institutional concerns *(15)*. These areas have ethical significance because they concern our vision for how best to advance the good life at the expense of and for others and in the face of different kinds and levels of risks. We have expanded this list of concerns to include issues related to biomedical ethics and social consequences. Furthermore, because animal biotechnology raises questions regarding the roles and responsibilities of scientists, we consider public trust in science another important area of concern that must also be explored.

3.1. Environmental Concerns

The biosafety of animal biotechnology represents a technically complex and emerging area of science. As applications of animal biotechnology are in their infancy, so are scientific approaches to characterize and measure the risks that these applications may pose to the larger environment. The diversity of animal species and the complexity of their respective types of interaction that both managed and unmanaged or natural ecosystems entails make it impossible to offer more than the most general discussion of issues relevant to biosafety in the present context. There is already extensive literature emerging for assessing the environmental risks of transgenic insects *(16,17)* and fish *(18,19)*. The aim here is to provide a general and conceptually oriented overview of the problems of biosafety as related to transgenic animals. Any attempt to assess or manage environmental risks from transgenic animals will require substantially more detailed scientific study of the species and environments involved.

Environmental risks are a function of hazard and exposure. An organism of any sort poses an environmental *hazard* when the presence of that organism in an environment can be interpreted as the possible source or cause of adverse events. The identification of hazards involves both a general and often speculative basis for linking the triggering event to subsequent outcomes and the normative judgment that these outcomes are unwanted, undesirable, or in some sense worse than other alternatives. However, many (if not most) hazards do not actually result in any harm. As such, an analysis of environmental risk also involves an account of *exposure*, the mechanisms that would produce the unwanted outcomes, and quantification of the likelihood for each stage or sequence of events comprising these mechanisms.

Characterizations of hazard and exposure for environmental risk, on the one hand, may be fairly broad and conceptual heuristic devices for thinking about the possible environmental consequences that might follow a triggering event; on the other hand, they might be technically specific and carefully determined measurements that reflect a high degree of empirical investigation and statistical sophistication. In either case, a

characterization of environmental risk may be distinguished from *risk management*, which indicates the principles, policy, and general plan that will be undertaken in deciding whether to mitigate, insure against, or simply accept the risk in question.

The intentional or accidental release of transgenic animals into the environment represents the triggering event for characterizing environmental risk from animal biotechnology. The NRC committee presumes that this release poses a hazard that could result in unwanted changes in the composition of plant and animal species comprising an ecosystem. The primary basis for this presumption is the recognition that some nontransgenic species have become invasive when introduced into new ecosystems, resulting in extensive changes in those environments that have disrupted both human use of the environment and the suitability of the environment as habitat for native species of plants and animals. The general approach that the NRC committee *(15)* recommends for biosafety is to draw on and model experiences with nontransgenic invasive species as a theoretical framework for anticipating risks from transgenic species. Thus, they argued that transgenic animals do not constitute a novel class of hazards when compared to their conspecifics.

Given this general approach to hazards, the presence of nontransgenic conspecifics in both wild and managed ecosystems provides an empirical basis for estimating exposure. Based on prior studies conducted for transgenic plants, the estimation of exposure involves two questions. First, do the transformations confer phenotypic characteristics on transgenic animals that could be expected to result in significantly different environmental effects from those observed for nontransgenic conspecifics? Second, is there a potential for transgenes themselves to migrate to other species, resulting in phenotypic effects on nontarget organisms that could, in turn, result in environmental impacts *(20)*?

Prevailing assumptions among biologists dictate that the only mechanism for gene migration in animals is through interbreeding with interfertile populations (wild or domesticated) extant in ecosystems. If this is correct, the probability of cross-species gene migration among animals is vanishingly small, suggesting that there is little need to worry about the second question in animal biotechnology risk assessment. However, it should be noted that experimental studies of environmental risk from transgenic plants resulted in a significant revision of prevailing assumptions about the potential of controlling environmental risks from transgenic plants through isolation strategies. Experimental risk analysis demonstrated significant potential for cross-species gene migration among plants *(21)*. These results testify to the need for experimental validation of critical assumptions.

If the prospects of cross-species gene migration can be discounted, estimating exposure from transgenic animals becomes a problem of first characterizing how transgenes will confer different phenotypic characteristics on transgenic animals and then estimating how these different characteristics will in turn lead to adverse environmental outcomes when compared to the behavior of nontransgenic conspecifics. This problem can be analyzed in terms of the likelihood that transgenic species will become established as breeding populations and the subsequent impact that established populations possessing the transgene might have on predator–prey relationships. The details of both reproductive fitness and predator–prey relationships involve considerable empiri-

cal knowledge that will be specific to the animal species and ecosystem involved. Any more detailed discussion of approaches to the assessment of biosafety risks thus involves considerable empirical and technical specification *(22)*.

The above discussion suggests that it is, in principle, possible to characterize the environmental risks of transgenic animals, although such characterizations may be difficult, especially in light of existing gaps in knowledge. However, the extent to which such gaps qualify the ability to understand environmental risks from transgenic organisms lies at the heart of hotly contested debates over the future of genetically engineered organisms of all kinds.

These debates have taken many forms, but the best known involve specification and application of the precautionary principle or the precautionary approach to environmental risks. The debate over precautionary approaches to genetically engineered organisms has often been subsumed into the politics of international trade because advocates of agricultural biotechnology have accused those who deploy the terminology of precaution of allowing protectionist aims to override scientific principles *(23,24)*. Nevertheless, there is a serious issue to be faced by anyone who considers the environmental risks of transgenic organisms in deciding how to use the characterization of risk that is developed by systematically analyzing hazard and exposure.

The possible responses to this question can be simplified for the purposes of exposition into two diametrically opposed alternatives. One approach was articulated in Bentham's statement of utilitarian ethics over 200 years ago. Bentham advocated an approach to quantifying the likelihood and value of consequences of an action that anticipates the general approach to estimation of hazard and exposure described above and argued that this approach allows determination of the risk-based elements of the expected value associated with that action. These elements can be weighed against expected benefits to determine the overall expected value, and the utilitarian approach dictates taking the course of action with the greatest overall expected value *(25)*.

Several analysts of the debate over genetic engineering have argued that mistrust in the ability to adequately anticipate the consequences of recombinant DNA techniques is closely tied to the rejection of the utilitarian approach in general. In place of an approach that accepts weighing costs and benefits, they see people advocating norms of respect for nature. This approach is far more prejudicial with respect to the ethical acceptability of biotechnology in general and dictates that transgenic animals would be acceptable only if we could assure ourselves that developing them was consistent with largely qualitative characterizations of human responsibilities toward the natural world *(26,27)*. This kind of argument has indeed been made by at least some advocates of precautionary approaches in environmental affairs *(28)*.

It is difficult to say how a path might be charted between these two extremes, and authors who have attacked precautionary approaches would almost certainly argue in favor of simply taking the utilitarian approach. Nevertheless, others have argued that precaution can be understood in terms of giving additional weight to catastrophic hazards without regard to their likelihood. *Catastrophic hazards* are adverse outcomes that have geographically widespread or extremely damaging effects, especially when these effects are irreversible *(22)*. Others argue that the high degree of uncertainty and ignorance that pervades ecological assessments provides a basis for extreme caution in

releasing organisms that would be likely to survive and interbreed with their conspecifics *(19)*. If the precautionary approach is understood in this way, it does not involve an abandonment of risk assessment so much as it recognizes circumstances in which a norm of minimizing the chance of worst-case outcomes should be substituted for the more typical utilitarian norm of seeking the greatest expected value.

3.2. Animal Well-Being and Health Issues

Animals typically used in agricultural or biomedical research (excluding insects) are considered sentient creatures that have a well-being or a good of their own. In contrast to the view of them as mere resources (as in traditional human-centered ethics) is the belief that these animals have a life that can go either better or worse for them. This last view is held by animal protection movements such as animal rights and animal welfare.* The well-being of these animals can be understood to have three major components. They include the animal's capacity to feel well both psychologically and physiologically, to function well, and to engage in species-specific natural behaviors *(39)*. These components of well-being are brought to bear on the question of permissible modification of animals by genetic engineering.

Genetic engineering has stimulated interest in the moral permissibility of animal use in research and challenges both the scientific community and the public sector to reexamine basic attitudes toward the moral status of animals and what is owed to them commensurate with their status and needs. Genetic engineering also raises questions about appropriate standards of well-being for research animals and spotlights the need for setting appropriate limits of modification and manipulation of animals.

Ethical concern regarding how modern biotechnology will affect animal well-being and health can take five general forms *(40)*:

1. That animals may suffer directly as a result of the effects of modification and manipulation.
2. That animals may suffer indirectly as a result of the effects of modification and manipulation.
3. That animals may suffer from consumption of or treatment with genetically modified products.
4. That, by using genetic transfer, the natures of animals are changed in substantial ways not for the benefit of the animals themselves, but for ours.
5. Procedural concerns related to the governance of animal use in general.

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*Although there is disagreement over the philosophical underpinning for taking animal interests seriously, four positions stand out. These include a sentientist view made popular by Singer *(29–31)*, which endeavors to optimize the total balance of sentient experience in a species-neutral way; a strong rights-based approach that is synonymous with Regan *(32,33)*, which holds that certain animals are "subjects-of-a-life" and hence have noninstrumental value, and by this view, any experimentation on animals is prohibited if they are not also direct beneficiaries of research. There is an ethics of care view imputed to Midgley *(34)* that considers our kinship and interspecies connectedness with some species as sufficient for establishing acquired duties to care for their well-being; and there is an integrity or "natures" view attributed to (among others) Rollin *(35,36)*, Rutgers and Heeger *(37)*, and Fox *(38)* and basically states that animals have an intrinsic nature or unique species-specific purposes that underscore the content of our responsibilities toward them, that is, they have "a nature, a function, a set of activities, intrinsic to [them] evolutionarily determined and genetically imprinted" *(35,36)* that is morally obligating in character.

3.2.1. Direct Effects

There is significant public concern that modifying the genetic constitution of animals will lead to increased physical pain and psychological suffering, whether inadvertent, unwanted, unexpected, or intentional. This concern is amplified given (1) widespread belief that we have special responsibilities, which include minimizing or not inflicting unnecessary harm, to care for animals in our charge; (2) the present underdeveloped state of the technology; and (3) the impossibility of anticipating the impact of modification on an animal's well-being, especially if the animal's constitution departs greatly from its evolutionarily determined genome.

Because the science and technology of genetic engineering are still in their inception, it is feared that genetic engineering will contribute to animal suffering by producing dysfunctional animals that must endure physical, physiological, and psychological harm, behavioral abnormalities, or health maladies. Although unhealthy transgenic animals will almost certainly be euthanized, an increase in the rate of euthanasia is not without ethical significance. Concern over the present inefficiency of production techniques is joined by questions over the utility value of animals in general and the morality of creating animals with pathological conditions to serve as research models for human beings. Concern for transgenic animals in this way is not without precedent.

The 1985 Beltsville pigs were among the first transgenic animals produced by the USDA Agricultural Research Service. Scientists microinserted the gene for human growth hormone into pig embryos in one of the early experiments that applied bioengineering to food animals so that they would grow faster, use less feed, and produce leaner meat. Nineteen animals made it to maturity, but they experienced painful arthritic conditions and endured physical deformities, ulcers, and decreased immune resistance. These crippled pigs were euthanized *(36)*.

Dolly, the famous cloned sheep from Scotland, was euthanized on February 14, 2003, after experiencing premature aging and virus-induced lung cancer. Dolly was 6 years old, approximately half the life expectancy of her breed. Her premature death, as did circumstances surrounding her conception, raises questions about the ethics and practicality of copying life *(41,42)* In the case of events leading up to her conception, Wilmut's team struggled approximately 300 times to fuse nuclei from adult cells with denucleated blastocysts. Of the 29 successful transfers to host wombs, only one clone, Dolly, was produced. Many fetuses were used and destroyed as the team also applied the same technique using nuclei from fetal and embryonic cells *(43,44)*.

The NRC committee cited a few examples highlighting direct deleterious effects of novel techniques on animals. They indicated that knockout and cloned mice showed increased levels of aggression and suffered impaired learning and motor skills in certain trials. A number of hoofed animals produced by either in vitro culture or nuclear cell transfer tended to have higher birth weights and longer gestation periods than conspecifics produced by artificial insemination. Of these animals, some experienced difficulty during birth and required specialized procedures like caesarean section and respiratory assistance and therapy *(15)*.

Another direct concern warranting attention includes the potential transmission of newly acquired diseases or traits from transgenic animals (such as those used in xenotransplantation) to conspecifics with no immunity against the disease.

This short litany of problems is an echo of a general concern that it is difficult to predict just how the psychological, behavioral, and physiological well-being of animals will be affected as a result of genetic modification of the very constitution of animals. Such incidents raise public concerns about the governance of science and accountability of scientists. In the mid-1980s, the same questions regarding responsibility, professional ethics, and accountability were sparked in lieu of *Silver Springs vs Dr. Taub*, and *University of Pennsylvania Head Injury Clinic baboons vs Dr. Genarelli (45)*. Scientists need to be sensitive to nonutility views of animals as well as practice good husbandry and care for research animals. It is thus important that the scientific community remain vigilant in their assessment of compatibility between the animal's well-being and its adaptability to its environment when pursuing research.

3.2.2. Indirect Effects

New applications of animal biotechnology, like xenotransplantation, raise secondary concerns related to creation of animals that deviate substantially from their traditional roles. In xenotransplantation of livestock animals, concerns related to management and housing of highly sophisticated and social source animals such as pigs and nonhuman primates used as research subjects raise eyebrows. To prevent or minimize transmission of diseases to potential human organ, cell, and tissue recipients, these animals must be housed in isolated and sterile living quarters. This form of housing may involve low stimulation and poorly enriched environments and may cause these animals to exhibit abnormal behaviors such as fear, anxiety, aggression, and patterns of stereotypical behaviors or boredom. Similar questions may be posed for transgenic animals developed to secrete pharmaceutical or industrial products in their milk. Whether subjecting animals to impoverished or frustrating environments can ever be justified remains a contentious issue. In any case, it demands serious attention by the scientific community, especially because this form of neglect or impairment of an animal's well-being is within the sight of many in the public.

3.2.3. Biotechnology Product Application

Genetic engineering may also be applied not directly to manipulate animals' genomes, but to produce drugs, therapies, and feed for animals. Issues associated with the approval of these products are, in one sense, no different from those for any other drug or additive. However, the use of advanced life science techniques may heighten controversy. For example, genetic engineering was used to produce recombinant bovine somatotrophin (rBST) to boost milk production of dairy cattle. Animal protection groups protested when rBST use was linked to increased incidence of mastitis and lameness and lower productivity *(46–48)*. The US Food and Drug Administration (FDA) concluded that these health problems were typical of high-production animals, and therefore that rBST should not be identified as a cause. However, regulatory agencies in other countries, including Europe countries and Canada, have cited animal health issues in refusing to approve rBST. The lesson of rBST is that researchers should be prepared for increased scrutiny (and possibly higher standards) when a biotechnology product has equivocal impact on animal health.

3.2.4. Changing the Nature of Animals

Although genome manipulation may produce animals that are able to transform feed with greater efficiency or animals better suited to their environments, the moral permissibility of altering or infringing the genetically encoded set of physical and psychological capacities that give rise to the basic interests of an animal (i.e., the "pigness of pigs" or "horseness of horses") remains a contentious subject. Moral harm is "perceived" to be committed when an animal is prevented from performing behaviors commensurate with the way it has evolved *(49)* or if the animal's genetically predetermined "set of functional needs" are thwarted *(38)*. Proposals for genetic modification that create duller or decerebrate animals so that they will be more conducive to conditions of intensive farming or sterile laboratory housing have been especially controversial among the public. Creating insentient beings purposefully for human ends and preventing them from living in accordance with their natural ends in life is perceived as a perversion of the sanctity of nature or natural boundaries.

Rollin *(36)* has suggested the principle of welfare conservation to help mitigate inhumane procedures related to genetic engineering. The principle states that genetic engineering is prohibited if it would make animals worse off than nongenetic animals in comparable circumstances; that is, it is unethical to create animals worse off with respect to suffering and deprivation comparable to conspecifics begotten through conventional breeding. Rollin's principle leaves two important implications:

1. A more palatable one: It is permissible to alter an animal's genetic constitution and biological function if it leads to less suffering or improved well-being.
2. A highly contentious one: It is permissible to modify an animal's experiential capacity if it relieves suffering, even if that suffering is caused by less-optimal living conditions.

In lieu of the perceived integrity of animals, Thompson has argued (with respect to implication 2) that, if it is wrong to alter a human being so the person would no longer be characteristic of human species, then without offering relevant differences, doing the same to an animal (i.e., depriving the pig of its pigness or the horse of what makes it the thing that it is) is equally wrong *(50)*. It is wrong to "estrange" animals from the functional needs characteristic of their species not only because it jeopardizes their well-being, but also because their perceived intactness is connected with their species identity. Genetic engineering that detracts from the animal's own good reduces them to mere means to human ends *(37,49)*.

3.2.5. Procedural Concerns Related to Animal Use

Besides these substantive issues regarding moral status is the concern that animal biotechnology is moving ahead in the absence of public discussion and consensus. The subjects of species integrity and whether it is permissible to modify animals if no benefits are conferred to the animals themselves have been of particular interest to animal protection groups seeking a voice in planning the research agenda. Furthermore, it would appear that public concern over the lack of clarity over what counts as adequate provisions for promoting health and normal development for research animals in our charge has been ignored by some sectors of science.

In the United States and Canada, IACUCs have stipulated norms for research since the mid-1970s. Although the institutional structure varies, similar committee approaches to animal ethics are now found across the globe. When functioning well, such committees deliberate carefully on the morality and prudence of research projects based on the principles of the 3Rs. Briefly, the 3Rs (reduction, replacement, and refinement) proposed by Russell and Burch in 1959 are three general principles for the governance of humane animal-based science and experimentation) *(51)*.

There is some doubt whether these committees will be able to offer appropriate guidance with respect to transgenic technologies without adequate revision or supplementation with other normative principles *(52,53)*. In particular, the 3Rs do not cohere with deeply held intuitions about animal and species integrity that constrain what is acceptable to do to sentient beings or animals in our charge. Furthermore, review of guidelines and regulations from government oversight agencies to keep up with contemporary standards is necessary and will go a long way to ensure that experiments are sufficiently controlled and offer adequate protections for animal research subjects (do not suffer unnecessarily; have appropriate standards of well-being; have adequate living conditions, good husbandry, and appropriate veterinary care; and are privy to humane end points). Reviewing outmoded guidelines may also help to anticipate and establish standards of "good welfare" instead of ameliorating or reacting to current conditions.

3.3. Food Safety and Consumer Autonomy and Sovereignty Issues

Animal products created through genetic engineering or cloning may pose unique disease and health risks when consumed and challenge existing aesthetic and cultural notions of food purity and standards of food quality. Here, the NRC *ad hoc* committee noted that the entry of genetically modified and genomically reprogrammed nonfood animals into the food supply was the most serious risk issue based on a strict expected value analysis of risk *(15)*.

Animals genetically modified to produce pharmaceuticals or other chemical or biologic properties in their eggs or milk may inadvertently find their way into the food supply. Strict monitoring procedures, regulations, and customized procedures meant to detect or anticipate implications of these new biotechnologies in the food supply may be necessary. The committee was also concerned that unused animals (such as male chicks and bull calves from dairy operations) engendered by new biotechnologies or that come into contact with biologically engineered products (i.e., conventionally bred and genetically modified animals fed with unapproved genetically modified foods) may inadvertently find their way onto grocery shelves in the absence of forward-looking measures or policies to ensure that they do not. Transgenic animals meant for food, like transgenic swine, fish, poultry, beef, dairy cattle, and sheep, will be screened using the principle of substantial equivalence. This requires that proteins not previously found in human diets will be subjected to extensive clinical trials for safety and quality before approval.

Other hazards associated with transgenic animals meant for consumption are as follows *(15)*:

1. They may induce allergens that could pose health risks.
2. Exposure to bioactive constitutive parts on consumption could give rise to illness.
3. There is the potential for toxicity from transgenically derived organisms, especially if the toxins manage to elude detection surreptitiously under conventional assessment methods.
4. Inappropriate gene expression may occur.
5. Activation of quiescent viruses is possible.
6. Nutritionally deficient substitutions that pose human health risks may be made.
7. Application of cloning on a large scale may result in monocultures that may be less resistant to disease, and thus communities of people may be susceptible to risk of famine or financial ruin *(54,55)*.

The committee noted that strict measures can be taken to mitigate the risks associated with items 1–5. They include monitoring the method of gene transfer and vigilance when it comes to how the genes are recombined or resequenced.

Not unlike risk analysis of environmental concerns, food safety issues are also typically assessed as a function of probability of unwanted outcomes occurring and their expected severity and immediacy. Again, experts are delegated the task of optimizing the ratio of bad consequences to good outcomes. Interpreting the problem of risk management solely as an optimization problem, however, bypasses concerns related to consumer sovereignty and autonomy in the food system.

Issues related to informed consent on the part of those who will be exposed to foodborne risks (whether real or perceived) cannot be treated as "costs" in an optimization problem. They raise questions about market, political, and social mechanisms to protect consumer autonomy and liberty of conscience *(56,57)*. Consumers may have concern for purity of food and may have aesthetic or religious reasons or moral arguments (such as wanting to support forms of farming as a lifestyle) that must also be considered. The lack of viable alternatives to genetically modified products impedes autonomous decision making and liberty of conscience (and is a form of covert coercion). Another concern is the absence of mechanisms of informed consent (such as standardized labeling) to help consumers decide on their own to avoid foods they deem incompatible with their moral, health, or religious values.

Apart from these infrastructural-minded matters, the dearth of public data on the subject of the safety of meat and milk and other products produced from genetically modified animals and somatic cell cloned organisms does not inspire confidence. Longitudinal studies and vigilant monitoring of the effects of new products and products fed to commercially bred animals are encouraged by private industry and government. Industry has been reluctant to make data on animal health public because of competitiveness concerns, yet with respect to food safety, it will almost certainly be critical to have published data available.

3.4. Policy and Institutional Concerns

How will animal biotechnology serve the public good? Might it perpetuate discrimination or be available only to well-capitalized outfits and people? Have government agents and scientists communicated likely applications and risks to the public, taken the time to help inform the public, and listened to public concerns before moving forward?

While pondering these questions, the NRC committee also questioned whether the current regulatory and legal framework supported the unique concerns raised by animal biotechnology and whether appropriate federal agencies had the technical capacity and resources to review the technology and address potential hazards. They also saw a need to clarify the responsibilities of individual scientists, academic institutions, private companies, and various government agencies associated with the development and application of animal biotechnology by clearly delineating the regulatory jurisdiction of the USDA, FDA, and the Environmental Protection Agency and reforming outmoded policies if necessary *(15)*. Of special concern was the lack of public engagement mechanisms to generate meaningful debate and improve public understanding of risk factors in a trustworthy and thorough manner at both national and international levels.

The NRC *(15)* indicated the need for broad public discussion with ethicists, scientists, policymakers, commercial agents, animal advocates, lawyers, biopharmaceutical representatives, physicians, citizen representatives, and other stakeholders on the ethical and social implications of developing and applying animal biotechnology in conjunction with the development of institutional guidelines, safeguards, and regulations (both nationally and internationally) to steer the course of the technology. At this time, broad public discourse to ensure that science and societal values remain aligned is a "serious political deficiency" *(48)*.

Institutional concerns also interface with the issues of food safety, the environment, animal well-being concerns, and biomedical concerns. Governments, with the aid of scientists and acting on behalf of their citizens, should stay on top of the technological advancements (so that they can report to their citizens). Governments should help improve the knowledge base so that citizens can weigh in on the risks and benefits for themselves, provide mechanisms by which citizens can act in ways commensurate with their convictions (i.e., labeling of altered foods), and monitor partnerships between publicly funded academic institutions and commercial industries (to forestall improprieties and conflicts of interest).

3.5. Biomedical Concerns

Animal biotechnology may also be applied to improve human disease resistance, as treatment alternatives, and to help offset the shortfall of human tissues and organs. However, biomedical uses of transgenic animals may pose trade-offs between benefits for individual patients and potential deleterious effects for society at large. At present, most projects involving animal biotechnology for biomedical purposes fall into one of three main categories:

1. The use of organs, live cells, and tissues for cross-species transfer or xenotransplantation
2. The production of biopharmaceuticals for human beings and animals
3. The creation and use of raw genetic materials for engineering other products

The relationship between biomedical concerns and increasing biotechnology to study gene function is not discussed in this chapter. The focus primarily is on xenotransplantation, but the issues discussed may be germane to categories 2 and 3 as well.

Xenotransplantation involves the transfer of tissues, living cells, and organs from one animal species to another. The potential for animal-to-human transplantation prom-

ises to increase the supply of viable organs, including lungs, kidneys, livers, pancreases, and whole hearts for human recipients. Tissue research promises bone transplants, skin grafts, and corneal transplants for accident, burn, and optical patients, respectively. Patients with diabetes, Parkinson's disease, Alzheimer's disease, or other diseases may have added hope of viable treatments through the fruitful xenotransfer of living cells from animals. Although promising, xenotransplantation has been questioned with respect to the merits and proficiency of the science and technology, the depth of the ethical discourse, and the absence of much needed national and global guidelines and regulations.

Some central concerns and questions associated with xenotransplantation include the following:

1. Personal health risks caused by immune rejection and infection despite the use of immunosuppressive drugs.
2. Potential spread of novel infectious diseases or viruses (i.e., xenozoonosis) from source animals to organ and tissue recipients and eventually to contact persons and to the public at large *(58,59)*. That is, unlike human-to-human transplants, using nonhuman donors leaves human recipients and their contacts susceptible to novel infections.
3. Legal issues. Individuals who currently participate in medical or clinical trials, must give their informed consent. Because of the threat of xenozoonoses, animal-to-human organ transplant recipients may be subject to invasion of privacy and be obligated to disclose personal information once protected under conventional patient–physician confidentiality statutes. These recipients may also be subjected to state-imposed restrictions on their right to self-determination, including life-long surveillance, quarantine, restricted travel (including prohibition to enter countries that forbid animal-to-human transplants), prohibition against procreation, or ban against blood, plasma, and organ donation. Recipients may also have to disclose their sexual partners and frequent social contacts and agree to mandatory postmortem examination. They may not, as most research subjects can, opt out of clinical trials *(60,61)*.
4. Business ethical issues. Animal biotechnology has the potential to be very lucrative if the prospects can be actualized. Should companies driven by profit and answerable to shareholders be mandated to exchange sensitive information and data to help the public weigh in on the costs and potential conflicts of interest? Are there appropriate international regulations and guidelines to regulate the business environment? Should governments allow clinical trials before or despite social consensus about the risks and how to manage them *(59,60)*?
5. Public health cost issues. In the event that transspecies transplants become accepted as standard medical practice, should public funds be committed for preclinical trials, clinical trials, postclinical screening and monitoring, animal care, and slaughter and disposal of the carcasses *(60,61)*? Who is responsible for the financial outlay for large-scale and long-term surveillance of organ and tissue recipients, close contacts, and their possible quarantine *(60,61)*? What are the obligations of national funding agencies, health care financing institutions, insurance companies and health maintenance organizations and pharmaceutical and biotechnology companies *(61,62)*?

Although xenotransplantation promises many things, undue attention to it as the ultimate medical elixir (or without substantial guarantees) may divert funding from equally viable alternatives that may also be less controversial. Alternatives that are less divisive or risky, such as making human donation more attractive and efficient through a more concerted effort to seek out and distribute organs; adoption of a "presumed

consent" policy of organ donation on death; investment in preventive measures that encourage healthy diets, appropriate exercise, and lower consumption of "vices" like alcohol and tobacco; the plausibility of human stem cell research; and mechanical and artificial gadgetry, for example, should not be ignored.

3.6. Other Social Issues

There are other ethical and policy issues to consider that do not fall neatly into the above categories. They include concerns over (1) distributive justice; (2) implications of animal biotechnology on what it means to be human; and (3) colliding sensibilities about animals and our responsibilities toward them. Although the decision point for addressing these issues is far from the working scientist's laboratory, researchers should have a basic understanding of them nonetheless.

3.6.1. Animal Biotechnology and Distributive Justice

Critics have alleged that application of novel animal biotechnology and precipitating changes to intellectual property rights may (absent regulation and public consensus) support the economic interests of industry giants such as pharmaceutical companies, agribusiness companies, and well-capitalized businesses to the detriment of smaller producers and rural communities (here and in the developing world), as well as have a negative effect on consumer choice. In the case of agriculture, for example, novel animal biotechnology that is too expensive for all levels of producers to adopt would give larger, well-capitalized agribusinesses a greater economic advantage over poorer ones (especially during the short run of transformation to the new technology). The development and marketing of this technology will likely be targeted toward producers in the former group; as a result, smaller producers who cannot compete or move quickly enough to adopt these new innovations may end up victims of bankruptcy. It is likely that the communities in which smaller producers are located may face irrevocable structural changes to their futures and way of life *(63)*.

3.6.2. Implications for Human Cultural Identity

Is animal biotechnology a good way to advance the quality of life? Even if the technology turns out to be safe, should it be pursued, especially if crossing the species barrier may have an adverse impact on traditionally cherished values of what it means to be human? What are the limits to interfering with "natural" species boundaries?

On November 13, 2002, under the auspices of Rockefeller University and the New York Academy of Sciences, a panel of North American experts convened to discuss the morality and science of injecting human embryonic stem cells into an early mouse embryo (a blastocyst) to test the potential of special stem cells to help fight disease. By producing this "embryonic chimera," scientists hoped to learn whether human stem cells (the kind that have the ability to grow into just about every tissue type) can contribute to the development of tissues within the mouse embryo *(64)*. Such research on human embryos is presently taboo.

In this particular instance, the panel focused primarily on questions related to the sanctity of the human genome and on how best to approach the subject of weighting benefits to individual patients against traditional conceptions of humanity. For example, the panel debated the nature of this chimera. That is, to what extent is this creature still a mouse if it produces human sperm or if its brain is made up mainly of human cells?

They also debated whether and just how this sort of experiment varied from previous experiments involving the insertion of human genes into other nonhuman animals, for example, into pigs to reduce organ rejection during xenotransplantation. They were also concerned whether ethically charged experiments like the present one would create public backlash to more mainstream forms of stem cell research.

3.6.3. Sensibilities About Animals

The perception of the moral status of animals is not uniform, and the instrumental view of animals as research subjects, genetic commodities to be manipulated and modified for human purposes held by most working in animal biotechnology collides with the view of animals as beings deserving of respect and sympathy and requiring good care and appropriate husbandry. The research community, entrenched in a utility view of animals, should be sensitive to contrasting views of animals as having value and integrity in their own right. Keener attention to the emotional and cultural significance of animals to the public as well as acknowledgment of the religious aspects of animal use and consumption are encouraged. In the latter case, scientists and regulatory bodies and funding agencies should be sensitive to just what forms of animal uses are taboo, socially sanctioned today, or sacrilegious and ensure that these animals and their products or relevant genetic material are not present in the food supply or in commercial products without informing the public.

So science and policymakers do not run with the ethically charged technology ungoverned, public discussion of the above issues is needed. Through public education, positive regulation and legislative prohibitions may be generated that do not stifle truly beneficial research and product development. As discussed in the next section, the social consequences of novel technology can be minimized by allowing the public (including producers) to debate on how technology should serve the public interests and on issues of just desert and fair commerce and resource distribution. The need for a well-functioning political mechanism for deliberating these issues is urgent. Regulation on the basis of social issues borne out of animal biotechnology should also be considered to ensure that policies are in step with the values and concerns of the nonscientific community.

4. Animal Biotechnology and the Role-Defined Responsibilities of Science

If the many promised societal benefits of animal biotechnology are to come to fruition, then there must be public acceptance both in the direction in which it is progressing and of products of animal biotechnology. Although better public understanding of the risks and benefits associated with animal biotechnology will go a long way in engendering such public acceptance, this is but one facet of what must be undertaken by the scientific community to promote animal biotechnology. The other facet (which is often taken for granted with technological innovation) concerns public perception of the trustworthiness and credibility of scientists or proponents of the new technology *(57,65)*. If animal biotechnology is to gain a foothold and flourish in the future, scientists should also be prepared to devote their time and energy to securing the confidence of the public in the scientific community itself as well as in their initiatives.

As the public becomes more scientifically literate, conscientious with respect to the concerns raised in Section 3, and suspicious of conflicts of interest that may arise from

research bankrolled by industry, the burden of proof rests with scientists. They must demonstrate that the increasing industry-driven science has not compromised the integrity and objectivity of the trusted professional *(66)* and prove that their technological innovation is safe and socially acceptable (or at least morally indifferent) and that these advances are undertaken in the interest of the public good.

In the case of animal biotechnology, rapid expansion and increasing specialization encourage knowledge gaps between the scientific community and the nonscientific public, which in turn places the public in a position of vulnerability. This vulnerability is amplified because of the inability to foresee dangerous consequences and unwanted outcomes associated with animal biotechnology. Relative to the lay public, scientists as "experts" or specialists are perceived as powerful authorities with decision-making capacity. As such, the responsibility of managing knowledge on behalf of the public good has been deferred to the technically skilled scientific community. But, as history has demonstrated many times, power inequilibrium can often lead to the exclusion and disenfranchisement of vulnerable parties by those in positions of privilege. The public's trust in the leadership of the scientific community should not be taken lightly by the scientific community.

In cultivating the public's trust and avoiding public suspicion, it is thus important that scientists recognize this social inequilibrium and their positions of privilege and make every effort not to let their positions of expertise detract from their public responsibilities. Instead, scientists as experts have a professional responsibility to reassure the public that animal biotechnology will be developed and applied in morally justifiable and socially responsible ways. This responsibility enjoins scientists to recognize the dignity and autonomy of others and to take measures to neutralize feelings of vulnerability by the public. Scientists can do this by being cognizant of the interests and values of others and by being aware that they are one part of a trust relationship.

The responsibilities associated with cultivating public trust encompass both personal and professional ethics. In general terms, they include establishing a climate of "participatory science," that is, of transparency and open communication, accountability, restraint, and leadership. Participatory science establishes a social component for scientists and serves to neutralize inequality among the various stakeholders by encouraging bridge building and partnership and by aspiring toward shared goals.

Presently, science, apart from being a field of study valuable in itself or aspiring to improve the quality of human life through problem solving and technological innovation, has also acquired advisory and regulatory roles in society *(67)*. In this last capacity, science and scientists are looked on to help people make good decisions as they aspire to live well. The voice of science has been an integral part in steering humankind along the path of a good life. Hence, the pursuit of knowledge and technological advancement is not a disinterested matter; it is not simply about excursions into curiosity for their own sake. Instead, knowledge and technological advancement are imbued with social, ethical, political, economic, or religions meaning. As such, scientists should take it on themselves to be cognizant of the ethical and social implications of their research and strive to understand better the various dimensions of risks and harms associated with the development and application of novel technology.

When it comes to questions of risk, science typically focuses on unwanted consequences, the probability of the actualization of various harmful scenarios, a valuation

of their respective levels of harm, and how to mitigate the harm *(65,68)*. For the public, risk is inextricably tied to trust and is not limited to consequences and statistical probability that harm will result from a given practice or technology or from the possibility of mistakes. The public views risk in terms of anxiety, vulnerability, and feelings of security and well-being *(65,69–71)*.

For the public, the element of risk also encompasses how they feel about their lack of control over the speed and direction of biotechnological development, unfamiliarity with the nature of the science and technology, fear and doubt in the ability of scientists and governments to respond adequately to a possible biotechnological calamity, and a lack of confidence in and suspicion of scientific authority. Disinterestedness by scientists in addressing larger ethical and social implications of their work, a nonchalant scientific attitude about changing the natures of animals, professional arrogance, undisclosed affiliations and commercial bankrolling, and a lack of identification with broad public values are also factors that account for how the public perceives it is at risk with respect to animal biotechnology *(70)*.

Hence, effective risk management includes sensitivity to how the public feels about and assesses risk and according responses to the public's vulnerability. A scientific community that engages the public in genuine reflection, commitment, and open communication will be seen as trustworthy and credible advisors. By including the public in open and conscientious deliberation (i.e., addressing their questions and fears thoroughly about the purposes and justification for applying and developing these new technologies and their attendant problems and prospects), scientists demonstrate their willingness to take seriously the public's ethical and social concerns *(48)*. Furthermore, forming these partnerships will help ensure that discussion related to the concerns raised in the Section 3 will be robustly discussed and debated to promote responsible development and application of animal biotechnology.

As mentioned, scientists working in the development of animal biotechnology are in prime position to anticipate unwanted consequences and to calculate degrees and probability of harm. This special expertise gives rise to leadership responsibilities that include educating the public so that they are reasonably science literate and well informed about the substantial issues. Scientists should provide the public with relevant information and alternatives or contingencies so the public may make considered decisions commensurate with their values and interests *(72)*. Leadership and accountability also involve self-reflection and cognizance of how scientists as a group understand themselves and their responsibilities and respond to challenges and public criticisms *(73)*. Thompson *(74)* suggested a few things that scientists can do to cultivate good habits and meet the goals of transparency, better public communication, restraint, and leadership. We delineate this list with some additions. Scientists should do the following:

1. Participate in citizen conferences regularly (both formally and informally), that is, be concerned about the issues about which the public is also concerned, consider the interests of other stakeholders at the table, and engage the public on the ethical impacts of scientific advances.
2. Engage critics with the same care as if writing journal articles and encourage peer-reviewed articles on ethical and social implications by scientists on their work and be prepared to show compelling reasons for the procedures that are adopted and for wanting to move forward.

3. Make explicit how animals are impacted by the different forms of genetic engineering and how this technology will influence the shape of human genetic engineering and cloning *(54)*.
4. Develop teaching curricula, including courses or degrees in bioethics in universities and high schools, which have ethics components and raise questions about the social roles and values assumptions of the scientific community, especially highlighting conflicts of interest and professional responsibility.
5. Encourage graduate students to take classes in ethics and public policy and to discuss the social implications of their work.
6. Make use of ethics centers and other public assets and mechanisms for discourse and critical exchange or include ethicists in research groups.
7. Make academic and commercial affiliations transparent, that is, disclose research sponsorships and industry collaborations, especially if partially supported by public monies *(66)*
8. Show self-criticism and reflectivity by demonstrating how professional ethical issues are attended, debated, reviewed, and awarded by the scientific community.
9. Ensure that no professional backlash befalls those in the scientific community who: (1) are willing to engage in ethical self-review of the community; (2) are critical of the direction that science may be progressing; and (3) are willing to expose the values and deficiencies of the scientific method.

5. Conclusion

Human beings have long depended on animals for help and as resources for different purposes and have a notable, albeit erratic at times, history of responsible use and care of these animals. Today, modern genetically based animal biotechnology offers new opportunities to employ the services of animals, but it also challenges us to revisit our responsibilities to both human beings and animals alike.

Animal biotechnology, for all its prospects, is beset with moral concerns that may or may not be surmountable. Because it involves intervening in the lives of others and may have unforeseeable and radical consequences, it is therefore urgent that the scientific community engage the public to be forthright about their responsibilities and to determine the risks and limitations of the applications in virtue of respect for the relevant stakeholders so that what is beneficial may not also be detrimental. Scientists alone should not be left to decide the direction and means of technological progress. Instead, both the scientific and nonscientific communities should come together to build a public science agenda as a way to anticipate and preclude corporate control of science or unscrupulous and socially unfettered individual research ambition.

Animal biotechnology has important implications for the nature of human relationship with animals, the environment, food safety, biomedical safety, distributive justice, and what it means to be human. Serious and thorough debate and dialogue among scientists, government and commercial agents, and the general public to lay the ethical foundation for the development and use of animal biotechnology are urgently needed before genetically modified organisms or cloned animals make their appearance on farms, in grocery stores, or in the environment. Such discourse is necessary to forestall unnecessary societal suspicion or prejudice that has befallen entry of genetically modified crops and foods of plant origin into the food supply. A vibrant public discourse will ensure that animal biotechnology will be developed and used consistent with the shared vision of responsible living and for the benefit of advancing the quality of life for both human beings and animals and not simply for economic or discriminatory gain of a few.

With any new technology, the public's attitude toward the research community is the key to its success. Responsible animal biotechnology development and application will be sanctioned by the public when scientists improve their image, have direct relationships with the public, and are keenly aware of their own assumptions and values. Responsible animal biotechnology enjoins scientists to consider the interests of the public, be aware of their leadership and advisory roles, and understand the implications of their work.

References

1. Guelph transgenic pig research program. Available on-line at: http:// www.uoguelph.ca/enviropig/. Accessed October 1, 2002.
2. Communications and Public Affairs. (2001) U of G's "Enviropig" a Success, New Study Reveals. July 31. Available on-line at: http://www.uoguelph.ca/mediarel/archives/000404.html. Accessed October 1, 2002.
3. Shapiro, H. T. (2000) Federal policy making for biotechnology, Executive Branch, National Bioethics Advisory Commission. In *Encyclopedia of Ethical, Legal, and Policy Issues in Biotechnology* . (Murray, T. H. and Mehlman, M. J., eds.). John Wiley and Sons, New York, pp. 241–257.
4. Wagner, W. E. (2000) Federal policy making for biotechnology, Congress, EPA. In *Encyclopedia of Ethical, Legal, and Policy Issues in Biotechnology*. (Murray, T. H. and Mehlman, M. J., eds.). John Wiley and Sons, New York, pp. 227–234.
5. Angelo, M. J. (2000) Agricultural biotechnology, law and EPA regulation. In *Encyclopedia of Ethical, Legal, and Policy Issues in Biotechnology* .(Murray, T. H. and Mehlman, M. J., Eds.). John Wiley and Sons, New York, pp. 26–37.
6. Miller, H. I. (2000) Agricultural biotechnology, law, and food biotechnology regulation. In *Encyclopedia of Ethical, Legal, and Policy Issues in Biotechnology*. (Murray, T. H. and Mehlman, M. J., Eds.). John Wiley and Sons, New York, pp. 37–46.
7. Browne, W. P. (2000) Agricultural biotechnology, law, and social impacts of agricultural biotechnology. In *Encyclopedia of Ethical, Legal, and Policy Issues in Biotechnology* .(Murray, T. H. and Mehlman, M. J., eds.). John Wiley and Sons, New York, pp. 46–56.
8. Tourine-Moulin, F., Vicari, M., and Ruano, M. (2000) International aspects, national profiles, France. In *Encyclopedia of Ethical, Legal, and Policy Issues in Biotechnology* . (Murray, T. H. and Mehlman, M. J., eds.). John Wiley and Sons, New York, pp. 703–711.
9. Kettner, M. (2000) International aspects, national profiles, Germany. In *Encyclopedia of Ethical, Legal, and Policy Issues in Biotechnology* . (Murray, T. H. and Mehlman, M. J., eds.). John Wiley and Sons, New York, pp. 711–722.
10. Macer, D. R. J. (2000) International aspects, national profiles, Japan. In *Encyclopedia of Ethical, Legal, and Policy Issues in Biotechnology* . (Murray, T. H. and Mehlman, M. J., eds.). John Wiley and Sons, New York, pp. 722–731.
11. Hasson, M. (2000) International aspects, national profiles, Scandinavia. In *Encyclopedia of Ethical, Legal, and Policy Issues in Biotechnology* . (Murray, T. H. and Mehlman, M. J., eds.). John Wiley and Sons, New York, pp. 731–739.
12. Bieri, F., Ghisalba, O., Kappeli, O., and Reutimann, H. (2000) International aspects, national profiles, Switzerland. In *Encyclopedia of Ethical, Legal, and Policy Issues in Biotechnology* . (Murray, T. H. and Mehlman, M. J., eds.). John Wiley and Sons, New York, pp. 739–747.
13. Ashroft, R.E., Capps, B., and Huxtable, R. (2000) International aspects, national profiles, United Kingdom. In *Encyclopedia of Ethical, Legal, and Policy Issues in Biotechnology* . (Murray, T. H. and Mehlman, M. J., eds.). John Wiley and Sons, New York, pp. 747–761.

14. National Research Council. (2000) *Incorporating Science, Economics, and Sociology in Developing Sanitary and Phytosanitary Standards in International Trade. Report by the Board on Agriculture and Natural Resources*. National Academy Press, Washington, DC, pp. 238–245.
15. National Research Council. (2002) *Animals Biotechnology: Identifying Science-Based Concerns. Report Prepared by the Committee on Defining Science-Based Concerns Associated With Products of Animal Biotechnology*. National Academy Press, Washington, DC.
16. Hoy, M. A. (2001) Transgenic arthropods for pest management programs: risks and realities. *Exp. Appl. Acarol.* **24**, 463–495.
17. Braig, H. R. and G. Yan. (2001) The spread of genetic constructs in natural insect populations. In *Genetically Engineered Organisms: Assessing Environmental and Human Health Effects* . (Letourneau, D. K. and Burrows, B. E., eds.). CRC, Boca Raton, FL, pp. 251–314.
18. Hallerman, E. M. and Kapuscinski, A. R. (1995) Incorporating risk assessment and risk management into public policies on genetically modified finfish and shellfish. *Aquaculture* **137**, 9–17.
19. Muir, W. M. and Howard, R. D. (2001) Methods to assess ecological risks of transgenic fish releases. In *Genetically Engineered Organisms: Assessing Environmental and Human Health Effects* . (Letourneau, D. K. and Burrows, B. E., eds.). CRC, Boca Raton, FL, pp. 355–383.
20. National Research Council. (2002) *The Environmental Effects of Transgenic Plants*. National Academy Press, Washington, DC.
21. Ellstrand, N. C., Prentice, H. C., and Hancock, J. F. (1999) Gene flow and introgression from domesticated plants into their wild relatives. *Annu. Rev. Ecol. Syst.* **30**, 539–563.
22. Kapuscinski, A. R. (2002) Controversies in designing useful ecological assessments of genetically engineered organisms. In *Genetically Engineered Organisms: Assessing Environmental and Human Health Effects* . (Letourneau, D. K. and Burrows, B. E., eds.). CRC, Boca Raton, FL, pp. 385–416.
23. Anonymous. (2000) Swapping science for consensus in Montreal. *Nat. Biotechnol.* **18**, 239.
24. Miller, H. I. and Conko, G. (2001) Precaution without principle. *Nat. Biotechnol.* **19**, 202–203.
25. Bentham, J. (1789/1948) *An Introduction to the Principles of Morals and Legislation*. Hafner, New York.
26. Saner, M. A. (2000) Ethics as problem and ethics as a solution. *Int. J. Biotechnol.* **2**, 219–256.
27. Magnus, D. and Caplan, A. (2002) Food for thought: the primacy of the moral in the GMO debate. In *Genetically Modified Foods: Debating Biotechnology* . (Ruse, M. and Castle, D., eds.). Prometheus Books, Amherst, NY, pp. 80–87.
28. M'Gonigle, R. M. (1998) The political economy of precaution. In *Protecting Public Health and the Environment: Implementing the Precautionary Principle* . (Raffensparger, C. and Ticknor, J., eds.). Island, Washington, DC, pp. 123–147.
29. Singer, P. (1990) *Animal Liberation*, rev. ed. Avon Books, New York.
30. Singer, P. (1979) *Practical Ethics*. Cambridge University Press, Cambridge, UK.
31. Singer, P. (1975) *Animal Liberation*. Avon Books, New York.
32. Regan, T. (2001) *Defending Animal Rights*. University of Illinois Press, Champaign-Urbana.
33. Regan, T. (1983) *The Case for Animal Rights*. University of California Press, Berkeley.
34. Midgley, M. (1983) *Animals and Why They Matter*. University of Georgia Press, Athens.
35. Rollin, B. E. (1998) On Telos and genetic engineering. In *Animal Biotechnology and Ethics* . (Holland, A. and Johnson, A., es.). Chapman and Hall, London, pp. 156–171.
36. Rollin, B. E. (1995) *The Frankenstein Syndrome: Ethical and Social Issues in Genetic Engineering of Animals*. Cambridge University Press, New York.
37. Rutgers, B. and Heeger, R. (1999) Inherent worth and respect for animal integrity. In *Recognizing the Intrinsic Value of Animals, Beyond Animal Welfare* . (Dol, M., Fentener van Vlissingen, M., Kasanmoentalib, S., Visser, T., and Zwart, H., eds.). Van Gorcum, Assen, The Netherlands, pp. 41–51.

38. Fox, M. W. (1990) Transgenic animals: ethical and animal welfare concerns. In *The Bio-Revolution: Cornucopia or Pandora's Box.* (Wheale, P. and McNally, R., eds.). Pluto, London, pp. 31–54.
39. Fraser, D., Weary, D., Pajor, E. A., and Milligan, B. N. (1997) Scientific conceptions of animal welfare that reflect ethical concerns. *Animal Welfare* **6**, 187–205.
40. Orlans, B. (2000) Research on animal, law, legislative, and welfare issues in the use of animals for genetic engineering and xenotransplantation. In *Encyclopedia of Ethical, Legal, and Policy Issues in Biotechnology.* (Murray, T. H. and Mehlman, M. J., eds.). John Wiley and Sons, New York, pp. 1020–1030.
41. Griffin, H. D. (2003) Dolly's Death Update. February 17. Available on-line at: http://www.roslin.ac.uk/news/press/articles/175.html. Accessed April 1, 2003.
42. Griffin, H. D. (2003) We are sorry to report that Dolly the sheep is dead. February 14. Available on-line at: http://www.roslin.ac.uk/news/press/articles/174.html. Accessed April 1, 2003.
43. Wilmut, I., Schnieke, A. E., McWhir, J., Kind, A. J., and Campbell, K. H. S. (1997) Viable offspring derived from foetal and adult mammalian cells. *Nature* **385**, 810–813.
44. Varner, G. (1999) Should you clone your dog? An animal rights perspective on somacloning. *Animal Welfare* **8**, 407–420.
45. Sideris, L., McCarthy, C., and Smith, D. H. (1999) Roots of concern with nonhuman animals in biomedical ethics. *Inst. Lab. Anim. Res. J.* **40**, 1–14.
46. Comstock, G. (1988) The case against BST. *Agric. Hum. Values* **5**, 36–52.
47. Krimsky, S. and Wrubel, R. (1996) *Agricultural Biotechnology and the Environment: Science, Policy and Social Issues.* University of Illinois Press, Urbana.
48. Thompson, P. B. (1998) Biotechnology policy: four ethical problem and three political solutions. In *Animal Biotechnology and Ethics.* (Holland, A. and Johnson, A., eds.). Chapman and Hall, London, pp. 243–262.
49. Bovenkerk, B., Brom, F. W. A., and Van Den Bergh, D. J. (2002) Brave new birds: the use of animal integrity in animal ethics. *Hastings Cent. Rep.* **32**, 16–22.
50. Thompson, P. B. (1997) Ethics and the genetic engineering of food animals. *J. Agric. Environ. Ethics* **10**, 1–23.
51. Russell, W. M. S. and Burch, R. L. (1959) *The Principles of Humane Experimental Technique.* Metheun, London.
52. De Cock Buning, T. (2000) Genetic engineering: is there a moral issue? In *Progress in the Reduction, Refinement and Replacement of Animal Experimentation.* (Balls, M., van Zeller, A.-M., and Halder, M. E., eds.). Elsevier Science, Amsterdam, The Netherlands, pp. 1457–1464.
53. Costa, P. (2000) Welfare aspects of transgenesis. In *Progress in the Reduction, Refinement and Replacement of Animal Experimentation.* (Balls, M., van Zeller, A.-M., and Halder, M. E., eds.). Elsevier Science, Amsterdam, The Netherlands, pp. 1719–1723.
54. Thompson, P. B. (1999) Ethical issues in livestock cloning. *J. Agric. Environ. Ethics* **11**, 197–217.
55. Rollin, B. E. (1997) Send in the clones ... Don't bother, they're here! *J. Agric. Environ. Ethics* **10**, 25–40.
56. Jackson, D. (2000) Labeling products of biotechnology: towards communication and consent. *J. Agric. Environ. Ethics* **12**, 319–330.
57. Thompson, P. B. (1997) Food biotecnology's challenge to cultural integrity and individual consent. *Hastings Cent. Rep.* **27**(4), 34–38.
58. American Medical Association Council on Ethical and Judicial Affairs. (1994) *Financial Incentives for Organ Procurement: Ethical Aspects of Future Contracts for Cadaveric Donors.* American Medical Association, Chicago.

59. Daar, A. S. (1997) Ethics of xenotransplantations: animal issues, consent and likely transformation of transplant ethics. *World J. Surg.* **21**, 975–982.
60. Nuffield Council on Bioethics. (1996) *Animal to Human Transplants: The Ethics of Xenotransplantation*. Nuffiled Council on Bioethics, London.
61. Bach, F. H., Fishman, J. A., Daniels, N., et al. (1998) Uncertainty in xenotransplantation: individual benefit vs collective risk. *Nat. Med.* **4**, 141–144.
62. Morris, P. J. (1997) Pig transplants postponed [editorial]. *BMJ* **314**, 242.
63. Comstock, G. (2000) *Vexing Nature? On the Ethical Case Against Agricultural Biotechnology*. Kluwer, Boston, MA.
64. Abraham, C. (2002) Scientists look at creating a human-mouse embryo. *Globe and Mail* November 28. Available on-line at: http://www.globetechnology.com/servlet/ArticleNews/tech/RTGAM/20021128/wxmous1128/Technology/techBN/. Accessed November 28, 2002.
65. Thompson, P. B. (1997) *Food Biotechnology in Ethical Perspective*. Chapman and Hall, London.
66. Sharpe, V. A. (2002) Science, bioethics and the public interest: on the need for transparency. *Hastings Cent. Rep.* **32**, 23–26.
67. National Science Foundation. (1994) *Science, Technology and Democracy: Research Issues on Governance and Change*. National Science Foundation Workshop, Washington DC.
68. Stich, S. (1978) The recombinant DNA debate. Philosophy and Public Affairs. **7(3)**, 187–205. Reprinted in Ruse, M., ed. (1989) *Philosophy of Biology*. Macmillan, New York, pp. 229–243.
69. Stern, P. C. and Fineberg, H. V. (Eds.). (1996) *Understanding Risk: Informing Decisions in a Democratic Society*. Washington, DC.
70. Thompson, PB. (1995) Risk and responsibility in modern agriculture. In *Issues on Agricultural Biotechnology*. (Mepham, T. B, Tucker, G. A., and Wiseman, J., eds.). Nottingham University Press, Nottingham, UK, pp. 31–45.
71. Thompson, P. B. and Dean, W. (1996) Competing conceptions of risk. *Risk Health Safety Environ.* **7**, 361–384.
72. Ziman, J. (1992) Not knowing, needing to know, and wanting to know. In *When Science Meets the Public*. (Lewenstein, B. E., ed.). American Association for the Advancement of Science, Washington, DC, pp. 13–20.
73. Kunkel, H. O. and Hagevoort, G. R. (1994) Construction of science for animal agriculture. *J. Anim. Sci.* **72**, 247–253.
74. Thompson, P. B. (1999) From a philosopher's perspective, how should animal scientists meet the challenge of contentious issues? *J. Anim. Sci.* **77**, 372–377.