

Animal Use in Biotechnology: Issues and Options — A New Zealand Perspective

A.C. David Bayvel

Animal Welfare Group, Biosecurity Authority, Ministry of Agriculture and Forestry, P.O. Box 2526, Wellington, New Zealand
E-mail: bayveld@maf.govt.nz

Summary — Although New Zealand has a relatively small national biotechnology research effort, there are a number of specific areas that have attracted attention in recent years. This has resulted from the interests and expertise of individual researchers, the priorities of both public and private sector research institutions, the importance of the livestock industries to the New Zealand economy, the high health status of New Zealand's cattle and sheep populations and, particularly, the absence of scrapie and bovine spongiform encephalopathy. A number of research activities are reviewed, with particular reference to the associated welfare and ethical issues. This includes reference to relevant legislation covering animal welfare and new organisms. Particular attention is given to public and political interest in the newer research areas. The challenges posed to researchers and regulators in relation to both public consultation and effective communication of the risks and benefits of the work proposed or being undertaken are addressed. The role of independent expert advisory committees (the National Animal Ethics Advisory Committee and the National Animal Welfare Advisory Committee) and the need for lay members of animal ethics committees to be fully conversant with the welfare implications and ethical considerations of the technology being used are also discussed.

Key words: *animal ethics, animal welfare, biotechnology, genetic modification, New Zealand legislation.*

Introduction

Dennis (1) puts the current biotechnology debate in historical context with the following comment:

Modification of the genome of animals has occurred throughout the ages. Initially, changes in genetic composition occurred spontaneously. With the beginning of agriculture, humans exerted influence on the process by selecting animals with desirable genetic traits. An animal with a spontaneous genetic mutation that increased feed conversion, boosted milk production, or produced more desirable carcass characteristics would be selected as breeding stock to improve the herd by perpetuating advantageous phenotypic changes. More recently, scientists accelerated the mutation process with irradiation and chemical mutagens. Many genetic loci were identified, mapped and studied using such tools. Genetic predisposition and resistance to diseases were detected.

The era of transgenic animals is a relatively new development, and the ability to manipulate and study the genome has increased greatly with the development of gene targeting technology. Like the rest of the developed world, New Zealand is actively involved in addressing the policy and regulatory challenges posed by genetic modification technology.

New Zealand has a strong background in traditional biotechnology. Innovation in the agricultural

industry has always been a significant contributor to increasing New Zealand's wealth. Improved pastures, aided with fertiliser, and constant improvements in stock through selective breeding (including artificial insemination) and animal health have helped improve New Zealand's productive capacity. New Zealand's biotechnology capabilities have enabled the development of economies of scale and scope, achieving consistently high productivity gains in agriculture. Freedom from the major infectious diseases of ruminants, including particularly the transmissible spongiform encephalopathies, has resulted in New Zealand being chosen as a site for international transgenic sheep research and as a favoured source for biological products, including blood, serum and vaccines.

From a regulatory perspective, New Zealand has two key pieces of legislation: the *Hazardous Substances and New Organisms Act 1996*, and the *Animal Welfare Act 1999*. Two ministerial advisory committees, the National Animal Ethics Advisory Committee (NAEAC) and the National Animal Welfare Advisory Committee (NAWAC) provide independent advice at a national level on both animal welfare issues and ethical issues arising from the use of animals in research, testing or teaching, including their use in biotechnology.

The *Animal Welfare Act (AWA)* demands that when animals are used for the purpose of research, testing or teaching, or for the production of biological products, that this only be carried out in accor-

dance with the requirements of an approved Code of Ethical Conduct, and after approval from an appropriately constituted local, institutional Animal Ethics Committee (AEC). The membership of AECs must include three external members, to ensure community input into the decision-making process on the use of animals for such purposes. These include a member nominated by the New Zealand Veterinary Association (NZVA), a member nominated by an approved animal welfare organisation, most commonly the Royal New Zealand Society for the Prevention of Cruelty to Animals (RNZSPCA), and a member nominated by local government. In the New Zealand experience, these members have been relatively easy to identify and have proved to be diligent, conscientious and effective. In recent years, in accordance with the provisions of the AWA, the NAEAC has focused on providing greater support to AECs and their individual members. Support has included articles in the NAEAC newsletter, a survey of AEC information and training needs, a recent series of workshops, and a number of specific publications targeted at AEC needs.

This regulatory system, thus, has a requirement for community involvement and a commitment to minimising the welfare impact on animals used in research, via the implementation of the principles of the Three Rs of Russell & Burch (2). There is, however, a concern that the system is relatively unfamiliar to the general public, particularly to those organisations and individuals with specific concerns regarding animal use in biotechnology.

The *Hazardous Substances and New Organisms Act* (HSNO Act) came into force for new and genetically modified organisms in July 1998. The Act states that its purpose is “to protect the environment and the health and safety of people and communities by preventing or managing the adverse effects of hazardous substances and new organisms”.

Hannah (3) emphasises that, “The Act explicitly makes genetically modified organisms (GMOs) new organisms and they remain new organisms and under the control of the Act until such time as they are approved for release”. To date, there have been no approvals for release of GMOs in New Zealand. Thus, all GMOs in New Zealand are still new organisms according to the HSNO Act. The legislation requires a public participation process for many of the types of application made under the Act. Those applications involving animals tend to attract a high level of public interest.

New Zealand is an active participant in the Australian and New Zealand Council for the Care of Animals in Research, Testing and Teaching (ANZCCART). ANZCCART’s mission is threefold:

- to promote excellence in the care of animals used in research and teaching;

- to ensure that the outcomes of the scientific uses of animals are worthwhile; and
- to foster informed and responsible discussion and debate within the scientific and wider community regarding the scientific uses of animals.

ANZCCART plays an important and independent role outside the Government regulatory and advisory committee structure.

ANZCCART has published a number of articles relating to the use of animals in biotechnology and in genetic modification research in its quarterly publication *ANZCCART News* (4–8). A number of valuable review papers have also been published in the proceedings of ANZCCART conferences (9, 10).

In addition, the Independent Biotechnology Advisory Committee (IBAC) was established in 1998, expressly to provide information to the public and the Government on biotechnology issues.

The 1999 report to the Ministry of Research, Science and Technology, *Ethical Issues of New and Emerging Technologies* (11), emphasised the importance of identifying effective mechanisms to engage the public and address putative concerns. In the New Zealand context, the Maori perspective on the ethical issues of new technologies is also an important additional dimension and this was addressed, in detail, by the 2000/2001 Royal Commission on Genetic Modification (12). The public response to the Royal Commission recommendations has illustrated the difficulty in reaching societal consensus on these issues.

Discussion

Legislative issues

The definition of animal in the AWA specifically states that an embryo in the first half of gestation is not considered to be an animal. The NAEAC has, however, developed a policy position on genetic modification research, which confirms that such research does fall under the Act in the case of mammals, due to the need to implant the embryo into a recipient dam as part of the overall research activity. AECs therefore address welfare issues involving the fetus in the last half of gestation, the dam, parturition itself and the health and welfare of subsequent progeny.

The animal welfare issues addressed by the AEC and the rationale for its decision are, in turn, taken into account when an application to develop a new organism in containment is considered by the Environmental Risk Management Authority (ERMA New Zealand). This is a good example of the complementary regulatory relationship between the Ministry of Agriculture and Forestry (MAF) and ERMA New Zealand.

To better align the definitions of animal and manipulation with the process of, and the risks involved with, genetic modification research, NAEAC is currently considering the case for recommending modifications to existing legislation. UK legislation is seen to provide a useful model, with its definition of “protected animal” and “regulated procedure”.

Benefits of genetic modification technology

Wells (article submitted) and a burgeoning list of other authors, including Smith *et al.* (13), Van Reenen *et al.* (14) and Dennis (1), have discussed both the benefits and welfare risks associated with cloning and transgenic research.

Animal cloning would provide many new opportunities in the following areas:

- livestock agriculture;
- human medicine;
- animal conservation; and
- production of transgenic animals.

Depending on the genes manipulated, the benefits associated with the production of transgenic animals include the following:

- human health products derived from the production of pharmaceutical proteins in bovine/ovine milk to treat conditions such as emphysema, cystic fibrosis and multiple sclerosis;
- organs for xenotransplantation, e.g. from pigs to humans, where the transgenic donor tissue no longer stimulates rejection in the recipient;
- models for human genetic diseases, e.g. Alzheimer’s disease, Parkinson’s disease, diabetes and various types of cancer, e.g. breast cancer, familial colon cancer;
- agricultural applications aimed at improving animal health and welfare and the quality or quantity of food or fibre products; and
- improved testing systems, e.g. transgenic mice show promise as substitutes for non-human primates to test the safety of attenuated polio vaccines.

Risks associated with genetic modification technology

Wells (article submitted) emphasises that animal cloning is currently an inefficient process, with high

losses during gestation, birth and the post-natal period. Gestation problems are associated with failure of the placenta to develop and function effectively, leading to specific medical conditions such as hydroallantois. He also stresses, however, that nuclear cloning is successful in producing physiologically normal animals, providing encouragement for the eventual development of efficient and safe practices.

Wells suggests that “the first application of agricultural cloning is likely to involve the production of small numbers of physiologically healthy, cloned sires for natural mating, whereas cloning on a larger scale will not be feasible or tolerated until efficiencies improve. Future improvements in the technology will, however, reduce the current animal welfare concerns and improve the future utility and acceptability of cloning technology”.

Animal welfare effects associated with the production of transgenic animals form a continuum from severely reduced animal welfare (e.g. inappropriate over-expression of growth hormone), to neutral (e.g. increased expression of bovine milk proteins), to enhanced animal welfare (e.g. increased pest and disease resistance).

Regulatory aspects of genetic modification technology

Existing New Zealand regulatory systems provide a relatively “low bureaucracy” framework to address ethical issues and the risks and benefits associated with this technology. Some critics, however, question whether the ethical issues can be adequately addressed at a local institutional level and argue that there should be a national decision-making process for genetic modification research. This appears to be a minority view.

Food safety is another very important consideration in relation to edible products arising from genetic modification technology. Wells (article submitted) confirms that information has been provided to national regulatory agencies in a number of countries to demonstrate compositional equivalence of food products derived from cloned livestock.

Societal attitudes to genetic modification technology

Around the world, genetic modification technology has attracted the attention of groups with fundamental concerns about attendant risks to the environment, human health, animal health and welfare and the role of private sector commercial interests. These concerns have, in turn, attracted considerable media attention which is, unfortunately, often of a sensational rather than an informative nature.

Different countries have used a variety of mechanisms to address this important and complex public policy issue. In New Zealand, a Royal Commission was established; in the UK, an independent Agriculture and Environment Biotechnology Commission (AEBC) has been formed; in The Netherlands, a report was commissioned from the Terlouw Commission on Biotechnology; to mention but a few. All these reports emphasise the economic and societal benefits of the technology, while stressing the importance of on-going controlled research and informed political and public debate.

Battye *et al.* (11) use the New Zealand examples of transgenic sheep being used to produce α -1 antitrypsin to treat emphysema and cystic fibrosis in humans and cattle being used to produce human myelin basic protein to alleviate the effects of multiple sclerosis as two cases that illustrate the dichotomy in the debate. "The negative public submissions to the [ERMA] cited religious and cultural objections and scientific uncertainty as the main reasons for not letting the trends proceed, while positive submissions emphasised the potential benefits to human health, even though there have been no human clinical trials to date".

In its report on *The Use of Genetically Modified Animals*, the UK Royal Society (15) cites the particular public interest in the welfare risks to animals and recognised that, "Those involved in GM biotechnology, whether in the development of legislation or in the application of scientific developments, should engage in an open and frank debate with the public and recognise concerns about this issue".

Conclusions

The majority of the animals used in New Zealand in biotechnology are associated with traditional areas of research or testing. The advent of new genetic modification technology has, however, attracted considerable public, political and media interest in recent years and has led to the establishment of the IBAC and a Royal Commission on Genetic Modification.

The Commission report supported the existing regulatory infrastructure and made a number of specific recommendations to enhance the current regime. This has led to some amendments to the HSNO Act, but no changes were considered necessary to the AWA. Both these Acts provide the opportunity for public participation and are seen to be progressive by international standards. The Royal Commission also recommended the establishment of a Bioethics Council (Toi Te Taiao) to specifically advise, provide guidelines and promote dialogue on the cultural, ethical and spiritual issues associated with biotechnology.

New Zealand sees recent scientific advances in the area of biotechnology as having the potential to make a significant future contribution to national economic well-being. It is also considered to be important to monitor and contribute to international debate in this area. The existing AEC-based regulatory system effectively addresses the welfare issues of associated animal use. Advances in genetic modification research have the potential to make major contributions to the health and welfare of both production and companion animals and to optimise and reduce the number of animals used in agricultural and biomedical research.

In promoting open dialogue between the public, government agencies such as MAF and ERMA, advisory committees such as NAEAC, NAWAC and IBAC, and the proposed Bioethics Council, New Zealand is actively addressing public concerns.

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