7a

Research ethics for animal biotechnology

Paul B. Thompson[#]

Animal biotechnology can be broadly categorized as encompassing the asexual reproduction of animals through cloning, and genetic transformation of animals through the manipulations made possible through recombinant DNA. The character and methods of such manipulations include the creation of 'knockout' animals intended to study gene function on the one hand, and also the insertion of genes originally identified in other species, or, colloquially, genetic engineering, on the other. This definition will clearly change and grow with theoretical and technological developments in genomics and systematic biology, but for the time being cloning and genetic transformation represent the main foci of animal biotechnology for the purpose of research ethics.

Bernard Rollin's 1986 paper *"The Frankenstein Thing"* articulated two ethical principles for animal biotechnology. One was the principle of conservation of welfare, to wit, that applications of biotechnology should result in animals that are no worse off with respect to suffering and frustration than traditionally bred animals. The other was his view that biotechnology should be used to make animals less likely to suffer in the various settings that they are to be used. This could be called the 'improvement of welfare' principle, and Rollin understood it to entail one uncontroversial and one very controversial conclusion. The uncontroversial conclusion was that there is nothing wrong with using biotechnology to address problems of animal health. The controversial one is that there is nothing wrong with using biotechnology to produce animals less capable of experiencing the suffering that humans inflict upon them.

Rollin's original article addressed the central question of research ethics for use of animals: what are researchers' responsibilities with respect to animals that they use in research? Many of the subsequent reactions to animal biotechnology have been less clearly relevant to this question, and many have ascended to a much broader level of generality, questioning, for example, the moral status of transgenic animals in general (Balzer, Rippe and Schaber 2000) or society's general responsibilities to transgenic animals (Bovenkerk, Brom and Van den Bergh 2002). In this paper I want to return to the narrower questions of research ethics. The approach that I will outline is a form of pragmatic bioethics (Keulartz et al. 2002). I begin with an overview of debate over animal biotechnology, followed by a brief discussion of animal welfare and research ethics. I argue that the key research-ethics questions demand a scientifically informed approach to animal welfare, which in turn demands an understanding of the interpenetration between ethics and animal-welfare science. I conclude with a discussion of how research-ethics committees can approach the evaluation of animal biotechnology in a more ethically satisfactory manner. My treatment of these issues reflects my background and main research interests with traditional livestock species

[#] Department of Philosophy, Michigan State University, East Lansing, MI, USA. E-mail: thomp649@msu.edu

that are intended for the production of animals for meat, milk and animal by-products, rather than mouse biotechnology where the focus has been on developing models for human disease.

Welfare and biotechnology: background

There is ample documentation of the public's interest in biotechnology's impact on animal welfare. In one of the early studies, animal biotechnology was found to be thought ethically problematic by a greater percentage of respondents than genetic engineering applied to human beings (Hoban and Kendall 1993). One British study found that public was more accepting of animal genetic engineering for biomedical research than for food production (Sparks, Shepherd and Frewer 1995), and another study by the same group found that the British public interpreted impact on animals as an ethical issue, rather than as an effect bearing on risk (Frewer, Howard and Shepherd 1997). There is evidence that respondents find animal cloning or transformation to be particularly problematic, as distinct from those who have general objections to the use of gene technologies as well as those who associate animal biotechnology with detrimental impact on animal welfare (Durant, Bauer and Gaskell 1998).

As early as 1992, the National Agricultural Biotechnology Council (NABC) held a meeting on animal biotechnology where animal welfare was a main focus of discussion. The consensus workshop of that meeting called for empirical research on the welfare of transgenic animals (McDonald 1991). NABC endorsed reasearch on both scientfic and philosophical dimensions of the animal-welfare question for a second time in 1995 (Thompson 1998). Similar recommendations were made in the Polkinghorne report (Ministry of Agriculture 1993) and by two subsequent committees in the United Kingdom (Bruce and Bruce 2000). A workshop of the European Centre for the Validation of Alternative Methods (ECVAM) published detailed recommendations for conducting research on the welfare of transgenic animals, though many were directed particularly toward biomedical applications such as the development of animal models for the study of human disease (Mepham et al. 1999).

There have also been many conceptual and philosophical papers on animal welfare and biotechnology. Rollin's 1986 paper presented an analysis that argued against the belief that simply introducing novelty into the genome could be construed as a form of harm. Instead, Rollin suggested that the entire ethical significance of animal biotechnology resides in risk to humans, environment and to the animals themselves. Rollin has extended but not substantially changed this analysis in subsequent writings, including his 1995 book. Less favourable philosophical viewpoints on animal biotechnology have been offered by Fox (1990), Linzy (1990), Verhoog (1992), Rifkin (1995), Ryder (1995) and Holland (1995). A complete and in-depth debate of the conceptual issues can be found in the contributions by scientists and philosophers to Holland and Johnson's Animal Biotechnology and Ethics (1998). Thompson (1997; 1999) and Appleby (1998) have published critical discussions of this literature that essentially support Rollin's analysis. De Cock Buning (2000) has argued that these less favourable approaches to understanding the moral issues behind genetic engineering of animals imply a deontological evaluation of the process of gene transfer and exclude the relevance of consequentialist norms, such as Rollin's principles, that emphasize the outcome with respect to animal welfare. He concludes

by expressing the hope that some middle ground could be struck between these approaches, but does not offer a principled way forward.

Expressions of public concern and ethical relevance notwithstanding, there are relatively few published articles discussing empirical studies of the welfare of genetically engineered or cloned farm animals. Van Reenen and Blokhuis (1993; 1997) report that adverse impact on the welfare of the transgenic cattle that they studied was limited to the experimental stage in which pre-implantation embryos were manipulated in vitro. Hughes et al. (1996) report no significant differences between transgenic and control sheep. Jaenisch and Wilmut (2001) report abnormal development in cloned sheep, but Lanza et al. (2001) report no abnormalities in a group of cloned cattle. A survey article by Mepham and Crilly (1999) extracts data from several research reports on transgenic farm animals that were not designed as studies of welfare to support the conclusion that transgenic animals may suffer from adverse welfare when compared to non-transgenic livestock. A recent survey article by Heap and Spencer (2000) cites anecdotal reports of adverse impact associated with both transgenics and cloning, but does not cite any empirical data.

In sum, public attitudes toward the ethical acceptability of animal biotechnology depend heavily on its impact on animal welfare. The need for empirical research on such impact has been endorsed by a number of groups representing scientific interests, as well (National Research Council NRC 2002). Given the relative paucity of published research on the topic, it is difficult to make any confident assertions about the relationship between welfare and biotechnology. This places researchers who must evaluate the ethics of work using biotechnology in a difficult position, the nature of which becomes clear when we frame the questions that must be asked within current approaches to research ethics.

Animal use in a research-ethics context

Research ethics takes an immediate concern with the conduct of research, though broader questions about the impact of science on society may also be appropriate. A procedural approach to the ethics of using animals in research has evolved within the science community over the last several decades. A procedural ethic is one in which the ethical justifiability of a particular course of action is tied to that course of action having been endorsed by a well characterized decision procedure. In contrast to procedural approaches, substantive ethical theories stipulate general principles or norms (such as the categorical imperative or the utilitarian maxim) and then interpret justification in terms of consistency with the stipulated principles or norms (see Russow 1999). The procedural nature of animal ethics within the context of scientific research is evident in the reliance on committee approval processes that are now commonplace across the globe.

Although the details for animal-ethics committees vary from country to country, the general approach to animal ethics within research institutions has been to require that researchers develop a protocol describing how animals will be used in a proposed experiment. These protocols are then reviewed by a committee which must decide whether or not the use of animals is acceptable. In most cases, this committee or a complementary one also has responsibility to ensure that actual practice is consistent with what has been approved in the protocol. The committee(s) itself (themselves) may be subjected to additional forms of oversight from authorizing or regulatory bodies. Thus, in the United States, institutions conducting animal research are required to constitute an internal Animal Care and Use Committee (IACUC) that will

review and approve protocols, as well as inspecting and certifying that animals used for research in the institution are in fact being used as indicated. Institutions and their IACUCs are inspected by the USDepartment of Agriculture, which has statutory authority to ensure that the provisions of the Animal Welfare Act are being upheld (National Research Council NRC 1996; Office of Laboratory Animal Welfare OLAW 2002).

The procedural IACUC-style approach to animal ethics ensures that animal interests are, at some level, being considered in the planning and conduct of research, at the same time that it allows for considerable flexibility in terms of specific administrative approaches. Not only will the administrative style of an institution result in different approaches, but also the nature of research being done at the institution may mean that different types of questions are appropriate. A drug company may be using rather different animals and conducting rather different kinds of studies from an agricultural college or a wildlife research institute, for example. It must be admitted that nothing in the procedural approach itself guarantees that the right ethical questions regarding animal use are being considered or that they are taken with an appropriate level of seriousness. Thus, the nature of the approval and oversight procedures at any given institution will reflect the culture and values of that institution (Rowan 1990). One interesting and ironic aspect of the culture within USinstitutions is a reluctance to using the word ‘ethics’ to describe what is essentially an ethical process, thus Americans have ‘care and use’ committees, while the rest of the world is more comfortable with animal-ethics committees (Jennings and Miller 2000; Marie et al. 2003).

Nevertheless, the evolution and development of the IACUC/ethics-committee approach has produced a fair amount of global agreement on the principles that tend to get used within the committee structure. First and foremost, animals count and scientists have ethical responsibilities for their care. Second and of almost equal importance, at least some human use of animals for research purposes is acceptable. Research ethics for animals remains fundamentally at odds with philosophical views that do not accept this fundamental tenet. Research ethics is thus committed to a broad interpretation of the view that the benefits or goals sought through research can, in some cases at least, outweigh or override harms to the animal research subjects on which that research is conducted. Third, research is acceptable because the committee members have approved it, either through a process of formal voting or a consensus procedure, and not because it conforms to some philosophical standard. (Donnelley 1990; Jennings and Miller 2000; Heitman 2002).

The third tenet is actually quite important, for it stipulates the procedural nature of the norms guiding animal research and creates a pluralistic structure for the application of substantive principles regarding animal use. A number of different standards, patterns of evaluation or principles of justification are available, and each member of the committee may apply their own judgment and standards to a protocol or policy. They are voting to approve or deny a protocol, not to decide a comprehensive philosophical view of animal ethics. Furthermore, the procedural pluralism of animal-research ethics qualifies the first two tenets in the following sense: although the benefits of research can in principle outweigh or offset harms to animals, this offsetting should not be thought of as involving a classical cost–benefit style of justification through optimization. Some members of a committee may be thinking that way, but others may not.

Beyond this, the details of animal research ethics can become almost overwhelming. One key question concerns the make-up of committees. Current U.S.

procedures require both a non-scientist and a member not affiliated with the institution conducting the research. These requirements can be interpreted to suggest that public concerns such as those noted above do indeed have a place within the procedural ethics of animal research. Furthermore, committees clearly need veterinary and animal-welfare expertise, as well as sophistication in experimental design. The ethical significance of these areas of expertise is sometimes summarized in terms of the 'Three R's'. Scientists should seek to reduce the number of animals being used. In practice this means that protocols are reviewed carefully with respect to whether experiments are decisive, including whether the number of animals is sufficient to generate data that will meet statistical requirements, but not exceeding the number in ways that inflict needless suffering or inconvenience on animal subjects. This requires expertise in statistics and research design. Scientists should seek to replace animals when possible, using computer or tissue models, perhaps, but also using species that have less complex and demanding cognitive needs. Replacement requires expertise in basic theory and in alternatives to animal use. Finally scientists should develop approaches that refine whatever adverse impacts may be unavoidable. Pain and discomfort should be treated with appropriate analgesics, husbandry and, in the extreme case, euthanasia (Russell and Burch 1959; Orlans 1990). Interpreting refinement within the context of an animal-ethics committee review involves standard veterinary expertise, but increasingly it also involves application of applied animal-welfare science.

Institutional animal-ethics committees should be constituted with these three broad areas of expertise in mind. Such committees typically involve representation from disciplines and research programmes conducting animal research, and as such are likely to include members with the requisite knowledge for reduction and replacement. Membership from attending veterinary staff is also required in the U.S., but veterinarians may or may not be cognizant of welfare science. None of the needed areas of expertise explicitly involve philosophy or ethics; hence one might wonder what role ethics would have in conducting the business of animal-ethics committees. But ethics and welfare science are intertwined. Thus it is useful to examine this element of the requisite ethical expertise for animal-research ethics more carefully.

Animal-welfare science

The science of animal welfare has grown considerably over the last two decades. It can be described generally as a blending of longstanding approaches to the assessment of animal health along with studies of animal behaviour and most recently cognitive and neuroscience methods for making comparative assessments of how animals fare with respect to different husbandry practices and environmental conditions. Animal-welfare science thus builds upon standard and relatively non-controversial veterinary approaches to animal health. Behavioural and cognitive research on animals grew out of the attempt to understand and model the functioning of individuals and animal populations in the wild. As it became evident that mechanistic, instinctual and physiological accounts of animals were unable to account for the complexity of animal behaviour in the wild, the application of cognitive ethological methods to animal welfare was a natural move (Bekoff 1994). However, much of the progress that has been made in animal-welfare science became possible only when researchers adopted rather pragmatic attitudes toward a number of conceptual and methodological problems that constrain research on animal welfare. Any application of science to the study of welfare issues associated with biotechnology will be subject to these

constraints. In addition, cloning and genetic transformation introduce additional complications into the basic problems of conceptualizing and measuring the welfare of farm animals.

Animal welfare is a multi-attribute, multi-disciplinary phenomenon

Considerable energy was expended during the early years of research on animal welfare debating the basis for an attribution or evaluation of comparative well-being. In fact, as with human well-being, there are a number of attributes to animal welfare, and attempts to formulate a reductive approach have not proved successful. Physiological indicators of health, such as growth rates and the absence of recognized disease etiologies are clearly relevant to welfare. Ongoing or cumulative experiences of pain and stress are elements of welfare, though it is doubtful that total absence of pain or stress would be consistent with acceptable levels of welfare in humans or livestock. Behavioural studies and evolutionary genetics suggest that animals of a given species have instinctual or functional needs for varying degrees of social contact, spatial orientation and sexual activity, as well as for performing certain behaviours. The scientific methods available to assess each of these attributes tend to be associated with different sub-disciplines in the animal sciences. Each of these sub-disciplines employs different experimental procedures that traditionally characterize dimensions of welfare not amenable to measurement by those procedures as elements that should be controlled through good experimental design. Thus one researcher's dependent variable is another's confounding factor. Animal-welfare researchers have thus faced the difficult conceptual problem of integrating methods and theories developed in quite disparate areas of science (Appleby 1999).

Welfare is an inherently normative concept

The very idea of welfare implies a normative valuation associated with a given state of affairs. To associate a given state of physiological functioning with an animal's welfare is to judge, at least implicitly, that this state is indicative of the animal's doing well or poorly. Nature, it could be said, is indifferent with respect to these various states; so to characterize them as elements of welfare is to interpret these states within a framework of valuation. Some of these evaluative elements are quite uncontroversial. For example, a disease process resulting in the death of an organism would readily be characterized as inimical to that organism's welfare. Yet such a characterization implies that life is better than death, and this, in turn, implies a perspective (perhaps that of the organism itself) from which such a value judgment can be made. Being a complex blending of multiple attributes, assigning value to a particular physiological or behavioural state is in fact often quite controversial. Such valuations are particularly susceptible to well-known fallacies. Anthropomorphism consists in presuming that a state or behaviour valued by human beings would similarly be valued by animals of another species. The naturalistic fallacy consists in presuming that a state or behaviour characteristic of animals in a 'natural' environment is, for that reason, particularly good, valuable or indicative of welfare. This fallacy is compounded by difficulties in ascertaining what environments would count as natural for domesticated animals. The ecological fallacy consists in presuming that what is good for the individual organism is good for the species, or vice versa.

There is a further fallacy that might be called the positivist fallacy. This consists in presuming that because the normative dimension of a phenomenon is elusive, ambiguous and subject to erroneous classification, it not only can but perhaps should

be ignored altogether. In its most extreme version, the positivist fallacy consists in the performative contradiction of asserting that science should be value-free. Of course, a value-free science could not include the normative assertion that it should be value-free, hence the contradictory nature of making such an assertion. According to numerous observers of the animal sciences, the positivist fallacy has played an influential role leading to the relative neglect of animal welfare in traditional agricultural research disciplines (Kunkel 2000; Rollin 1989). In fact, as a domain of applied science dedicated to increasing yield, productivity and the enhancement of sensory, nutritional and economic value of food commodities, the agricultural sciences presume elusive and occasionally contested value judgments in their most basic goals and concepts. The neglect of animal welfare thus involves a rather selective and arbitrary application of the positivist fallacy within the context of agricultural research.

Some normative approaches to animals are more conducive to scientific studies of welfare than others

David Fraser (1999) describes two broad approaches to animal ethics. Type I is characterized by Peter Singer and Tom Regan, two philosophers prominently associated with animal advocacy. This view is characterized by an attempt to develop a single ethical principle that would be used to derive a normative valuation for individual animal lives. Type-I animal ethics does not discriminate according to taxonomic differences among animals, and presumes that a single normative criterion – generally associated with sentience – can be used to derive standards for human conduct oriented to animal welfare. Type-II animal ethics, which Fraser associates with a number of less well-known philosophers, takes a more inductive philosophical approach that attempts to specify principles for ethical treatment of animals that is sensitive to different species cognitive and behavioural capabilities, as well as to different practices of husbandry that might emerge given particular economic, technological and political preconditions. Fraser argues that Type-II animal ethics is more conducive to application within animal welfare science, and that given the inherently normative basis of welfare, is in fact essential to the development of coherent research programmes in animal-welfare science.

Type-II ethics can be characterized as a form of philosophical pragmatism (Thompson, forthcoming). Here, the philosophical starting point is to review why the situation at hand might be thought problematic. As already indicated, animal-welfare science is most relevant to problems of refinement: finding ways to mitigate the pain and discomfort suffered by experimental animals. Here, standard veterinary indicators of animal health can be used along with behavioural cues, such as stereotypies and avoidance behaviour, to make assessments of animal preferences. These welfare indicators are combined with an attempt to assess cognitive capabilities and functional or instinctual drives typical of a species. In addition, both the evolutionary history of the species (including domestication events, for domesticated species) and the ecological history of environmental conditions in which founder animals for current populations have lived are used to provide a background framework for comparing a protocol as designed to possible alternatives. Although this inductive and comparative approach does not yield criteria that permit one to judge given measures of welfare to be unambiguously acceptable or unacceptable, a pragmatic approach to ethics does facilitate amelioration of animal-welfare problems within the parameters set by experimental design.

Welfare science and animal biotechnology

Given a pragmatic and procedural approach to animal-research ethics, it is now time to explore briefly a few of the questions and approaches that are most relevant to animal biotechnology. The Principle of Conservation of Welfare that Rollin (1986; 1995) proposed as the standard of welfare for agricultural biotechnology states that, all things considered, transgenic and cloned animals should not be worse off than founder animals or other animals of the same species used for similar research purposes. Rollins' Principle of Conservation of Welfare permits applications of biotechnology that make animals better off than the comparison group. It should be possible to apply animal-welfare science to transgenic and cloned animals in collecting a variety of standard veterinary measures of health and development, augmented by behavioural studies. Such data could be compared against standard ranges of value considered to be typical of healthy animals, and also to data taken for non-transgenic, non-cloned animals in control groups. This comparison would provide the basis for an empirically informed assessment of how these animals fare in comparison to conventionally bred animals kept under comparable circumstances. At the risk of stating the obvious, I will explore the ramifications of such an approach in more detail.

If the procedures used in gene transfer or cloning are themselves the source of detrimental (or positive) effects on animal welfare, we would expect that welfare indicators for a sufficiently large and random sample of cloned and transgenic animals would diverge from those of conventional livestock to a statistically significant degree. Given the standard conditions of variability associated with measurements of welfare, we should not expect that all data will provide an unequivocal indication of any one result, at least until a number of studies have been conducted. The current situation, in which relatively few studies have been conducted, does not provide a sufficient basis for making a scientifically informed judgment. The existence of at least a few studies indicating no significant impact on scientifically measured indicators of welfare does show that techniques of transgenesis and cloning do not necessarily lead to detrimental impacts on animal welfare, and we should not underestimate the significance of even this limited result. It does provide a temporary basis for animal-ethics committees to use when evaluating studies involving cloned and transgenic animals. Nevertheless, any scientifically informed judgment about the effect of biotechnology on animal welfare will require a significantly larger number of studies.

There are confounding factors that clearly apply to transgenic animals. The choice of genes used in transformation may substantially affect the measurements that are associated with specific welfare indicators. It is generally accepted that a subclass of possible genetic modifications would be expected to produce detrimental results for animal welfare. Animals developed as models of human disease, for example, would not be characterized as successful transformations unless they exhibit a given disease in a large percentage of individuals, hence they would be expected to perform less well than a typical individual with respect to welfare indicators. As a second example, it is now widely hypothesized that the transformation associated with the famous Beltsville pigs – increased production of growth hormone – was contrary to animal health. In such cases, successful incorporation and expression of the transgene can be expected to have a detrimental impact on animal welfare. Thus, there will be a subpopulation of transgenic animals for which the welfare comparison is unfavourable, but which do not provide evidence that the techniques for producing transgenic animals are responsible for the negative impact on welfare, as distinct from

the expected functioning of the transgene. It may not be possible to discern which transgenes have detrimental effects without experimentation. There may, of course, prove to be similar confounding factors for cloning, particularly if cloning is practiced primarily on a subpopulation of founder animals that is atypical with respect to other welfare indicators.

A second set of possible confounding factors are derived from welfare indicators associated with reproductive health. Both transformation and cloning involve in-vitro manipulation of embryos and blastocysts. In-vitro fertilization and implantation is itself associated with reduced levels of reproductive success, and the manipulations associated with biotechnology can be expected to lower the survival rate of blastocysts, as well as live births. If such data are incorporated into comparisons between conventional in-vitro fertilization and either transgenic or cloned animals, it will almost certainly skew the resulting assessment against animal biotechnology. Comparison with in-vivo fertilization will be even worse. Yet however issues associated with reproductive success are finally evaluated, keeping these issues separate from those associated with live-born transgenics and clones would appear to be warranted. For the near term, all transgenic and cloned animals must be regarded as experimental. It is reasonable to expect that current rates of reproductive success may not be typical of those that would be associated with more mature technology. As such, meaningful welfare comparisons of reproductive-success data may be premature. Furthermore, it is far from clear how to apply scientifically measurable indicators of welfare to prenatal and even early neonatal individuals. If such comparisons are to be made on a scientific basis, there will need to be a corresponding development in the conceptualization and testing of measures for animal welfare during the earliest stages of life.

There are a number of practical issues that will arise in conjunction with any attempt to apply animal-welfare science to biotechnology. Once concerns the specific indicators and measures that would be deployed in any attempt to make comparative assessments of welfare. The ECVAM working group attempted to specify a number of fairly specific indicators in their 1999 report focused on laboratory animals (Mepham et al. 1999). While it may be useful for the NRC committee to provide some general guidance on welfare measures, it is questionable as to whether any specific set of indicators would be appropriate for all transgenic and cloned animals. One can expect that there will be significant differences depending on species and the nature of a genetic transformation, not to mention differences that depend on the number of animals and the experimental conditions in which measurements can be taken. The ECVAM group also recommended that all experiments involving transgenic animals involve an animal-welfare component. Yet data beyond the most rudimentary indicators of health and development might not be particularly indicative of welfare for transgenic and cloned animals in certain cases. Collection of data and operation of controls may, in some cases, involve costs that would not be justified by the scientific results that could be expected to be obtained. However, these practical difficulties should not be allowed to result in a continuation of the current paucity of meaningful scientific data on the welfare of transgenic and cloned animals.

Conceptual and philosophical issues

Although it should possible for animal-welfare science to make a significant contribution to our understanding of welfare issues associated with animal biotechnology, there are a few conceptual and philosophical issues that do not appear to be resolvable on scientific grounds. Many issues revert back to the difference

between Fraser's Type-I and Type-II (or pragmatic) animal ethics. It is not clear that every approach Fraser has classified under the Type-I heading would be opposed to animal biotechnology. Singer's utilitarianism, in particular, might be applied in a manner that would find some applications of biotechnology to be morally permissible. Nevertheless, there is a growing philosophical literature that opposes genetic engineering and cloning on grounds that are not particularly amenable to the empirical, inductive and comparative approach of animal-welfare science. There are two broad types of argumentation that are relevant. One associated with Fox (1990), Verhoog (1992) and Rifkin (1995) puts forward the idea that animal genomes possess a form of integrity such that modification is in every case a violation of integrity and morally forbidden. The second involves the claim that modification is not consistent with the animal's own good, and as such involves a form of disrespect. Ryder (1995) and Holland (1995) offered versions of this argument, and a recent article by Balzer, Rippe and Schaber (2000) uses a similar claim to suggest that biotechnology is in all cases inconsistent with the dignity that should be accorded to all animals. Balzer et al. note that current Swiss law requires respect for the dignity of creatures and argue that this forms a basis for opposition to biotechnology on legal grounds.

Arguments that stress the genetic integrity of animals may be subject to a scientific evaluation. At a minimum, it would be useful to debate whether the notion of genetic or genomic integrity can be supplied with any scientifically grounded basis. However, it seems most likely that this will be a topic for geneticists, evolutionary theorists and possibly ecologists. Animal-welfare science will play at most a supporting role to these other disciplines in biology. It may appear that welfare science could be brought to bear on arguments emphasizing an animal's own good. However, these arguments emphasizing dignity suggest that the underlying ethical problems follow from a viewpoint that interprets animals as of purely instrumental value for human uses. As such, this philosophical approach follows not from an empirical assessment of how animals fare in particularly situations, but from an assessment of the human attitudes that lie behind animal use. Though the philosophical merits of both arguments should be analysed and debated within the context of animal ethics, neither will be deeply affected by empirical considerations derived from animal-welfare science.

A more interesting and relevant set of conceptual issues arise in connection with genetic modifications that improve the well-being of animals both in biomedical research applications and in livestock-production settings by changing their capacities to experience various forms of stress or deprivation. This issue has been debated extensively in connection with Bernard Rollin's discussion of whether it would be unethical to change an animal's telos. 'Telos' is a term Rollin adapted from Aristotle's philosophy to summarize the behavioural, functional and cognitive drives that are most deeply associated with the welfare or well-being of animals of a given species. Thus, nesting behaviour or various forms of social grouping would be characteristic of the telos for some animals, but not for others. Rollin (1995) has argued that not only is there is no reason why it should not be permissible to modify an animal so that certain drives or needs characteristic of founding individuals are absent in the modified progeny, but also that for animals that intended to mimic painful disease conditions, such forms of modification may be ethically mandatory as a form of refinement. In some cases, arguments stressing integrity or dignity have been an attempt to find some grounds on which to oppose this result.

The modification of functional needs and drives also leaves open the possibility that one might relieve welfare problems associated with livestock production by using

genetic engineering to produce a new breed that would not be vulnerable to stressors that lead to these problems. This is not a possibility that is unique to biotechnology. Conventionally bred species of blind hens display lower levels of stress in typical confined layer production systems. Standard measures of welfare would thus indicate the use of blind hens would be preferable to sighted hens. Yet few are willing to follow this application of welfare logic (Sandøe et al. 1999). This suggests that at least some applications of biotechnology that would be supported by the comparative analysis of animal-welfare science will be found questionable on ethical grounds. This is a curious result. It seems unlikely that people would reject a modification that made livestock less susceptible to a production-related disease, such as mastitis, yet the judgment that it is not acceptable to solve welfare problems by making animals less susceptible to stress is widely supported by anecdotal analysis. This may be more of a philosophical than a scientific problem, yet it does suggest that there may be some possible areas of ethical, conceptual and philosophical ambiguity where the application of animal-welfare science will be less than straightforward.

Meeting public expectations

These conceptual issues bring us back to the broader context of public interest in the ethics of animal biotechnology. The existence of ethical puzzles about using biotechnology to pursue the goals of refinement suggests that there is an additional way in which animal biotechnology is problematic. Some strategies for mitigating animal suffering may be at odds with our culturally based views about what it is acceptable to do. Animal-ethics committees intently focused on achieving the goals of refinement may find themselves at odds with the broader public if they sanction transformations that would substantially alter the basic characteristics of a species. Rollin's suggestion that it would be a good thing to develop a strain of decerebrate lab animals incapable of feeling pain is unlikely to win wide public approval, at least over the short run, and even less radical uses of biotechnology in the service of refinement can certainly run afoul of ethical norms that have been articulated in terms of respecting the intrinsic value of research animals. It is in responding to this tangle of issues that the pragmatism of my approach becomes most evident.

First, the *sine qua non* of pragmatism is its unrelenting focus on the problem at hand. Other philosophical schools have tended to presume that deep and enduring philosophical disputes such as the irreconcilability of deontology and consequentialism or the puzzle of *Moralität* and *Sittlichkeit* lie at the heart of every moral issue. Pragmatists try to avoid prejudging the philosophical issues, and are especially attentive to what Todd Lekan (2003) calls 'determination problems', where the exact nature of what is at issue is precisely what needs philosophical attention. In the present instance there are at least two problems that are deeply entangled. One is that we are not at all sure of what the right thing to do is in the cases that have been reviewed in the preceding section. This problem is grounded in the lack of clarity regarding ethical responsibilities that scientists owe to research animals. The examples of blind hens and decerebrate mice indicate a puzzle over the way that researchers' duties to animals ought to be discharged, and there is every reason to believe that no convincing solution to it is on the near horizon. As Bernard Gert argues in his contribution this volume, the issues are beyond the reach of common morality. The other problem is that animal-ethics committees need some guidance on how to proceed on a provisional basis when there is a high degree of confusion and moral uncertainty. This problem is particularly acute in light of the significant degree of public interest in the ethics of agricultural biotechnology, and it is useful to

understand this problem as grounded not in responsibilities to animals, but in the responsibility of scientists to the broader public.

Scientists are accorded special roles in society in order to carry out their work, and in exchange the public is entitled to expect that scientists are conducting their business in a thoughtful and deliberative manner. Animal-ethics committees are an institutional response to this public expectation. They address both substantive concern with the care and treatment of research animals and also the need for public accountability with respect to the care and treatment of animals. The procedures and records of committee activities provide a basis for the public to see whether researchers are taking their responsibilities to animals seriously. Looking toward institutions that can cope with vagueness, indeterminacy and a plurality of relevant norms and perspectives is also a characteristically pragmatic response. Pragmatists tend to favour procedural norms in such instances, especially when procedural approaches have the capacity to provide some basis for taking action in the short term without foreclosing the possibility for revisiting an issue (or taking a different stance with respect to apparently similar cases) as experience and learning accumulate. Pragmatists also see normative standards as products of social interaction; hence the institutional and procedural orientation of animal-ethics committees represents a characteristically pragmatic response to the problem of public expectations.

Members of the public can appreciate the conceptual and philosophical difficulty of issues such as those that have been discussed above. Public opinion about the way that such questions should be settled will almost certainly be as diverse and divided as that of the philosophers themselves, and research-ethics committees cannot be expected to settle the issues, especially not in the context of reviewing protocols. However, it is reasonable to expect that even these difficult issues are being taken seriously. It would be ethically problematic if researchers used the uncertainty and philosophical difficulty of determining what our responsibilities are with respect to cloned or transgenic animals as an excuse for ignoring the potential problems altogether. Hence there is an ethical responsibility both to grapple with these issues and to be able to demonstrate to the public that researchers have not taken a cavalier attitude with respect to them. This is not to say that the philosophical puzzles of duties to research animals are resolved. What can be said is that the puzzles are being taken seriously, and that, by implication, responsibilities to animals are being taken seriously.

A pragmatic approach to procedures for addressing researchers' responsibilities to research animals should produce an amelioration of problems associated with animal use, and should be oriented toward public, institutional learning that extends beyond the particular individuals who happen to sit on committees at any given time. With this in mind, it is possible to offer the following suggestions as part of the approach for IACUCs and animal-ethics committees to take in response to the challenges posed by animal biotechnology.

At a minimum, committees should have records that indicate what research is being done with cloned and transgenic animals. These records should describe cloning methods and/or the nature of the genetic transformation in functional terms. This is a minimal requirement for being able to monitor and document whether cloned and transgenic animals suffer unusual health or well-being problems. If record keeping is tightly linked to protocols, this means that generic protocols for performing a broad class of biotechnology experiments will not be acceptable.

Since there are few public data on the general effects of biotechnology on animal health and well-being, committees should encourage the collection, sharing and

publication of such data whenever doing so is compatible with larger research purposes and institutional policies.

Particular experiments involving genetic transformations that could substantially alter the functional characteristics of animal health or behavioural and cognitive needs or functioning of research animals should be discussed on a case by case basis, and committee records should indicate that they have been discussed. A proper animal-ethics committee will include members who can and will articulate the rationale for concern about such experiments, even if they themselves may not endorse this rationale.

Committees should develop a forum in which the broad ethical acceptability of animal biotechnology is discussed. Such a forum may involve committee workshops and policy discussions, or general workshops and seminars made available to the entire faculty of researchers.

These are provisional suggestions that may need to be revised as committees (and society at large) learn more about animal biotechnology. For now, they provide a basis for research to continue while a great deal of philosophical uncertainty and confusion remains over the relationship between biotechnology and animal welfare.

Beyond the procedural research ethic for animal use, there are broader questions for the research agenda. Although the few studies that have been published show that animal biotechnology can be consistent with standards typically applied to the welfare of research animals, the small number of studies, the equivocal results and anecdotal reports of occasional welfare problems indicate that there is a need for continued and better research on the welfare of transgenic and cloned animals. Such research should be conducted under the still developing but now established paradigm of animal-welfare science. Studies will need to be conducted with some sophistication in order to avoid confounding factors. Given standard methodological and philosophical issues associated with assessment of animal welfare, it will continue to be possible to draw different conclusions from the same data and to aggregate results in ways that either favour or disfavour the comparison of biotechnology to more traditional programmes of livestock breeding. There should thus be a sustained effort within the scientific community to arrive at a consensus on which blend of standards and which forms of reporting data provide the most meaningful assessment of the welfare question. There should also be some effort to help members of the broader public, especially those interested in animal protection, evaluate highly aggregated or generalized statements about the link between biotechnology and animal welfare with a critical eye.

In closing with such a long list of ‘should’ statements and specific recommendations for animal-welfare committees, it may appear that the field of research ethics for animal biotechnology is left in a state of philosophical disarray. While it is obvious that many unsolved problems remain, the shift to a procedural-pragmatic approach that institutionalizes a process for combining seriousness of purpose, consideration for animals, philosophical pluralism and social learning should be regarded as a significant achievement. The problems with which I close are much more focused and amenable to amelioration (if not final solution) than are the grand puzzles of intrinsic value and the metaphysics of human–animal relations. I regard that as progress.

References

Appleby, M.C., 1998. Genetic engineering, welfare and accountability. *Journal of Applied Animal Welfare Science,* 1 (3), 255-173.

Appleby, M.C., 1999. *What should we do about animal welfare?* Blackwell Science, Oxford.

Balzer, P., Rippe, K.P. and Schaber, P., 2000. Two concepts of dignity for humans and non-human organisms in the context of genetic engineering. *Journal of Agricultural and Environmental Ethics,* 13 (1), 7-27.

Bekoff, M., 1994. Cognitive ethology and the treatment of non-human animals: how matters of mind inform matters of welfare. *Animal Welfare,* 3 (2), 75-96.

Bovenkerk, B., Brom, F.W.A. and Van den Bergh, B.J., 2002. Brave new birds: the use of animal integrity in animal ethics. *Hastings Center Report,* 32 (1), 16-22.

Bruce, D.M. and Bruce, A., 2000. Animal welfare and use. *In:* Hodges, J. and Han, I.K. eds. *Livestock, ethics and quality of life*. CABI Publishing, Wallingford, 53-78.

De Cock Buning, T., 2000. Genetic engineering: is there a moral issue? *In:* Balls, M., Van Zeller, A.-M. and Halder, M.E. eds. *Progress in the reduction, refinement and replacement of animal experimentation*. Elsevier Science, Amsterdam, 1457-1464. Developments in Animal and Veterinary Sciences no. 31.

Donnelley, S., 1990. Animals in science: the justification issue. *Hastings Center Report,* 20 (3 Suppl.), 8-13.

Durant, J., Bauer, M.W. and Gaskell, G. (eds.), 1998. *Biotechnology in the public sphere: a European sourcebook*. The Science Museum, London.

Fox, M.W., 1990. Transgenic animals: ethical and animal welfare concerns. *In:* Wheale, P. and McNally, R. eds. *The bio-revolution: cornucopia or pandora's box*. Pluto Press, London, 31-54.

Fraser, D., 1999. Animal ethics and animal welfare science: bridging the two cultures. *Applied Animal Behaviour Science,* 65 (3), 171-189.

Frewer, L.J., Howard, C. and Shepherd, R., 1997. Public concerns in the United Kingdom about general and specific applications of genetic engineering: risk, benefit and ethics. *Science, Technology and Human Values,* 22 (1), 98-124.

Heap, B.A. and Spencer, G.C.W., 2000. Animal biotechnology: convergence of science, law and ethics. *In:* Hodges, J. and Han, I.K. eds. *Livestock, ethics and quality of life*. CABI Publishing, Wallingford, 27-52.

Heitman, E., 2002. The human care and use of animals in research. *In:* Bulger, R.E., Heitman, E. and Reiser, S.J. eds. *The ethical dimensions of the biological and health sciences*. 2nd edn. Cambridge University Press, Cambridge, 183-191.

Hoban, T.J. and Kendall, P.A., 1993. *Consumer attitudes about food biotechnology*. North Carolina Cooperative Extension Service, Raleigh, NC.

Holland, A., 1995. Artificial lives: philosophical dimensions of farm animal biotechnology. *In:* Mepham, T.B., Tucker, G.A. and Wiseman, J. eds. *Issues in agricultural bioethics*. Nottingham University Press, Nottingham, 293-306.

Holland, A. and Johnson, A., 1998. *Animal biotechnology and ethics*. Chapman and Hall, London.

Hughes, B.O., Hughes, G.S., Waddington, D., et al., 1996. Behavioural comparison of transgenic and control sheep: movement order, behaviour on pasture and in covered pens. *Animal Science,* 63 (1), 91-101.

Jaenisch, R. and Wilmut, I., 2001. Don't clone humans! *Science,* 291 (5513), 2552.

Jennings, M. and Miller, J., 2000. Harmonizing IACUC practices. *In:* Balls, M., Van Zeller, A.-M. and Halder, M.E. eds. *Progress in the reduction, refinement and replacement of animal experimentation*. Elsevier Science, Amsterdam, 1705-1711. Developments in Animal and Veterinary Sciences no. 31.

Keulartz, J., Korthals, M., Schermer, M., et al., 2002. Ethics in a technological culture. *In:* Keulartz, J., Korthals, M., Schermer, M., et al. eds. *Pragmatist ethics for a technological culture*. Kluwer Academic Publishers, Dordrecht, 3-21. The International Library of Environmental, Agricultural and Food Ethics no. 3.

Kunkel, H.O., 2000. *Human issues in animal agriculture*. Texas A&M University Press, College Station.

Lanza, R.P., Cibelli, J.B., Faber, D., et al., 2001. Cloned cattle can be healthy and normal. *Science,* 294 (5548), 1893-1894.

Lekan, T., 2003. *Making morality: pragmatist reconstruction in ethical theory*. Vanderbilt University Press, Nashville.

Linzey, A., 1990. Human and animal slavery: a theological critique of genetic engineering. *In:* Wheale, P. and McNally, R. eds. *The bio-revolution: cornucopia or pandora's box*. Pluto Press, London, 175-188.

Marie, M., Edwards, S., Von Vorell, E., et al., 2003. *Animal bioethics courses in Europe: state of the art*, Paper presented at the IVth EurSafe Congress, Toulouse, 20-22 March.

McDonald, J.F. (ed.) 1991. *Agricultural biotechnology at the crossroads: biological, social and institutional concerns*. National Agricultural Biotechnology Council, Ithaca. NABC Report no. 3.

Mepham, T.B., Combes, R.D., Balls, M., et al., 1999. The use of transgenic animals in the European union: the report and recommendations of ECVAM workshop 28. *Alternatives to Laboratory Animals,* 27 (1 Suppl.), 21-43.

Mepham, T.B. and Crilly, R.E., 1999. Bioethical issues in the generation and use of transgenic farm animals. *Alternatives to Laboratory Animals,* 27 (1 Suppl.), 847-855.

Ministry of Agriculture, Fisheries and Food, 1993. *Report of the Committee on the Ethics of Genetic Modification and Food Use (the Polkinghorne Committee report)*. HMSO, London.

National Research Council NRC, 1996. *Guide for the care and use of laboratory animals*. National Academy Press, Washington DC. [http://www.nap.edu/readingroom/books/labrats/]

National Research Council NRC, 2002. *Animal biotechnology: science based concerns*. National Academy Press, Washington DC. [http://www.nap.edu/books/0309084393/html/]

Office of Laboratory Animal Welfare OLAW, 2002. *Institutional Animal Care and Use Committee guidebook*. 2nd edn. National Institutes of Health, Bethesda. [http://grants.nih.gov/grants/olaw/GuideBook.pdf]

Orlans, F.B., 1990. Policy issues in the use of animals in research, testing and experimentation. *Hastings Center Report,* 20 (3 Suppl.), 25-30.

Rifkin, J., 1995. Farm animals and the biotechnology revolution. *In:* Wheale, P. and McNally, R. eds. *Animal genetic engineering: of pigs, oncomice and men*. Pluto Press, London, 19-38.

Rollin, B.E., 1986. The Frankenstein thing. *In:* Evans, J.W. and Hollaender, A. eds. *Genetic engineering of animals: an agricultural perspective*. Plenum, New York, 285-298. Basic Life Sciences no. 37.

Rollin, B.E., 1989. *The unheeded cry: animal consciousness, animal pain and science*. Oxford University Press, Oxford.

Rollin, B.E., 1995. *The Frankenstein syndrome: ethical and social issues in the genetic engineering of animals*. Cambridge University Press, Cambridge.

Rowan, A.N., 1990. Ethical review and the animal care and use committee. *Hastings Center Report,* 20 (3 Suppl.), 19-24.

Russell, W.M.S. and Burch, R.L., 1959. *Principles of humane experimental technique*. Metheun, London.

Russow, L.M., 1999. Bioethics, animal research and ethical theory. *The ILAR Journal,* 40 (1), 15-21.

Ryder, R., 1995. Animal genetic engineering and human progress. *In:* Wheale, P. and McNally, R. eds. *Animal genetic engineering: of pigs, oncomice and men*, Vol. 1-16. Pluto Press, London.

Sandøe, P., Nielsen, B.L., Christensen, L.G., et al., 1999. Staying good while playing God: the ethics of breeding farm animals. *Animal Welfare,* 8 (4), 313-328.

Sparks, P., Shepherd, R. and Frewer, L.J., 1995. Assessing and structuring attitudes towards the use of gene technology in food production: the role of perceived ethical obligation. *Basic and Applied Social Psychology,* 16 (3), 267-285.

Thompson, P.B., 1997. Science policy and moral purity: the case of animal biotechnology. *Agriculture and Human Values,* 14 (1), 11-27.

Thompson, P.B., 1998. Report of the NABC ad-hoc committee on ethics. *Journal of Agricultural and Environmental Ethics,* 10 (2), 105-125.

Thompson, P.B., 1999. Ethical issues in livestock cloning. *Journal of Agricultural and Environmental Ethics,* 11 (3), 197-217.

Van Reenen, C.G. and Blokhuis, H.J., 1993. Investigating welfare of dairy calves involved in genetic modification: problems and perspectives. *Livestock Production Science,* 36 (1), 81-90.

Van Reenen, C.G. and Blokhuis, H.J., 1997. Evaluation of welfare of transgenic farm animals: lessons from a case study in cattle. *In:* Nilsson, A. ed. *Transgenic animals and food production: proceedings from an international workshop in Stockholm, May 1997*. Royal Swedish Academy of Agriculture and Forestry, Stockholm, 99-106.

Verhoog, H., 1992. The concept of intrinsic value and transgenic animals. *Journal of Agricultural and Environmental Ethics,* 5 (2), 147-160.