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Food Standards Australia New Zealand
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Application A1110 from Monsanto Australia Limited for approval for food derived from insect-protected soybean line MON87751 with OECD Unique Identifier MON-87751-7 (also referred to as MON87751), engineered against lepidopteran insect pests through expression of Cry proteins.

PSGR recommends Food Standards Australia New Zealand (FSANZ) reject Application A1110. The food regulation review process of FSANZ has a legislated mandate to protect public health and safety. In approving this Application, FSANZ would not be meeting this duty of care.

1. A main area of concern is human ingestion of the Cry proteins (*Bacillus thuringiensis* (Bt))

Transgenes express in the xylem of plants: leaves, fruit, flowers, pollen, nectar, and guttation fluid. Whatever part of a transgenic plant is used as a food or food ingredient, consumers will ingest transgenes, even if as minute fragments, from whatever part/s of the plant they consume.

Protection against lepidopteran insect pests is conferred by *Bacillus thuringiensis g*enes which will be expressed in the whole plant.

A study in 2013 examined the hematotoxicity and genotoxicity of four Bt spore-crystals, in this case engineered to express individually Cry1Aa, Cry1Ab, Cry1Ac or Cry2A. It demonstrated that Bt spore-crystals induced hematotoxicity, particularly to the erythroid lineage. This corroborated published literature demonstrating that alkali-solubilised Bt spore-crystals caused in vitro hemolysis in cell lines of laboratory subjects, including human erythrocytes. It suggested that the plasma membrane of susceptible cells (erythrocytes, in this case) may be the primary target for these toxins. The researchers concluded that the results showed that the Bt spore-crystals can cause hematological risks to vertebrates, increasing their toxic effects with long-term exposure.

With the advent of transgenic food plants expressing δ-endotoxins, the bioavailability of Cry proteins has increased.[1]

It is known synergistic and additive effects both between Bt toxins and other compounds do occur. It is also known that synthetically produced Bt toxins can show much higher toxicity than native proteins. Even small changes in the structure of the proteins can cause huge changes in their toxicity. These effects render higher toxicity and give rise to unexpected risks.[2]

There have been no studies on potential health impacts due to combinations of the toxins or synergies with external factors such as protease inhibitors, or with residues from spraying. In general, the mode of action of Bt toxins is not fully understood and controversially debated.[2]

Developers of transgenic crops claim Bt has a history of safe use. They point to organic farmers and others who use Bt for natural insect control. However, with transgenic crops Bt genes are inserted into the plant and the Bt-toxin produced in transgenic plants is thousands of times more concentrated than natural Bt spray. It is, in fact, designed to be more toxic.[3] It has properties of an allergen, and unlike the spray, cannot be washed off the plant. If there is a known allergen in the normal crop any application for a transgenic crop should be refused under the Precautionary Principle and Cartagena Protocol.

Moreover, studies confirm that even the less toxic natural bacterial spray is harmful. When dispersed by plane to kill gypsy moths in the Pacific Northwest, about 500 people reported allergy or flu-like symptoms.[4] [5] Similar symptoms are reported by farm workers in India, caused by handling Bt cotton.[6] [7]

More significant is the incidence of animals dying when grazed on Bt cotton stubble.

Post mortems showed severe irritation and black patches in both intestines and liver (as well as enlarged bile ducts).[8] In a feeding study by India's Deccan Development Society, all sheep fed Bt cotton plants died within 30 days; those that grazed on natural cotton plants remained healthy. Of 13 buffalo grazed on Bt cotton plants all became sick the next day and all died within three days.[9]

There is support for the specificity of the association of transgenic foods and specific disease processes. Multiple animal studies show significant immune dysregulation, including upregulation of cytokines associated with asthma, allergy, and inflammation.[10] [11] [12]

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[1] 'Hematotoxicity of Bacillus thuringiensis as Spore-crystal Strains Cry1Aa, Cry1Ab, Cry1Ac or Cry2Aa in Swiss Albino Mice', Mezzomo et al., J Hematol Thromb Dis 2013, 1:1, http://dx.doi.org/10.4172/jhtd.1000104; http://foodrecap.net/wp-content/uploads/2013/05/nailing-cry-toxin-harmful-to-mice.pdf

[2] Potential synergies that can enhance Bt toxicity in SmartStax, Analyses of Levine et al., 2008a and MacRae 2008, Report Number MSL0021104 and MSL 0020554. 28 June 2011. https://www.testbiotech.org/sites/default/files/SmartStax_Bt_Synergies_Testbiotech.pdf

[3] See for example, Dutton et al, 'Uptake of Bt-toxin by herbivores feeding on transgenic maize and consequences for the predator Chrysoperia carnea,' Eco Entomology 27 (2002): 441–7; and Romeis et al, 'Bacillus thuringiensis toxin (Cry1Ab) has no direct effect on larvae of the green lacewing Chrysoperla carnea (Stephens) (Neuroptera: Chrysopidae),' J Insect Physiology 50, no. 2–3 (2004): 175–183.

[4] Report of health surveillance activities: Asian gypsy moth control program, Olympia, WA: Washington State Dept. of Health, 1993).

[5] M Green et al., 'Public health implications of the microbial pesticide Bacillus thuringiensis: An epidemiological study, Oregon, 1985-86,' Amer. J. Public Health 80, no. 7(1990): 848–852.

[6] Ashish Gupta et al, 'Impact of Bt Cotton on Farmers' Health (in Barwani and Dhar District of Madhya Pradesh),' Report, Oct–Dec 2005.

[7] Sunday India, 26 October 2008

[8] 'Mortality in Sheep Flocks after Grazing on Bt Cotton Fields—Warangal District, Andhra Pradesh', Report of the Preliminary Assessment, April 2006, http://www.gmwatch.org/archive2.asp

[9] http://www.responsibletechnology.org/doctors-warn

[10] Finamore et al, 'Intestinal and peripheral immune response to MON 810 maize ingestion in weaning and old mice'. J Agric. Food Chem. 2008; 56(23):11533-11539. Kroghsbo et a;. 'Immunotoxicological studies of genetically modified rice expression PHA-E lectin or Bt toxin in Wistar rats', Toxicology. 2008; 245:24-34.

2. The effects on human health of transgene ingestion

While DNA is claimed to be mostly degraded during the industrial process and in the digestive tract, small fragments were detected in body tissues such as leukocytes, liver, spleen and gut bacteria.[13] Fragments of orally administered phage M13 and plant DNA were found to be taken up by phagocytes as part of their normal function as immune system cells.[14] Fragments could pass into other organs, including the foetus. Animal studies reveal the potential for conditions presenting now and in the short- and long-term future. As shown above, transgenes have proven fatal in the field.

Ingestion effects may not be as immediate as the effects from direct spraying. However, with multiple daily helpings of transgenes, cumulative effects will stack up, particularly as soy is a common ingredient in a large volume of processed food products. Other transgenic crops forming part of the human diet may add to the effects or interact in ways we do not yet understand. Effects over long periods are uncertain simply because no one is looking, or dare not risk using human guinea pigs in trials, or risk their careers by suggesting this is crucial research. Instead, industry and regulatory agencies have given transgenes a tick of approval without initiating independent long-term studies and without monitoring consumers.

In 2004, researchers proved soy transgenes moved from ingested food to bacteria in the human gut.[15] Professor Dr Han-Hinrich Kaatz found the transgene conferring resistance to glufosinate ammonium had transferred in bees' guts to microbes.[16] No regulator has supported further independent studies.

3. Bioaccumulation and potential health results associated with residues

Bioaccumulation is a normal process of growth and nurturing of organisms. All animals - including humans - bioaccumulate ingested material and can bioaccumulate substances in the body to levels that can cause harm. A typical food chain bioaccumulation process is plant uptake from soil or spray, animal eating plant, human eating animal or plant. Each step can result in increased bioaccumulation including toxins where absorption of a substance is at a rate greater than that at which the substance is lost or eliminated.

While official bodies accept the word of developers and those with vested interest continue to deny the possibility of adverse effects, this does not mean there are none. Animal studies reveal the potential for conditions presenting now and in the short- and long-term future. For example, in one study, mouse embryos exposed to glufosinate in vitro developed apoptosis (fragmentation of the cells leading to cell death) in the neuroepithelium of the brain.[17] An earlier study found all embryos in treated groups had specific defects including overall growth retardation, increased death of embryos, hypoplasia (incomplete g/ml, and cleft lips at 20µ development) of the forebrain at 10g/ml.

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[11] Malatesta M, Boraldi F, Annovi G, et al. 'A long-term study on female mice fed on a genetically modified soybean: effects on liver ageing. Histochem Cell Biol. 2008; 130:967-977. Velimirov et al, 'Biological effects of transgenic maize NK603xMON810 fed in long term reproduction studies in mice', Report-Federal Ministry of Health, Family and Youth. 2008.

[12] Kilic A, Aday M. A three generational study with genetically modified Bt corn in rats: biochemical and histopathological investigation. Food Chem. Toxicol. 2008; 46(3):1164-1170.

[13] 'Foreign (M13) DNA ingested by mice reaches peripheral leukocytes, spleen, and liver via the intestinal wall mucosa and can be covalently linked to mouse DNA', Schubbert et al, Proc. Natl. Acad. Sci. USA Vol. 94, pp. 961–966, February 1997 Medical Sciences, http://www.pnas.org/content/94/3/961.full.pdf

[14] On the fate of orally ingested foreign DNA in mice: chromosomal association and placental transmission to the fetus. Schubbert et al, Mol Gen Genet. 1998 Oct;259(6):569-76. http://www.ncbi.nlm.nih.gov/pubmed/9819049

[15] 'Assessing the survival of transgenic plant DNA in the human gastrointestinal tract', Netherwood et al., Nat Biotechnol. 2004 Feb;22(2):204-9. Epub 2004 Jan 18. http://www.ncbi.nlm.nih.gov/pubmed/14730317.

[16] London Observer, May 28, 2000. http://www.theguardian.com/science/2000/may/28/gm.food/print.

[17] 'Foreign (M13) DNA ingested by mice reaches peripheral leukocytes, spleen, and liver via the intestinal wall mucosa and can be covalently linked to mouse DNA', Schubbert (TWO BBs) R, et al, Proc. Natl. Acad. Sci. USA, Vol. 94, pp. 961–966, February 1997, Medical Sciences, http://www.pnas.org/content/94/3/961.full.pdf

Described as a "crisis" the number of US citizens with chronic health conditions is rapidly increasing: rising from 44.7% (118 million people) in 1995 – the year the first large scale planting of transgenic crops occurred - to 47.7% (149 million) in 2015. The rate is predicted to rise to 49.2% (149 million) in 2030.[18] In a 2012 study based on official statistics, researchers found 117 million US adults have at least one of 10 chronic conditions examined (hypertension, coronary heart disease, stroke, diabetes, cancer, arthritis, hepatitis, weak or failing kidneys, current asthma, or chronic obstructive pulmonary disease [COPD]). One in four adults has multiple chronic conditions.

While there will be multiple reasons for this rise in chronic diseases, professional medical bodies point to the evidence accumulating that consuming transgenes has adverse effects on human health. Medical professionals and veterinarians in the US are advising patients, pet owners and farmers not to eat transgenic foods or feed them to pets or livestock. The results of not doing so are reported to be substantial improvements in health and well-being, human and animal.[19]

The International Assessment of Agricultural Knowledge Science and Technology for Development (IAASTD), part of the United Nations Environment Programme, issued a report co-authored by over 400 international experts and sponsored by the UN and the World Bank. It concluded: "The safety of GMO foods and feed is controversial due to limited available data, particularly for long-term nutritional consumption and chronic exposure" and "the approval process of GM crops is considered inadequate."[20]

The Australian Medical Association has said, "Genetically modified foods have been developed and introduced without regard for full and independent safety evaluation, or full and adequate public consultation or rigorous assessment of health impacts."[21]

A British Medical Association report concluded that with regard to the long-term effects of transgenic foods on human health and the environment, "many unanswered questions remain" and that "safety concerns cannot, as yet, be dismissed completely on the basis of information currently available".[22]

The American Academy of Environmental Medicine[23] (AAEM) has stated, "GM foods pose a serious health risk in the areas of toxicology, allergy and immune function, reproductive health, and metabolic, physiologic and genetic health, and are without benefit. There is more than a casual association between GM foods and adverse health effects. There is causation as defined by Hill's Criteria[24] in the areas of strength of association, consistency, specificity, biological gradient and biological plausibility. The strength of association and consistency between GM foods and disease is confirmed in several animal studies." It further states, "Multiple animal studies show significant immune dysregulation," including increase in cytokines, which are "associated with asthma, allergy, and inflammation." All are on the rise in the US. The AAEM highlights animal studies showing altered structure and function of the liver, including altered lipid and carbohydrate metabolism as well as cellular changes that could lead to accelerated aging and possibly lead to the accumulation of reactive oxygen species (ROS).[25] Kidney, pancreas and spleen changes have been documented.[28] [26]

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[18] http://www.fightchronicdisease.org/sites/fightchronicdisease.org/files/docs/GrowingCrisisofChronicDiseaseintheUSfactsheet_81009.pdf
[19] http://www.cdc.gov/pcd/issues/2014/13_0389.htm
[20] http://www.unep.org/
[21] https://ama.com.au/
[22] http://bma.org.uk/
[23] http://www.aaemonline.org/gmopost.html
[24] Hill, AB. The environment and disease: association or causation? Proceeding of the Royal Society of Medicine 1965; 58:295-300.
[25] Malatesta et al, 'A long-term study on female mice fed on a genetically modified soybean: effects on liver ageing. Histochem Cell Biol. 2008; 130:967-977. Velimirov et al, Biological effects of transgenic maize NK603xMON810 fed in long term reproduction studies in mice. Report-Federal Min Health, 2008. Kilic & Aday, 'A three generational study with genetically modified Bt corn in rats: biochemical and histopathological investigation. Food Chem. Toxicol. 2008; 46(3):1164-11707

The cumulative effects of ingesting increasing quantities of multiple and substantially different sequences of transgenes on a daily basis, potentially for a lifetime has not been pursued officially. Effectively, populations, especially in the US, and especially the most vulnerable of society – foetuses, infants and children, the elderly, and those with challenged immune systems - have unknowingly acted as guinea pigs for an ongoing experiment, the results of which no official body is monitoring or evaluating.

There is also a deficiency of independent substantive data on the potential interactions of chemicals that a transgenic product has been designed to resist and an absence of data to assess potential health risks to humans through unique combinations of chemicals in food that are accepted as probable or feasible. This is an unmanaged risk.

4 The premises on which evaluations are based

It is safe to say transgenic food crops have been evaluated mainly by US regulatory bodies, which authorities declared them safe for human consumption. It is also a fact that almost all of the 'safety' testing has been carried out by the company developing the novel DNA, not by independent scientists.

In Alliance for Bio-Integrity et al v Shalala (1998) over 44,000 pages of files produced by the US Food and Drug Administration (FDA) at the behest of the Court revealed it had declared genetically engineered foods to be safe despite disagreement from its own experts, and that it falsely claimed a broad scientific consensus supported its stance. Internal reports and memoranda disclosed agency scientists repeatedly cautioned that foods produced through recombinant DNA technology - that is, genetically engineered organisms - entail different risks than do their conventionally produced counterparts and that this was consistently disregarded when FDA policy was written in treating transgenic food crops the same as conventional ones.

In taking this stance, the agency violated the US Food, Drug and Cosmetic Act in allowing genetically engineered foods to be marketed without testing on the premise that they are 'generally recognized as safe' (GRAS) by qualified experts.

The consensus of scientists working for the FDA at that time was that transgenic foods were inherently risky, and might create hard-to-detect allergies, poisons, gene transfer to gut bacteria, new diseases, and nutritional problems. They urged rigorous long-term tests.

From this irresponsible start, applications have continued to be approved without independent testing.

The 2014 'Hot Debate' at New Zealand's Lincoln University featured six experts discussing transgenic organisms. Dr Jon Hickford and Dr Tony Connor, proponents of genetic engineering technology, stated transgenic foods were safe to eat.

They were asked (a) if they could provide 10 human studies to support this statement, and (b) would they also advise where the diagnostic tools are available for health professionals to identify if GE foods in the human diet are contributing or not to illnesses.

Drs Hickford and Conner admitted there are no safety studies nor are there any diagnostic tools for monitoring public health impacts of GE foods.[27]

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[26] Finamore et al. Intestinal and peripheral immune response to MON 810 maize ingestion in weaning and old mice. J Agric. Food Chem. 2008; 56(23):11533-11539.
[27] http://www.scoop.co.nz/stories/PO1404/S00063/myths-revealed-about-safety-of-ge-food.htm.

After two decades of growing commercial transgenic crops, the results to consumers unknowingly ingesting transgenes continue to be questioned. Proponents of genetic engineering technology continue to assert that transgenic organisms are safe because the FDA's policy of substantial equivalence considers such organisms are equivalent to their conventional counterparts. This is a contentious issue discredited by a substantial body of experts, the debate focussing on the methodology used to determine criteria for substantial equivalence. A 2015 study[28] reads:

"Systems biology, which aims to understand complexity of the whole organism as a system rather than just studying its parts in a reductionist manner, may provide a framework to determine appropriate criteria, as it recognizes that GM, small or large, may affect emergent properties of the whole system."

Using a computational systems biology method the researchers coupled "known perturbations on five biomolecules caused by the CP4 EPSPS GM of Glycine max L. (soybean), with an integrative model of C1 metabolism and oxidative stress (two molecular systems critical to plant function). The results predict significant accumulation of formaldehyde and concomitant depletion of glutathione in the GMO, suggesting how a 'small' and single GMO creates 'large' and systemic perturbations to molecular systems equilibria."

Regulatory agencies could utilize a systems biology approach using a combination of in silico, computational methods and "subsequent targeted experimental in vitro and in vivo designs, to develop a systems understanding of 'equivalence' using biomarkers, such as formaldehyde and glutathione, which predict metabolic disruptions, towards modernizing the safety assessment of GMOs."

The study findings clearly show that transgenic organisms are not substantially equivalent to conventional organisms and show that significant damage is done at the cellular level to foods that have been engineered.

PSGR urges FSANZ to give serious attention to how they assess risks and why they approve virtually every Application made using scientific analysis released by overseas regulators of questionable integrity. The US FDA has admitted it operates under a directive "to foster" the US biotech industry.[29] New Zealand and Australia should not follow suit.

4 Conclusion

There remains no official monitoring of effects on the human population and consumers have virtually no notification of the risks related to commercial transgenic crops via labelling or freedom of information.

With US consumers increasingly growing aware of the potential results of ingesting transgenic DNA, the fastest growing sector in its grocery industry is for foods free of transgenes, that sector now estimated to be at close to one third of the market. This is the result of consumer pressure, and from medical professionals recommending foods free of transgenes with consequent improved health for patients.[30]

New Zealand remains well positioned to help meet that demand for GE-free food and its population would benefit from such a stance.

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[28] Do GMOs Accumulate Formaldehyde and Disrupt Molecular Systems Equilibria? Systems Biology May Provide Answers. DOI: 10.4236/as.2015.67062, V. A. Shiva Ayyadurai* and Prabhakar Deonikar, Systems Biology Group, International Center for Integrative Systems, Cambridge, MA, USA. http://www.scirp.org/journal/PaperInformation.aspx?PaperID=57871#.Varc06Sqqkq

[29] Alliance for Bio-Integrity http://www.biointegrity.org/list.htm.

[30] http://www.aaemonline.org/gmopost.html.

PSGR urges FSANZ to:

- Undertake in-depth research using independent scientists to evaluate Applications with long term testing and not to take as an authority the questionable decisions of US regulators.

- Uphold public safety by banning transgenic foods from the New Zealand food supply, as there is no scientific proof that they are equivalent to non-transgenic foods or that they are safe.

If transgenic foods continue to be approved for the New Zealand food supply FSANZ should insist on comprehensive mandatory labelling to identify them, to warn of potential health risks, and to give consumers a choice.

FSANZ should reject Application A1110. The food regulation review process of FSANZ has a legislated mandate to protect public health and safety. In approving this Application, FSANZ would not be meeting this duty of care.

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Ends