Witness Brief Form 2

Royal Commission on Genetic Modification

1. Name of Witness

Maewan Ho

2. Name of "Interested Person" (on behalf of whom the Witness will appear)

GE Free New Zealand (RAGE) in Food and Environment Incorporated

3. Witness Brief Executive Summary

Executive Summary

Provide an overarching summary of the evidence and recommendations made [in respect of items (1) and (2) of the Warrant]. The Executive Summary should be no more than **3** pages in length

Please note that individual section summaries will be required and therefore the Executive Summary should focus on summarising the issues addressed in the brief and provide cross references to the sections in which the issues are covered rather than summarising the substantive content

ES6.1 I obtained my B.Sc. Biology (1964) and Ph. D. Biochemistry (1967) from Hong Kong University, and was Postdoctoral Fellow in Biochemical Genetics, University of California San Diego, from 1968 to 1972. An award of a Fellowship of the US National Genetics Foundation took me to London University in the United Kingdom, where I became Senior Research Fellow in Queen Elizabeth College. I then became Lecturer in Genetics (from 1976) and Reader in Biology (from 1985) in the Open University, and since retiring in June 2000, Visiting Reader in Biology at the Open University and Visiting Professor of Biophysics in Catania University, Sicily. My career so far spanned more than 30 years in research and teaching in biochemistry, evolution, molecular genetics and biophysics, with over 200 publications including 10 books. Since 1994, I have been scientific advisor and spokesperson for the Third World Network on biotechnology, biosafety and related issues, and have produced many reports and papers on the subject for policy-makers and the general public, as well as articles for peer-reviewed scientific journals.

ES6.2 In 1999, I co-founded the Institute of Science in Society (ISIS) of which I am Director. ISIS is a not-for-profit organisation promoting socially and ecologically accountable science and the integration of science in society. ISIS also represent a group of scientists around the world (currently 364 from some 40 countries), who have co-signed a World Scientists Statement and Open Letter to All Governments, calling for a moratorium on environmental releases of GMOs on grounds that they are unsafe, and to revoke and ban patents on life-forms and living processes, on grounds that they are unethical (Appendix 1).

ES6.3 In this Witness Brief, I explain why GMOs are different, how they are made, why they are inherently unreliable and unsafe, and how current regulatory processes fail to protect health and biodiversity. The risks have to be balanced against the potential benefits.

ES6.4 The creation of genetically modified organisms (GMOs) is a new departure from conventional selective breeding and introduces new hazards. This view is shared by many

scientists, including those advising the United States and United Kingdom Governments (see Appendix 1). The techniques and the nature of artificial constructs (GM constructs) made are the same in all applications, whether in agriculture or in biomedicine, and so are the hazards involved.

ES6.5 Conventional selective breeding involves crossing varieties within a species or between closely related species with similar genetic makeup. That is because genetic barriers prevent reproduction between unrelated species and limit the exchange of genetic material between them.

ES6.6 Almost by definition, genetic engineering involves designing artificial GM-constructs to break down all species barriers and to invade genomes. There is thus no limit to the new genes and new combinations of genes that can be made in the laboratory, nor to the GMOs created, which may never have existed in billions of years of evolution.

ES6.7 Most of the genetic material used is isolated from a wide variety of dangerous bacteria, viruses and other genetic parasites, including antibiotic resistance genes that make bacterial infections untreatable.

ES6.8 GM-constructs generally contain strong genetic signals, *promoters*, which enable the foreign genes to be expressed at very high levels continuously effectively placing those genes outside the normal metabolic regulation of the GMO. The most common promoter used in plants is from the cauliflower mosaic virus (CaMV).

ES6.9 The genetic engineer cannot target or control where the GM construct containing the foreign genes are inserted in the genome. Each GM line is the result of one or more 'transformational' events in a single plant cell in which the GM construct integrates into the cell's genome. On account of the uncontrollable, random nature of the transformational process, each transformed cell, and hence the GM line derived from it, will be distinct, despite the fact that the same GM-construct(s) and plant cells are used.

ES6.10 GM constructs are also structurally unstable, and are frequently rearranged, deleted or repeated in part or in whole. The resultant GMOs, likewise are unstable and do not breed true, so significant genetic and epigenetic changes may occur in subsequent generations, multiplying the unpredictable risks to health and biodiversity. Current regulatory systems do not take this into account.

ES6.11 There are four special safety concerns arising from GMOs (Appendix 2):

1. Effects due to the exotic gene products introduced into the GMO.
2. Unintended, unexpected effects due to random insertion of GM constructs; and interaction between foreign genes and host genes.
3. Effects associated with the nature of the GM-constructs.
4. Effects of gene flow, especially secondary, horizontal spread of genes and GM-constructs from the GMOs to unrelated species.

ES6.12 Examples of hazards from the exotic gene products introduced are the Bt toxins originating from the soil bacterium *Bacillus thuringiensis*, engineered into GM crops to kill insect pests, which are found to harm beneficial insects such as lacewings, and endangered species such as monarch butterflies and the black swallowtail. One of them, the Cry9C in Aventis'

Starlink GM maize intended for animal feed, is known to be a potential allergen for human beings, and is behind the recent massive recall of contaminated taco shells in the United States. Current safety tests are inadequate to address even this problem

ES6.13 The most notorious case of unexpected, unintended effects due to toxins or allergens involved a genetically engineered batch of tryptophan in the United States that killed 37 and made 1500 seriously ill in 1989. Current safety tests do not address unintended effects at all.

ES6.14 Safety concerns have been raised over the 35S promoter from the cauliflower mosaic virus (CaMV) that is in practically all GM crops already commercialized or undergoing field trials (Appendix 3). CaMV is closely related to human hepatitis B virus, and less closely, to retroviruses such as the AIDS virus. Although the intact CaMV specifically infects plants of the cabbage family, its isolated 35S promoter is promiscuous across domains and kingdoms, and is active in all plants, algae, yeast, bacteria as well as animal and human systems. It can substitute in part or in whole for promoters of other viruses to give infectious viruses. It is known to have a 'recombination hotspot' where it is prone to break and join up with other genetic material, hence increasing the likelihood for horizontal gene transfer and recombination. It has the potential to reactivate dormant viruses, which have now been found in all genomes, plants and animals included, and to recombine with other viruses, dormant or otherwise, to create new viruses. In addition, the fact that it is active in animal and human cells means that, if transferred into their genomes, it may result in over-expression of certain genes that are associated with cancer.

ES6.15 GM constructs can spread by ordinary cross-pollination to create herbicide-tolerant weeds and superweeds. Another consequence is the spread of the novel genes and GM-constructs for over-expression, as well as the antibiotic resistance marker genes, which are in a high proportion of GM crops. This will multiply the unpredictable physiological impacts on the organisms to which the genes and gene-constructs are spread, and hence on the ecosystem.

ES6.16 By far, the most serious consequences are from the horizontal transfer of GM constructs to unrelated species, in principle, to all species interacting with the released GMO (Appendix 4). There is already evidence for transfer of GM genes from GM plant material to soil bacteria and fungi. Recent experiments in 'gene therapy'also show that GM constructs can readily invade cells and genomes of animals and human beings (Appendix 5).

ES6.17 The hazards from horizontal transfer of GM constructs are summarised as follows,

- Creation of new viruses by recombination between the viral genes or promoters in GM construct and viruses in the environment.
- Creation of new bacterial pathogens by recombination between the bacterial genes in the GM construct and bacteria in the environment.
- Spread of drug and antibiotic resistance marker genes in the GM construct to other bacteria making infections much more difficult to treat.
- Random, insertion of GM genes into cells with harmful effects, including cancer.
- Reactivation of dormant viruses that cause diseases by the CaMV and other viral promoters in GM constucts.
- Multiplication of ecological impacts due to all the above.

ES6.18 Unfortunately, current regulatory systems do not take horizontal gene transfer into account, and many dangerous GM constructs and GM genetic material are discharged into the

environment, and even recycled as food, feed and fertilizer, in direct violation of the precautionary principle (Appendix 6).

ES6.19 The negative socioenomic and ethical impacts of GM technology should also be taken into account. Patents on life-forms and living processes amount to corporate ownership of life that destroy livelihoods, compromise food security, violate human rights and dignity and are contrary to public good. Biomedical applications, in particular, are having disastrous consequences on the social and moral fabric of civil society, with no clear benefits to improving health (Appendix 7).

ES6.20 Supporters of GM agriculture are still speaking of potential benefits after more than 20 years, because there has been none so far. Evidence is emerging that GM crops are agronomically as well as ecologically unsustainable. Transgene instability give rise to inconsistent performance in the field, yield drag and other failures. Global market for GM crops has collapsed as people all over the world are rejecting them and opting for organic sustainable agriculture.

ES6.21 In contrast, agroecological approaches since the 1980s, which combine local farming knowledge and techniques with contemporary western scientific knowledge, have led to improved yields, as well as social, economic, health and environmental benefits for tens of millions in the developing as well as the developed world.

ES6.22 The genetic modification approach is based on a discredited, mechanistic paradigm at odds both with the scientific findings of the new genetics (Appendix 8) and with our aspiration for a safe, healthy, just and compassionate world.

Appendices

I. World Scientists Open Letter to All Governments on GMOs (with many references to scientific and other literature) www.i-sis.org

II. Ho, M.W. (1999). Special Safety Concerns of Transgenic Agriculture and Related Issues Briefing Paper for Minister of State for the Environment, The Rt Hon Michael Meacher in *Seminario Internacional sobtre Direcito da Biodiversidade, I* . Available on http://www.biotech-info.net/special_concerns.html

III. Scientific papers on the cauliflower mosaic virus promoter (all available on http://www.i-sis.org

1. Ho, M.W., Ryan, A. and Cummins, J. (1999). The cauliflower mosaic viral promoter – a recipe for disaster? *Microbial Ecology in Health and Disease* 11, 194-197.
2. Cummins, J., Ho, M.W. and Ryan, A. (2000). Hazards of CaMV promoter. *Nature Biotechnology* 18, 363.
3. Ho, M.W., Ryan, A. and Cummins, J. (2000). Hazards of transgenic plants with the cauliflower mosaic viral promoter. *Microbial Ecology in Health and Disease* 12, 6-11.
4. Ho, M.W., Ryan, A. and Cummins, J. (2000) CaMV 35S promoter fragmentation hotspot confirmed, and it is active in animals. *Microbial Ecology in Health and Disease* (in press).

IV. Ho, M.W. (2000). Horizontal gene transfer, and Ho, M.W. (2000). Techniques and dangers of genetic engineering. Commentaries to appear on the website of SCOPE - a NSF-funded research project involving *Science* Journal and groups at the University of California at Berkeley and the University of Washington in Seattle; for a slightly different version of the commentaries see Ho, M.W. (2000). Horizontal gene transfer – hidden hazards of genetic engineering www.i-sis.org

V. Ho, M.W., Ryan, A., Cummins, J. and Traavik, T. (2000). *Unregulated Hazards: 'Naked' and 'Free' Nucleic Acids*, ISIS and TWN Report www.i-sis.org; also Ho, M.W., Ryan, A., Cummins, J. and Traavik, T. (2000).Slipping through the regulatory net: 'naked' and 'free' nucleic acids (submitted).

VI. ISIS News#6 October 1000 www.i-sis.org , especially "Dangerous GM wastes recycled as food feed and fertilizer" Mae-Wan Ho and Joe Cummins, "EU Directive on deliberate release still inadequate" Angela Ryan; and
Use and abuse of the precautionary principle. By P.T. Saunders, submitted to US Senate on Biotechnology, July 2000.

VII. Ho, M.W. (2000). The Human Genome – The Biggest Sellout in Human History. ISIS-TWN Report, October 2000 www.i-sis.org

VIII. Ho, M.W. (1999). *Genetic Engineering Dream or Nightmare? Turning the Tide on the Brave New World of Bad Science and Big Business*, Gateway, Gill & Macmillan, Dublin.

Evidence by Section (as specified in the matters set out in the Warrant)

Evidence by Section

Witness briefs are to be structured in line with the matters specified in the Warrant and the sections numbered accordingly

Each section should stand alone, and include a section summary, identifying the issues addressed in the section

Witness briefs may address **all** or only **some** of the sections (as specified in the Warrant). However section numbers should be retained, for example, if a brief addresses matters (a), (c) and (e), the sections shall be numbered (a), (c), and (e), rather than a, b, and c

Witness briefs may, within each section, adopt a sub-section approach using different headings; however, each paragraph should be consecutively numbered

Section B (c)

B (c) the risks of, and the benefits to be derived from, the use or avoidance of genetic modification, genetically modified organisms, and products in New Zealand, including:

(i) the groups of persons who are likely to be advantaged by each of those benefits

(ii) the groups of persons who are likely to be disadvantaged by each of those risks

Section B (c) Summary

I can see no clear public interest in genetic modification in any of the areas, for reasons already stated. However, I recognize the need for supporting basic research under well-contained conditions, especially in areas relevant to biosafety. In the meantime, there should be much more investment of public funds into research and development of sustainable, organic agriculture and holistic health.

B (c)(i)

1.1 Biotech corporations should stand to gain, and have gained mainly from the sale of herbicides tied to herbicide-tolerant GM crops. The human genome project has also generated enough propaganda to boost their shares in the stock market. In the long run, they will stand to lose. The demise of Monsanto was an object lesson. The collapse of the GM market is already having an effect on corporate investment in agricultural biotechnology. It may not be long before the biomedical bubble bursts

B (c)(ii)

1.1 Everyone will be hurt by the risks involved, as GM constructs will pollute our land, air and water. Even corporate bosses will not be immune to new viral and bacterial pathogens, nor from the potential of cancer from horizontal transfer of GM constructs. In the short term, farmers will suffer most both because of the collapse of the GM market and the intensification of corporate control, especially in the form of patented seeds that they are not allowed to resow.

Section B (d)

B (d) the international legal obligations of New Zealand in relation to genetic modification,

genetically modified organisms, and products
Section B (d) Summary

1.1 The Cartegena International Biosafety Protocol under the UN Convention on Biological Diversity was negotiated in the Conference in Montreal, Jan. 2000, at which New Zealand was a party. The Biosafety Protocol is intended to regulate the transboundary movement and use of GMOs, and has been signed by 65 countries to-date. It is based on the precautionary principle. Many countries and regions are actively drafting national biosafety laws as a result. There is also general recognition that the Biosafety Protocol is not strong enough, and hence national/regional law will have to be stricter.

Section B (e)

B (e) the liability issues involved, or likely to be involved, now or in the future, in relation to the use, in New Zealand, of genetic modification, genetically modified organisms, and products
Section B (e) Summary

1.1 Liability has been agreed in principle in the Cartegena Biosafety Protocol. The recent incident involving the contamination of taco shells by Aventis' Starlink GM maize will set a precedent in liability. Aventis is reported to be buying back all contaminated corn and compensating farmers.

Section B (f)

B (f) the intellectual property issues involved, or likely to be involved, now or in the future, in relation to the use in New Zealand of genetic modification, genetically modified organisms, and products
Section B (f) Summary

1.1 There are strong moves by many G77 countries against Trade Related Intellectual Property Rights at the World Trade Organization, especially with regard to patents on GMOs, genes and cell lines. There is also growing opposition to the EU Patents Directive dealing with biotech patents from many European countries. Strong evidence is emerging that these patents are stifling research and innovation. New Zealand may want to take those considerations into account.

Section B (h)

B (h) the global developments and issues that may influence the manner in which New Zealand may use, or limit the use of, genetic modification, genetically modified organisms, and products
Section B (h) Summary

1.1 I have debated and lectured in nearly 30 countries around the world within the past 3 years. There is strong resistance to GM crops everywhere: farmers because corporate monopoly, and consumers on account of safety. Resistance has spread finally to the US, the largest producer by far, as world market for GM produce has collapsed. Between 1999 and 2000, planting of GM crops has decreased by 24% in maize, 13% in cotton and 9% in soya. Argentina, the second largest producer is having second thoughts, while Canada, the third, is growing 10% less GM canola.

Section B (i)

B (i) the opportunities that may be open to New Zealand from the use or avoidance of genetic modification, genetically modified organisms, and products
Section B (i) Summary

The demand for organic, non GM produce is growing exponentially worldwide. There is every incentive to avoid GM crops and to switch to organic.

Section B (j)

B (j) the main areas of public interest in genetic modification, genetically modified organisms, and products, including those related to: **(i)** human health (including biomedical, food safety, and consumer choice) **(ii)** environmental matters (including biodiversity, biosecurity issues, and the health of ecosystems) **(iii)** economic matters (including research and innovation, business development, primary production, and exports) **(iv)** cultural and ethical concerns
Section B (j) Summary

1 The risks are inherent to genetic modification, at least in its present form, and include,

- new toxins and allergens, resulting directly from the gene products introduced or indirectly due to the inherent uncontrollable nature of the process and the interaction between foreign genes and host genes
- creation of superweeds due to spread of GMOs introduced or the GM genes and constructs by cross-pollination
- harm to nontarget beneficial species of predators or pollinators
- spread of antibiotic resistance marker genes by horizontal gene transfer to bacterial pathogens, making infections untreatable
- creation of new bacterial pathogens by horizontal gene transfer and recombination
- creation of new viruses and reactivation of dormant viruses by horizontal gene transfer and recombination
- risks of cancer from horizontal transfer of GM constructs into animal and human cells
- multiplication of ecological impacts due to all of the above.

2. Compelling evidence of actual and suspected hazards already exist, but regulatory oversight is still lacking. There is also no evidence of actual benefits of GM crops. On the contrary, evidence has emerged indicating inconsistent performance, yield drag and increase in herbicide use.

3. Many of the potential benefits have been promised ever since the beginning of genetic engineering, and all the signs are that they will never be realized. For example, nitrogen fixation involves at least 50 genes. Similarly, drought and salt tolerance are due to many genes scattered over the entire genome. In fact, many salt and drought tolerant plants already exist, as do plants for bioremediation which clean up polluting heavy metals and so on.

4. I have not been asked to address biomedical applications explicitly. But even there, many of the benefits claimed are illusory, and the risks to health as well as the social moral fabric of civil society far outweigh the benefits (Appendix 7).

B (j)(i) (ii)

Risks and benefits of GM Technology and Its Applications

1.1 In order to understand the risks as well as the potential benefits of GM technology, it is necessary to understand why GMOs are different and how they are made, why they are inherently unreliable and unsafe, and how current regulatory processes fail to protect health and biodiversity. The risks are serious and uncontrollable, and must be balanced against the potential benefits.

1.2 One of the major shortcomings of current regulatory systems is their fragmented state, reflecting the fragmented state of the science. Those busy exploiting the technology for biomedicine are unaware of what is happening in agriculture and *vice versa*. Many applications are not regulated because they fall between the scopes of different directives and regulatory bodies (1,2, Appendix 6). Regulators pay lip service to the precautionary principle which is enshrined in the International Biosafety Protocol under the UN Convention on Biological Diversity negotiated in Montreal in January 2000, and to which the UK and New Zealand are parties. In practice, however, regulators have been adopting the *anti*-precautionary approach, and confusion abounds over how scientific evidence is to be interpreted and used (3, Appendix 6).

GMOs are a new departure from conventional selective breeding

1.3 The creation of genetically modified organisms (GMOs) is a new departure from conventional selective breeding and introduces new hazards. This view is shared by many scientists, including those advising the United States and United Kingdom Governments (4, Appendix 1). The techniques and the nature of artificial constructs (GM constructs) made are the same in all applications of GMOs, whether in agriculture or in biomedicine, and so are the hazards involved.

1.4 Conventional selective breeding is restricted to crossing varieties within a species or between closely related species with similar genetic makeup. That is because genetic barriers prevent reproduction between unrelated species and limit the exchange of genetic material between them.

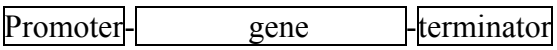
1.5 GMOs are created in the laboratory by genetic engineering, techniques that modify the genetic material directly. The genetic material is deoxyribonucleic acid or DNA. DNA is made up of long strings of four different units, A, T, C, G repeated apparently at random for millions or billions of times. The exact sequences matter, as they code for specific proteins and enzymes that make up intricate structures of the organism and enable the organism to transform

material and energy to grow, develop and do all the things that constitute being alive. The totality of all the genetic material of an organism is its genome, which is organized in a specific way typical of a species, and represented in every cell of the organism.

1.6 In making GMOs, genetic material from different sources are cut and recombined to make artificial GM-constructs that are transferred into the genomes of organisms. So, genes can be combined from widely disparate sources, and transferred between species that would never interbreed in nature. In other words, the GM-constructs are designed to overcome species barriers and to invade genomes. There is thus no limit to the new genes and new combinations of genes that can be made in the laboratory, nor to the GMOs created, all of which may never have existed in billions of years of evolution.

What genetic materials are used in GM constructs and how are GMOs made?

1.7 Most of the genes used in GM constructs originate from a wide variety of bacteria and viruses that cause diseases and other genetic parasites which spread drug and antibiotic resistance genes. A gene is never used by itself. It needs a start and a stop signal, a promoter in front and a terminator. The promoter-gene-terminator together form a unit GM-construct known as an 'expression cassette' which looks like this:



1.8 Very often, the three parts of the expression cassette originate from different sources. The promoter is usually from a virus, which makes the gene over-express at very high rates continuously, to make lots of the protein gene product. This is something that never happens in a healthy organism, and effectively puts the gene outside the normal metabolic regulation of the GM organism. The most common promoter used in plants is from the cauliflower mosaic virus (CaMV), a plant pathogen. The CaMV 35S promoter is in practically all GM crops already commercialized or undergoing field trials.

1.9 Apart from the expression cassette containing the gene of interest, it is necessary to have at least one other cassette containing an antibiotic resistance gene with its own promoter and terminator. This enables the genetic engineer to select for cells that have taken up the GM construct with the antibiotic, which kills off all other cells. Two or more expression cassettes are linked or stacked in series in a typical GM construct.

2.0 For ease of handling and bulking up GM constructs, and for transferring them into genomes, genetic engineers make a large variety of artificial gene carrier or vectors (5) by combining parts of the most aggressive natural vectors, viruses, plasmids and transposons.

2.1 A virus consists of genetic material wrapped in a protein coat. It sheds its overcoat on entering a cell and can either hi-jack the cell to make many more copies of itself, or it can jump directly into the cell's genome. Plasmids are pieces of 'free', usually circular, genetic material that can be indefinitely maintained in the cell separately from the cell's genome and replicates with the cell. Transposons, or 'jumping genes', are blocks of genetic material which have the ability to jump in and out of genomes, with or without multiplying themselves in the process. Genes hitch-hiking in genetic parasites therefore, have a greater probability of being successfully transferred into cells and genomes. Genetic parasites are *vectors* for gene transfer.

2.2 Natural genetic parasites are restricted by species barriers, so for example, pig viruses will infect pigs, but not human beings, and cabbage virus will not attack tomatoes. It is the protein coat of the virus that determines host specificity, which is why naked viral genomes (the genetic material stripped of the coat) have generally been found to have a wider host range than the intact virus. Similarly, the signals for propagating different plasmids (such as the 'origin of replication') and transposons are usually specific to a limited range of host species, although there are exceptions.

2.3 Artificial vectors, however, are especially designed to overcome species barriers and to invade genomes, so a vector may transfer, say, GM constructs containing human genes spliced into it, to the genomes of all other mammals, or of plants. Artificial vectors greatly enhance horizontal gene transfer, or gene transfer across species barriers.

2.4 In making GMOs, the GM construct is generally spliced into an artificial vector and vector sequences often end up in the resultant GMO, even parts of the vector that are not intended to do so. This gives rise to uncharacterized, unknown sequences that may not be safe.

2.5 The genetic engineer cannot control or target where and in what form the GM construct becomes integrated into the genome. Each GM line is the result of one or more 'transformational' events in a single plant cell, in which the GM construct integrates into the cell's genome. An entire plant is grown from that cell, the progeny of which constitutes the GM line. *Because transformation is random, each transformed cell, and hence the GM line derived from it, will be distinct, despite the fact that the same GM-construct(s) and plant cells are used*.

2.6 GM constructs are also structurally unstable, and are frequently rearranged (scrambled up), deleted or repeated in part or in whole when they are integrated into the host genome. The resultant GMOs, likewise, are unstable and do not breed true, as significant genetic and epigenetic changes may occur in subsequent generations (6-8, see Appendix 6), multiplying the unpredictable risks to health and biodiversity.

2.7 Thus, unless there are good molecular genetic data documenting the genetic stability of the GM line, it is impossible to guarantee that it is stable or uniform to begin with, or that it will not change further in subsequent generations, especially with regard to properties that affect safety.

2.8 Unfortunately, regulators in Europe, USA and Canada, all appear to be unaware of this. They have not required industry to submit molecular genetic data in sufficient detail to document genetic stability, or to allow identification of the GM line unambiguously (9). Instead, they are effectively granting blanket approval for GMOs from multiple transformation events plus all progeny arising from them, variously backcrossed to non GM varieties.

2.9 European Commission legislation actually requires that new plant varieties be tested for Distinctness, Uniformity and Stability (DUS) prior to being placed on the National List of a Member State, and prior to marketing. There is no evidence that any GM line has passed this test, which requires the molecular genetic data mentioned above. Incidentally, this also invalidates patents on transgenic lines and organisms.

Special safety concerns arising from GMOs

3.0 There are four special safety concerns arising from GMOs (10, Appendix 2):
1. Effects due to the exotic gene product(s) introduced into the transgenic organisms.
2. Unintended, unexpected effects due to random insertion of GM constructs; and interaction between GM genes and host genes.
3. Effects associated with the nature of the GM-constructs.
4. Effects of gene flow, especially horizontal spread of genes and gene-constructs from the GMOs to unrelated species.

Hazards from the exotic gene product(s) introduced

3.1 The exotic genes introduced into GM crops are mainly from bacteria and non-food species. Furthermore, the expression of these genes is often greatly amplified by strong viral promoters. In practice, that means all species interacting with the GM plants - from decomposers and earthworms in the soil to insects, small mammals, birds and human beings - will be exposed to large quantities of proteins new to their physiology. Adverse reactions may occur in all species, including immune or allergic responses. For example, Bt toxins from the soil bacterium *Bacillus thuringiensis*, engineered into GM crops to kill insect pests, are found to harm beneficial insects such as lacewings, and endangered species such as monarch butterflies and the black swallowtail (4, see also Appendix 6). One of them, the Cry9C in Aventis' Starlink GM maize intended for animal feed, is a potential allergen for human beings, and is behind the recent massive recall of contaminated taco shells in the United States (11).

3.2 The safety tests for new gene products are very inadequate. There is an on-going public hearing on a GM 'line' Chardon LL (Aventis – T25 Maize), approved for animal feed, which the Government is proposing to put on the UK National List (12), and I can use that case as an example.

3.3 Chardon LL contains a gene, *pat*, coding for the enzyme phosphinotricin acetyltransferase (PAT), which imparts resistance to the broad-spectrum herbicide glufosinate. The gene originates from the soil bacterium, *Streptomyces viridochromogene,* which has never been part of our food chain, nor animal feed. The *Streptomyces* genus includes plant (13) as well as human and animal pathogens (14). One feeding trial was conducted in rats for 14 days on the extracted protein, obtained, not from Chardon LL, but from GM oil seed rape. Rats are monogastrics and have a completely different digestive system from ruminants, which have four stomachs and keep the plant material longer. Furthermore, the feeding experiment was never completed, and no histological data on the state of internal organs were ever presented. As has argued by Dr. Arpad Pusztai and others, feeding studies must be done on *young* animals, as the young are more susceptible to adverse effects, and histological examinations are crucial.

Hazards from random gene integration and interaction with host genes

3.4 The random, uncontrollable insertion of GM constructs into the host genome and interaction of exotic genes with host genes is well known to give many developmental failures and gross abnormalities in animals. In microorganisms and plants, unexpected toxins and allergens have been found. The most notorious case involved a genetically engineered batch of tryptophan that killed 37 and made 1500 seriously ill in 1989 (4, Appendix 1).

3.5 Current regulation does not require characterization for unintended toxins and allergens. Hence, no attempts were made to do so in the case of Chardon LL. The characterisations that

were carried out were undiscriminating. Nevertheless, significant differences were often found between GM and non GM counterparts, but were explained away by appealing to variations in other varieties of the species under the principle of 'substantial equivalence'. In other words, Chardon LL could have the worst characteristics of all the varieties within a species, and still be considered substantially equivalent.

3.6 No feeding studies were done with GM plant material of Chardon LL, and hence its safety is unknown and unproven. Ewen and Pusztai carried out feeding studies with GM potatoes, from which they concluded that significant effects may be due to the transformation process or the GM construct, and not just the gene product itself (15). As yet, no Governments have attempted to repeat those investigations. In the case of Chardon LL, they seem to be avoiding the issue altogether by accepting feeding data on the novel protein alone.

Hazards from the GM construct

3.7 Safety concerns have indeed been raised over the 35S promoter from the cauliflower mosaic virus (CaMV) that is in the GM-constructs of practically all GM crops already commercialized or undergoing field trials. In a series of scientific papers (16-19, Appendix 3), my colleagues and I point out that

- CaMV is closely related to human hepatitis B virus, and less closely, to retroviruses such as the AIDS virus. Related viruses can more readily exchange genes than non-related ones, and they use similar regulatory signals such as promoters.
- The CaMV 35S promoter can substitute in part or in whole for promoters of other viruses to give infectious viruses.
- Although the intact CaMV specifically infects plants of the cabbage family, its isolated 35S promoter is promiscuous across domains and kingdoms. It is active in all plants, algae, yeast, and bacteria, and as we recently discovered in the scientific literature 10 years old, also in animal and human systems. The conventional wisdom among plant molecular geneticists is that CaMV 35S promoter is only active in plant and plant-like species. Why have they not checked the literature before using it so widely?
- The CaMV 35S promoter has a 'recombination hotspot' where it is prone to break and join up with other genetic material, hence increasing the likelihood for horizontal gene transfer and recombination (see below).

3.8 These findings suggest that CaMV 35S promoter has the potential to reactivate dormant viruses, which have now been found in all genomes, plants and animals included, and to recombine with other viruses, dormant or otherwise, to create new viruses. In addition, the fact that the promoter is active in animal and human cells means that, if transferred into their genomes, it may result in over-expression of genes that are associated with cancer. The case is compelling for recalling all GM crops containing the CaMV 35S promoter from environmental release on grounds of safety.

3.9 Chardon LL does have a CaMV 35S promoter and is hence subject to all the potential hazards that it brings. In addition, it has an origin of replication from the pUC plasmid vector which is also transferred into the GM plant, plus further stretches of uncharacterized, unidenfied sequences of unknown function and safety, as mentioned in ISIS' written objection (20). The origin of replication, claimed not to be active in plant cells, will be active in bacteria to which the GM construct is transferred. This signal enables the GM construct linked to it to be maintained in the bacteria as an independently replicating plasmid, hence enabling the GM construct to be multiplied and spread widely by horizontal gene transfer.

Hazards from gene flow, especially horizontal gene transfer

4.0 GM constructs can spread by ordinary cross-pollination to non GM plants of the same species or related species. The most obvious effects of cross-pollination already identified are in creating herbicide-tolerant weeds and superweeds (4, Appendix 1). Another consequence is the spread of the novel genes and GM-constructs for over-expression, as well as the antibiotic resistance marker genes. This will multiply the unpredictable physiological impacts on the organisms to which the genes and gene-constructs are transferred, and hence on the ecosystem.

4.1 By far, the most serious consequences are from the horizontal transfer of GM constructs to unrelated species, in principle, to all species interacting with the released GMO (21, Appendix 4) microorganisms, earthworms and arthropods in the soil, insects, birds, mammals, human beings. This is not just a theoretical possibility. There is already evidence that GM genes from GM plant material can transfer to soil bacteria and fungi. Recent experiments in 'gene therapy' have also amply documented that GM constructs, of the same form as those used in GM crops can readily invade cells and genomes of animals and human beings (22, Appendix 5). One of the routes of 'gene therapy' is oral administration, ie, swallowing.

4.2 What is the probability of horizontal gene transfer in the gut? An important factor is whether the GM genetic material is sufficiently broken down in processed food and animal feed. The UK Government's own commissioned research has repeatedly shown that most commercial processing either left the genetic material intact or in large fragments (23, 24). The scientists advised against using GM material in animal feed (23).

4.3 In fact, government scientists have pointed out that the possibility of horizontal gene transfer starts in the mouth, which contains dangerous bacteria that can take up antibiotic resistance genes (25) and similar bacteria are present in the respiratory tract. They warn of dangers to farm workers and food processors from GM pollen and dust (26). But, of course, such dangers would apply to the general public as well. Several months ago, Prof. Hans-Hinrich Kaatz from the University of Jena in Germany, reported that GM genes have transferred via GM pollen to bacteria and yeast living in the gut of bee larvae (27). This raises the issue of the safety of GM honey.

4.4 Chardon LL has an ampicillin resistance gene, *AmpR*, which came from the pUC18 plasmid vector used in gene transfer. It is reported to be non-functional because its promoter is lost. However, this gene is notorious for its ability to mutate and extend the ability of the enzyme encoded to break down new generations of □-lactam antibiotics (penicillin and chemically similar derivatives). It may regain function through mutation or recombination on being transferred horizontally, as was also pointed out by the Government's own scientific advisors (26). There is an entire class of genetic elements in bacteria called integrons that can take up an antibiotic resistance gene and provide it with a ready-made promoters (see ISIS' written objection, ref.20, and reviewed in ref. 28). It should also be noted that a rearrangement of the GM construct, which brings the CaMV 35S promoter next to the inactivated ampicillin-resistance gene, would restore function to that gene. The CaMV 35S promoter works in bacteria.

4.5 The hazards from horizontal transfer of GM constructs are summarised as follows,

- New viruses that cause diseases due to recombination between viral genes and viruses in the environment. Recombinant infectious viruses have been recovered in many GM plants

containing GM viral genes that are supposed to make the plants resistant to viral infections (reviewed in ref.18, Appendix 3).

- New bacteria that cause diseases due to recombination between bacterial genes and bacteria in the environment.
- Spread of drug and antibiotic resistance genes to bacteria, making infections much more difficult to treat. The transfer of antibiotic resistance genes from GM plant material to soil bacteria and fungi has been found both in the laboratory and in the field (21, Appendix 4), and there is no reason to expect that Chardon LL's ampicillin resistance gene will not be transferred.
- Harmful effects, including cancer, as the result of random insertion of GM constructs into cells. This possibility is amply demonstrated in 'gene therapy' experiments where similar constructs are introduced into cells in tissue culture (22, Appendix 5).
- Dormant viruses reactivated by the CaMV and other viral promoters. Recombinant replicating viruses routinely arise when gene therapy vectors are 'packaged' in cultured cells that contain dormant viruses (22, Appendix 5).
- Multiplication of ecological impacts due to all the above.

4.6 There is now overwhelming evidence that horizontal gene transfer and recombination are responsible for the resurgence of drug and antibiotic resistant infectious diseases worldwide within the past 25 years (28). We have reviewed the evidence extensively and questioned whether genetic engineering, in enhancing horizontal gene transfer and recombination, may have contributed, and will continue to do so if unchecked.

4.7 The current regulatory systems do not take horizontal gene transfer into account (1, 2, Appendix 6, see also Section B(n), this Witness Brief). There is no requirement for industry to monitor and report on horizontal gene transfer. On the contrary, dangerous vectors, GM constructs and GM genetic material are either being released directly into the environment, or are being recycled as food, feed, fertilizer and landfills (1, Appendix 6). We have repeatedly drawn attention to the dangers of horizontal gene transfer to no avail. Our Government as well as the biotech companies have been acting in violation of the precautionary principle as well as with sound science (3, Appendix 6). Governments as much as the biotech companies may well be held legally responsible for any harm from GMOs.

4.8 The version of the precautionary principle most relevant for GMOs is one stating that when there is reasonable suspicion of serious irreversible harm, lack of scientific certainty or consensus must not be used to postpone preventative action. I hold that *the precautionary principle is part and parcel of sound science because science, as opposed to fundamentalist religion, is an active knowledge system*. Scientific evidence is always uncertain and incomplete, and the proper role of scientific evidence, therefore is to set precaution. Dr. Peter Saunders, Professor of Applied Mathematics and co-Founder of ISIS, shows how the precautionary principle is just codified common sense that people have accepted in courts of law as much as statisticians have accepted in setting the burden of proof (3, Appendix 6).

4.9 Society accepts with the law that a person is assumed innocent until proven guilty beyond reasonable doubt, because, so the saying goes: "It is better that a hundred guilty men should go free than that one innocent man should be convicted." If we seriously want to protect health and the environment, then we must acknowledge that there is already reasonable suspicion that GM technology is hazardous, and that the effects are uncontrollable and irreversible. The burden of proof, therefore, should be on industry to establish it is safe beyond reasonable

doubt, particularly as there is no evidence of benefit or need (see below). Unfortunately, our regulatory systems have operated the other way round. The burden of proof is on civil society to establish it is harmful before it can be rejected.

5.0 Statisticians have actually been practising precaution by setting a 5% probability as the 'level of significance'. It means that to justify introducing something new, one should assume a 'null hypothesis' that there is no difference between the new and the old, unless the improvement observed is such that there is only a 1 in 20 chance for getting observed difference. The same goes for safety testing. One starts with the null hypothesis that there is no difference between GM and non GM. However, the failure to show that GM is significantly harmful does not mean it proves GM is safe. Many factors can contribute to this failure, including insufficient number of experiments and experiments badly designed and executed. Unfortunately, such failures have been taken as evidence that GM is safe.

We should reject the GM approach

5.1 The scientific evidence of actual and suspected hazards arising from GM technology is sufficiently compelling for hundreds of scientists around the world to call for an immediate moratorium on further environmental releases in accordance with the precautionary principle as well as sound science (4). The scientists also demand a ban on patents on life-forms and living processes, on grounds that they amount to corporate ownership of life that destroy livelihoods, compromise food security, violate basic human rights and dignity and are contrary to public good. Biomedical applications, in particular, are having disastrous consequences on the social and moral fabric of civil society, with no clear benefits to improving health (29, Appendix 7).

5.2 Many of the potential benefits have been promised ever since the beginning of genetic engineering, and all the signs are that they will never be realized (8). For example, nitrogen fixation involves at least 50 genes, at least half of which have to be transferred into plants; and it is pretty difficult to transfer even one successfully and stably. Similarly, drought and salt tolerance are due to many genes scattered over the entire genome. In fact, many salt and drought tolerant plants already exist, as do plants for 'bioremediation', which clean up the environment from polluting heavy metals and so on.

5.3 There are no clear benefits from GM crops so far. Evidence is emerging that GM crops are agronomically as well as ecologically unsustainable. Transgene instability due to gene silencing, rearrangement and loss of GM constructs give rise to inconsistent performance in the field, yield drag and other failures (4).

5.4 Global market for GM crops has collapsed as people all over the world are rejecting them and opting for organic sustainable agriculture. In contrast, agroecological approaches since the 1980s, which combine local farming knowledge and techniques with contemporary western scientific knowledge, have led to improved yields, as well as social, economic, health and environmental benefits for tens of millions in the developing as well as the developed world.

5.5 We should reject the entire genetic modification approach based on a discredited, mechanistic paradigm at odds both with the scientific findings of the new genetics and with our aspiration for a safe, healthy, just and compassionate world (30, Appendix 8).

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Section B (n)

B (n) whether the statutory and regulatory processes controlling genetic modification, genetically modified organisms, and products in New Zealand are adequate to address the strategic outcomes that, in your opinion, are desirable, and whether any legislative, regulatory, policy, or other changes are needed to enable New Zealand to achieve these outcomes
Section B (n) Summary

1.1 I am not aware of any regulatory system that adequately addresses the risks of genetic modification. The most glaring omission is the exclusion of naked and free nucleic acids, including many dangerous GM constructs, from the scope of the Biosafety Protocol. No regulatory process has required monitoring for horizontal gene transfer and its ecological and health impacts. On the contrary, transgenic wastes containing large amounts of GM constructs are being recycled as food, feed, fertilizer and landfills, according to current practice in the biotech industry.

B (n)

Inadequate regulation exists in Europe on both contained use and deliberate release of GMOs.

Contained use

1.1 Serious flaws in the regulation on contained use were pointed out in a comprehensive scientific review published in 1998 (1). This paper was submitted to the World Health Organization, European Commission, the Biosafety Conferences at the UN, as well as to the UK Health and Safety Executive, with additional comments from myself and others.

1.2 More recently, we raised the matter again in an update calling attention to the increasing variety and volume of 'naked' and 'free' nucleic acids produced in the laboratory and

biotech factories under contained use, which are in fact not contained at all, but discharged in one form or another into the environment (2), as sanctioned by the current EC Directive on Contained Use (Council Directive 90/219/EEC), last amended in 1998. Our paper was circulated at the Montreal meeting on Biosafety in January, and contributed to the strength of the Cartegena Biosafety Protocol that was agreed in the last hours of that conference. But there has been no real change since to the Directive on Contained Use. This Directive is fundamentally inadequate for the following reasons.

1. The scope covers only genetically modified micro-organisms; transgenic animals, fish and plants are not included. It also excludes nearly all classes of naked or free nucleic acids, vaccines, gene therapy vectors and other pharmaceutical products, except for viroids (infectious naked RNAs that cause diseases in both plants and animals).
2. Notification only and not explicit approval is needed for use of Group I GM microorganisms, (GMMs), considered nonpathogenic or otherwise safe; however, there is no agreement among EU nations on which microorganisms are pathogens or not; and it is effectively left up to industry to decide
3. For Group I GMMs, only 'principles of good microbiological practice' applies, ie, there is no containment.
4. 'Tolerated release' of Group I GMMs are allowed to take place, without treatment, directly into the environment.
5. No treatment of GM DNA or RNA is required to break them down fully before release.
6. There is no requirement to monitor for escape of GMMs or GM constructs, horizontal gene transfer, or impacts on health and biodiversity.

1.3 We presented evidence on the dangers of horizontal gene transfer, among which are the creation of new viral and bacterial pathogens and the spread of antibiotic and drug resistance among the pathogens. Particularly of note is that virulent genes are transferred in mobile units, so that non-pathogens can be converted into pathogens in one or a few quantum steps.

1.4 Despite our efforts, successive versions of the Directive have been relaxed and shaped by the European Federation of Biotechnology. This industry-dominated group have produced a series of 'safe biotechnology' papers, the latest, published this July (3), specifically addresses DNA content of biotechnological wastes.

1.5 The paper admits that DNA persists in soil and aqueous environments, that it is transferred to bacteria and cells of animals, and that it may become integrated into their genomes.

1.6 But they defend current practice by claiming 1) Horizontal transfer of GM DNA occurs, if at all, at very low frequencies, especially in nature, 2) The persistence of foreign DNA depends on selective pressure, especially in the case of antibiotic resistance marker genes, and 3)DNA taken up is unlikely to be integrated into the cell's genome unless designed to do so.

1.7 The first claim is unwarranted. Evidence of horizontal gene transfer from transgenic plants to soil bacteria has been obtained in the laboratory as well as in the field (4) although the researchers themselves are downplaying the findings, in violation of the precautionary principle. The second assumption has been shown to be false. There is now

substantial evidence that antibiotic resistance can and does persist in the absence of the antibiotic (5) mainly because biological functions are, as a rule, all tangled up with one another, and cannot be neatly separated. The third point is false as well, for it has been demonstrated in gene 'therapy' experiments that naked DNA-constructs, not intended for integration, have nevertheless become integrated into the genome. Integration occurs not only in somatic cells, but also in germ cells (2)

1.8 The most dangerous aspect of current practice, defended by industry, is that solid wastes, heat-treated, or autoclaved, containing large amounts of intact or incompletely degraded GM constructs and transgenic DNA are being recycled or disposed of as food, feed, fertilizer, land reclamation and landfill.

1.9 Only in cases where GM constructs are specifically made to transform higher organisms, such as gene vaccines and genetic pill applications (for gene therapy) is there a recognition that there may be a need to "inactivate waste by validated procedures rendering DNA nonfunctional by either reducing DNA fragment size below functional entities or altering the chemical composition and structure of the DNA." However, no such validated procedures exist.

Deliberate Release

2.0 The EU Directive 90/220/EEC on Deliberate Releases of GMOs is currently being amended.

2.1 European Parliament voted on the amendments in June 2000, but major issues remain outstanding between the texts proposed by the European Council of Ministers (representing the member nations of the EU), and that of the European Parliament.

2.2 The new directive is much tighter than its predecessor in terms of assessing the environmental impact of GMOs but serious inadequacies remain.

2.3 There is no requirement for the molecular characterisation of each transformed line over a number of generations (6) to ensure genetic stability, and there is still no requirement to monitor for horizontal gene transfer.

2.4 Parliament rejected the amendment that attempted to prevent horizontal gene transfer. This amendment is the most important in terms of safety. An industry spokesman said it would have "killed off the whole technology" (7). Not so long ago, industry has been claiming that horizontal gene transfer does not happen, or happens at extremely low frequency, and is therefore not a safety concern (see above). Whilst Parliament has officially acknowledged that horizontal gene transfer is a natural phenomenon, it fails to provide measures for adequate monitoring or prevention. The risks associated with horizontal gene transfer present the greatest hazards to health and the environment and could result in widespread genetic pollution of the environment (see Section B(c) of this Witness Brief)

2.5 The European Commission called for a ban on the use of antibiotic resistance marker genes due to the risk of horizontal gene transfer, but the European Parliament voted only for a phasing it out by 2005. The Commission also wanted released pharmaceutical products included in the scope, as agreed in the Cartegena Biosafety Protocol, but Parliament voted them out too. Industry was further let off the hook regarding specific

liability for environmental harm associated with their products. However, this may be only a temporary measure as Parliament is already committed to introducing liability rules by 2001.

2.6 A conciliation process is underway. The Directive will be enacted during the French presidency and the French are especially sensitive regarding safety issues. Dominique Voynet, the French Green Minister, insisted the political moratorium will remain in place until there is legislation to ensure GM products can be traced through the entire production chain, from field to plate. But without collecting molecular data for each transformed line over generations and adequate monitoring for horizontal gene transfer, GM genetic material will be passing through this new regulatory net unchecked (2).

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