

# **The Welfare of Transgenic Animals**

**Notes from workshops held in Sydney and Melbourne  
on 28 and 30 November, 2001**

*This project was assisted with funding from the Animal Welfare  
Committee, National Health and Medical Research Council*

## **ANZCCART workshops on *The welfare of transgenic animals***

The Board of ANZCCART decided to hold these workshops in recognition of growing interest in and concern for the welfare of transgenic animals. This is of particular concern to members of animal ethics committees (AECs), who are charged with the responsibility of approving, modifying or rejecting applications from scientists to use animals for research purposes. This involves an assessment of the costs and benefits associated with the proposed procedure. Costs include compromised animal welfare, either as a direct result of the procedure or sometimes indirectly, for example deleterious physical expressions of genetic manipulation.

The workshop was held in Sydney (at the University of NSW) on 28 November and in Melbourne (at the Victorian College of Pharmacy, Monash University) on 30 November. The program was the same for each workshop, but some speakers only gave their paper at one venue.

The workshops were sponsored by the Animal Welfare Committee of the NHMRC. Each was well attended, with a total of 110 persons attending the two workshops.

Robert Baker  
22 February, 2002

### **Program**

#### **Opening and welcome by Dr Robert Baker, Director, ANZCCART**

#### **Transgenic animal production – what are the ethical issues?**

Dr Miranda Gott – NSW National Parks and Wildlife Service - For both workshops

#### **Welfare of transgenic animals – what are the problems?**

Dr Denise Noonan (Monash University) - For both workshops

#### **The animal rights perspective.**

Sydney - Mr Keith Edwards, Animals Australia  
Melbourne – Ms Glenys Oogjes, Animals Australia

#### **An AEC lay member's perspective**

Sydney - Ms Jane Burns  
Melbourne - Ms Patricia Baitz

#### **How to measure animal welfare?**

(3 x 10 minute papers, each with 5 minutes discussion)

#### **A scientist's view, including phenotype analysis of transgenic animals**

Sydney - Dr Rosemary Sutton  
Melbourne- Dr Alan Harris

#### **How to measure welfare of transgenic laboratory animals.**

Dr Alana Mitchell - -For both workshops.

#### **How to measure welfare of transgenic farm animals, including the use of an audit tool.**

Dr John Barnett (VIAS) for both workshops

#### **Legislative control (State and Federal)**

Sydney – A/Professor Margaret Rose (Animal Research Review Panel, NSW Agriculture)  
Melbourne – Dr Jane Conole (Animal Welfare Bureau, Victorian Department of Natural Resources)

#### **Summary of workshop**

Dr Robert Baker (ANZCCART)

# Ethical issues about transgenic animal production

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This paper examines questions of where ethical issues about transgenic animals stem from, how we make ethical decisions, and whether ethical issues concerning transgenic animal production are different from those in the production of non-transgenic animals. It examines one example of an application of a utilitarian approach to making decisions about transgenic animals, and some of the many ethical questions arising from the consequences of transgenesis.

## **Sources of ethical issues**

Ethical issues associated with genetically modified animals are sometimes discussed as though they are synonymous with welfare issues, although they arise from many sources, primarily:

- Our views and beliefs about animals and nature, and the relationship of animals with human beings.
- The demonstrable and possible consequences of producing and using transgenic animals, including those related to animal welfare, ecology and the environment, economic and social factors, and human health.

## **A generalised framework for making ethical decisions**

As scientists, welfarists, members of Animal Ethics Committees, and members of the broader community, how do we weigh ethical issues about the use of animals? Most people take an approach that philosophers might describe as “preference utilitarianism”. Simply, we examine the relative weight of benefits that will be gained by a particular use of an animal compared to harm that will be done by that use, but tempered by the level of consciousness that we ascribe to the species, and the level of empathy that we feel for it. Our decision making process often includes “intrinsic” objections to certain uses, uses that are objectionable of themselves, irrespective of the weight of benefit that might arise from the use. Intrinsic objections lie at the heart of much opposition about the creation and use of transgenic animals.

That kind of approach is quite appealing as a means of making practical decisions about the use of animals because a cost-benefit analysis is the system we use to make many everyday decisions, and because by bringing empathy into the decision, we are more likely to arrive at a conclusion with which we feel emotionally comfortable. A number of writers in the field have proposed that, just as a decision based purely on emotion is not able to be morally defended, so any ethical stance based exclusively on logic and reason is likely to fail the test of application to real-life situations. Other disagree, stating instead the view that moral decisions about the acceptability of genetic engineering should be made solely on “a rational and considered basis” (Reiss and Straughan, 1996 p.45).

Broadly speaking, the application of this approach to a range of situations delivers three types of outcomes:

- Some uses are generally acceptable, often because their costs (usually welfare, health and environmental) are perceived as negligible.
- Some uses are acceptable only where the benefits are sufficiently great and outweigh any perceived costs.
- Some uses are intrinsically unacceptable, irrespective of the magnitude of benefits or costs.
- Intrinsic objections to transgenic animals are underpinned by a range of social and personal beliefs:
- *Religious teachings about the place of humans in nature and in relation to a creation deity.* Most religions have something to say about the place of humans relative to other life forms, whether it be one of human dominion over animals, an ethos of stewardship, or explicit instruction about avoidance of association with certain animals. Transgenesis challenges those teachings, and is seen to place humans in the position of ‘playing God’ by creating new life forms or tinkering with the blueprints of life forms.
- *Personal beliefs about respect and consideration owed to other life forms.* These beliefs are often explained in terms of views about the sentience of other life forms, their aesthetic appeal, ecological value, or wonderment at their biological complexity.
- *Concepts of the “natural” or acceptable in nature.* This often may be expressed in terms of a religious belief, evolutionary process, or ecological dependency. Transgenesis is often perceived as involving the creation of life forms by means not found in nature.
- *Concepts of species barriers.* Beliefs in barriers between species, in particular between humans and other species, are deeply ingrained and common to most cultures, irrespective of how we view humans in relation to other life forms or our personal beliefs about the consideration owed to other life forms. The ‘otherness’

of other forms of life is an awareness formed in early childhood. In common belief, species are defined in terms of breeding barriers, and transgenesis is seen as breaching those barriers.

- *The economic nexus – “patenting and ownership of life”*. The commonly-held belief that patenting and ownership of transgenic life forms is wrong seems at odds with the general acceptance of the ownership of non-transgenic life forms (livestock, pets, strains of plants). The apparent contradiction may be explained in terms of a more subtle view of the human-animal relationship, and a belief in the existence of a ‘natural purpose’ for animals. Ownership of non-transgenic life-forms may be seen as a relationship based on stewardship or custodial responsibility, whereas the patenting of transgenic life forms is seen to subvert human obligations inferred in that traditional relationship, and implies no natural purpose for the organism other than a human-defined one.

#### ***How important are intrinsic ethical objections?***

Several surveys of public opinion about biotechnology have identified moral or ethical factors as contributing to opposition to genetic manipulation (see review in Hamstra, 1998). Although surveys such as one from the UK in 1985 found that 70% of respondents thought genetic engineering was ‘morally wrong’ (Reiss and Straughan, 1996), later surveys suggest that public attitudes are based on quite complex and subtle calculations of cost, benefit and ethical considerations, such that the level and nature of intrinsic objections is more difficult to pinpoint.

Identification of intrinsic objections which could contribute to public policy and regulation of genetic engineering is not without problems. Intrinsic objections are based heavily on beliefs rooted in personal experience, hence identifying a set of widely acceptable intrinsic objections that could be applied in a consistent manner is likely to be difficult.

Proponents of genetic engineering sometimes don’t take intrinsic ethical objections with a great deal of seriousness, assuming that any opposition that does not focus on welfare or health or environmental concerns is simply an emotional reaction to the introduction of a new technology that is without any kind of rational basis, and can be expected to disappear as people become accustomed to the new technology (Banner report 1995). Nevertheless, it’s quite clear that some intrinsic ethical objections are strongly held, and can’t be remedied by addressing welfare or environmental concerns, or by appeals to logic, or by examples which demonstrate some inconsistency of reasoning, or by promises of vast benefits that genetic engineering may bring at some time in the future.

#### ***An application of a utilitarian ethical approach to transgenic animals: The Banner report***

In 1995, the UK’s Ministry of Agriculture Fisheries and Food delivered a seminal report about the ethical implications of emerging technologies, including genetic modification, on the breeding of farm animals. Commonly referred to as the Banner report, it articulated three principles for animal use (p. 8):

- “Harm of a certain degree and kind ought under no circumstances to be inflicted on an animal.
- “Any harm to an animal, even if not absolutely impermissible, nonetheless requires justification and must be outweighed by the good which is realistically sought.
- “Any harm which is justified by the second principle ought, however, to be minimised as far as is reasonably possible.”

The Banner report regarded intrinsic objections seriously and didn’t take the view that, simply because those views were often expressed with some degree of emotion, that they were irrational or invalid. It also took the view that an assessment of ethical matters simply on the basis of a cost-benefit analysis, without acknowledgment of the intrinsic objectionableness of some actions, is not acceptable to the majority of the community, nor is it a good basis for public policy. Cost-benefit analysis could not be the sole test of ethical acceptability, it said.

The Banner report summarised the range of intrinsic ethical objections as arising from a belief that some use of animals:

“...involves an essentially improper attitude towards them, expressing, in effect, the view that animals are no more than the raw materials for our scientific projects or agricultural endeavours...” Such an attitude “fails to take account of the fact that the natural world in general, and animals in particular, are worthy of our respect as possessing an integrity or good of their own, which we ought not simply to disregard.” (p. 12)

The Banner report took the view that transgenesis was not intrinsically objectionable, but some of its applications could be. Whether the nature of the genetic modification involved the transfer of genetic material between species, or simply modification within a species' genome, was irrelevant to its ethical acceptability.

Using these principles, the Banner report divided the use of emerging technologies on animals into three categories:

- *Uses which are generally acceptable within the requirement for minimization of harm* included techniques such as embryo transfer, that can be used in the development of transgenic animals.
- *Uses which are justified only in particular circumstances where substantial good is expected* included the use of animals for xenotransplantation (animals raised for the transplantation of bodily organs into humans), currently viewed as a use of transgenic animal production that will be achievable in the near future.
- *Uses which were identified as intrinsically objectionable* included genetic modification of a type which "can be thought to constitute an attack on the animal's essential nature".

The concept of an essential nature is not new, being similar to the Aristotelian concept of telos, the end state or goal of an animal, and the basis of arguments put forward by modern-day ethicists such as Holmes Rolston and Michael Fox. Its critics argue that the concept of an essential nature is useless as the basis for an ethical system because it is not practically possible to draw up a set of rules which objectively defines the essential nature of a cow or pig or chicken.

Rather than trying to provide rules about what constitutes an attack on essential nature, the Banner report (pp.14-15) cited three hypothetical examples to illustrate their view of what was, and was not, acceptable:

- *Genetic modification that increases the protein content of cows milk.* The Banner report took the view that this kind of modification "seeks to enhance a particularly desirable trait...does not affect the animal's defining characteristic, nor threaten the achievement of its natural ends or good...but respects its essential nature and well-being."
- *Genetic modification that causes poultry breeding stock to produce only female chicks.* The Banner report took the view that this kind of modification "would not deprive the chicken of the freedom to express normal behaviours", although acknowledged that it is more radical in the sense that the end result may not be argued to be a straight-forward enhancement of a particularly desirable existing trait.
- *Genetic modification that decreases the sentience and responsiveness of pigs, thus making them more sedentary and quicker to put on weight.* The Banner report took the view that this kind of modification, irrespective of any benefit to profit margins, is ethically objectionable because the human ends and purposes override the ends and purposes which are natural to the animal, and is an attack on the animal's essential nature.

***"Transgenic animal production is no different from conventional breeding methods"***

The proposition is often put that transgenic animal production is indistinguishable from traditional breeding methods, and since the traditional breeding methods are ethically acceptable, so is transgenic animal use.

Transgenic animal production can be both qualitatively and quantitatively different from animals bred by traditional methods. Transgenic animals can be made to display novel characteristics which cannot be achieved by traditional breeding and treatment methods, and so can be used for some entirely new purposes, and for a wider range of existing purposes (such as acting as medical models for a wider range of conditions).

Transgenesis also enables us to expand uses to which we can put animals at a far more rapid rate than does conventional breeding methods. It is different, even if the nature of the difference is primarily the rate of change which is made possible. Irrespective of whether the nature of that difference between particular transgenic and non-transgenic methods is more one of rate of change made possible rather than qualitative change, it does not follow that there are no ethical differences - just that perhaps the ethical boundaries are difficult to define.

Bruce and Bruce (1998) discuss the ethical trap of gradualism: because there is general acceptance of the fact that humans have used pigs for meat for millennia, and more recently for medical uses such as skin and heart valve transplants, therefore there is no ethical difference between those uses and xenotransplantation. To accept that view is to assume that we condone all use of animals, or any use for which there is some human benefit, simply because we condone some uses.

It doesn't follow that our acceptance of a current practice implies or requires that we accept a similar practice – sometimes it just forces us to reassess our acceptance of the current practice. So an outcome of deeper consideration of the ethics of genetically modified animals may be a reassessment of our ethical acceptance of non-transgenic current farming and breeding practices.

Transgenic animals are certainly different from non-transgenic animals in that it is much harder to *make ethical decisions* about their use, and this is a very real problem for regulatory groups as well as the public. Leaving aside the question of which intrinsic objections should contribute to regulation, the main problem is that the level of uncertainty around both costs and benefits is so much higher for genetically modified animals. It is that much harder to predict the nature of undesirable outcomes, and to estimate the probability of achieving an outcome, whether undesirable or those which might be the objective of the work. It is also much easier to produce extreme and unforeseen outcomes.

This uncertainty is principally due to genetic engineering being a leading-edge technology that we understand imperfectly, and our attempts to manipulate genes towards particular outcomes are, to a large extent, experimental. Secondly, the technology has evolved more rapidly than our capacity to regulate it, and has been driven in part by commercial interests, both which may have resulted in some lack of access to information that would allow those risks and benefits to be evaluated more accurately.

### ***Ethical issues derived from consequences***

Many ethical questions arise from the consequences (animal welfare, environmental, human health, social and economic) of the development and use of transgenic animals. Some commonly voiced concerns are presented here, with examples of their origins.

*Is it ethical to use transgenic animals where the purpose of that genetic modification means that disease or disability or environmental degradation will be inevitable?* The often-cited example is that of oncomice, mice genetically modified to inevitably develop cancers. A second example is the Australian proposal to release transgenic bacteria which will make ruminant stock animals more immune to the poisonous effects of fluoroacetate. This proposal was rejected by the Genetic Manipulation Advisory Committee after widespread criticism on environmental grounds. The genetic modification would have enabled livestock grazing to be expanded and intensified in areas of native vegetation which was previously protected by its naturally high levels of fluoroacetate, with probable effects on the conservation of native fauna and flora. The high risk of spread to feral ruminant populations was also of concern.

*Is it ethical to establish transgenic animal lines where there is much greater “wastage” of animals?* Some sources of wastage include low success rates of current techniques to create novel lines of transgenic animals (often cited at 2% or less), and inherent phenotypic instability that requires culling of variant animals in order to keep the transgenic line “pure”. A third source may be variable demand for a wide range of animal lines, placing pressure on businesses that supply animals to manage their stock animals in ways which increase economic efficiencies but require more culling.

*Is it ethical to use transgenesis to address welfare concerns and downgrade conditions of care?* Transgenesis is often cited as having the potential to reduce welfare problems in animal production, in particular reducing disease susceptibility. However, it could be argued that (using the example from the Banner report), the transgenic pig that has been modified to have decreased sentience and responsiveness is less likely to experience suffering from its condition, and hence that the genetic modification produces a net welfare benefit for the individual. Taken one step further, the view could be taken that such a pig would be equally content in a smaller enclosure than those given to its non-transgenic pigs.

If it were possible to produce a transgenic chicken that was less aggressive, based on an argument that it would reduce the need for practices such as de-beaking, would that be ethical? The issue would have to be weighed against the question of whether there are other ways to reduce pecking that don't involve a genetic modification – ways such as larger and better designed housing and avoidance opportunities.

*Is it ethical to develop transgenic animals where benefits are not primarily for health, welfare or environment?* For example, are economic efficiencies, human comfort (such as baldness cures or pets with novel characteristics), or scientific curiosity and public acclaim (such as the much-publicised plan by the Australian Museum to clone the Tasmanian tiger) sufficiently ethical reasons to develop transgenic animals?

### ***Do we need some transgenic applications?***

Discussion of pros and cons of particular transgenic proposals is sometimes played out without much consideration of the *need* for some transgenic applications. There seems to be an assumption that, risk factors providing no barrier, the “market” for transgenic animals should be the primary determinant of what new transgenic animals should be developed. However, the question of need may be quite strong in the public mind. It may explain the apparently greater acceptance of transgenic animals for medical uses than for food production which is evident in some surveys (see Hamstra, 1998).

The public is quite ready to ask questions such as: “Why do I need transgenic cows which have higher-protein milk when I already have a protein-rich western diet?” and “Why do I need a transgenic pig which produces meat at a lower cost when non-transgenic bacon is only \$7 per kilo?” The question of need has not been seriously considered in public debate, nor addressed by proponents of biotechnology.

### **Conclusion**

Ethical concerns about transgenic animal use stems from both intrinsic objections, and the purpose and consequences of transgenic animal production. Intrinsic objections won't disappear from public belief or public policy simply because they might be emotionally expressed or viewed as difficult to apply in a consistent manner.

The use of transgenesis to improve animal welfare outcomes should not be assumed to be a preferable alternative to developing, exploring and implementing better practices in the way animals are housed and treated.

It doesn't necessarily follow that because we accept some uses of animals, we accept all uses, or that our acceptance of current practices about non-transgenic animals implies or requires that we accept a similar practice for non-transgenic animals. Considering whether transgenic animal production is ethically similar to non-transgenic animal production suggests that both forms deserve deeper ethical consideration, preferably as a whole rather than separately.

### **References:**

- Banner report (1995). *Report of the Committee to Consider the Ethical Implications of Emerging Technologies in the Breeding of Farm Animals*. UK Ministry of Agriculture, Fisheries and Food.
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- Reiss, M.J. and Straughan, R. (1996). *Improving Nature? The science and ethics of genetic engineering*. (Cambridge University Press, Cambridge.)

# The welfare of transgenic animals – what are the problems?

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These notes are a summary only of the presentation given in Sydney and Melbourne by Dr Noonan.

## ***Why is genetic manipulation undertaken?***

- as a result of the biotechnology revolution;
- for economic reasons;
  - e.g. to increase productivity
  - to reduce costs
  - because of the availability of venture capital
  - because it has the potential to solve difficult problems.

## **Benefits for humans**

- new knowledge about the function of genes;
- new knowledge about control of cell differentiation;
- development and ageing;
- new knowledge
  - about organ transplantation
  - better animal models of human genetic diseases (e.g. by gene deletion)
  - about organ transplantation
- better animal models of human physiology: animals with human genes, cells and tissues
- tissue engineering; repair and replacement of organs
- xenotransplantation;
- stem cell technology
- animal products
  - pharmaceuticals
  - neutraceuticals
- safer products
- more efficient animal production
- cheaper products
- preservation of rare and elite genes (insurance against loss of an individual animal or a breed/population);
- more livestock with elite genes.

## **Benefits for animals**

- increased innate disease resistance;
- new health products (vaccines, pharmaceuticals, neutraceuticals);
- safer products
- better nutrition/greater ability to utilize food;
- conservation of endangered species (preservation of genetic variability of a population).

## **Animal welfare concerns**

### ***Potential for pain and suffering***

- outcome uncertain: imperfect control of genetic manipulation;
- micro-injection methods = less control;
- homologous recombination = more control.



### ***Large numbers of animals are needed to create genetically modified animals***

- donors of cells, tissues
- recipients/surrogate mothers;
- success rate low;
- many “unwanted” animals are created that lack the genetic modification.

### ***Potential for pain and suffering: problems caused by embryo manipulations***

- late gestation foetal deaths;
- oversized offspring;
- deaths of embryos;
- birth problems;
- malformation;
- phenotype not “normal” and may reduce chances of survival;
- slow to reach developmental milestones;
- behaviour may be abnormal or different (e.g. feeding, activity);
- effects on fertility, reproduction and ability to rear offspring;
- animal models of human genetic disease (e.g. cystic fibrosis);
- increase in productivity increases risk of “production-related” disease (e.g., mastitis in dairy cattle; leg weakness in poultry);
- increased level of animal care and attention may be required;
- risks of loss of genetic diversity and genetic “fitness” of a breed or species may lead to a reduced capacity for species survival (e.g., due to reduced lifespan – “aged DNA”).

### **References**

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*Innovation, ethics and animal welfare: public confidence in science and agriculture*. Proceedings of the joint AWAC/ANZCCART Conference held in Wellington, New Zealand, 18-19 November, 1999. ANZCCART, 2000.

*Farm Animals in Research – can we meet the demands of ethics, welfare, science and industry?* Proceedings of the Conference held at University of Adelaide, 30 November-1 December, 2000. ANZCCART 2001.

## The animal rights perspective

Glenys Oogjes and  
Keith Edwards  
Animals Australia

We treat humans differently from the way we treat all other species – we do things to non humans that we can't or won't do to humans. We have constructed a barrier around ourselves saying we are different, and that we can justify our actions towards other species. In terms of research, testing and teaching we have institutionalised this through legislation and through the establishment of separate ethics committees for experimentation with humans and non humans.

The difference between humans and non humans is generally regarded as being clearly defined. However, animal rights people and others question the construct that we have made. They ask is the barrier that we have constructed around our species so clear?

Consider the approach that has been adopted in New Zealand in relation to experimentation with the 'great apes':

The NZ Animal Welfare Act (1999), in a section dealing with *Restrictions on use of non-human hominids*, both the Director General of the Agriculture Department and the National Animal Ethics Committee are given an overview role before any research on these particular animals can be accepted. The Act then is very clear that permission to use a great ape for research should and would only be permitted if:

- (a) the use of the non-human hominid in the research, testing, or teaching is in the best interests of the non-human hominid; or
- (b) the use of the non-human hominid in the research, testing or teaching is in the interests of the species to which the non-human hominid belongs and that the benefits to be derived from the use of the non-human hominid in the research, testing, or teaching are not outweighed by the likely harm to the non-human hominid.

There are then strong powers and obligations upon the Director General in the Act to withdraw permission if he/she believes that the activity is **no longer** in the best interests' of the non-human hominid itself, or the species, or the benefits are then seen to be outweighed by the likely harm to the great ape.

Professor David Penny of Massey University makes the point that the law will not prohibit all experiments– just those that are not in the best interests of the apes. He suggest that in this respect, the legislation comes very close to protocols used in experiments with human children (*ANZCCART News* Sept 99 12(3) 3-4)

***So perhaps, the distinction between our treatment of humans and non humans is not now so clear.***

What if we replaced the word 'hominid' with the word 'animal'. We would now have a clear view of what the animal rights view would be for all animals.

***With that background, you should start to get an idea of where we are coming from in terms of our view of the use of transgenesis. While the membership of Animals Australia is diverse, it agrees on the following approach to all animal research:***

*Animals Australia/ANZFAS is opposed to animal experimentation and calls for its abolition. Change is overdue. Animals should not be viewed as mere tools for research and education. A commitment by governments, research and educational institutions and the community is required to bring about a radical change in methodology in research and teaching to reduce and subsequently eliminate the use of animals in these areas.(Extract from Animals Australia/ANZFAS Policy.)*

Our primary concern, the reason for the policy, is that the use of non-human animals is unethical. Put simply we believe it is unfair and unwarranted to have animals bred and used for a purpose that does not benefit **them**. Most animal based research, particularly medical research, is aimed at assisting humans not the animals on whom the research is done. Most work with agricultural animals is, at best, aimed at the maintaining or improving the health of the species, but almost invariably related to increasing production and thus the viability of further exploitation of the species. And of course there is no question of consent being given. You cannot ask a non-human animal (except a few great apes with sign language) whether they

consent. But it is clear that if and when it means any suffering, dislocation from con-specifics, or particularly impending death, they would say 'no thanks'.

A further reason for opposition to animal research put up by other groups is that it is 'unscientific'; meaning that animal research may tell us a lot about the individual or the species being studied, but it cannot reliably be extrapolated to humans. This is an important and fundamental consideration. However, we see it as merely adding to the ethical basis of our opposition because even if a particular experiment was seen to directly provide an insight into a human or other species problem, but it adversely affects an animal's life, it would still be ethically wrong.

While *Animals Australia* has been engaged in the debate about animal ethics committees and the quest for better conditions for animals and animal welfare concerns in general, and for greater emphasis on non-animal alternatives, it should not be forgotten that our fundamental position is an animal rights perspective, rather than an animal welfare perspective. It is within this framework that we consider the rapidly growing use of transgenesis (the production of transgenic animals used in research, for agricultural production reasons and for human health work, xenotransplantation).

### Particular issues

- **Reinforcing concept of animals as tools** The development of transgenic lines of animals further promotes the concept of these animals simply being tools for use in achieving a desired outcome rather than recognizing them as individual sentient beings. The ability to patent these lines further reduces the level of concern for these animals.
- **Impacts on animals.** The processes involved in the development of transgenic lines of both laboratory and farm animals potentially have major impacts on the animals involved. Particular areas where problems can occur are in the experimental processes related to the in vitro production and transfer of embryos and during the gestation and birth of manipulated animals. In farm animals, compared with artificial insemination, procedures used before and after the actual microinjection e.g., in vitro culture and embryo transfer) may lengthen gestation, increase birth weight, and cause higher incidences of calving difficulties and perinatal loss.
- **The high risks of modifying genes.** While modification of the genome is high technology, it can lead to unexpected results. At the Pest Animal Control CRC they tampered with the mouse pox virus (a relatively low grade disease for most mice) in order to see if they could interfere with reproduction (stop fertilisation of the ova, thus lead to reduction in mouse plagues, in theory). In doing so the modified mouse pox virus overwhelmed all the natural resistance mechanisms to mouse pox, even in those mice previously immunised (a 50% reduction in efficacy) and genetically immune, and killed most infected mice. That is, they inadvertently produced a killer disease from a low-grade, but easily transmitted, one. Imagine this technology in the hands of terrorists or careless scientists!
- **Increased numbers of animals.** While it is argued that the use of transgenic animals in research may result in the use of fewer animals, in the short term at least the numbers will be greater. The potential for increased animal use is two-fold: 1) the extra numbers involved in developing the strain, and then 'breeding it up', mean more animals are likely to be needed just so that some transgenic animals will be actually used in research, and 2) there is a commonly expressed desire to keep that breeding line in existence. The temptation is to keep breeding the line just in case it might be needed for experimental purposes rather than freezing down embryos for future possible use. Both these aspects fly in the face of the national *Australian Code of Practice for the Care and Use of Animals for Scientific Purposes* (1997) principle of reducing the number of animals used in research (Reduction).
- **Production of spare parts.** Transgenic animals, especially pigs, carrying a human gene have been developed to overcome the chronic shortage of organs available for transplantation into humans. The potential risks to humans of the introduction of viruses from the source animals is well documented and it seems less likely that non human primates will be used a source of tissues or organs, not because of any concern for the non human primates but because of increased risks of transmitting simian pathogens to humans.
- **Consent.** Fancy calling pigs and baboons 'donor' animals! They may be the 'source' animals, but they certainly did not give informed consent to have their organs snatched ('harvested') and die so that an individual of another species could have their lives extended.

- **Public debate/approval.** Animal rights activists abhor such activities. Perhaps the broader community does too. Have they been asked; have we had a proper debate? Who says that monies going into this research may not be better placed encouraging/educating/promoting prevention of some diseases through lifestyle choices, or through a much greater acceptance and availability of human organs.
- **Not the best way to go.** In any event – related to xenotransplantation – are we all being ‘fed a line’ that it is imminent. 25% of human heart transplant patients die within 12 months, and 50% of those who receive a human lung die before 2 years (Ref: From a report by Dr Gill Langley and Joyce d’Silva, published by BUAV and CIWF called *Animal Organs in Humans: Uncalculated Risks and Unanswered Questions* October 1998, ISBN 1 870356 21 7). So why are we being told that pig and baboon organs are the way to go? Disease prevention and artificial organs are likely to be better bets.
- **Gene-pharming** or the production of drugs or other pharmaceutically active compounds in non human animals by adding human genes, so that animals secrete proteins for use with diseased humans is another source of concern. It is seen as just another, but unwelcome, extension of current farming of non human animals for the purposes of producing food, fibre or products such as aphrodisiacs (deer velvet).
- **The ecological aspects of transgenic animal production are of concern.** Animals can and will escape and may cross breed with wild animals. There is a real need for risk analysis for the escape of transgenic animals. What is the risk of escape, what is the risk of such an animal surviving post escape, is there a wild population of the species with which the escapees can breed and what are the potential risks of the new gene once incorporated in the wild populations? In Australia there are free living populations of pigs and goats and most importantly there are free living populations of fish. Transgenic fish farmed in pens may readily escape to breed with wild populations with an unknown resultant effect on these wild populations.
- One up-side might be that because the transgenic animals are more valuable, then they might be better cared for as we seem to care for non human animals in proportion to their value to us. Of course this may come at the expense of a more ‘free’ lifestyle.

#### **Where is the boundary between transgenes and humans?**

An interesting question in the context of this workshop is whether growth in the use of transgenic animals further breaks down the wall separating us from other species? While at the moment the proportion of the human genome being inserted into the genome of nonhumans is minuscule, at what stage will we start ascribing to transgenic animals carrying human genes, the same values we ascribe to humans?

To digress slightly - remember in George Orwell’s *Animal Farm* when, after the revolution and the non human animals had taken over the farm, there had subsequently been a reconciliation between the pigs and the humans and the humans had returned to the farm and were celebrating with the pigs in the farm house.

The other animals had gone up to the window of the farm house and were looking in, wondering what was going on and

“as the animals outside gazed at the scene, it seemed to them that something strange was happening. What was it that had altered the faces of the pigs? ... Some of them had five chins, some had four, some had three. But what was it that seemed to be melting and changing.”

After watching for a while longer, they realised

No question, now, what had happened to the faces of the pigs. The creatures outside looked from pig to man, and from man to pig, and from pig to man again: but already it was impossible to say which was which.” George Orwell, *Animal Farm*, 1945.

So there we have it: Now we can alter an animal’s genes to make the animal more like us, yet we still reject the other ways in which the animal is already like us.

When will we reach the point that all sentient beings have the right to be treated in a considerate manner, not because they look alike but because we recognise that they all have qualities which demand that we take equal consideration of their interests into account in our dealings with them?

## The welfare of transgenic animals – An AEC lay member's perspective

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Lay members or Category D members on Animal Ethics Committees, as I was told in 1996 I think it was when I was approached as a possible new member, are chosen on the general rule of thumb that they enjoy listening to *The Science Show* on the radio or watching *Quantum* or *Catalyst* on television. Lay members therefore do not have the unifying characteristics of Categories A and B members in veterinary science or medicine, or Category C members in animal welfare. Category D members are as varied as the proverbial person in the street whom in fact they represent.

My background is in the arts, as an administrator rather than as an arts practitioner, but my years of experience in this field have shown me that there could be similarities between science and the arts in attempts to bring along the members of the general public to understand what is going on and also to dispel misconceptions, or apathy, which may be worse.

I have been and am still somewhat complacent about my ignorance of complex scientific data, but complacent only because I am confident in the knowledge and high ethical standing of my Committee colleagues in Categories A, B, and C. I know that they will answer any questions I could pose or explain in terms I can understand. It has been my experience that all the science-based and animal welfare based people on the Committee seem to be good teachers and also have the capacity to be inclusive in discussions on protocols. They are faced with the layperson on the Committee as an obligatory given. Its not a matter of choice for them, but it seems to me that apart from the benefit to everyone on the Committee in having the protocols explained in language the layperson can understand, maybe the presence of the Category D members is a constant reminder of the majority of the population out there who need to be 'brought along,' so to speak, in an everyday knowledge of contemporary science.

Category D is described in the *Australian Code of Practice for the Care and Use of Animals for Scientific Purposes* as "an independent person who does not currently and has not previously conducted scientific or teaching activities using animals". It made me wonder, not why, because I think it is laudatory and necessary for there to be a 'person of the people representative' in the loop when matters of ethics are involved, but how the good sense of those who proposed this inclusion originally prevailed. From the viewpoint of the arts I think that if it were obligatory to have a science person, with no knowledge of arts practice, as a member on the various grants and other arts committees the reaction would be that it was a waste of a committee place. The layperson on Church committees is an age old and accepted practice. Maybe science and the Church have that in common.

I am typical of those in the general public motivated to interrogate sources readily available to them on radio, TV, the Internet, the and newspapers to research a range of subjects. In this case it was transgenic animals. It made me think that perhaps the problem of scientists is not how to get information out, because there is something written every day on biotechnology but how to control what gets out, in the sense that a little knowledge can be a dangerous thing. I was surprised to find that the term transgenic animal has been around since the late 1960s or early 1970s but only since 1981 has DNA microinjection in mammals been applied to. That is only a relatively short time for the knowledge about transgenic animal technology to become known beyond the scientific community, much less for the non-scientific community to have an opinion on the ethics of such science. It might be useful for me to explain what basic facts on transgenic animals my reading has delivered to me. I can guarantee that it is more information than a straw poll of 20 of my alert and enquiring friends can muster.

- Transgenic animals are created by DNA microinjection, by embryonic stem cell-mediated gene transfer and by retrovirus-mediated gene transfer;
- embryonic stem cell mediated gene transfer is the method of choice for gene inactivation and hence the so-called "knock-out" mice;
- success rate in terms of live birth of animals containing the transgene in retro virus gene transfer is low and it is common practice to freeze and store embryos containing the transgene – I ask myself is this where the interestingly named mortal and immortal cells arise ?

- the creation of transgenic animals is allowing a shift in the use of higher order animal species to lower order species and is allowing for change in numbers of animals - which is good news;
- apart from wide ranging medical research usage, transgenic animal creation is of great interest in the pharmaceutical industry, to test products and produce drugs. To the layperson this can sound alarms that commercial controls may be not always in the public interest;
- experience in the laboratory is a requirement in industry standards for keeping transgenic animals - that signals to the layperson that there are special rules relating to student researchers and others who enter any laboratory holding transgenic animals;
- there are guidelines which scientists must follow which cover justification of the rationale for creation of the particular transgenic animal and welfare issues in the creation process; and
- bio-safety for the animal care staff and for the animals is paramount and includes special cages and special protective clothing.

My main sources for the above information are my downloading of the Guidelines from the Canadian Council on Animal Care (<http://www.ccac.ca/index.htm>) and the Monash University Animal Welfare Committee (<http://www.monash.edu.au/regrant/animal-ethics/index/htm>).

The NSW Animal Research Act 1985 No 123 and Regulations, and the Australian Code of Practice for the Care and Use of Animals for Scientific Purposes, 6<sup>th</sup> Edition, 1997 are among the documentation which all members of the UNSW AEC receive on appointment. These spell out the responsibility of the AEC in research involving genetic manipulation and the role of the National Health and Medical Research Council Animal Welfare Committee and the Genetic Manipulation Advisory Committee (since reconstituted) in Canberra from whom registrations and licenses must be obtained.

All of the above I found reassuring when I began to consider some of the issues which spring to mind when thinking about transgenic animals from a layperson's perspective.

Some of the questions were:

- (i) was the language of science necessarily arcane?
- (ii) the Guidelines on Transgenic Animals set down by the Canadian Council on Animal Care seem to have achieved the high ground on the internet. Has Australia posted similar Guidelines which I missed? How frequently do working scientists refresh their memories on the relevant parts of the Animal Research Act relating to experimental manipulation of animals' genetic material in order to pass this information on to any students in their responsibility? How much and when do graduate and undergraduate student scientists learn about animal research licenses and the Code of Practice?
- (iii) what is being done at University level, in CSIRO, or in other science bodies, specifically to inform and maybe educate the general public on issues arising from genetic engineering in animals and if the discussion and debate became general, would this impede scientific progress in an inordinate manner?
- (iv) who owns the research if Universities become too reliant on the corporate sector to fund them? What about the question of patents? How is the law weighted?
- (v) where, apart from the AEC, are lay people brought within the scope of discussion on ethics and animal research?

These are a sample of the myriad of questions that can confront a layperson who thinks about the subject of transgenic animals. They reflect my realisation, albeit late in my term as Category D member of the AEC, that I have assumed, and I am sure correctly, that there must be sufficient checks and balances in the system to assure the non-professional observer that nothing untoward should occur in animal research in Australia. Other wider questions relating to genetic manipulation that arise for those of us who view it from afar relate to where it is all leading.

Over the last couple of weeks there has been a flurry of information arising from latest research results in animal and plant gene manipulation, and newspapers have been full of discussion on the cloning of the human embryo. The distinction between creation of transgenic mice and the cloning of human embryos may be a mile apart for scientists but it is a distinction that only those in the know can make. It is perhaps the ever changing end point of genetic research that is cutting the layperson off from a reasonable comfort zone, and that should be a warning sign for scientists.

I list here are some of the pieces in the Sydney Morning Herald and on ABC Radio National that in the last month I have read or heard which will give you a taste of how prevalent the subject of this Workshop and extensions of it are becoming in the general media. It made me wonder whether there is any monitoring of this

in the scientific community and whether the prevalence of material is after all part of a master plan to inform and educate the general public. Am I right?

I read a piece in the Sydney Morning Herald on 16 October, 2001 which confirmed that a British couple had sidestepped British regulations and sought help in the USA in order that they could give birth to a baby with an immune system which matches that of their four year old son who suffers from leukaemia. The 'designer baby' is due by the end of this year.

I heard Lord Robert Winston during a recent Press Club address decrying what he called the over-hyping of genome technology which he said was like talking of the invention of the axle rather than the wheel. But as a lay person, although I find Robert Winston is enormously reassuring and straightforward, is he adequately addressing public perceptions when he plays down concerns in this area?

On 22 November, 2001 the Editorial of the *Sydney Morning Herald* stated: "The achievements of genetic research constitute one of the great successes of modern science. Some of the benefits offered by the new technology, however, challenge long-established codes of behaviour. They also present legal and ethical dilemmas involving the improper use of genetic information as it affects employment, insurance, commercial gain and government services. Clearly a balance is needed between encouraging the advances of genetic science and technology and protecting Australians from loss of privacy and unfair genetic discrimination".

The ABC Background Briefing program of 11 November was an address delivered in the UK in October this year by Professor George Monboit on Global Democracy. George Monboit is a young professor in philosophy, environmental science and politics, and a columnist for *The Guardian* newspaper. He convincingly argues that democratic governments such as Britain, the US, France and Germany are increasingly being held to ransom by corporate lawyers and non-elected bureaucrats whose strings are really being pulled by corporations. And so we get, according to George Monboit's research, genetically engineered growth hormones injected into US beef which is able to be sold according to trade regulations of the World Trade Organisation into Europe and those countries refusing to accept it are hit with trade sanctions.

On 19 November the ABC had a lead news item from the University of California on the transfer of genes from the bacterium *E.coli* to the ovarian cells of a Chinese hamster. The report was followed by a CSIRO spokesperson explaining what a break through this is and emphasising that the delivery of genes into target cells has been a major challenge. My reaction as a lay person was *Why a Chinese hamster?*

The ABC *Encounter* program on 25 November dealt with the International Meeting on Biotechnology in Salzburg in October when 60 scientists, philosophers, lawyers and medical specialists from all over the world came together to think about the ethical and legal implications of the explosion of knowledge in animal and plant genetics. As a member of the general public I found this most reassuring and also it told me about the International Bioethics Committee of UNESCO, which in January 1999 drafted the Universal Declaration on the Human Genome and Human Rights. I learned also that the Australian Health Ethics Committee and the Australian Law Reform Commission have issued a recent paper on protection of human genetic information and that there was a Gene Technology Act promulgated in Australia in 2000, and that cloning of genetic material is prohibited by law in some Australian States. These are all significant occurrences protecting the highest standards of practice and ethics in Australian science and it shocked me a bit as a member of the general public to find out about them as a supplementary piece of information from an International Conference in Salzburg.

I want to underline the vigilance which I can see as a layperson is required of scientists to be aware of and to counter where necessary the wide ranging opinion and comment which is out there on what scientists are doing in the area of genetic engineering and how the *genie out of the bottle* is impossible to control.

I can't resist the chance to return to the question of language for a moment. I wonder if science achieves the highest rate of acronym use of all language exchange. My guess is that if acronyms were not widely used scientists would have to live longer than the general population to communicate! DNA is now so widely used in everyday parlance and seems to be the key to all mysteries but I'm sure if you stopped 20 people in the street and asked what the initials DNA stood for, very few would be able to say deoxyribose nucleic acid, and I until a week or so ago I'm one of the 20 and I love crime novels dealing with forensic medicine!

I am not advocating any change in language usage by scientists except maybe an appeal for clarity of meaning, but as in cricket, or wine making, or the arts, it can't be denied that terms can develop which can sound somewhat quaint and unusual to the uninitiated. With a wry smile I draw your attention to the scientific use of the terms 'mortal' and 'immortal' cells. A lay person might think that there was fodder here for assuming

that scientists sometimes play God. By the same token the term 'knock-out method' to describe gene inactivation in embryonic stem cell mediated transfer is down to earth and self-explanatory.

In summary here are some of matters for consideration I'd like scientific researchers to consider from a layperson's perspective :

- consider the role of the lay member on the AEC and your attitude to their inclusion. How comfortable would you feel if, for example, an investigative journalist (with impeccable ethical credibility as a given) was appointed as a Category D member on your AEC?
- consider the channels through which members of the general public inform themselves on the areas of research scientists carrying out and how easy it is for misinformation to arise if scientists do not become aware of the level of ignorance which prevails in the general community;
- consider ways of involving general public discussion as a means of information and education and whether you think this would impede or enhance your work; and
- in our best interests, develop fool-proof ways of dealing with big business interests and scientific research, and assure us that patents and products are less important than human rights and ethical probity. Remember that the general public must rely entirely on the scientific community in all these matters, and the delegation of this responsibility should constantly register with you.



## An AEC Lay Member's Perspective

**Patricia Baitz**  
**Category D member**  
**Monash University Animal Welfare Committee**

Ms Baitz described the four categories of AEC members and then referred to the category of animal technician, which has not yet been formally recognised by the Code of Practice, but which is mandatory in some states (e.g., S.A.). It is these people who provide much basic and vital information to AECs and yet don't often receive accolades.

She explained that her talk would be in two parts – the problems which face a lay member of an AEC and some of the issues about the production and use of transgenic animals.

It is very difficult to define a lay person and very difficult for such a person on an AEC to obtain necessary information. It is necessary to be proactive – to ask for help and to go into the laboratory.

A Category D person is supposed to represent the wider community, but it is very hard to put aside one's own philosophies and opinions, to be dispassionate and to try to represent the broad feelings of the community.

Ms Baitz thanked Dr Noonan and her colleagues at Monash University for their advice and provision of books for background information. While this can be daunting, it is also interesting and a necessary part of being able to comprehend complicated scientific jargon.

A lay person should always look at the aims of and at the justification for any project. For proposals involving the production and use of transgenic animals, she always looks more carefully at:

- the numbers of animals proposed;
- the care of the animals;
- staffing levels;
- whether the care is going to be different because the outcome is unpredictable;
- monitoring of the animals, which is difficult because there is often no prior experience and the researchers are deliberately constructing a defect or even a disease;
- how thorough are the observations that are reported in the monitoring sheets?
- can problems occur in later generations?
- the three Rs of Reduction, Replacement and Refinement
  - can these really be applied to transgenic animals?
  - replacing is not appropriate, rather creating
  - we may be replacing a poor model with a good model;
- does the end justify the means?
- the use of transgenic farm animals can result in high production and possible reduced losses through disease, but problems can arise – e.g., the Beltsville pigs in the USA.

Ms Baitz concluded by saying that while this is a fascinating and exciting stage in the history of science, we must educate ourselves and be forever vigilant.

## A scientist's view, including phenotype analysis of transgenic animals

**Dr Rosemary Sutton**  
**Children's Cancer Institute**  
**Sydney**

Dr Sutton explained in her introduction that her paper would describe a line of transgenic mice which develop a form of cancer called neuroblastoma.

When planning experiments to induce cancer in mice, there are a number of factors to consider. It is important to weight the potential benefits against the cost of doing the research and so it is necessary first to consider whether *in vitro* alternatives are possible. In setting up the experiment, a number of parameters need to be defined. It is often wise to do a pilot experiment, which may reveal the need to redefine the experimental design. When working with animals with induced cancer, it is very important to detect tumours early, so that the effects of treatment can be measured early and euthanasia of the mice can be done as early as possible. This needs to be before the animals are compromised by the cancer they are developing and may involve the use of appropriate analgesics.

Dr Sutton then described the work undertaken in her laboratory on neuroblastoma, which is a type of cancer in children, with a 40% mortality rate. In about one third of all neuroblastomas is an oncogene, which, when amplified in the tumours in children, results in only about 15% survival. Her research focuses on neuroblastomas removed from children and studies genes which have been altered. She also uses transgenic mice to enable research which could not be done on humans, to study the events occurring in early tumour development and to test possible treatment strategies.

These tumours often develop in humans and in mice in the nerves coming from the spinal cord. These tumours can occur in nerve ganglia in the thorax and abdomen, which are difficult to detect. The histology from the transgenic mouse tumours is very similar to those from humans. About 30% of the transgenic mice develop tumours, usually at about 14 weeks of age. When the mice have inherited the transgene from both parents, there is a 100% incidence of the tumour. These mice develop tumours very early, at about 6 ½ to 9 weeks of age. It is incumbent on researchers to minimize pain and distress to these mice. Proposed treatment can start in these mice from as early as three weeks of age. Her research group is currently testing treatments to stop the action of the oncogene. The treatment is administered under anaesthesia and is given from four to ten weeks of age.

The mice are monitored carefully for the development of tumours and are euthanased when they cause distress. The results have been encouraging, with a significant reduction in the size of tumours. Further experimental work is required before it can be used in children.

The key issues in assessing the welfare of mice with cancer relate to the skills and attentiveness of the technical staff looking after the mice. This includes watching their behaviour for any signs of abnormality, including nesting behaviour, respiration and movement, as well as coat condition. Body weight needs to be carefully monitored and the tumours have to be palpated regularly to gauge their size and rate of growth.

Her group is interested in developing other techniques for the early detection of tumours, such as blood and urine testing and ultrasound scanning. The possibility of marking the tumour cells so that they and fluorescent is also under investigation.

## A scientist's view, including phenotype analysis of transgenic animals

**Dr Alan Harris**  
**Walter and Eliza Hall Institute of Medical Research (WEHI)**  
**Melbourne**

Dr Harris referred his work at WEHI over the past 15 years on the mechanisms of apoptosis, or cell death. This began with the observation that a type of human lymphoma was characterized by a recurrent chromosome translocation. This occurred also in a mouse model and is related to a gene known as MIK. His group then made transgenic mice that expressed this gene in their B lymphocytes.

Small amounts of this gene construct were then injected into fertilized mouse eggs and the eggs transferred into pseudo-pregnant mice. Some of these become pregnant and the young born have to be screened to identify those which have incorporated the new DNA and are therefore transgenic. Of 100 progeny born, somewhere between 5 and 30 are likely to be transgenic. The remainder have to be discarded for experimental purposes.

The gene is expressed in the transgenic mice by the development of lymphomas, enlarged lymph glands, often visible around the neck. They are always killed before becoming clinically unwell and each affected mouse has its lymph nodes palpated daily. Occasionally the lymphomas are not evident by palpation and occur in the Peyer's patches, areas of lymphoid tissue in the wall of the small intestine.

How do the tumours develop in these mice? The tumours develop in individual mice at different ages, so it is not possible to predict their occurrence. All mice therefore have to be carefully monitored.

With regard to our research on cell death, this originated from other scientists' observations of another chromosome translocation in human lymphoma. At a particular locus on chromosome 14 is a gene which, when over-expressed, keeps cells alive rather than allowing them to die. Unlike MIK which promotes cell proliferation for cell growth, this gene, BCL2, doesn't affect cell growth, but inhibits cell death. So our laboratory made transgenic mice expressing BCL2. We noticed that the size of the spleen was much larger in these mice than in normal mice. This was due to an excess of Lymphocytes, because of the effect of the BCL2 gene on inhibiting cell death. This gave them a longer lifespan and also made them resistant to various agents known to kill lymphocytes. These mice did not have a high frequency of tumours. He then looked at what the effects were of a contribution of MIK and BCL2 in mice, by crossing the two strains.

The mice bearing both of these genes developed tumours extremely rapidly and all had died by five weeks of age. This was an example of different genes involved in cancer when combined becoming more tumorigenic. This led to the current understanding that, for a cell to make the transition from being normal and becoming malignant requires multiple cooperative mutations.

What then is the role of normal BCL2 in mice when it is not being over-expressed? Does it play a role in increasing the viability of normal cells? One way of testing this is to "knock-out" the gene. This has been done with BCL2 by a number of other laboratories and resulted in a whole series of problems. Such mice are very small, have short ears and don't grow well. They die at one to six weeks of age, mainly from kidney disease. Their immune system collapses soon after birth, so B and T lymphocytes nearly all die. This suggests that BCL2 is actually required in the normal mouse to keep the cells alive.

There are two factors in the control of cell death which have been recognised in recent years. There are proteins made in cells which are anti-cell death proteins and there are also endogenous proteins in cells that can actually cause cell death. It appears that there is a balance between cell killers and promoters within any cell. There may be a variety of proteins which can do this, perhaps used differently in different cell types.

A transgenic mouse has been made in his laboratory in which the gene called BIM encoding a protein which seems to promote cell death has been knocked out. When one of the two alleles of BIM was knocked out, it essentially cured the BCL2 knock out mice of their kidney disease problem. This suggests that in the mouse kidney there is a form of balancing between BCL2 and BIM, so that if the protective effect of the BCL2 is knocked out, the cells die, whereas if the BIM is knocked out, it is brought back into balance and the cells survive.

The last point is that BCL2 knock-out mice go grey after about five or six weeks of age. The few that survive the kidney disease go grey, whereas if BIM was also knocked out, the mouse coat colour was almost normal, with just a few flecks of grey hairs. This shows that in the pigment producing cells that cause hair colour there is also a balancing act between BCL2 and BIM genes.

These are just a few examples of how transgenic characteristics can be expressed in mice. Some are expected and some are unexpected.

# How to measure welfare of transgenic farm animals

Dr Alana Mitchell  
Science Link Pty Ltd  
Animal Welfare Liaison Officer for the NHMRC

## ANZCCART WORKSHOP ON THE WELFARE OF TRANSGENIC ANIMALS

- Statistics from Great Britain indicate that the use of transgenic animals increased by more than 10-fold between 1990 and 1999, to account for about 20% of all procedures using animals.
- It's probable that a similar change has taken place in Australia.
- There are no national statistics recorded for the use of animals in research in Australia because animal welfare is a matter for State and Territory legislation and each State and Territory operates somewhat differently.
- The *Australian Code of Practice for the Care and Use of Animals for Scientific Purposes* is the unifying aspect of animal welfare nationally.
- A major concern in relation to transgenic animals, particularly mice, is the number of excess animals required to establish a transgenic line, and to produce the required number of animals with the correct gene complement for experimentation. This poses a dilemma in the context of the 3Rs on which the Code of Practice is based.

## RUSSELL AND BURCH IN 2001

- I pose three questions as discussion points.
  1. *Is the concept of reduction as described by Russell and Burch 40 years ago still applicable to the creation of transgenic animals in 2001?*
  2. *Would the concept of 'relative' reduction (which is achievable), rather than 'absolute' reduction (which is highly unlikely), provide a more realistic basis on which AECs could consider an application?*
  3. *Having accepted transgenic technology, should the focus be on wellbeing of the animals and refinement rather than reduction?*

## THE CODE

- *The current Code has one section entitled Experimental manipulation of animals' genetic material which is specific for transgenic animals.*
- *In addition, general information about caring for experimental animals, which is applicable to transgenic animals, can be found throughout the Code.*
- *One of the issues for discussion in the imminent review of the Code is the section on transgenic animals.*

## CONCLUSION

Where transgenic animals are concerned, it remains important to 'expect the unexpected'. Even with the best information, and the best of intentions, it is not possible to predict with certainty how the introduction of a transgene, or the knockout of an existing gene, will impact upon the experimental animal.

This means that extra vigilance is required by researchers, animals technicians and AECs to ensure that potential causes of pain and distress to experimental animals are quickly detected and treated or eliminated.

## Welfare audits for farm animals and implications for transgenic animals

**John L. Barnett**  
**Animal Welfare Centre**  
**Victorian Institute of Animal Science**

For the last 2½ years a collaborative project has been underway to develop a comprehensive welfare audit for the chicken meat industry. This is a landmark project in that it provides the world's first comprehensive animal welfare audit for an entire industry, in this case for the chicken meat industry from the hatchery to the processing plant. It provides an agreed set of questions for an auditor to use that have been developed in conjunction with inputs from a number of stakeholders and that are based on good farming practices in the industry.

Currently, the only welfare requirements for farm animal industries to abide by are 'codes of practice' for individual industries. These 'codes' are developed by SCARM (Standing Committee on Agriculture and Resource Management) and agreed to for national adoption by ARMCANZ (Agriculture and Resource Management Council of Australia and New Zealand). Such national/state codes are either adopted without change or there may be some minor modifications by individual States and Territories to meet local requirements. A perceived negative aspect of codes of practice for farm animals is that they are seen as generally reflecting only minimum welfare standards. One benefit of a welfare audit is that, in time, it will assist in changing the perception of an industry that is seen as only complying with minimum welfare standards to one of an industry striving to achieve high welfare standards.

While this welfare audit documentation for the chicken meat industry and similar projects that are underway for the pig and dairy industries are being developed for animals of normal genotypes, there is no reason why the principles cannot be utilised for transgenic animals.

Some of the principles are to decide on the industry sectors to be covered and to form an appropriate Management Group that is manageable in size, representative of all stakeholders and has the appropriate expertise or networks to obtain required information. For the chicken meat audit the Management Group had representatives from industry, the welfare lobby, legislators and research and teaching staff. It was also attempted to have a consumer representative, but there are few consumer organisations in Australia. For transgenic animals it would be very worthwhile including a consumer representative, or at least one or two community representatives, similar to the position held by category D members on AECs. The chicken meat industry was divided into the following sectors: hatchery, broilers, breeder rearers, breeder layers and pick-up, transport and processing sectors.

For transgenic animals, the first decision is to decide on what the industry is. There is no reason why audit documentation for farm animal species cannot be developed or modified to include issues of concern for transgenic animals. Currently, the number of transgenic farm animals is probably small and the major part of the transgenic industry is laboratory animals for research and laboratory animals and perhaps transgenic farm animals for pharmaceutical developments and production. Thus, this industry is part of the laboratory animal industry and it will be necessary to develop documentation for different species and strains and include the range of transformations, from simple to complex. Deciding on the industry sectors will vary, depending on the species and strain, but areas that should probably be included for all species/strains are parent stock and gestation, neonatal and postnatal development, rearing, breeding and transport and relocation.

Another important principle is to have terms of reference to ensure a project, once started, is completed on time. While every attempt should be made to reach consensus, this may not always be possible. Some useful clauses along the following lines are suggested for inclusion in terms of reference:

- i) Recognise that the research group is responsible for completing the project and therefore may need to make decisions contrary to individuals' opinions. Notwithstanding this recognition, attempts will be made to reach a consensus.
- ii) Recognise that it is not the intention of the audit documentation to change the 'code of practice', although it may identify areas that require change.

It is important to identify to the Management Group what welfare audits will not achieve. They will not achieve either quick changes to current industry practices or resolution of controversial issues. Nevertheless, they can identify and encourage adoption of best practice, identify areas that may require further examination and identify areas in relevant Codes of Practice that may require resolution. In relation to transgenic animals it would need to be made clear that this would not be the forum to resolve ethical issues surrounding the production and use of such animals. Nevertheless, it is an appropriate forum to raise such issues and to include them in background/training sections of the documentation, so that industry is made aware of the breadth of the issues. The focus of a welfare audit is on the practical animal and facility management issues that contribute to welfare.

While animal houses associated with research institutions and breeding establishments in Australia are licensed and audited, there is no agreed audit documentation, based on the experiences of developmental problems and best practice, such as those being developed for the agricultural animal industries. As well as providing standardised audit documentation, an important benefit is for self-assessment to determine how facilities are performing compared to industry targets and to identify areas for improvement. There is community concern about animal experimentation and a greater concern about transgenic manipulations of both plants and animals. These concerns are recognised by States having separate sections in legislation for animal experimentation and a separate body involved with issues of genetic manipulation. If industries do not address community concerns themselves, there is likely to be further regulation imposed. A recommendation from ARMCANZ at the end of the year 2000 for the egg industry, provides some guidance. They have recommended that the industry develop a quality assurance (QA) program that includes food safety, biosecurity and welfare. In the future, it is likely that those industries that have QA programs that include welfare and that have some external auditing will receive less scrutiny from government.

Industry-wide feedback was obtained for the chicken welfare audit by circulating drafts for comment to all chicken meat companies and revised documents were subsequently provided to companies as both hard copies and on a CD. Each booklet has audit questions, background information on the purpose of the questions and how the questions/practices relate to welfare and the Codes of Practice for welfare for both the transport and keeping of poultry. Examples of recording sheets are also included to assist farmers/unit managers demonstrate compliance with an audit. The audit questions include both critical questions, which are defined as those where "if something goes wrong the welfare of the birds is irrevocably damaged" and good practice questions which reflect the current state of knowledge and its practical implementation in the industry. For a number of areas there are 'targets' for farmers/unit managers to aim for, based on current industry information on good farming practice, or that act as a trigger for attention. The audit questions have been based around management tasks that are routinely conducted. Thus, welfare is integrated into routine farm and animal management and is not considered as a separate task. The purpose of the audit documentation is threefold: firstly, to provide documented evidence of high quality animal care by identifying and encouraging best practice for each sector of the industry; secondly, to identify and monitor equipment and animal problems associated with quality animal care; and thirdly to identify and monitor human resource issues associated with quality animal care.

While it was not possible to evaluate all sectors of the audit, there was some evaluation of all booklets 'on-farm' to provide feedback on the validity of the questions and any perceived difficulties in implementing the audit. Also, there was a more comprehensive evaluation of the broiler audit. Twenty-four broiler farms contracted to one company were used. The company provided production data for the 3 previous batches of birds and the farms were ranked from 1-24 according to their performance. Pairs of farms with similar performance were allocated to treatment and control groups. The 12 treatment farms received the audit document and were asked to complete the recording sheets. The 12 control farms did not receive a copy of the audit document and were asked to continue recording what they normally would have done such as mortalities, culls, feed supplied and body weight. Growers participated in the study for 3 batches of birds. At the end of the third batch, the audit was conducted for the period from 2-5 weeks of age; this time period was chosen to avoid variation due to pick-up schedules. As expected, record-keeping was better at the treatment farms and there was also a significantly lower mortality (1.37 vs. 1.74 %) in the first week after placement.

While a reduced mortality can be considered a welfare benefit, and some production advantage may be expected from implementing the welfare audit, because of the close link between welfare and production, any production advantage should be considered as just a bonus from implementing the welfare audit. A welfare audit is seen as having a number of advantages. These are: an immediate improvement in animal welfare; public reassurance of high welfare standards; market protection and development by having systems in place to minimise industry-wide risks; a mechanism for recommending upgrades to welfare codes of practice; generally higher standards of animal welfare than the minimum standards currently in the codes of practice; demonstrated industry commitment to welfare; continual improvement in animal welfare; certainty for all;

intangible benefits including improved production, better maintenance of equipment, fewer crises and improved staff training; less focus on industries with QA by government, welfare groups and the public; improved relationships between industry and welfare groups and the potential to reduce conflict between industry, government and welfare groups; improved industry sustainability.

The model described above, that covers some of the procedures adopted in developing a welfare audit for an agricultural industry, has some obvious parallels for a similar undertaking for transgenic animals. It allows a range of stakeholders to see the processes/procedures/outcomes (by appropriate on-site visits), it allows for precise definition of the issues and the development of reasonable targets and review points (based on industry experience and current practices) and it provides for a process whereby a consensus can be reached. It also provides a forum for people with different views to openly discuss some of the ethical issues and provides a means of people getting an appreciation of others' views in a non-threatening situation. The issue of having agreed and standardised welfare targets is one that is generally lacking for most commercial animal enterprises.

Some important components in developing the model are the need for a management group that includes wide representation and particularly includes non-industry stakeholders e.g. RSPCA and/or Animals Australia, agreed terms of reference, availability of a confidentiality agreement for participants, if it is deemed to be required and acknowledgement that it is a process cannot be rushed, as the stakeholders have to learn a degree of trust and this takes time.

Specifically, in relation to transgenic animals, as well as laboratory and farm animals, there is already considerable experience and expertise available. Development of a welfare audit, based on the model described above, can take advantage of this experience and expertise and provide some very useful and credible documents for use as a standardised audit tool. It could be used by organisations that are currently involved with transgenic animal production and those who wish to develop such animals. The suggested targets to be developed are similar to those that would be used for conventional species, such as specific targets for growth rates, survival at birth, to weaning and during rearing and temperature, housing and ventilation targets. Less tangible, but equally important targets, such as appearance, sound and behaviour at specific stages of development and best methods of euthanasia are also suggested for development. In addition, because of an awareness of problems associated with transgenic animal production, the list of targets could be expanded, depending on the species, to include birthing difficulties, standing and competency of movement at birth, teat seeking, sucking and suckling behaviours (as indicators of potential viability), and behavioural tests to indicate appropriate rates of development such as learning tests, social behaviour observations and tests and fear tests. The latter is predicated on the view that fear of novelty develops at appropriate stages of development for the species. The purpose of targets, and the requisite record keeping, is firstly to provide some standards for determining compliance with an audit and secondly to provide early identification of problems and intervention. Thus, the process is one that encourages continual improvement, on an industry-wide basis.

The process outlined above is a way of capturing the knowledge and expertise that is already available and subsequently applying the knowledge and measuring the outcomes, using existing audit procedures that are already in use for the transgenic animal industry. It is highly likely that the expertise and knowledge is available, but bringing it together is a costly process, probably in terms of dollars and certainly in terms of time.



## Legislative Control (State and Federal)

**Associate Professor Margaret Rose  
(Animal Research Review Panel, NSW Agriculture)**

I was asked to talk about State and Commonwealth legislation and the first comment I will make is that governments get involved in an issue in response to expressions of community concern. It is certainly true that in the first instance with regard to animal welfare generally that there has been community concern in this country, particularly with regard to animal experimentation, which has resulted since about the mid-1980s in various State legislatures putting in place either amended or new legislation that relates specifically to the use of animals in research and teaching. An Australian House of Representatives Committee also responded in the early 1990s to community concerns about the use of gene technology and genetic manipulation with the report *Genetic manipulation – the threat or the glory* (1992). There are a couple of comments about that report that I think are worth noting.

First, with regard to animal welfare, the committee concluded that what needs to be established is whether there is anything inherent in genetic manipulation of animals which makes it particularly likely to cause pain or suffering or to cause more pain or suffering than the use of traditional selective breeding techniques. There was some interesting discussion about animal experimentation per se. With regard to the use of genetic manipulation, the report said it increased the ability to create animals which suffer diseases to which human beings are prone and the ethical justification for such work must depend on the extent of pain or suffering likely to result in each case as well as the likely benefits.

They noted as well that the increased use of animals as models in the study of human diseases presumably will reflect an increased possibility of decreasing human pain or suffering by developing treatments for human disease and, more generally, an increased use of animals and experiments may be morally justifiable.

The report also considered the inheritance of harmful effects, which I think is particularly relevant to the scientific use of transgenic laboratory animals, rather than farm animals, because specifically in these areas, we are deliberately choosing to seek to manipulate genes for the purpose of either understanding the functions of the genes and therefore producing animals which will have a defect as a result of that, or specifically attempting to induce the disease. Those are issues that may well have particular risk and potential harm to the animal.

The Committee concluded that the possibility of causing heritable, harmful changes to laboratory or farm animals is a matter of legitimate concern, but they also said it wasn't unique to genetic manipulation. They went on to say the moral justification or lack of justification of intentionally developing animals susceptible to an illness or medical treatment is surely the same regardless of the method used to achieve that result. The important question is whether the genetic manipulation techniques are more or less likely to produce unintended harmful, heritable changes than traditional selection techniques. They went on to suggest that in fact traditional selection techniques may have a disadvantage, in that it is difficult to control what characteristics other than the one being sought may be passed on to the progeny.

The Committee concluded that genetic manipulation holds the promise of enabling a precise alteration of the carefully selected and limited part of the genome and as genetic manipulation techniques are further developed, that it actually may reduce the chances of unintentionally causing harmful changes to farm animals or others which are able to be passed to subsequent generations. However, the Committee believed that the animal welfare authorities should be obliged to enforce the existing rules and regulations. This is the only government enquiry within the last ten years in this country that related to gene technology.

The outcome from that enquiry related to two recommendations for further action. Firstly, the Committee recommended that the Australian Code of Practice for the Care and Use of Animals for Scientific Purposes should be amended to require observation of genetically modified animals by researchers for a sufficient number of generations of those animals to ensure the detection of any latent effects and to report any such findings to institutional Animal Ethics Committees. They also recommended that there should be Commonwealth Legislation with regard to gene technology which has come to fruition with the Gene Technology Act (2000).

If you go to the website of the Office of the Gene Technology Regulator [www.ogtr.gov.au](http://www.ogtr.gov.au) will find information about the Gene Technology Act and how it might relate to transgenic animals. When you look at the aims of the Act and the information about it on this site, the Act is really to set up a regulatory framework that is concerned with two things. One is to provide some form of regulatory control over the use of genetically modified material and the other is to relate specifically to assessment or risks for human health and environmental welfare. To do that it has a mechanism through the Office of the Gene Technology Regulator and via institutional bio-safety committees. It is also putting in place a mechanism for community input via three committees which have been established. These are the Gene Technology Technical Advisory Committee, the Gene Technology Community Consultative Committee and the Gene Technology Ethics Committee.

I was quite surprised that the notion of animal welfare as a risk is not within the ambit of this Federal legislation and I think we are all in the situation where we need to work through with that. There is a fair amount of detail to help us work through specifically what we need to put in place if we are involved in using genetically modified animals and to help us in doing that you will find a handbook on the Regulation of Gene Technology in Australia, which again you can browse. It is 172 pages, which you can download from the site to give you some information regarding the housing and the containment of transgenic animals. The guidelines for certification of facilities are also downloadable .

The other federal legislation which is relevant to our use of genetically modified animals and transgenic animals relates to the requirements of AQIS (Australian Quarantine and Inspection Service), specifically regarding the issues relating to quarantine requirements for importation of laboratory mice. We also have the Australian Wildlife Protection Act.

In the 1997 edition of the Code of Practice there is a specific section that relates to genetically modified organisms. Now it may not use the word transgenic, but I think it's worthy to note that specific requirements were put in place at that time. In Section 3 of the Code there are four things that relate to transgenic animals.

One is that all work involving the introduction of foreign DNA and inter-mammalian cells or whole animals, must be conducted in accordance with guidelines issued by what was then known as GMAC and is now the Office of the Gene Technology Regulator. All proposals to manipulate the genetic material of animals, their germ cells or embryos, must be submitted to an AEC for approval. Investigators must inform the AEC of known potential adverse effects on the well-being of the animals. The clinical condition of animals in which the genetic material has been manipulated experimentally must be monitored for unusual or unexpected adverse effects and investigators must report such effects to the AEC.

That is what is now set in the basic requirements for the national Code of Practice and as we know, that national Code has been incorporated by reference into State legislation in various ways. It essentially sets the framework for any national issues with regard to animal welfare. Although we don't have Commonwealth legislation in terms of animal welfare, we do have this umbrella policy under the national Code and we do have the Office of Gene Technology Regulation requirements as well as the AQIS requirements.

Where might we be wanting to go for the future? In thinking about that, I had a look to see what was happening overseas and there has in fact been quite a lot of activity with government inquiries with regard to transgenic animals and genetic engineering in the last few years. The first of these (in 1998) was the report on the use of transgenic animals from the European Union (EU) and it is embodied in a report that is in an issue of the journal *ATLA* (27, supplement 1, November, 1999). I would like to share with you some of the comments or recommendations which are coming back from these reports. With regard to the EU, the conclusions they made are that genetic modification of animals has a potential to cause unexpected detrimental effects in the progeny that are sometimes severe and which we have also identified in the Code of Practice. They have discussed the approval for a program of transgenic animals which should be reviewed periodically with regard to costs and benefits, independent competence and continuing assessment of the impact on the animals, the issue of providing people with information and the need for data bases of up to date information regarding the effects of transgenic procedures on animal welfare. They have also talked about the areas where we really do need to get some more information which include the kinds of things that are actually involved in terms of impact on the animals. It starts with an initial production of the transgenic animal and what procedures the parents are put through as well as what is the potential risk to the offspring and the future generations of those offspring. It may relate to potential risks of what are known and predicted and what is unpredicted.

The EU Report has also put forward some suggestions in terms of how we actually can take this technology and how we manage it and how we manage our colonies in terms of the three Rs. One of the things that really becomes critical is looking at issues like reduction, replacement and refinement. For various reasons we may want to be keeping certain strains. Keith Edwards' suggestion (at this workshop) about cryogenic preservation of embryos is one of the strategies that should be put in place. It may not always be possible in certain areas, but we then may need, for example, to look at maintaining heterozygotes rather than homozygotes and simply breeding homozygotes when we actually need that particular strain. One of the overriding things in the ATLA report is the need to be careful in assessing, monitoring and evaluating.

There are three reports originating from the UK. The first of these is the Boyd Group report from 1992. The Boyd Group is essentially a 'think tank' that relates to ethical issues with animal experimentation. This report is available on the web and is really good – [www.boyd-group.demon.co.uk/](http://www.boyd-group.demon.co.uk/). It has clearly identified the animal welfare issues as well as the ethical concerns. The two most recent UK reports that I found interesting and useful were from the Royal Society and from the Animal Procedures Committee of the Home Office. One of the things that was interesting about both of these reports was that each was the result of public comment and both were looking at the broad issue of genetically modified animals and biotechnology. The vast majority of responses they received from the wider community related to animal welfare. The Royal Society Report and the Animal Procedures Committee Report each raise issues about animal welfare related to the preparation of genetically modified animals, the induction process, the implantation process, together with queries and concerns about high levels of foetal mortalities. There was also a note in the Boyd report about a high probability of a high mortality rate with death occurring, and that it was hard to obtain some of these data. There was also the prediction of risks as a consequence of altering the genes and that related to both unintended and expected harmful effects.

One of the important issues is that the public debate about genetically modified animals must take account of wider issues than the science alone. The Royal Society stressed the importance of informing the debate on the basis of sound scientific evidence. We need to have a broad public debate about the issues, but at the same time we need to look at ways in which we can underpin that.

One of the issues raised in the Animal Procedures Committee Report related to the numbers of animals used. With regard to the principle of reduction, there is a real argument of whether the use of transgenic animals is going to reduce the numbers of animals we use or whether it is going to increase the numbers. At the moment the trends would seem to suggest that we are actually going to increase the numbers of animals which are being bred, but not necessarily increase the numbers of animals which are going to be part of an experiment. An issue is record keeping, as well as the ways in which animals may be bred excess to demand. One of the issues to come through, particularly from the Animal Procedures Committee Report, has been the question of how numbers are reported.

In terms of the effects on the welfare of genetically modified animals, one of the other issues the Home Office report brought out and which I think is really worth taking on board is considering the impact and implications for housing and environmental needs of those animals. Quite often the way in which we are housing and caring and providing that environment for the animal may be significantly altered by the effects of genetically modified and transgenic animals. We can ameliorate some of these effects by looking more critically in the ways at which we manage those animals.

The key issues relate to really assessing the full scope of the impact of the procedures on the animals.

The question of how we monitor has become critical and it's one that has also arisen in Australia. One of the things that we might think about doing is setting up a much broader data base. If you go to data bases such as that of Jackson Laboratories (USA) you will get some information about welfare implications of particular transgenic lines, but it is not necessarily information that is widely available. An important issue is the ways in which we can share information about what are the welfare implications for particular transgenes in a particular situation, so that we actually share that information across institutions. This is something really worth taking on board as a way of monitoring carefully, looking at strategic ways of monitoring. It brings on board the need to come up with an agreed type of proforma and I would like to find a way to focus on the critical questions and to start developing the data base. Individuals are doing it in institutions. If we could start finding ways of sharing that, we could be making a significant contribution to refining the procedures and the use of animals in terms of transgenics. So I think in terms of us being able to implement the 3 Rs of Replacement, Reduction, Refinement, we do have some potential there for Refinement. With Reduction, we need to go back and look at all of that again, more critically. But monitoring is quite clearly a key issue and for future revisions of the Code it's one that comes forward.

Finally, the New South Wales government recently put out a document, *Biofirst*, which is a response to community issues. One of the main planks of this documents relates to bio-ethics, of which animal welfare and gene technology and genetic manipulation are part. The document includes the NSW Government's comments about this relationship. The challenge for government is to optimize progress in medical and agricultural research and clinical practice. There are potential social, environmental and economic benefits that can be made available to the community while ensuring that appropriate ethical, safety and environmental studies are maintained.

We talked a lot about the way in which the community is involved and the interface between science and the broader community about these issues. They are clearly not issues for the scientific community alone.

## The welfare of genetically modified animals: legislative control (state and federal)

Jane Conole  
Bureau of Animal Welfare  
Department of Natural Resources and Environment

In Australia there are two major areas of legislative control of genetic modification in animals, the regulation of gene technology and the regulation of the use of animals in science.

The regulation of gene technology is by Commonwealth legislation, the Gene Technology Act 2000 that describes a nationally consistent scheme which involves each State enacting legislation that is almost identical to the Commonwealth Act. For example, in Victoria the Gene Technology Act was passed in 2001 and is virtually the same as its namesake. The stated purpose of these Acts is to protect the health and safety of people and protect the environment. This will be achieved by licensing people to “deal” with Genetically Modified Organisms (GMOs) and developing policy principles and codes of practice. The Office of the Gene Technology Regulator in Canberra began its duties as described by the Commonwealth Act in June 2001 and performs these functions with input from a variety of sources.

The Office of the Gene Technology Regulator (OGTR) receives applications from industry and institutions for licenses or accreditation to deal with GMOs. The Commonwealth Act also describes the formation of a Ministerial Council for Gene Technology and a number of committees to be involved in the work of the OGTR. These committees are the Gene Technology Technical Advisory Committee, the Gene Technology Community Consultative Committee and the Gene Technology Ethics Committee. These committees are involved in the development of policy principles and codes of practice. The OGTR also interacts with other commonwealth regulators as necessary.

The Gene Technology Act 2000 is virtually silent on animal welfare. The only explicit mention is that the membership of the Gene Technology Ethics Committee must include someone with skills or experience in animal health and welfare. Therefore there is scope for animal welfare issues to be addressed by this committee.

The regulatory framework for gene technology in Victoria, as an example of a state involved in this scheme, is that there is a local public service unit to co-ordinate Victoria’s involvement in the Commonwealth system, the Minister for Health is a member of the Commonwealth Ministerial Council for Gene Technology and there are two local committees formed to advise the Minister. These committees are the Biotechnology Safety and Ethics Interdepartmental Committee and the Victorian Biotechnology Ethics Advisory Committee. The form that the Ethics Committee will take is yet to be decided, but its role could include advising the Minister on animal welfare issues, which could then be raised in the Ministerial Council for Gene Technology.

Diagrammatic representations of the Commonwealth and Victorian regulatory framework for gene technology are available from the Victorian Biotechnology Safety and Ethics Unit website (<http://www.dhs.vic.gov.au/phd/biotech/index.htm>).

Examination of the regulation of gene technology shows that it barely touches on the welfare of genetically modified animals at present. This may well be because it is expected that other legislation will provide adequate control, for example the legislation which regulates the use of animals in science.

Regulation of the use of animals in science is state based; there is no federal legislation. In Victoria regulation is provided by the Prevention of Cruelty to Animals Act 1986. In part 3 of this Act regulation is provided by the licensing of establishments and the requirement that Animal Ethics Committees (AECs) approve scientific procedures on animals. Other states and territories have very similar controls. In Victoria licensed establishments and AECs must operate in accordance with the Victorian Code of Practice for the care and use of animals for scientific procedures. This Code of Practice is essentially an A4 document that says that you must comply with the Australian Code of Practice for the care and use of animals for scientific purposes. All the States and Territories have or are in the process of adopting the Australian Code by a variety of means.

The purpose of the Australian Code is to ensure the humane care of animals used for scientific purposes through AEC approval and adherence to the principle of the three R's, i.e. the replacement, reduction and refinement of animal use in science. AEC approval must be on the basis of a cost/benefit analysis of the proposed work, i.e. does the projected benefit of the work outweigh the expected cost to the animals (section 1.2). However in new genetically modified strains this evaluation may not be possible because the cost to the animals can not be foreseen. The Code includes some specific responsibilities of investigators working with genetically modified animals (section 3.3.54-57). These responsibilities include informing the AEC of known potential adverse effects, monitoring for unexpected adverse effects and reporting the latter to the AEC. In genetic modification projects it is very important that AECs receive reports from the investigators of the actual effect of genetic modification on the animals. The results of receiving these reports may be to instigate different monitoring requirements, establish new humane end points and even re-evaluate the cost/benefit analysis of the project in light of the actual cost to the animals. To this end, AECs should establish systems of reporting the phenotype of genetically modified animals in order to comply with this section of the code.

The Australian Code of Practice for the care and use of animals for scientific purposes is currently in the early stages of revision and comment is welcomed (contact the NHMRC, Canberra).

In the future we may have genetically modified animals that are no longer used for scientific procedures but are part of normal agriculture or other industries. Currently in Victoria the protection of the welfare of these animals would be through the earlier parts of the Prevention of Cruelty to Animals Act, Parts 1 and 2 which define cruelty and provide for the development of Codes of Practice which specify procedures for the care and use of animals. We are yet to see whether these legislative tools adequately protect the welfare of genetically modified animals when they leave the scientific establishments.

In conclusion, the Commonwealth and Victorian Gene Technology Acts are virtually silent on animal welfare and therefore the legislative control of the welfare of genetically modified animals in Victoria is by part 3 of the Prevention of Cruelty to Animals Act. In other states legislative control is by similar legislation, all of which describe the means to license (or equivalent) establishments, form the all-important Animal Ethics Committees and adopt the Australian Code of Practice for the care and use of animals for scientific purposes.

## ANZCCART WORKSHOPS

### SUMMARY

**Dr Robert Baker**  
**Director**  
**ANZCCART**

Dr Baker referred to his introduction to these workshops, when he suggested four possible outcomes. These were: -

- **A better understanding of ethical and practical issues relating to transgenic animals.**
- **Means to measure the welfare of transgenic animals, including the use of an audit tool**
- **Notes from these meetings to be provided to all registrants and made available from ANZCCART's website.**
- **ANZCCART to produce a set of guidelines similar to those from the Canadian Council on Animal Care?**

While the first three had been very comprehensively addressed, no decision was reached on the last.

Both workshops had been well served by very knowledgeable speakers. Dr Miranda Gott had dealt very well with the ethical issues involved in the production of transgenic animals. She pointed out that some of the problems, as well as some of the public opinion about this, cannot be quantitated, as they are intrinsic— they are what is known as “gut feelings”, but are real and need to be taken into account. Dr Gott referred to the cost-benefit analysis required when proposing to use animals in science. This applies particularly to the production and use of transgenic animals, but can be more difficult, as it does not always answer the objections of some members of the public. She asked what is justifiable and what is not in terms of transgenic animals and cited as examples the use of transgenic animals in medical research, animal production and the maintenance and breeding of endangered species. The last example was not really addressed by these workshops, and relates to the welfare of species rather than of individuals. Nevertheless, the cost-benefit analysis still needs to be applied to individuals.

Dr Denise Noonan covered a lot of ground in her paper. She addressed the benefits from genetic manipulation of animals in detail, as well as the inherent problems. She looked at benefits from the perspectives of animal and human health and welfare.

Keith Edwards and Glenys Oogjes gave similar papers, which provided a clear presentation of the animal rights movement's view on animal experimentation and genetic manipulation in particular. They asked the very valid question whether there should in fact be a boundary between what we do to humans and what we do to non-human species of animals? They cited the inclusion in the recent New Zealand animal welfare legislation (Animal Welfare Act, 1999) of specific constraints on invasive experimentation on great ape species.

Ms Jane Burns and Ms Patricia Baitz provided eloquent and very useful perspectives on the difficult role of a Category D (lay) member on an AEC. This is particularly so when dealing with complex technology such as genetic manipulation and is difficult when the members do not have a scientific background and where there is the use of jargon, such as in describing transgenic techniques. Ms Burns asked the workshop to consider whether there should be Australian guidelines to the use of transgenic animals similar to those published by ANZCCART's Canadian counterpart, the Canadian Council on Animal Care?

The afternoon sessions comprised three short papers on how to measure welfare of transgenic animals. Drs Rosemary Sutton and Alan Harris described some of their own research using transgenic animals and how phenotypic expression can be used as a measure of transgenesis.

Dr Alana Mitchell from the NHMRC described the role of the NHMRC's Animal Welfare Committee and the Code of Practice, with regard to the production and use of transgenic animals. The Code of Practice is currently being revised and the new edition is likely to include more about this area.

Dr John Barnett then drew on his experience developing and using an audit process for assessing the well-being of farm animals. In answer to the question whether an audit process is needed for laboratory animal welfare, he pointed out that this is already in place in some states (e.g., NSW) and in New Zealand and is being developed in other states and territories. The audit tools are available and can be adapted from his model for farm animals to laboratory animals.

Associate Professor Margaret Rose (NSW) and Dr Jane Conole (Victoria) comprehensively covered the legislative process at the state and national level.

Dr Baker thanked all of the speakers for their contributions and the Animal Welfare Committee of the NHMRC for sponsoring the workshop.