Witness Brief Form 2

Royal Commission on Genetic Modification

1. Name of Witness

Joseph Cummins

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

Joseph Cummins

EDUCATION

1. NAME AND LOCATION OF HIGH SCHOOL: Stadium High School, Tacoma, Wash. 1951

2. UNIVERSITIES AND DEGREES, WITH DATES:

   B.S., (Horticulture) Washington State University, 1955
   Ph.D., (Cell Biology) University of Wisconsin, 1962

3. FELLOWSHIPS/SCHOLARSHIPS, WITH DATES:

   Postdoctoral Fellow, Univ. of Edinburgh. (Prof. J.M. Mitchinson, Dept. of Zoology) 1962-64

   Postdoctoral Fellow, McArdle Lab. for Cancer Research (Univ. of Wisconsin, Prof. H.P. Rusch) 1964-66

   Postdoctoral Fellow, The Karolinska Inst., Stockholm (Prof. J.E. Edstrom) 1969

PREVIOUS ACADEMIC/PROFESSIONAL EMPLOYMEN

Visiting Assistant, Prof. Radiology, Dept. of Radiology, Case-Western Reserve University, Cleveland, Ohio, 1967

Assistant Professor, Biol. Sci., Dept. of Biol. Sci., Rutgers University, New Brunswick, N.J.,

1966-67

Assistant Professor, Dept. of Zoology, Univ. of Washington, Seattle, Washington, 1967-71

Assistant Professor to Professor Emeritus 1972 to 1996
Teaching: Advanced Genetics (molecular genetics), microbial genetics, microbiology, human genetics, environmental pathology and toxicology (medical faculty) and graduate topics in environmental issues.

Professional Associations: American genetics society, American society for cell biology, and Society for Environmental Mutagens along with that sit or sat on boards of environmental organizations. Received a number of recognitions for participating in and advising environmental issues.

Publications
Career total : over 210 publications

Over 70 peer reviewed journal articles

Over 5 chapters in books

Numerous reviews, reports to government agencies, reports in meetings proceedings and popular magazines

Current Activities

Actively engaged in preparing reviews and reports in areas related to genetic engineering, global pollution with persistent organic pollutants and pesticides.

Summary

6.1 It is often claimed that there is no evidence that genetically modified (GM) crops pose potential threats to human health. (1.0 – 3.10) GM food and crops are products whose fundamental genetic make-up has been altered using genetic engineering. Genes from bacteria, viruses or animals including human have been introduced into the seeds of the crops that make up GM food. These genes are introduced to fight pests such as weeds, insects, fungus, bacteria, virus or nematodes. (1.0 – 1.11)

6.2 Presently GM crops on the market have been modified to fight pests , later releases may deal with nutrition and shelf life of the GM foods. Several years ago a GM tomato with very long shelf life was introduced but then removed when consumers found the tomatoes did not taste good. However, the safety of GM crops is still in question because crop approval has been based on a concept called “substantial equivalence”. Substantial equivalence is the doctrine that maintains that if GM crops are grossly similar to crops that have not been genetically modified they are equivalent to those crops and need not be labeled in the market and they need not be tested similarly to the test required for pesticides or pharmaceutical drugs. Governments in Canada and the United States employ that doctrine to evade labeling and testing the GM crops before they are marketed. (2.0 – 3.8)

6.3 In the following witness brief I will discuss some examples in which GM crops or biopesticides have been evaluated in a manner that indicates that evidence of hazard or unsubstantial equivalence has been ignored or downgraded. (1.6 – 1.11) (2.0 – 2.7) (3.0 – 3.10)

4. 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 Relevant Matters

The Warrant has set the Commission the task of receiving representations upon, inquiring into, and investigating, the matters set out in Section B (a) – (n) below

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

B (j) (i) Risks to Human Health – including food safety

- Bacillus thuringiensis and its toxins as biopesticides: (1.0 – 1.11)
- Glyphosate tolerant (Roundup Ready) corn in a demonstration of substantial equivalence: Glyphosate-Tolerant Corn: "The Composition and Feeding Value of Grain from Glyphosate-Tolerant Corn Is Equivalent to That of Conventional Corn (2.0 – 2.7)
- Genetically Modified (GM) Baculovirus Vectors to Control Insect Pests and for Gene Therapy: (3.0 – 3.8)
- Concluding Statement (3.9 – 3.10)

B (j)(i)

1.0 Bacillus thuringiensis and its toxins as biopesticides:

Biopesticides are microbes or natural chemicals produced by organisms that are used to control disease causing organisms (pests) such as insects or bacteria. In the United States the Environmental Protection Agency (EPA) regulates plant pesticides used directly or as a part of genetically modified (GM) crops. Bacillus thuringiensis (Bt) and its toxins are far and away the most significant biopesticides. Bacillus thuringeinsis is a common spore forming bacterium.

1.1 Certain of its varieties produce toxins that are effective in controlling specific insect pests; as well each variety may produce a number of toxins of varying toxicity and specificity. Normally GM crops are modified with a single toxin gene from among a number available to deal with a particular insect pest; frequently the toxin genes are synthetic copies of the bacterial gene. The toxin proteins bind to the cell membrane at particular target site and create pores that enhance water uptake into the cell, ultimately causing that cell to burst.

1.2 The toxins used with GM crops are selected so that insect cells are attacked while mammalian cell membranes are not. In bacterial biopesticides some toxins do bind to mammalian cells but overt toxicity to mammals is prevented by the acid environment of the gut (the insect gut is normally alkaline). Bacluus thuringiensis spores are normally applied to crops as a biopesticide, such spores are known to cause allergy in farm workers

(Bernstein,I,Bernstein,J,Miller,M,Tiewzieva,S,Bernstein,D,Lummus,Z, Selgrade,M,Doerfler,D and Seligy,V "Immune responses in farm workers after exposure to Bacillus thuringiensis pesticides" 1999 Environ Health Perspect 107,575-82).

1.3 The spores are normally washed off crops prior to marketing so do not pose a threat to consumers. The toxins in GM crops are a part of the cells of the crop and cannot be washed out of the crop.

1.4 Psuedomonas flourescens genetically modified with toxin gene from Bt toxins are marketed as encapsulated Bt toxin. Such products have been marketed to organic producers without acknowledging that the products are genetically modified.

1.5 The EPA listing and reviews of Bt pesticides and toxins are listed on the EPA website: http://www.epa.gov/oppbppd1/biopesticides/ai/all_ais.htm

- 1.5.1 "Bacillus thuringiensis Berliner
- 1.5.2 Bacillus thuringiensis Cry1IA(c) & Cry I(c) delta-endotoxin in killed Pseudomonas fluorescens
- 1.5.3 Bacillus thuringiensis Cry1A(b) delta-endotoxin and the genetic material necessary for its production in corn
- 1.5.4 Bacillus thuringiensis Cry1A(b) in corn from PV CIB4431
- 1.5.5 Bacillus thuringiensis Cry1A(c) delta-endotoxin and the genetic material necessary for its production in cotton
- 1.5.6 Bacillus thuringiensis Cry1F protein and the genetic material necessary for its production (plasmid insert PHI8999) in corn plants (pending)
- 1.5.7 Bacillus thuringiensis Cry3A delta-endotoxin and the genetic material necessary for its production in potato

1.5.8 Bacillus thuringiensis Cry3Bb protein and the genetic material necessary for its production (Vector ZMIR14L) in corn plants (pending)
1.5.9 Bacillus thuringiensis K Cry1A(b) delta-endotoxin and the genetic material necessary for its production in corn produced by HD-1 gene from PV pZ01502
1.5.10 Bacillus thuringiensis K Cry1A(c) delta-endotoxin and the genetic material necessary for its production in corn
1.5.11 Bacillus thuringiensis K Cry1C in killed Pseudomonas fluorescens
1.5.12 Bacillus thuringiensis subsp. aizawai
1.5.13 Bacillus thuringiensis subsp. aizawai GC-91
1.5.14 Bacillus thuringiensis subsp. israelensis
1.5.15 Bacillus thuringiensis subsp. israelensis EG2215
1.5.16 Bacillus thuringiensis subsp. kurstaki
1.5.17 Bacillus thuringiensis subsp. kurstaki BMP123
1.5.18 Bacillus thuringiensis subsp. kurstaki delta-endotoxin in killed Pseudomonas fluorescens
1.5.19 Bacillus thuringiensis subsp. kurstaki EG2348
1.5.20 Bacillus thuringiensis subsp. kurstaki EG2371
1.5.21 Bacillus thuringiensis subsp. kurstaki EG2424
1.5.22 Bacillus thuringiensis subsp. kurstaki EG7673 Coleoptera Toxin
1.5.23 Bacillus thuringiensis subsp. kurstaki EG7673 Lepidoptera Toxin
1.5.24 Bacillus thuringiensis subsp. kurstaki EG7826
1.5.25 Bacillus thuringiensis subsp. kurstaki EG7841
1.5.26 Bacillus thuringiensis subsp. kurstaki M200
1.5.27 Bacillus thuringiensis subsp San Diego delta-endotoxin in killed Pseudomonas fluorescens
1.5.28 Bacillus thuringiensis subsp. tenebrionis
1.5.29 Bacillus thuringiensis subsp tolworthi Cry9C delta-endotoxin and the genetic material necessary for its production in corn fm PV pRVA9909

1.6 In general the EPA reviews of the Bt and toxins biopesticides roundly ignored the finding that Bt was allergenic to farm workers. The EPA review of the Bt toxin Cry 9 is found at: http://www.epa.gov/oppbppd1/biopesticides/cry9c/cry9c-peer_review.htm

1.7 “The results of intraperitoneal injection of corn powder extracts into BN rats indicate that both the control and transgenic corn powders are able to induce IgE or reagininc antibody responses by the PCA assay. The use of corn powder immunogen decreases the rate of the immune response to the Cry9C protein compared to the bacterial preparation.

1.8 However, the lowest responding dose for Cry9C was similar for the two preparations (between 0.1 and 0.4 µg Cry9C). The control challenge test with the heterologous antigen of control corn powder or transgenic corn powder in the day 42 sera samples indicated that there was significant reactivity from the corn portion of the extracts themselves in the PCA assay. It is unclear, given this background reactivity, how conclusions can be made about the reactivity of the Cry9C protein alone.

1.9 The PCA results from oral sensitization with ovalbumin II, control corn extract, bacterial Cry9C and transgenic corn (apparently supplemented with bacterial Cry9C) indicated that an IgE or reagin antibody response was elicited in naïve Sprague-Dawley rats. Ovalbumin sensitized serum produced a low frequency of responders and a weak dose

response between the 5.0 and 50.0 mg/kg dose levels on days 28 through 42. The control corn also produced a positive oral sensitization response but this was only examined at the 50 mg/kg dose. Oral dosing with bacterial Cry9C gave a positive PCA response as did the Cry9C amended transgenic corn extract.

1.10 The frequency of response to bacterial Cry9C began to diminish in day 42 sera. The Cry9C amended transgenic corn had a higher frequency of responders and the frequency remained high on day 42 PCA response. Western blot analysis indicated that Cry9C protein bands could be recognized in the rat sera from both exposure routes."

1.11 These results on an allergic (IgE) response was associated with Cry9 in corn powder. Considering that the Cry 9 containing corn was fed millions of farm animals and probably as many humans eating corn products contaminated with corn designated only for animal use any evidence of IgE response to Cry 9 corn should not be allowed to be buried.

2.0 Glyphosate tolerant (Roundup Ready) corn in a demonstration of substantial equivalence: Glyphosate-Tolerant Corn: "The Composition and Feeding Value of Grain from Glyphosate-Tolerant Corn Is Equivalent to That of Conventional Corn *(Zea mays* L.)" Ravinder S. Sidhu,* Bruce G. Hammond, Roy L. Fuchs, Jean-Noel Mutz, Larry R. Holden,Beverly George, † and Tammy Olson ‡

2.1 Monsanto Company, 700 Chesterfield Parkway North, St. Louis, Missouri 63198
J. Agric. Food Chem. 2000, *48,* 230□-2312

2.2 Abstract: Glyphosate-tolerant (Roundup Ready) corn line GA21 has been developed by genetic modification to tolerate glyphosate, the active ingredient in Roundup herbicide. The purpose of this study was to evaluate the compositional and nutritional safety of corn line GA21 compared to that of conventional corn. Compositional analyses were conducted to measure proximate, fiber, amino acid, fatty acid, and mineral contents of grain and proximate, fiber, and mineral contents of forage collected from 16 field sites over two growing seasons.

2.3 The nutritional safety of corn line GA21 was evaluated in a poultry feeding study conducted with 2-day old, rapidly growing broiler chickens, at a dietary concentration of 50-60% w/w. Compositional analysis results showed that, except for a few minor differences that are unlikely to be of biological significance, the grain and forage of GA21 corn were comparable in their composition to that of the control corn line and to conventional corn. Results from the poultry feeding study showed that there were no differences in growth, feed efficiency, adjusted feed efficiency, and fat pad weights between chickens fed with GA21 grain or with parental control grain. These data taken together demonstrate that Roundup Ready corn is as safe and nutritious as conventional corn for food and feed use.

2.4 The research group from Monsanto pointed out that substantial equivalence (the idea that genetically modified (GM) crops are equivalent to crops that are not genetically modified in terms of nutrition and composition) is crucial to the regulation of GM crops. Their research efforts included comparing GM corn containing primarily a gene that made the corn resistant to the herbicide glyphosate. The corn was then fed to chickens and the chicken fed GM corn or corn that was not GM. The investigators believed that their

results proved that the GM corn was substantially equivalent to corn that was not modified.

2.5 The investigators believed that their conclusions were valid even though GM corn was found to be about 9% lower in calcium content a difference that was statistically significant. The GM corn was also found to be statistically significantly different in the content of the amino acids serine and tyrosine from unmodified corn. The chickens fed GM corn or corn that was unmodified were not significantly different but the research report briefly and hidden mentions that the GM corn fed the chickens had never been exposed to the herbicide glyphosate. Major alterations in corn metabolism would only be triggered in the presence of the herbicide.

2.6 The Monsanto researchers claimed that GM corn was not substantially different from unmodified corn even though the two were statistically significantly different! They seem to have convinced government regulators that statistical significance just doesn't count when you have faith in your company's product. The regulators and editors did not even wince when the experimental chickens were fed herbicide tolerant corn that had never been exposed to herbicide!

2.7 Statistical significance should count and the corn was clearly substantially different from unmodified corn. Feeding chickens GM corn that was not exposed to herbicide was clearly a strange thing to do.

3.0 Genetically Modified (GM) Baculovirus Vectors to Control Insect Pests and for Gene Therapy:

Baculovirus are viruses that infect insects; they are very stable and may remain dormant in the environment for years before infecting insects. The virus can be purified and produced in quantity to be used in insect control. Since the virus multiplies and persists, its use in pest control seems promising.

3.1 The virus alone has a relatively low killing power and slow action. When a gene for a potent toxin such as scorpion toxin or a gene effecting a juvenile hormone is added to the virus it kills faster and fewer insects survive infection. Numerous field tests of modified virus sprayed on crops have been undertaken often accompanied by loud expressions of concern from the public. Soon after GM virus were developed for insect control it was found that baculovirus were capable of infecting human liver cells and produced relatively little toxicity to the infected cells.

3.2 For that reason baculovirus vectors were developed to treat liver disease. Interestingly, the fact that baculovirus can infect human liver cells seems to have been ignored by those developing the virus for commercial pest control. The following discussion will deal with the use of baculovirus vectors and their safety. I understand that there has been a great deal of pressure to hasten approval of the GM baculovirus for pest control.

3.3 Ecological considerations for the impact of recombinant baculovirus insecticides have been studied extensively (Richards et al 1998). The study emphasized baculovirus containing scorpion toxin because that construction has been most widely studied. Impact on non-target insects is extrapolated from insects of related phylogeny, a practice difficult to defend. The recombinant baculovirus were very persistent and capable of reshaping an

ecosystem. Modification of baculovirus host range specificity has been achieved by inserting or deleting genes (Theim 1997).

3.4 Baculovirus is a circular DNA duplex, it replicates in the insect cell nucleus and replication is prone to the generation of defective genomes by deletion (Wu et al 1999). The mode of virus replication seems to make the recombinant virus highly unpredictable and prone to generating potentially undesirable variants. This important finding has not yet influenced the risk analysis of recombinant baculovirus insecticides and gene therapy vectors.

3.5 The scorpion toxins used with recombinant baculovirus have been selected to avoid human neurotoxicity and as much as possible toxicity to non-target animals. However, the allergenicity of toxins and their behavior (as for example in autoimmunity) in human liver infection has not yet been studied. In insect control the depressant toxin was more effective than the excitatory toxin in recombinant baculovirus (Gershburg et al 1998).

3.6 Recombinant baculovirus containing Bacillus thuringiensis toxin have not proven successful in controlling insect pests (Martens et al 1995). However, recombinant baculovirus modifying juvenile hormone proved effective in insect control (Bonning et al 1999). Recombinant baculovirus containing an antisense fragment to the c-myc oncogene proved effective in target insect control (Lee et al 1997). The behavior of the myc oncogene recombinant vector bears careful study regarding non-target animals and its impact during human liver infection.

3.7 Baculovirus vectors efficiently transfer genes into human liver cells (Hofmann et al 1995; Boyce and Bucher 1996). The vectors transferred into human liver tissues most effectively in perfused liver tissue because serum components hampered virus transfer (Sandig et al 1996).Human conditions causing defects in complement should allow liver transfer of recombinant baculovirus. Inhibitors of complement facilitate baculovirus gene transfer (Hofmann and Strauss 1998). Hybrid baculovirus-adeno virus vectors have been used to deliver genes to human cells (Palombo et al 1998). Baculovirus vectors have been used to deliver hepatitis B to human liver efficiently to allow study of hepatitis B drug therapy (Delaney et al 1999).

3.8 In conclusion baculovirus vectors are being used to control insect pests because they are effective and persist for a long time in the environment. Baculovirus vectors are also being used in gene therapy of human liver. These areas of research seem to exist as two solitudes and the risks of one are not evaluated in the context of the other. The most disconcerting finding is the one showing that replication of the baculovirus is inherently unpredictable. However, there may be some that believe that we should all have unlabelled liver gene therapy with our salad.

References

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2.Boyce,F and Bucher,N Baculovirus-mediated gene transfer into mammalian cells” 1996Proc. Natnl Acad Sci USA 93,2348-52

3.Delaney,W,Miller,T, and Isom,H "Use of the hepatitis B virus recombinant baculovirus-Hep G2 system to study the effects of beta 2',3' dideoxy 3'thiaceydine on replication of hepatitis B virus and accumulation of covalently closed circular DNA"1999 Antimicrob Agents Chemother 43,2017-26
4.Gershburg,E,Stockholm,D,Froy,O,Rashi,S,Gurevitz,M and Chejanovsky,N "Baculovirus mediated expression of a scorpion depressant toxin improves the insecicidal efficacy achieved with excitatory toxins" 1998 FEBS Lett 422,132-6

5.Hofmann,C,Sandig,V,Jennings,G,Rudolph, Schlag,P and Strauss,M "Efficient gene transfer into human hepatocytes by baculovirus vectors" 1995 Proc. Nantl Acad Sci USA 92,10099-103

6.Hofmann,C and Strauss,M "Baculovirus mediated gene therapy in the presence of human serum or blood facilitated by inhibition of the complement system" 1998 Gene Ther 5,531-6

7.Lee,S,Qu,X,Chen,W,Poloumieko,A,MacAfee,N,Morin,B,Lucarotti,C and Krause,M "Insecticidal activity of a recombinant baculovirus containing an antisense c-myc fragment" 1997 J Gen Virol 78,273-81

8.Martens,J,Knoester,M,Weijts,F,Groffen,S,Hu,Z,Bosch,D and Vlack,J "Characterization of baculovirus insecticides expressing tailored Bacillus thuringiensis Cry1A9b) crystal proteins" 1995 J Invertebr Pathol 66,249-57

9.Palombro,F,Mociotti,A,Recchia,A,Cortese,R,Ciliberto,G and LaMonica,N "Site specific integration in mammalian cells mediated by a new hybrid baculovirus-adeno-associated virus vector" 1998 J Virol 72,5025-34

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3.9 **Concluding Statement:** The experiments discussed in the above brief suggest that there should be great concern about the use of substantial equivalence to evaluate crops. First, because it is not a useful concept for recognizing and eliminating injurious toxins. Second, because the concept is not being used properly, even ignoring clear differences in composition. Last those employing the concept to approve GM crops seem unwilling to remove approved crops from the market when they are shown to be unsubstantially equivalent.

3.10 Furthermore, the GM biopesticides seem to be approved or pushed for approval with inadequate safety evaluation and concern for their long term impact. The field of genetic engineering seems to be moving forward with undue haste and employing humans as experimental organisms. The profession would probably greatly improve its outlook if criminal charges could be laid against researchers and their university or company officials when injurious procedures effecting humans or the environment are implemented without full regards for the rights of humans to decline participation in the procedure or when foreseeable environmental damage is ignored. Charges could be laid based on the depraved indifference of researchers and the officials that direct them.