

chapter |

# 9.

Medicine

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## Key issues:

- Genetic modification is widely accepted in the prevention, diagnosis and treatment of disease
- Genetic therapy offers hope of treatment and cure for people with genetic based illnesses
- Confusion exists over differences in the regulation of dietary supplements, food and medicine
- Significant future opportunities for advancement in health are offered by genetic modification.

## Introduction

1. Genetic modification is widely used in biomedical research and the study of disease. New Zealand currently makes widespread use of genetic modification in medicine and many genetically modified products and processes have been safely used for more than two decades. Almost all medical applications of gene technology use products derived from live genetically modified organisms, rather than live genetically modified organisms themselves.
2. This chapter discusses existing and potential uses of genetic modification technology and the benefits of using genetic modification in medicine. It looks at uses in the prevention, diagnosis and cure of disease. Particular focus is given to the use of genetic modification technology in vaccines. Other aspects considered include the possible impact of live genetically modified treatments on the environment, products with medicinal properties for human use, animal remedies, the increasing potential of foods as a way to deliver pharmaceuticals or vaccines, and the regulation and control of dietary supplements.
3. New Zealanders appear to be more comfortable with the use of genetic modification technology in medicine than with most other uses. The Commission's survey showed that 71% of the public felt genetic modification

had more advantages than disadvantages in relation to medicines and vaccines. This was a higher proportion of advantages than identified for other uses of genetic modification. Approval for genetic modification was highest in the areas of medical research (65% of respondents) and medicines and vaccines (64%).<sup>1</sup>

4. Public submissions also acknowledged potential health benefits from genetic modification. Approximately 10% (1045 submitters) of public submissions mentioned targeted treatments generally, cures for specific diseases, the eradication of inheritable diseases, use of gene therapy or the use and development of nutraceuticals.<sup>2</sup> Of these submitters 43% (447) said that non-specific medical uses were an acceptable application of genetic modification technology.

5. Most submitters supported current use of genetic modification in medicine. Several advocated the potential benefits of continuing and extending its use. A minority of submitters expressed reservations or outright opposition when it came to using genetic modification in medicine.

## Human treatments and issues

### Current uses in health

6. Many submitters and witnesses gave detailed information about the type of products used and their availability and use in New Zealand. Associate Professor Ingrid Winship, a clinical geneticist called as a witness by Auckland Healthcare Services [IP91], said that genetic modification technology was used in New Zealand for the investigation and diagnosis of genetic disorders and congenital metabolic diseases in the areas of:

- prenatal diagnosis of a mutation from which the foetus was at risk
- diagnosis confirmation for an individual who manifested a disorder
- carrier detection
- predictive testing prior to the onset of symptoms of individuals who are at risk of developing a late onset genetic disorder where, should the mutation be present, the disorder is inevitable
- predisposition testing of individuals prior to the onset of symptoms, where a mutation may make the individual susceptible to a disorder, but where, should the mutation be present, the disorder is not inevitable (for example, familial colorectal cancer)
- treatment of congenital metabolic diseases in newborn babies
- ongoing monitoring.<sup>3</sup>

7. Current and future specific uses of genetic modification in medicine are discussed in the following sections.

## Existing and potential benefits

8. We received many submissions emphasising the benefits of genetic modification in medicine, from universities, Crown Research Institutes, medical organisations and patient groups. Specific benefits suggested by submitters highlighted New Zealand’s potential in a number of areas.

### More treatments and cures

9. The Cystic Fibrosis Association of New Zealand [IP39] contended that “genetic modification offers the only possibility for a cure for a genetic condition such as cystic fibrosis. There is no other option.” The Association considered it was “inconceivable that anyone could decide not to allow research into genetic modification to proceed in New Zealand”.<sup>4</sup>

10. The Researched Medicines Industry Association of New Zealand (RMI) [IP55] noted that, while New Zealand currently had more than 20 protein products of genetic modification that were formulated as medicines, the American FDA had approved 76 genetically engineered biotechnology medicines for human use. It expected there would be applications soon in New Zealand for approval of many of these medicines.

11. In addition, the RMI said that, among pharmaceutical and biotechnology companies in the United States, there were 369 new biotechnology medicines in the development “pipeline”, targeting more than 200 diseases. Nearly half of these new medicines (175) targeted various forms of cancer, some using novel approaches. Infectious diseases, such as hepatitis, genital herpes, urinary tract infections and tuberculosis, were the focus of another 39 biotechnology medicines development projects. Autoimmune diseases, such as rheumatoid arthritis and systemic lupus erythematosus, and digestive disorders, such as Crohn’s disease and acute pancreatitis, were the targets respectively of 39 and 11 new medicines in the research pipeline.

### Large scale supply of replacement human proteins

12. The RMI noted that the potential for large scale production of replacement human proteins that would otherwise be in short supply had already been demonstrated with insulin for diabetics and erythropoietin for anaemic cancer patients. Diabetes Youth New Zealand [IP60] told us “the lives of about 32,000 New Zealanders are absolutely reliant on continued access to GE insulin”.<sup>5</sup>

### Eliminating contamination risks

13. Genetic modification makes it possible to eliminate the risks of contamination by infectious pathogens through avoiding raw material from human and animal sources. Recombinant Factor VIII is used to treat haemophilia

and human growth hormone to treat growth-deficient children. Deon York, a young haemophiliac presenting for the Haemophilia Foundation of New Zealand [IP48], told us:

Genetically modified products must provide safer and more effective treatment of haemophilia. The world haemophilia population has been one group particularly affected by HIV [the virus causing AIDS] and HCV [the virus causing a type of hepatitis that is difficult to treat]. ... We continue to be reminded of the effects of transmitting viruses or prions [the infectious agents of mad cow diseases, see chapter 8 (Food), page 191] via the public blood donor system. Now we have CJD [Creutzfeldt-Jakob disease] as a concern.<sup>6</sup>

14. The Haemophilia Foundation saw human gene therapy as “a bright light on the horizon after the traumas brought about by haemophilia and the past consequences of its therapy”.<sup>7</sup> These relate to the so-called “bad blood” problems associated with blood contaminated with hepatitis B and C, and HIV.

15. In its public submission the Ministry of Health noted that, because there are no antibodies produced as a reaction to recombinant human insulins, manufacturers have greater control over the contents and can produce a purer product with less risk of infection. New Zealand Vice Chancellors Committee [IP18] referred to a paper by Dr Sean Devine which said “human health” would be a “winner”<sup>8</sup> because drugs sourced from genetically modified organisms had a lower risk of HIV infection than those derived from human blood or blood products.

### **Precise and effective new medicines with fewer side effects**

16. Dr Parry Guilford from the Department of Biochemistry at the University of Otago [IP19] explained the use of gene technology in screening synthetic or naturally occurring chemical compounds that may be active against cancer. He argued that “identification of the cellular targets of these compounds meant more rapid development of drugs and greater opportunities to modify drugs to have more effect and fewer side effects”.<sup>9</sup> Dr Gillian R Woollett, a witness called by RMI, gave the example of Humulog, a more rapidly reacting variant of insulin which could be given at mealtimes, which was more convenient than administration 45 minutes or more before eating. Auckland Healthcare Services noted that “the very specific, accurate and safe treatments that have been established on the basis of genetic modification technology have introduced a marked improvement in the health of people affected”.<sup>10</sup> Auckland Healthcare Services specifically mentioned Pulmozyme in the treatment of cystic fibrosis, insulin in the treatment of diabetes and Ceredase in the treatment of Gaucher disease.

## The use of insulin in diabetes<sup>11</sup>

Today more than 15 million people with diabetes worldwide use insulin derived from genetically modified organisms (recombinant human insulin). In New Zealand about 15,000 type 1 diabetics are completely reliant on this insulin for survival. The number of New Zealanders with type 2 diabetes is estimated at 185,000, and 17,000 or more of these people also use insulin for blood glucose control.

New Zealand was one of the first countries to get recombinant insulin approved, in 1983, very soon after the first worldwide commercial use in the United Kingdom. Before this date, serious diabetics received insulin extracted from pig and cow pancreases. Ageing populations, wider insulin use and obesity meant more and more insulin was being used. Insulin from the equivalent of up to 70 pig pancreases a year is typically used by a diabetic and there were looming supply problems.

Patients can develop resistance to the action of injected insulin. Occasionally this is because of allergenicity to the insulin molecule itself, but more often it is to the chemicals used to modify the speed at which it works, and to contaminants. It was because of this that in 1985 the availability of recombinant insulin was widened, and in 1986 beef insulin use was discontinued in New Zealand. This was before there were concerns about mad cow disease.

Genetic technology makes it possible to produce large quantities of recombinant human insulin at relatively low cost. The first biosynthetic insulin made, and still used, is physically, chemically and biologically identical to the insulin made in healthy human pancreases, except that it is produced by genetically modified organisms in a contained fermentation system.

To avoid the need to attach other chemicals to the insulin molecule to alter the speed and length of time an insulin injection worked, research led to the development of another insulin molecule with a single chemical change known as Humalog™. The first patent in the world for manufacturing this was granted in South Africa on 29 January 1986 [Patent no. 85/4083] and in New Zealand on 3 November 1988 [Patent no. 212243]. Both patents expire on 29 May 2005, and after this time other companies than Novo Nordisk will be able to manufacture insulin in this way.

Better insulin leads to better blood sugar control and a reduction in the nasty complications of diabetes such as blindness, amputations, kidney failure and heart attacks.

### Benefits to the health system

17. The Cystic Fibrosis Association gave evidence of potential cost savings in the public health service, noting that there was considerable potential economic gain for the Government and the health sector from having available a cure for, or significant relief from, serious symptoms for a number of genetic conditions. These included savings from fewer routine clinic visits, reduced hospitalisation, smaller volumes of expensive medication taken continuously and fewer services and payments required of the Department of Work and Income. There would

also be more people working reliably in full time employment and contributing to the economy. The Malaghan Institute of Medical Research [IP10] emphasised public health benefits, arguing that the public stood “to benefit enormously in the sphere of health as new knowledge about the human genome and the genomes of pathogenic organisms accumulated and this information is applied to the human condition”.<sup>12</sup>

### **Only source of hope**

18. Representatives from some patient groups consistently reminded us that gene therapy was their only hope for a cure. Margaret Nicholls, the mother of two sons with cystic fibrosis, told us that their family illness is caused by a deletion of genetic material from chromosome 7. After the cause of cystic fibrosis was identified in 1989, “the hope of all the cystic fibrosis community was centred on finding a way for correct gene material to be placed, somehow, in the lung so that it would behave normally”.<sup>13</sup> Lysosomal Diseases New Zealand [IP99] called Jenny and Paul Noble, parents of two severely disabled children, as witnesses. They told us that “if there had been a cure, we as a family would not be suffering now”.<sup>14</sup> Patient groups argued that any risks of such treatments were borne by the person receiving the treatment and that, with adequate provision for informed consent, the advantages far outweighed any disadvantages.

### **Maori perspectives**

19. Maori were also more inclined to accept genetic modification in medicine than in the environment. Some, however, were not. Some witnesses expressed concern that genetic modification in medicine was misdirected. Representing the New Zealand Maori Council [IP105], Maanu Paul, despite confirming that he himself was a diabetic, said he remained unconvinced of a need for genetic modification in medicines when it was used to treat symptoms rather than address a cause. Similarly, Tim Rochford, lecturer in Maori health and a witness called by Te Runanga o Ngai Tahu [IP41], maintained that the potential medical benefits held out for genetic modification were unproven, misleading and did not address the environmental causes of many illnesses suffered by Maori:

It is important to understand that while there is a genetic influence on type 2 diabetes, the principal determinant is poverty related stress. Type 2 diabetes clusters in the most deprived communities in developed countries. It is an illness that appears to have a particular impact on indigenous people. It is thought that this is a reflection of accelerated aging caused by cultural dislocation, racism and poverty. In clinical terms it is possible to trace the path from chronic stress to the development of type 2 diabetes, hypertension, heart disease, increased risk of cancers and mental health disorders.<sup>15</sup>

20. Nga Wahine Tiaki o te Ao [IP64] expressed particularly forceful opposition towards any use of genetic modification.
21. In answer to a question about the use of genetic modification technology for children with growth deficiency syndromes and the impact on such children if these genetically modified products were taken away, Dr Fiona Cram, for Nga Wahine Tiaki o te Ao, stated that a clear distinction should be made between “what is a medicine and what is sheer experimentation”.<sup>16</sup> Nga Wahine Tiaki o te Ao considered that “this is experimentation”, and did not support its use in New Zealand. Alternative therapies needed to be explored as treatments for growth hormone deficiency before genetic modification therapies were used.
22. On the other hand, Des Ratima (Ngati Porou, Ngati Kahungunu) said at the Wellington regional hui at Waiwhetu Marae that:
- In parts of genetic engineering I think there are things we should embrace. If we can get rid of the diabetes ... and cancer that affects our people so drastically, then lets pursue that ... and the reason I say that is that we can control those measures.<sup>17</sup>
23. Other possible benefits from medical research were detailed by a number of witnesses and are discussed in chapter 6 (Research).

## Actual and perceived risks

24. A witness for the Human Genetics Society of Australasia [IP59], Dr Joanne Dixon, a clinical geneticist, said that risks would arise from genetic modification techniques unless there was adequate regulation, monitoring, auditing and reporting, and if New Zealanders did not understand the process. She added that some already-identified risks included allergic reactions and other failures of experimental therapies. The purpose of such experiments was, in part, to identify safety as well as efficacy issues. If all new therapies were adequately trialled and monitored after general introduction, harm should be minimised. With regard to therapeutic risk, Dr Dixon noted that New Zealanders already evaluated and then accepted the risks associated with untested, unproven and possibly unsafe “alternative” therapies.
25. Groups such as Physicians and Scientists for Responsible Genetics New Zealand (PSRG) [IP107] and the Green Party of Aotearoa/New Zealand [IP83] expressed general concern but recognised the potential for medical applications. PSRG saw the benefits in medicine as being “enormous” but said that the potential could only be realised if all associated risks were adequately mitigated. They saw these risks as the possible creation of previously unknown diseases and disease vectors such as bacterial pathogens or viruses, possible side effects from experimental genetic therapies, and novel selective pressures producing possible

new strains of existing pathogens. Jeanette Fitzsimons, MP and Co-leader of the Green Party, said she had listened to the extensive testing process for new pharmaceuticals described by Professor Garth Cooper, a witness appearing for the University of Auckland [IP16]. Ms Fitzsimons said the testing “does lower the risk from genetically modified medicines to the point where they are probably not dissimilar to the risks from other synthetic medicines, and that is why we are not opposed to the development of genetically engineered medicines in the laboratory”.<sup>18</sup>

26. The Commission is confident that the international research process, and the regulatory systems in place, or recommended by this Report, will ensure risks will be assessed as the technology progresses. As discussed in chapter 4 (Environmental and health issues), the degree of risk will be related to the gene construct used. Further, as recommended in chapter 6 (Research), we call for additional research in the form of environmental impact studies on the effects of genetically modified organisms and their products.

## Current and future specific uses

### Therapeutic treatments

27. In a background paper prepared for the Commission, Dr Michael Berridge<sup>19</sup> identified many genetically modified medicines in use in New Zealand. Dr Winship noted that genetic modification therapy is currently used in many medical specialties of clinical medicine, including cardiology, endocrinology, renal medicine, respiratory medicine, gastro-enterology, neurology, haematology and oncology. The therapeutic agents used are nearly all protein products derived using DNA technology and include products such as insulin, growth hormone and interferon.

28. The following table details the current commercially available therapeutic uses of genetic modification in New Zealand. It is based on information as at 1 October 2000 supplied by Dr Winship and Dr Berridge. Only two of the products in the table, insulin and hepatitis B vaccine, are used outside a hospital setting. Most are used in highly specialised, uncommon situations. Other therapeutic treatments are available free of charge from pharmaceutical companies as part of research trials and are therefore not on this list.

### Vaccines

29. Genetic modification enables a substantial expansion in the range of diseases for which vaccines can be developed. For example in the future vaccines may be available for diseases such as melanoma, asthma and psoriasis. The three

## Therapeutic uses of genetic modification commercially available in New Zealand

Products available	Medical use in New Zealand
Insulin	Diabetes
Growth hormone	Childhood growth retardation
Interferon- $\alpha$	Hairy cell and chronic myeloid leukaemias, Kaposi sarcoma, hepatitis B and C
Interferon- $\beta$	Multiple sclerosis
Interferon- $\gamma$	Chronic granulomatous disease
Erythropoietin	Anaemia associated with kidney failure
G-CSF	Neutropenias, stem cell collection
GM-CSF	Marrow transplantation
Factor VIII	Haemophilia
Factor VIII antibody inhibitor	Haemophilia
Factor IX	von Willibrand disease
Tissue plasminogen activator (TPA)	Heart disease and stroke (dissolves blood clots)
Interleukin-2	Cancer and cancer immunotherapy
Adenosine deaminase	Severe combined immunodeficiency (SCID)
DNAase (Pulmozyme®)	Cystic fibrosis
$\alpha$ -1 antitrypsin	Cystic fibrosis and emphysema
Follicle stimulating hormone (FSH)	Infertility
Alglucerase (Ceredase®)	Gaucher disease
TNF- $\alpha$ receptor Ig	Arthritis
IL-1 receptor-Ig	Arthritis
IL-1 receptor antagonist	Osteoporosis
Hepatitis B vaccine	Prevention of hepatitis and liver cancer
Cholera vaccine (live)	Prevention of cholera approved but withdrawn
Herudin	Anticoagulant
PDGF-A	Diabetic ulcers
Stem cell factor	Stem cell peripheralisation and transplantation
Monoclonal antibody treatments	Organ rejection Non-Hodgkins lymphoma (B-cell) Acute organ rejection Childhood RSV infection

genetically modified human vaccines currently used in New Zealand are produced from a genetically modified organism, but are not themselves genetically modified organisms. These are the vaccines for hepatitis A, hepatitis B and pertussis (acellular).

30. Most of the detailed evidence we received on vaccines related to use in animal welfare. These are discussed below in a section on animal remedies. Similar issues apply to human and animal vaccines.

31. Dr Glenn Buchan, a senior lecturer in immunology and a witness for the University of Otago, said:

The development of new and improved vaccines cannot be left to chance . . . The search for a vaccine against HIV, the causative agent of AIDS, has continued for over two decades now.<sup>20</sup>

32. He said this was due to the slow, haphazard and unreliable nature of existing technologies, which had failed to safely attenuate the virus and had failed to produce an effective vaccine from the killed virus. Dr Buchan considered that:

GE supplies a powerful tool which allows us to understand how the body responds to infection, how microbes become disease causing and how vaccines can be designed to protect against existing and new diseases that may appear.<sup>21</sup>

33. Not all submitters were as optimistic about the effectiveness of the new technology in vaccines. Dr Michael Godfrey, Medical Director of the Bay of Plenty Environmental Health Clinic and a witness appearing for PSRG, told us that the hepatitis B vaccine, which was genetically modified, “could cause a variety of immune and neurological health problems”<sup>22</sup> However, Dr Garth Cooper, Professor of Biochemistry and Clinical Biochemistry at the University of Auckland, for which he appeared as a witness, argued the importance of the genetically modified hepatitis B vaccine to the health of New Zealanders. He said he was responsible for oversight of a programme that was currently using recombinant [genetically modified] hepatitis B vaccine to eradicate hepatitis B virus from Maori, Pacific Island and Asian populations in New Zealand where it was:

currently estimated that probably around . . . 40,000 to 50,000, primarily Maori, are infected with the virus, and . . . all their contacts are at risk. [This vaccine has] probably be[en] administered to around three quarters of a million New Zealanders over the last 20 years in an attempt by the health system to protect New Zealanders from the ravages of the hepatitis B virus.<sup>23</sup>

34. The Commission was told that the genetically modified organisms in these vaccines are highly attenuated (their ability to reproduce is severely curtailed).

35. We consider that, in terms of safety, genetically modified vaccines are comparable to or better than their non-genetically modified counterparts.

36. When live genetically modified organisms are used in medicine, it is generally in vaccines. In New Zealand only one vaccine, the cholera vaccine, has contained live bacteria. These were genetically modified to remove the gene coding for the active cholera toxin. This vaccine was introduced into New Zealand in 1998. The Ministry of Health advised us in its public submission that in May 2000 it realised, in discussions with the Ministry for the Environment while preparing for this Royal Commission, that the vaccine fell within the regulatory frameworks of both the Medicines Act 1981, as a medical product, and the Hazardous Substance and New Organisms Act 1996 (HSNO), as a “new organism”, and that because of an oversight, approval from the Environmental Risk Management Authority (ERMA) had not been sought. ERMA then requested that the distributor recall the product. The Ministry of Health is negotiating with suppliers of alternative vaccines that would not require approval under HSNO. However, the Ministry considers that the medicine is more effective than other cholera vaccines and does not pose a significant risk to human safety. Another genetically modified vaccine, for rotavirus, was in the approval process at the time the cholera vaccine oversight was found, and was then withdrawn from the process. It is likely that, because of the increasing international trend toward developing live genetically modified vaccines, more medicines in future will require double approval unless legislation is modified.

### **Diagnostics**

37. Genetic modification technology is routinely used in diagnostics in New Zealand. We were told of many applications, typically in medical research and, in particular, the management of genetically-determined human health conditions. Most submitters supported the continued use of genetic modification technology in diagnostics.

38. In diagnostics, products of genetic modification and genetic modification techniques are used in two main areas: the identification of genetic differences, and the use of this information in the subsequent treatment of illness and disease. Use of genetic modification in diagnosis enables more accurate diagnosis, prevention and treatment of disease, and more accurate prescribing and patient management. Literally thousands of genetically modified products are used in clinical and diagnostic medical laboratories throughout the country. The Council of Medical Colleges in New Zealand [IP37] said in its submission that without continued access to genetic modification in diagnosis “many diagnostic tools would have to be removed”.<sup>24</sup>

39. Genesis Research and Development Corporation [IP11] noted that genetic modification technology is used in screening for HIV and hepatitis B viruses in infected blood products and donated organs. The New Zealand Biotechnology Association [IP47] told us of benefits, including: increased understanding of the genetic contributors to diabetes, the development of new opportunities for cancer treatment, better understanding of the genetic basis for differences in response to drug treatment, and in particular the possibility for better tailored treatment in psychiatric illness.

40. The University of Auckland drew attention to the importance of genetic modification technology in underpinning programmes for early detection of prostatic carcinoma. It maintained that a “removal of this test is likely to place all older males at increased risk of prostatic cancer”.<sup>25</sup>

41. Dr Dianne Webster, Clinical and Technical Head of the National Testing Centre [IP44], noted that New Zealand currently used genetic modification technology to test for seven metabolic disorders, but that overseas, technologies were available that would allow “screening for maybe up to 20 more”.<sup>26</sup> Dr Webster spoke of more than 500 inherited metabolic disorders or inborn errors of metabolism that affected various kinds of body chemistry. Dr Webster estimated that in New Zealand metabolic disorders were associated with about one birth in 1000, that is about 60 births each year.

42. Dr Christine Morris, Senior Researcher in Cancer Genetics, Christchurch School of Medicine, who was called as a witness by the Human Genetics Society, spoke about the widespread application of FISH (protocols using fluorescent *in situ* hybridisation) in human genetics research, and in clinical testing in laboratories. Dr Morris said FISH-related techniques were routinely used in laboratories in Auckland, Hamilton, Wellington, Christchurch and Dunedin. Dr Morris added that the use of these techniques in the diagnostic setting was:

... expected to grow exponentially over the next few years as the molecular basis of each of the approximately 4000 or so human genetic conditions unfolds. Their use in research is inevitable for as long as human genome mapping and the investigation of natural and disease-related genetic-related variations continues.<sup>27</sup>

43. We also received evidence of the beneficial use of genetic modification technology in relation to members of a particular family who because of genetic predisposition had a high risk of contracting stomach cancer. The affliction was regarded as a curse on the family. It meant that many members of a particular whanau and hapu developed cancer, necessitating major surgery. The E-cadherin gene predisposed one quarter of the family towards cancer. Maria Tini (Te Arawa, Ngai Tahu) said at the hui at Tamatekapua, Rotorua, use of diagnostic

techniques involving genetic modification enabled the family to identify those members who were predisposed to this cancer:

... in November 1996, an agreement was entered into with the Cancer Genetics Laboratory, Biochemistry Department, University of Otago, for a cancer genetic research project to study the basis for familial gastric cancer prevalent within members and descendants of our whanau. The research project was a joint venture between the parties. The project involved analysing genes from blood samples, histology material, archived biopsy samples and tumor material or tissue, in the hope of identifying a cancer predisposition gene. The research project and information obtained would be used for diagnostic purposes only, in the hope that it may lead to a better understanding of the genetic factors that may lead to the early onset of familial gastric cancer within the whanau and its descendants. Stomach cancer, like all cancers, can be treated more effectively if detected early. The aim of the project was to develop a genetic test to enable people at very high risk of getting stomach cancer to be identified before the person becomes sick. That way treatment protocols and clinical surveillance can start before the cancer has spread.<sup>28</sup>

44. Maria Tini told us that “dispelling the notion of the curse through knowledge, information and ongoing education has been fundamental to the whanau growth, development and survival”.<sup>29</sup>

45. We also heard at the Auckland regional hui at Orakei Marae from Dr Jan Bryant (Nga Puhi, Ngati Porou) who was involved as a doctor with the whanau who have adrenoleucodystrophy:

[It's] a very sad issue to see the offspring with adrenoleucodystrophy, and the fact that some of their mokopuna make it, others don't. So ... along with what [Dr David Jansen] said, if what we can do is bring these tools and this genetic research [to these people], then it is a tool for us to help our whanau.<sup>30</sup>

46. We accept the evidence we heard about the value of genetic modification technology in diagnostic medicine.

### **Gene therapy**

47. There are two types of gene therapy. Germ line therapy changes the genetic make-up of an individual in a way that can be transmitted to future generations, for example to correct an inheritable genetic disease such as Huntingtons disease or cystic fibrosis. Somatic therapy on the other hand involves changes to the genetic make-up of an embryo or a person in such a way that the changes are not passed on to future generations. The Ministry of Health told us that somatic gene therapy had been used in New Zealand in recent years to treat a few children with a rare fatal disease, but with limited success. We are also aware of a small number of instances where New Zealanders have been treated with somatic therapy

overseas as part of research trials. Apparently these treatments have been at least partially successful.

48. Gene therapy also includes some treatments for cancer, as detailed by Dr Woollett of RMI, which operate by manipulating genes and their properties so that they induce the body's own cells to replace defective tissue or grow new tissue.

49. The techniques used for some forms of somatic gene therapy are similar to those used with vectored vaccines, in that a vector, such as a harmless virus, is used to carry the new DNA into the cells where it is needed. With a vectored vaccine, the new gene produces a protein, which triggers an immune response. In contrast, gene therapy aims to replace a defective gene with a normal copy, to correct the problem caused by the mutation. The concerns associated with gene therapy are therefore similar to those for vectored vaccines and revolve around the high level of uncertainty about the safety of using viruses for these therapies.

50. As identified above, these therapies have provided considerable hope to families affected by genetic diseases. The Royal Society of New Zealand [IP77a] among others said that it was essential that this therapy be available in New Zealand for the benefit of patients. In reality, however, any practical use of these therapies lies well into the future. Dr Winship, when a witness for Auckland Healthcare Services, told us that in her opinion this would not happen in the next two decades. She also said that if continued research and clinical uses of genetic modification technology were prevented, there may be serious adverse consequences for people with acquired and genetic diseases who would be disadvantaged in the investigation and management of their health problems.<sup>31</sup>

51. Recent genome research has identified many unexpected similarities between mammalian genomes. This means that New Zealand agri-scientists who have been researching animal genetics are now at the forefront of research relevant to human health. Lysosomal Diseases stated research into a cattle disease at Massey University in the 1970s and 1980s led to the finding that it was the same genetic variation as a type of lysosomal disease in humans, and also as a certain sheep disease:

Significant research into Alpha-Mannosidosis in Aberdeen Angus cattle, carried out at Massey in the '70s and '80s, greatly assisted overseas researchers in the development of bone marrow transplant as a treatment option for a number of lysosomal storage diseases [LSD]. This work also provided significant baseline information for use in other related research which in turn has led to GM products for these diseases.

Similar work on another LSD – Batten disease – at Massey and Lincoln, using a naturally occurring sheep model, has provided the world with significant knowledge about this

disease. Although Batten is a very rare disease, it is also probably closer than any other disease to the biochemical pathway of other major diseases such as CJD [Creutzfeldt-Jakob disease] and Alzheimers. The animal model of Batten is therefore one of the likely pathways to understanding and hopefully treating or controlling these major health problems.<sup>32</sup>

52. Lysosomal Diseases described the various therapies currently available for sufferers of these severe diseases, and the limitations of those therapies. Its conclusion was gene therapy is well suited to treatment of lysosomal diseases as these are caused by mutations in a single gene. Further, it told us that gene therapy would be useful where the disease affects the brain as conventional treatments often cannot reach the brain.

53. While families burdened by inherited disease have great hope for gene therapies, others are concerned about the wider implications of this new technology. The New Zealand Catholic Bishops' Conference [IP38] called for a prohibition on germ line therapy for a defined period while New Zealand grappled with the uses of genetic modification that have less serious consequences. It also argued that while “in principle we would also see germ line therapy to be an ethically acceptable therapeutic intervention, providing safety issues are resolved and the welfare of future generations can be assured”,<sup>33</sup> it also argued that “we all share the human gene pool and it is not the property of any one of us, so our decisions in this respect need to be agreed upon collectively, rather than being individual decisions”.<sup>34</sup>

54. No submitters disputed that gene therapy could have positive therapeutic effects for sufferers of genetic diseases. However, many drew a line between therapeutic effects and genetic enhancement, also called eugenics. Hana Jensen (Tainui), Trustee of Raupatu Maori Lands Trust and Huakina Trust, said at the Ngaruawahia national hui:

To Maori, it would raise an ... ethical question as to what would be done with the failures. Selective beings and breeding may give a wonderful looking shell but no wairua within the shell.<sup>35</sup>

55. The New Zealand Organisation for Rare Diseases [IP98] said our beliefs would lead to personal choices about the use of this therapy; but our choice should not deny others opportunities, choices or benefits.

56. The Catholic Bishops' Conference, among others, opposed any use of gene therapy for enhancement purposes.

57. Toi te Taiao : the Bioethics Council should consult widely and develop guidelines for the uses of gene therapy, including therapeutic uses.

58. The coding of the human genome and the prospect of individuals having access to more complete information about their own precise genetic make-up has intensified the debate over individual privacy. Many submitters expressed concern about the prospect of having to relinquish ownership of knowledge relating to their genes, about being under pressure to produce information about an existing or expected medical condition and also about prejudice towards those with an existing or expected medical condition. The Youth Forum participants made the following comments on a mural they constructed: “All Beethoven’s family had some irreversible physical problem. If we had used genetic modification technology on him, would there have been a Beethoven?” and, “Should parents be able to choose traits in their children? My daughter will have blonde hair, blue eyes, be the prettiest, the most intelligent ...”.<sup>36</sup>

59. In gene therapy applications in New Zealand there may be an area not covered by legislation, even if the Assisted Human Reproduction Bill before Parliament becomes law. This bill will require all assisted reproduction procedures up to the stage of fertilised eggs to be approved by medical ethics committees, whether undertaken in public or private medical facilities.

60. Biotechnology is evolving so rapidly that the bill does not cover the newest technologies, for instance use of stem cells, which may open the possibility of gene therapy and “genetic enhancement” clinics. Genetic Technology Advisory Committee (GTAC) and Standing Committee on Therapeutic Trials (SCOTT) approvals are required for any gene therapy trial where the primary aim of the project is research. GTAC approval is required for any gene therapy carried out in public hospitals or medical facilities. Both bodies require formal ethics committee approval. However if a gene therapy were to complete phase 3 trials overseas and become available commercially, then use in New Zealand might not trigger any compulsory ethical committee oversight. The only ethical oversight of a private medical facility then would be with the professional colleges of the doctors and nurses offering the service. To avoid the need for prescriptive and possibly incomplete legislation in such contentious areas as gene therapy and cloning, general approval from the Bioethics Council and case-by-case local medical ethics committee approval should be legally required wherever the procedure is carried out, and regardless of who is paying for it.

### **Recommendation 9.1**

**that all gene therapy, whether in the public or the private sectors, require formal medical ethical oversight.**

## **Xenotransplantation**

61. Xenotransplantation involves the transference of a body organ from one species to another, although use of the term is usually restricted to a transfer from an animal to a human. The need for xenotransplantation arises because of the widespread worldwide shortage of human organs for transplantation, worsened by a low donation rate, increased demand with medical advances and decreases in the number of road deaths.

62. This technology is at a very early developmental stage. There are no examples in New Zealand of xenotransplantation in humans, even as part of research trials. However, pigskin is used as a temporary cover for badly burned patients, and pig heart valves have been used for many years to replace human valves damaged as a result of rheumatic fever. We are aware that xenotransplantation technology could be used in animal medicine to preserve the breeding potential of very valuable livestock and, while this may not raise the same ethical objections as in human use, the scientific risks are similar.

63. The evidence presented about xenotransplantation largely focused on the medical risks involved, specifically the risks of importing viruses from one species to another. The issues of porcine (pig) endogenous retroviruses (PERV) and human endogenous retroviruses (HERV) were raised. Endogenous retroviral DNA sequences are found in the chromosomes of all mammals, but currently their significance is unclear. Submitters varied in how they regarded these retroviral sequences. Some believed that they were harmless, and would not be affected by xenotransplantation. Others were very concerned about possible potential reactivation of the retroviral sequences.

64. Concern was expressed that xenotransplantation could cause a situation where either a HERV or PERV was reactivated and caused disease. Alternatively the strong promoters, often part of the modified gene, could accidentally turn on a PERV or HERV. We heard evidence that many scientists working in the field shared these concerns and were actively researching these potential problems. We agree clarification is needed before human trials can take place.

65. Associate Professor Richard Squires, a witness called by the New Zealand Veterinary Association [IP28], said “some virologists [were] deeply concerned that the transplantation of PERV-containing porcine organs into immunocompromised HERV-containing humans may eventually lead to emergence of new variant viruses, similar to one of the HERVs, but pathogenic”.<sup>37</sup> He noted that “deep concern, about what is, at this stage, a theoretical threat, has delayed progression of clinical trials with xenotransplantation”.<sup>38</sup>

66. One problem with PERVs relates to genetically modifying a pig to reduce the glycosylation in the membrane, a major cause of organ rejection in humans.

This would mean humans with pig organs would not need to take the toxic drugs that are needed to prevent rejection in the absence of genetic modification technology. However, if membrane glycosylation is reduced or removed, the pig's immune-recognition system could be damaged and a currently subdued PERV might reactivate and cause diseases that are transferred with the organ. Dr Squires said virologists claimed there was potential for one or more of these new viruses to pose a threat to the health, not only of the unfortunate organ recipients from whose bodies they might emerge, but also to society at large as contagion spread.<sup>39</sup>

67. The Ministry of Health advised that the Health Research Council referred clinical trials involving xenotransplantation to its SCOTT committee, whether or not genetic modification was involved. We have confidence in the professional judgment exercised by members of this committee. However wider consultation on these difficult issues is now appropriate.

68. The use of animal organs to prolong human life has both ethical and cultural implications. Organisations concerned with animal welfare, such as SAFE (Save Animals from Exploitation) [IP85], considered the use of transgenic animals to provide replacement parts for humans as exploitation. SAFE also described specific animal welfare concerns, for example that “donor cattle are frequently subjected to hormonal injection, artificial insemination and surgical removal of embryos or slaughter; sometimes the oviducts are removed by castration, or embryos are collected by flushing of the oviducts”.<sup>40</sup> Other submitters were concerned with the use of specific animals. We heard from the New Zealand Jewish Community [IP80] that Jewish dietary laws do not allow the consumption of pigs or the use of any product derived from pigs.

69. Joanna Paul, a witness for the Quaker Spiritual Ecology Group, Religious Society of Friends [IP50], objected to the mixing of animal and human parts in an unnatural way:

... trying something out on an animal ... seems a very crude way of finding whether that's going to work for a human being. ... There's a qualitative difference between that kind of thing and actually unhousing a mouse. ... I think that to make something what it is not is a sin and a crime. ... I think we have to regard the specificity of things as a sacred trust ... this is a new language we have to talk because it's a new problem.<sup>41</sup>

70. At the Wanganui hui, Pare Bennett spoke against the mixing of mauri, saying that:

No Rangi-tu-ha-ha nga mea katoa, tona whakairatanga ka hono te wairua me te tinana o nga tipu, o nga kararehe, o nga tangata katoa. He tino motuhake enei ahuatanga ki a matou. Ko tenei hoki te kakano i ruia mai i Rangiatea; te kakano o te maramatanga, te

tapu o nga mea katoa. Ka waihotia e nga tipuna enei ahuatanga motuhake mo matou nga uri hei tiaki mo ake tonu ake.

(All things emanate from the heavens, where the spirit and the body are joined, of plants, of animals, of all peoples. These are basic tenets to us, for this is the seed that was sown in Rangiatea, the seed of clarity, the most sacred of sacreds. These things were left by our ancestors as legacies for us to perpetuate forever. However, we maintain that by tampering with the genetic make-up of things, we make this thing not sacred, this is our grave concern.)<sup>42</sup>

71. We consider that more research is required before xenotransplantation could be considered seriously as an option. However, when eventually the issue arises as a practical question, either in the context of growing organs in New Zealand or the importation of an organ, the issue will first need to be referred to the Bioethics Council. Should the Council recommend in principle in favour of proceeding, the question of approval in the specific instance can be decided under the existing regulatory mechanisms.

72. It is noted that, if the Council decided to reject the use or importation of genetically modified organs for transplantation, ethical issues would remain since New Zealanders are likely to travel overseas to take advantage of the technology wherever it may be permitted.

### **Recommendation 9.2**

**that Toi te Taiao : the Bioethics Council develop ethical guidelines for xenotransplantation involving genetic modification technology.**

### **The convergence of food and medicine**

73. When is medicine a food and food a medicine? We heard evidence on a wide range of products ingested by humans that supplemented or enhanced normal dietary intake. Genetic modification makes it more possible for a substance to be both a food and a medicine. Several issues were raised (see below):

#### **Problems of definition**

74. Because of the speed of change, the current terminology is confusing. There are no internationally recognised definitions. Submitters used a plethora of terms, including “dietary supplements”, “functional foods”, “nutriceuticals” and “nutraceuticals”, that lacked clear and concise definition. Several categories of products were new and appeared to be evolving. The distinction between others appeared to be blurred. It was evident to us that it was unclear, both in legislation and in the wider public mind, what was essentially a food and what was

essentially a medicine. Confusion appears to be exacerbated by the use of the term “natriceutical” by the alternative health product industry.

### **Inconsistent regulation**

75. The confusing terminology is reflected in inconsistent regulation. Different regulatory arrangements apply to various products intended for human consumption. The Ministry of Health gave us information on the regulatory arrangements applying to medicines and foods. Since 1981 medicines and foods have been regulated separately under different statutes. Previously, medicines, foods and dietary supplements were all regulated under the Food and Drug Act 1969, but in 1981 regulation was divided between the Medicines Act 1981 for restricted medicines and the Food Act 1981 for food or dietary supplements. The Ministry explained that the Medicines Act and associated medicines regulations gave a framework for the approval of medicinal products. Medsafe, a unit of the Ministry of Health, approves medical products for distribution.

76. Under the Medicines Act, the Medicines Regulations 1984, the Misuse of Drugs Act 1975 and the Misuse of Drugs Regulations 1977, Medsafe regulates products used for a therapeutic purpose. The objective of the medicines legislation is to manage the risk of avoidable harm associated with the use of medicines. The legislation is designed to ensure that medicines meet acceptable standards of safety, quality and efficacy, that the manufacture, storage and distribution of medicines complies with standards applying right up to delivery to the end-user, and that information about the selection and safe use of medicines is provided to health professionals and consumers. Medsafe achieves this through pre-marketing approval of products and post-marketing surveillance.<sup>43</sup>

77. We heard evidence that submitters had confidence in Medsafe’s regulation. Sue Kedgley, Member of Parliament and a witness for the Safe Food Campaign [IP86], told us under cross-examination that genetically modified food should undergo “the same safety testing regime as genetically engineered pharmaceuticals”.<sup>44</sup>

78. We understand that dietary supplements are defined and regulated under statute but that other products are not. The Ministry of Health pointed out that dietary supplements are defined in the Dietary Supplements Regulations 1985 as “any amino acids, edible substances, foodstuffs, herbs, minerals, synthetic nutrients and vitamins sold singly or in mixtures in controlled dosage forms as cachets, capsules, liquids, lozenges, pastilles, powders, or tablets which are intended to supplement the intake of those substances normally derived from food”. These products come under legislative arrangements for food rather than medicine.

Other products alluded to by submitters, such as nutraceuticals and functional foods, appeared to lack consistent definition or legislative provision.

### **Joint trans-Tasman arrangements**

79. We were advised of discussions between the Australian and New Zealand Ministers of Health to establish a single joint trans-Tasman agency to replace Medsafe. The new agency would be responsible for evaluating medicines and medical devices, setting standards, compliance monitoring and enforcement activities.

80. Ian Lindenmayer, Managing Director of the Australia and New Zealand Food Authority (ANZFA), noted nutraceuticals and functional foods were “a very topical issue to the extent that the regulatory environment in New Zealand and the regulatory environment in Australia ... are different”.<sup>45</sup> He commented further that when the newly adopted joint Food Standards Code of Australia and New Zealand (Joint Food Treaty) became the source of the standards for the two countries it would be awkward to have “a group of products such as dietary supplements, which are regulated as dietary supplements still in New Zealand but regulated as foods in Australia”.<sup>46</sup>

### **Functional foods and nutraceuticals: foods or medicines?**

81. Functional foods and nutraceuticals are not specifically defined in legislation or regulations, but these terms are being increasingly used by industry. The meanings appear similar. Nutraceuticals are generally taken to be products that are extended to provide enhanced nutrition, for example vitamin A-enriched rice. Functional foods, on the other hand, were described by one source as being similar in appearance to conventional foods, and intended for consumption as part of a normal diet, but with modifications to take on physiological roles beyond simple nutrition.<sup>47</sup> The addition of plant sterols to margarine was given as an example. However, there is little published data or any consensus on just what comprises a functional food.

82. It is also becoming increasingly unclear whether functional foods and nutraceuticals are essentially foods or medicines. Dr Ross Clark, molecular geneticist and witness called by Auckland UniServices [IP23] confirmed “there is no clear distinction between what is considered a drug and what is considered to be a food”. He added that “the ‘health food’ industry highlights this blurred distinction. In the future this distinction will become even further blurred”.<sup>48</sup>

### **Foods with medicinal properties**

83. The increasing potential for developing and producing nutraceuticals and functional foods with medicinal properties and uses was constantly stressed. Dr Clark spoke of New Zealand’s ability to “leverage off its agricultural

sector and become a world leader in novel, high value nutraceutical products”.<sup>49</sup> Submitters, including the New Zealand Wool Board [IP30], the New Zealand Dairy Board [IP67] and the Foundation for Research, Science and Technology [IP21] stressed opportunities for the development of nutraceuticals. The New Zealand Arable-Food Industry Council [IP56], the New Zealand Feed Manufacturers Association/Poultry Industry Association of New Zealand/Egg Producers Federation of New Zealand [IP35], the New Zealand Grocery Marketers Association [IP54] and Comvita New Zealand [IP74] outlined the potential for New Zealand to develop functional foods.

84. Dr Brian Jordan, a witness called by Arable-Food Industry Council, told us that “New Zealand has real potential to use its biological base as the ‘science platform’ of a molecular revolution in health ... and functional foods”.<sup>50</sup> The Grocery Marketers Association predicted “the range of these specialised functional foods will significantly increase over the next few years as technological advances occur in the food industry”.<sup>51</sup> The Association presented a chart of the potential health benefits from genetically modifying plants. This indicated that potatoes could have increased levels and better distribution of starches that would make them easier to process and less prone to absorb fat when fried. Tomatoes could have higher lycopene levels to increase their antioxidant effects. Garlic could have higher allicin levels to lower cholesterol.

85. Given the likely expanded market for foods with enhanced medicinal properties, we have decided that clarity in terminology and a clear and robust regulatory system are priorities. Putting aside for the moment the issue of genetic modification, there appear to be three broad categories of product involved in this market: dietary supplements, functional foods and “pharmaco foods”.

86. Dietary supplements are products containing extracts, concentrates or synthetic versions of food substances. They are defined and regulated under the Dietary Supplements Regulations (discussed above). Functional foods are foods with enhanced nutritional value and include foods that have been genetically modified to enhance their nutritional value, including products generally referred to as nutraceuticals.

87. “Pharmaco food” is a new term we are using to encompass a new and evolving product. A pharmaco food is essentially a vehicle to convey a specific medicine or vaccine. We envisage applying this term to all foods that are genetically modified to deliver a particular therapeutic agent, such as a vaccine or a pharmaceutical. Historically medicines and vaccines have been delivered by a variety of means, including pills, capsules, drinks and injections. A pharmaco food would simply be another delivery mechanism for such medicinal purposes. The term would be used for products such as a proposed banana incorporating a

hepatitis B vaccine. In our view the regulation of these pharmaco foods should be the responsibility of Medsafe, as discussed below.

## Regulatory regimes

88. The regulatory issues for dietary supplements, functional foods and pharmaco foods were similar to those for medicines, food and crops. Because the risks involved in consuming medicinal products, foods and nutritional supplements are similar and vary only with the degree of concentration, volume consumed and frequency of consumption, the same standards of testing, monitoring and ongoing surveillance should apply to all.

89. The critical issues raised with us involved regulatory costs to industry, the safety of products consumed by humans and the requirements for labelling. We consider these issues can all be addressed under a clear, concise and robust regulatory arrangement.

### Labelling

90. The evidence concerning labelling is discussed extensively in chapter 8 (Food). We consider the issues are the same for dietary supplements, functional foods and pharmaco foods, which are all intended for human ingestion. It seems to us unnecessary to make distinctions among them.

91. The Ministry of Health believed some dietary supplements fell outside the scope of the Joint Food Treaty. If this were the case, “the labelling provisions of Standard A18 would not apply to all dietary supplements produced using gene technology”.<sup>52</sup> (Standard A18 requires all ingredients to be labelled if of genetically modified origin.) They noted however that dietary supplements were still covered by the provisions of section 9(4) of the Food Act 1981, “which prohibit the sale of food unfit for human consumption, and section 10 which prohibits misleading labelling”.<sup>53</sup>

### Regulatory oversight

92. As mentioned above under “Inconsistent regulation”, the approval regimes for nutritional products and medicines are covered by separate legislation with foods generally covered by the Food Act and medicines by the Medicines Act. The approval bodies established under this legislation also vary. Food approval, as discussed in chapter 8 (Food), is the responsibility of ANZFA in administering the Joint Food Treaty. Medicines approval is within the ambit of Medsafe, as discussed above.

93. These regimes apply to all products, irrespective of whether genetic modification technology is involved. The approval regime is further complicated if a product involves genetic modification. It then requires approval by ERMA

under HSNO. This means that some products require two approvals, others three. For example, a live genetically modified organism that is a vaccine requires approval from ERMA and Medsafe. If the compound is ingested as “food”, further approval is required from ANZFA. Milk from a cow genetically modified to incorporate a vaccine (in a product such as butter or ice cream), would need three approvals: from ERMA, because a genetically modified organism is involved, from Medsafe because it is a medicine, and from ANZFA because it is a food.

94. These regulatory requirements cause confusion and compliance is expensive. Many submitters gave evidence on the extent and impact of these expenses and this discussion is covered in chapter 6 (Research).

95. Medicines and medicinal products involving genetic modification fall within four product categories: medicines, pharmaco foods, functional foods and dietary supplements. Attention should be given to streamlining the approval processes so as to reduce costs and confusion. This process could be achieved by extending the role of Medsafe to encompass approval of such products.

96. In the situation where multiple approvals are currently required for genetically modified medical products grown in New Zealand (such as the earlier example of a vaccine incorporated into butter or ice cream), we recommend that the existing ERMA approval regime should continue if the original transgenic organism is developed and grown in New Zealand. This would allow ERMA to fully assess the environmental impacts of the product. For medical products not developed or grown in New Zealand, we recommend that an extended Medsafe be the only approval authority required. These suggestions are summarised in the table opposite.

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### **Recommendation 9.3**

**that products be clearly defined in legislation as medicines, pharmaco foods, functional foods or dietary supplements.**

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### **Recommendation 9.4**

**that imported medicines and pharmaco foods that include live genetically modified organisms be approved for use by Medsafe without a requirement for additional approval from the Environmental Risk Management Authority.**

**Recommended approval process for genetically modified products**

<b>Type of product</b>	<b>Regulatory oversight*</b>	<b>Label</b>
Food	<ul style="list-style-type: none"> <li>• ANZFA for approval</li> <li>• Food Authority for surveillance of compliance with standards</li> </ul>	ANZFA
Dietary Supplement	<ul style="list-style-type: none"> <li>• ANZFA for approval</li> <li>• Food Authority for surveillance of compliance with standards</li> </ul>	ANZFA plus Medsafe requirements
Functional Food	<ul style="list-style-type: none"> <li>• ANZFA for approval</li> <li>• Food Authority for surveillance of compliance with standards</li> </ul>	ANZFA
Pharmaco Food	<ul style="list-style-type: none"> <li>• Medsafe for approval</li> <li>• Ministry of Health for surveillance</li> <li>• Food Authority for surveillance of compliance with standards</li> </ul>	ANZFA plus Medsafe requirements
Medicines	<ul style="list-style-type: none"> <li>• Medsafe/Ministry of Health</li> </ul>	Medsafe

\* For products grown or produced in New Zealand, ERMA approval required in addition.

## Animal remedies

### Veterinarian medicines and nutritional supplements

97. Evidence we received on the genetic modification of animal feed focused mostly on lysine, the amino acid that is added to corn and fed to livestock. Adding lysine means a far greater proportion of corn can be used in chicken diets, and used more efficiently. Bob Diprose, Executive Director of the Poultry Industry Association of New Zealand, presenting for the Feed Manufacturers Association/Poultry Industry Association/Egg Producers Federation, told us that for the year ended 1999 it was estimated that 1200 tonnes of the amino acid lysine was used in the livestock industry in New Zealand. Lysine is a product of genetically modified bacteria, similar to tryptophan, produced in fermenter vats. (See box in chapter 4: Environmental and health issues.)

### Vaccines for animals

98. The Veterinary Association cited several benefits to be obtained from the continued use of genetic modification technology in animal treatment. Most of this evidence centred on the use of so-called “new generation” of genetically modified vaccines. The Association said that such vaccines would reduce animal suffering, make New Zealand’s animal industries more efficient and reduce the use of antibiotics in animals. It also emphasised that genetically modified vaccines with “markers” would allow tests that could distinguish between vaccinated animals and those which had been exposed to disease. It regarded such vaccines as “an unique and efficient tool for the eradication and control of diseases which are [not] endemic or normally exotic to New Zealand”.<sup>54</sup> Such diseases would include foot and mouth disease.

99. Professor Emeritus Bill Manktelow of Massey University’s Veterinary School, called by the Veterinary Association, spoke of the “considerable advantages” of genetically modified vaccines over conventional products, saying they were “often more effective, often safer”<sup>55</sup> and that they provided opportunities to vaccinate against more diseases than was previously possible. He stressed New Zealand’s “enviable high standard of health in its livestock” and said that maintaining this high standard was “a vital and continuing task for our biosecurity defences”.<sup>56</sup>

100. The benefits of further research and development of such new vaccines were stressed by Dr Kenneth McNatty, a scientist at Wallaceville Animal Research Centre, presenting evidence on behalf of AgResearch [IP13]. He identified the need for improved vaccines to prevent major farm animal diseases such as tuberculosis, Johne’s disease, helminthosis and campylobacteriosis.<sup>57</sup>

Dr McNatty stressed the views of the Veterinary Association with his comments that “vaccines should substantially reduce the amounts of drugs and chemicals required for farming, and substantially reduce the billion dollar impact of farm animal diseases on the New Zealand economy”.<sup>58</sup> As an example, he cited the case of a bovine tuberculosis vaccine that had the potential to eliminate the disease from wildlife, and thus reduce control costs of more than \$40 million per year. Meat New Zealand [IP31] also identified potential vaccine uses as alternatives to chemical drenches in animals such as cattle and sheep. It said “chemical drench resistance in ruminant animals continues to develop on New Zealand farms and we need new techniques to control this problem”.<sup>59</sup>

101. Vaccines were discussed under four classes:

- **Live attenuated vaccines** These are currently used in New Zealand for immunisation of cats. The Veterinary Association gave the example of Leucogen, a vaccine against feline leukaemia virus, also known as feline AIDS. These vaccines consist of disease microorganisms that have been genetically modified so that they no longer have their virulence, but can still induce immunity. Such vaccines could also be made by introducing into harmless microorganisms sequences of DNA containing code for the production of proteins that induce immunity.
- **Subunit vaccines** These vaccines typically contain parts of the disease-causing microbe that will induce immunity. Parts of the organism required for it to cause disease are absent. Although these vaccines could be produced using non-genetic modification technology, the new technology has greatly advanced opportunities for their production. Subunit vaccines have widespread acceptance and use in New Zealand and overseas. In the past many conventional animal vaccines have been made from whole live weakened (attenuated) microorganisms, a method with several risks. These include mild disease, severe side effects, reversion to full virulence in the field and infection of other non-target animal species. Subunit vaccines reduce these risks.
- **(Naked) DNA based vaccines** These vaccines are not currently used in New Zealand. The Veterinary Association told us these vaccines are similar to other vaccines derived from genetic modification, but that they “rely entirely on the animal’s own cells to take up the injected DNA and cause the host animal cell to make the foreign antigenic (immunity inducing) protein”.<sup>60</sup> Several submitters gave evidence of their concerns about the impact of naked DNA in the environment at large, among them Professor Terje Traavik, Head of the Department of Virology at the University of Tromsø School of Medicine in Norway, who appeared as a witness for Greenpeace New Zealand [IP82], Friends of the Earth (New Zealand) [IP78], and

Environment and Conservation Organisations of New Zealand [IP102]. He described a series of virus infection trials carried out at his university in which naked genomic DNA was injected into rabbits and mice and, contrary to “what was known from the literature, ... so-called conventional wisdom”<sup>61</sup> and the researchers’ expectations, the DNA was not broken down but instead produced illness. Professor Traavik also noted that:

... the problem is ... we know in the case of a few, perhaps rare, combinations of nucleic acids and circumstances, nucleic acids will be able to be taken up from the mucous membranes. However, we have no knowledge of the sequences, structures or environmental factors that can contribute to such stability [ie, failure to break down]. Nor can we therefore, at the present time, predict what type of DNA will avoid rapid breakdown in the organism and which environmental factors may contribute to this.<sup>62</sup>

We are aware that Professor Traavik’s research was carried out from 1989 to 1993, and that since that time his findings and those of others have been used to develop vaccines.

- **Vectored DNA vaccines** These are not available in New Zealand. However, the Veterinary Association said it understood the United States Department of Agriculture had approved a vaccine for immunising chickens against Newcastle and fowl pox diseases. Although fowl pox was present in New Zealand, it was not significant, and there was no problem here with Newcastle disease. The Association also said that, in the event that Newcastle disease became established here, availability of the vaccine from an overseas source provided “another strategic option”.<sup>63</sup>

102. We regarded the evidence on the potential use of vaccines for animals as significant for two reasons. First, the technology has the potential to impact on New Zealand’s primary sector. Second, the technology used for animal vaccines, including the research and development of such vaccines, has implications for humans.

103. We consider moves to have these “new generation” vaccines more widely available in New Zealand are likely to be made first for animal remedies. We cannot ignore the possibility that a threat to New Zealand’s biosecurity in the form of a major livestock disease may be the impetus for such increased use.

104. As noted earlier in this chapter, we have concerns about the potential environmental impact of live genetically modified organisms. Such effects do not at the moment appear to be a major problem in New Zealand, and we cannot say what effect, if any, they would have on the environment. However, New Zealand should anticipate the likely increased availability and use of such products in relation to both humans and animals.

105. The Veterinary Association recommended that:

... for any GM-based product proposed as an animal remedy, provision of adequate information on efficacy and the genetic modification involved in its manufacture must become a statutory requirement for any application for its registration.<sup>64</sup>

### **Recommendation 9.5**

**that, in respect of applications for approval as Animal Remedies of genetically modified organisms or products manufactured by processes using genetic modification techniques, the specified information which the Director-General of Agriculture and Forestry requires to be contained in applications under the Agricultural Compounds and Veterinary Medicines Act 1997 include full information on the efficacy and the form of the genetic modification used in manufacture; and**

**that such information be included as one of the categories of relevant risks and benefits under section 19 of the Act.**

## Emergency use of genetically modified organisms

106. Submitters questioned the adequacy of the statutory powers for emergency use of genetically modified organisms. We are also aware that it is not possible to hold as a stockpile enough animal vaccine to respond to a major outbreak of all diseases.

107. The Veterinary Association told us that stockpiling of vaccines for control of possible outbreaks was becoming a common phenomenon overseas. For example, the United States Department of Agriculture currently held a stockpile of a vaccine against avian influenza.

108. New Zealand's ability to respond quickly to any outbreak of disease in animals and humans was raised with the Commission. We made enquiries of relevant government agencies, including the Ministry of Health, the Ministry for the Environment, the Ministry of Agriculture and Forestry, and ERMA, to ascertain what legislative powers they had to authorise emergency imports of a genetically modified organism.

109. Currently three statutes cover the possible use of organisms in emergencies, or in relation to them. These are HSNO, the Biosecurity Act 1993 and the Health Act 1956.

110. In terms of HSNO, section 46(1) lists the types of emergency situations in which the Act applies. If the emergency is not within these categories, an application for the importation or release of a new organism must be made to ERMA under normal application procedures. Any other import or release is illegal.

111. If the situation meets the conditions in section 46(1), an emergency can be declared and sections 47 and 48 apply. These sections allow for emergency applications for importation or release of organisms, in foreseeable emergencies only. If the emergency or the use of the organism in relation to it was unforeseeable, HSNO does not apply to the importation or use of that genetically modified organism, provided it is not one of the prohibited organisms in the second schedule of the Act.

112. ERMA advised that it expected most emergencies were likely to be declared, in which case HSNO would apply.

113. The Ministry for the Environment told us that “section 49 of the HSNO Act, in order to provide a workable solution to the minimisation and remediation of emergencies, must be interpreted narrowly. Foreseeable therefore must mean ‘foresight of the use of the exact organism’ or ‘foresight of the exact emergency’”.<sup>65</sup>

114. There are powers under sections 144–145 of the Biosecurity Act to declare an emergency. Provisions under this section allow for action to be taken to manage or eradicate the organism in respect of which the emergency has been declared.

115. The Health Act also has provision for the control of infectious diseases in emergencies, and these are in addition to the powers conferred under the Biosecurity Act. The Ministry for the Environment also advised that expanded public health emergency provisions are being considered for inclusion in a proposed Public Health Bill, which is intended to replace the Health Act.

116. In anticipated disease outbreaks rapid importation of vaccines may be required. Where the emergency provisions under HSNO, the Biosecurity Act and the Health Act are invoked to control the outbreak of disease in humans or animals, but it could reasonably be argued that such an outbreak was foreseeable, rapid importation of vaccines or medicines containing live genetically modified organisms may not be possible.

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### **Recommendation 9.6**

**that, as protocols identify useful therapeutics for serious disease control, approvals through Environmental Risk Management Authority (ERMA) and Medsafe be sought in advance for the importation of live genetically modified organisms in the form of vaccines.**