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Managing Risks Associated with Outdoor Use of Genetically Modified Organisms

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Foreword

In February 2014 the Council of the Royal Society of New Zealand considered a request from Federated Farmers to review the validity of scientific conclusions underpinning Auckland Council, Far North District Council, Kaipara District Council and Whangarei District Council Draft Proposed Plan Change to the District /Unitary Plan for Managing Risks Associated with Outdoor Use of Genetically Modified Organisms (GMO) Draft Section 32 Report (January 2013). Professor Barry Scott FRSNZ and Professor Clive Ronson FRSNZ are the authors of this focused review of scientific and technical assertions in that Report, on behalf of the Royal Society of New Zealand. Economic and cultural aspects relating to the outdoor use of GMOs were outside the scope of this review. We thank the authors and peer reviewer Dr Tony Conner FRSNZ for undertaking this work.

Sir David Skegg FRSNZ, President, Royal Society of New Zealand

Benefits and risks

In assessing benefits and risks, both the magnitude and the likelihood of each need to be taken into account; this is the approach taken in New Zealand by agencies such as the Environmental Protection Authority[1] and Food Standards Australia New Zealand[2]. There is an element of risk associated with most human activities but it is the weighing up of magnitude and likelihood that is important in the decision making process. The Report's section on benefits and risks, however, does not include these considerations in the issues it raises.

In considering the risks, the Report highlights the impact of rare events and uses the emergence of bovine spongiform encephalopathy (BSE) in United Kingdom cattle as the example. It is important to point out that the BSE outbreak in the UK was a consequence of food manufacturing practices and had nothing to do with Genetic Modification (GM). In fact, current scientific evidence strongly supports the opinion that GMOs do not impose any greater risks as a result of their genetically modified status[3]. Any risks imposed are a result of the host organism and the trait it expresses, and are the same for an organism expressing a particular trait created by GM or by conventional means[4].

1 http://www.epa.govt.nz

2 http://www.foodsafety.govt.nz/science-risk/risk-assessment/overview.htm

3 Conner A. J., Glare T. R. and Nap J-P. (2003) The release of genetically modified crops into the environment - Part II. Overview of ecological risk assessment. Plant J. 33, 19–46

4 Leyser O. (2014). Moving beyond the GM Debate. PLOS Biol. 12, e1001887

Environmental Risks

The Report highlights a number of potential risk areas associated with the outdoor use of GMOs, but only one supporting reference is supplied in relation to these assertions[5]. The reference[5] is largely opinion-based and is very selective in the arguments it makes. Furthermore, certain errors of fact are made, which might have been avoided had the publication been subjected to scientific peer review. For example:

- " … *plants created by conventional plant breeding are not hazardous*". While this is likely to be true if the starting material has already been selected over many years and has been shown to be safe, there are many scenarios where this will not be the case. For example: kiwifruit are allergenic to certain individuals[6]; crossing a commercial tomato cultivar with a wild relative to introduce disease resistance has the potential to introduce a range of of traits that could be undesirable for some consumers[7]; and the potato cultivars 'Lenape' (USA and Canada) and 'Magnum Bonum' (Sweden) were both withdrawn due to excessive glycoalkaloid content in their tubers following successful breeding for pest and disease resistance[8].

- "*Techniques so far do not allow for site-specific insertion*". This may have been true in 2005, but is certainly not so now, with a variety of methods now available to allow the insertion of genes at specific sites in a genome, including zinc finger nucleases (ZFNs), transcription activator-like effector nucleases (TALENs) and clustered regularly interspaced short palindromic repeats (CRISPR)/Cas9 technologies[9].

The specific areas highlighted in the Report as environmental risks are addressed below:

Non-target effects

The Report highlights the potential non-target effects of GMOs. For example, GMO crops that produce Bt insecticide can negatively impact non-target insect populations. However, field studies have shown that these negative impacts are markedly lower than those that occur with conventionally managed crops. The scientific consensus is that the use of insect-resistant biotech crops constitutes a major advance over the use of broad-spectrum synthetic insecticides for control of insect pests since they are environmentally more benign[10]. A well-publicised case in New Zealand involved the purportedly significant detrimental effect of Bt-expressing maize pollen on the monarch butterfly. This concern arose from laboratory studies in which the pollen was fed to the butterfly. However, subsequent large-scale field trials demonstrated no detrimental effects; for example, it was noted that when the maize was in flower the monarchs were not present. Thus, in this instance, while the potential hazard was high, exposure was negligible resulting in effectively zero risk[11].

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5 Antoniou M., Robinson C., and Fagan J. (2012) GMO Myths and Truths: An evidence-based examination of the claims made for the safety and efficacy of genetically modified crops. Earth Open Source, UK. 123 pp.

6 Bublin M., Mari A., Ebner C., Knulst A., Scheiner O., Hoffmann-Sommergruber K., Breiteneder H., Radauer C. (2004) IgE sensitization profiles toward green and gold kiwifruits differ among patients allergic to kiwifruit from 3 European countries. J. Allergy Clin. Immunol. 114, 1169–1175.

7 Labate J. A. and Robertson L. D. (2012) Evidence of cryptic introgression in tomato (*Solanum lycopersicum* L.) based on wild tomato species alleles. BMC Plant Biol. 12:133.

8 Zitnak A. & Johnston G. R., (1970) Glycoalkaloid content of B5141–6 potatoes. Am. Potato J. 47, 256–260.

9 Voytas D. F. and Gao C. (2014) Precision genome engineering and agriculture: opportunities and regulatory challenges. PLOS Biol.12, e1001877.

10 Gatehouse A. M. R., Ferry N., Edwards M. G. and Bell H. A. (2011) Insect-resistant biotech crops and their impacts on beneficial arthropods. Phil. Trans. R. Soc. B 366, 1438–1452; Yu H-L, Li Y-H; Wu K-M (2011) Risk assessment and ecological effects of transgenic *Bacillus thuringiensis* crops on non-target organisms. J. Integr. Plant Biol. 53, 520–538.

11 Sears M. K., Hellmich R. L., Stanley-Horn D. E., Oberhauser K. S., Pleasants J. M., Mattila H. R., Siegfriedi B. D., and Dively G. P. (2001) Impact of *Bt* corn pollen on monarch butterfly populations: A risk assessment. Proc. Natl. Acad. Sci. U. S. A. 98, 11937–11942.

Invasiveness

Plant 'weediness' or 'invasiveness' is an inherent property of the plant:

- Old Man's Beard is highly invasive because of its vigorous scrambling properties[12].
- Clover is weedy because its seeds are long lived and can be widely dispersed. As a legume, it can grow on nitrogen poor soils[13].
- By contrast, domesticated crops such as potatoes and maize are not invasive[14].

In making a risk assessment of the potential invasiveness of a GMO or a naturally occurring plant species, the most important consideration is the inherent biological properties of the starting organism[15]. Single GM changes are very unlikely to change the persistence of a crop species, unless it involves the introduction of herbicide resistance genes, used in an environment with increased use of herbicide. The 'weediness' of the plant then becomes linked to the general agricultural practice that the plant is used in[16].

The bullet points on effects on non-target species, invasiveness and rare events given in the Report are taken directly from *Community Management of GMOs: Issues, Options and Partnership with Government*. (Simon Terry Associates, March 2004). However, we note that the references given in the source publication in support of these concerns are largely opinion pieces, rather than evidence based articles.

Horizontal gene transfer

Horizontal gene transfer (HGT) refers to any process in which a recipient organism acquires genetic material from a donor organism other than by vertical transmission (normal sexual reproduction). It is not restricted by species boundaries and HGT has been shown between organisms as diverse as bacteria and plants and animals[17].

HGT has long been recognised as a major force in microbial evolution and, with advances in large-scale sequencing technologies, it is also being recognized as a significant contributor to the evolution of eukaryotic genomes, with most transferred genes coming from bacteria[18]. Evidence for HGT is most often seen between organisms that are intimately associated (e.g., in mutualistic or parasitic relationships)[19]. For example, it is likely that there has been frequent transfer of genes from bacterial endosymbionts to their invertebrate hosts over an evolutionary time scale[20]. Such large evolutionary timescales make it impossible to observe HGT involving plants and animals in real time.

Statements in the Report relating to horizontal gene transfer are largely based on the publication *GMO Myths and Truths: An evidence-based examination of the claims made for the safety and efficacy of*

12 Ogle C. C., La Cock G. D., Arnold G. and Mickleson N. (2000) Impact of an exotic vine *Clematis vitalba* (F. Ranunculaceae) and of control measures on plant biodiversity in indigenous forest, Taihape, New Zealand. Austral Ecol. 25, 539–551.

13 Baker M.J . and Williams W. M. (Eds) 1987. White clover. CABI, UK. 534 pp.

14 Conner A. J., Glare T. R and Nap J-P. (2003) The release of genetically modified crops into the environment - Part II. Overview of ecological risk assessment. Plant J. 33, 19–46

15 Warwick S. I., Beckie H .J., and Hall L. M. (2009) Gene flow, invasiveness, and ecological impact of genetically modified crops. The year in evolutionary biology 2009: Ann. N.Y. Acad. Sci. 1168: 72–99.

16 Conner A. J., Glare T. R. and Nap J-P. (2003) The release of genetically modified crops into the environment - Part II. Overview of ecological risk assessment. Plant J. 33, 19–46

17 Bock R. (2010) The give-and-take of DNA: horizontal gene transfer in plants. Trends Plant Sci. 15, 11–22.

18 Keeling P. J. (2009) Functional and ecological impacts of horizontal gene transfer in eukaryotes. Curr. Opin. Genet. Dev. 19, 613–619.

19 Bock R. (2010) The give-and-take of DNA: horizontal gene transfer in plants. Trends Plant Sci. 15, 11–22; Dunning Hotopp, J. C. (2011) Horizontal gene transfer between bacteria and animals. Trends Genet. 27, 157–163.

20 Dunning Hotopp J. C. (2011) Horizontal gene transfer between bacteria and animals. Trends Genet. 27, 157–163.

genetically modified crops[21]. In the introduction to the publication's section on HGT, it is stated that "*The EU-supported website GMO Compass states, "So far, horizontal gene transfer can only be demonstrated under optimised laboratory conditions." Alternatively, they argue that if it does happen, it does not matter, as GM DNA is no more dangerous than non-GM DNA*." This statement from GMO Compass is an accurate reflection of the majority scientific opinion as expressed in the peer-reviewed scientific literature[22]. However the *GMO Myths and Truths* article then goes on to claim that "*The consequences of HGT from GM crops are potentially serious, yet have not been adequately taken into account by regulators*." We contend that the arguments used to support this claim in the body of the section do not stand up to scientific scrutiny.

Concerns over antibiotic resistance

HGT among bacteria is a major contributor to microbial evolution including to the emergence of new strains of pathogens and to antibiotic resistant strains. The recent emergence of Gram-negative pathogens expressing New Delhi Metallo-beta-lactamase-1 (NDM-1) is one example of the profound effect of HGT. The associated carbapenemase enzyme makes bacteria resistant to carbapenem antibiotics, which are a mainstay for the treatment of Gram-negative antibiotic-resistant bacterial infections. Bacteria that produce carbapenemases are very difficult to treat. Other recent studies using next generation sequencing (NGS) have indicated that antibiotic resistance has been acquired by *Streptococcus pneumoniae* by genetic transformation within patients. These examples show that HGT of antibiotic resistance genes can occur rapidly. A major factor thought to contribute to this spread is the misuse of antibiotics. The message is that, where selective pressure occurs, traits that allow adaptation to that pressure can be acquired by bacteria through HGT.

With respect to GM plants, there is no evidence of HGT of antibiotic resistance genes from plants to bacteria[23]. If it does occur, it would be at such a vanishingly small frequency that it would have no impact on the overall frequency of HGT of such genes in the environment. It should also be noted that new-generation transgenic plants often do not contain antibiotic-resistance genes.

21 Antoniou M., Robinson C., and Fagan J. (2012) GMO Myths and Truths: An evidence-based examination of the claims made for the safety and efficacy of genetically modified crops. June 2012, Earth Open Source, UK. 123 pp.

22 Brigulla M. and Wackernagel W. (2010) Molecular aspects of gene transfer and foreign DNA acquisition in prokaryotes with regard to safety issues. Appl. Microbiol. Biotechnol. 86, 1027–1041.

23 Brigulla M. and Wackernagel W. (2010) Molecular aspects of gene transfer and foreign DNA acquisition in prokaryotes with regard to safety issues. Appl. Microbiol. Biotechnol. 86, 1027–1041.