FS65

Proposed Kaipara District Plan:
Form 6 - Further Submission

Clause 7 of Schedule 1, Resource Management Act 1991

This is a further submission that is either in support of or in opposition to any submission already received by Kaipara District Council on any Proposed Kaipara District Plan topic **except for Light** in the Proposed Kaipara District Plan. No new submission points can be made.

All submissions and Summary of Submissions can be viewed on our website here: www.kaipara.govt.nz/kaipara-district-plan-review/proposed-district-plan-submissions

Note: *The topic of Light was notified for further submissions on 21 October 2025 prior to all other topics due to the hearing for Light being confirmed for 17 December 2025.*

Note: You can only make a further submissions on the submission points identified in an original submission on the Proposed Kaipara District Plan.

1. Further submitter details *(mandatory information)*

Full name of individual/organisation making further submission:
Life Sciences Network Incorporated

Contact person ***(if different from above):*** Dr William Rolleston

Email address: wrolleston@lifesciencesnetwork.nz

Postal address: P O Box 2117, Washdyke, Timaru

Postcode: 7941

Preferred method of contact: ✔ **Email** ☐ **Post**

Contact phone number: 027 246 0634

Do you have an agent who is acting on your behalf? ☐ **Yes** ✔ **No**

If you would like a copy of your submission sent to your agent, enter their email address below *(otherwise leave blank)*

Agent email address:

2. Eligibility to make a further submission *(for information on this section go to RMA Schedule 1, clause 8)*

I am (select one of the following options):

☐ A person representing a relevant aspect of the public interest.
In this case, also specify below the grounds for saying that you come within this category.

✔ A person who has interest in the proposal greater than the interest that the general public has.
In this case, also specify below the grounds for saying that you come within this category: or

☐ The local authority

3. My reasons for selecting the category ticked above are:

(For example: Any person representing a relevant aspect of the public interest would likely include public interest environmental groups

OR

Any person that has an interest in the proposed policy statement or plan greater than the interest that the general public has is likely to include owners of land and users of resources directly affected by plan provisions. It is also likely to include iwi and hapu where their interests are directly affected.)

The Life Sciences Network (LSN) is an organisation which has, since May 2000, represented the interests of science and industry (including agriculture) in the public debates on science issues, in particular the regulation of genetic modification. LSN was considered by the Royal Commission on Genetic Modification (2000-01) to have an interest greater than the general public and was thus awarded interested person status.

4. Request to be heard at hearings

☑ Yes, I wish to be heard at the hearing in support of my further submission; or

☐ No, I do not wish to be heard at the hearing in support of my further submission.

If others make a similar submission, I will consider presenting a joint case with them at the hearing.

☑ Yes ☐ No

Signature of further submitter:
(or person authorised to sign on behalf of person making further submission)

(A signature is not required if you are making your further submission by electronic means)

Date 11th December 2025

Important information:

1. This Form 6 is for further submissions on every topic with the Proposed Kaipara District Plan (apart from Light).
2. You must serve a copy of your further submission on the original submitter **within five working days after it is served** on Kaipara District Council.
3. The Kaipara District Council must receive this further submission before the closing date and time for further submissions **(5.00pm on Monday 15 December 2025).**
4. All information provided in your further submission is considered public under the Local Government Official Information and Meetings Act 1987 and will be published to progress the process for the Proposed Kaipara District Plan and will be made publicly available. Your further submission will only be used for the purpose of the Proposed Kaipara District Plan.
5. Submitters who indicate they wish to speak at the Hearing will be emailed all relevant information relating to the Hearing. If you don't have an email address, it will be posted.

Note to person making submission:

Your further submission (or part of your further submission) may be struck out if the authority is satisfied that at least one of the following applies to the further submission (or part of the further submission):

- It is frivolous or vexatious;
- It discloses no reasonable or relevant case;
- It would be an abuse of the hearing process to allow the further submission (or the part) to be taken further; and/or
- It contains offensive language.

Send your further submission:

Post it to: District Planning Team
Kaipara District Council
Private Bag 1001
Dargaville 0340

OR

Email to: districtplanreview@kaipara.govt.nz

OR you can hand-deliver this further submission form along with any attachments to: any Kaipara District Council service centre (Dargaville at 32 Hokianga Road or Mangawhai at 6 Molesworth Drive). Please be aware that our service centre doors close at **4.00pm**.

Please refer to District Plan Review on our website www.kaipara.govt.nz where all information and updates are located.

If you need any assistance at all, please contact the District Planning Team on 0800 727 059 or email us at districtplanreview@kaipara.govt.nz.

Further Submissions must be received
by: **5pm – Monday 15 December 2025**

5. Further Submission/s on all remaining topics (excluding the LIGHT topic) on the Proposed Kaipara District Plan:

Name of original submitter	Original submitter number	Original submission point number	Support or oppose	Reasons for supporting or opposing	I seek that the whole (or part [describe part]) of the submission be allowed (or disallowed) ***Give precise details***
Example *John Smith*	*Example* *600*	*Example* *600.001*	*Example* *Support*	*Example* *I support because I believe…..*	*Example* *I seek that the whole of the submission point be allowed*

YOU ARE WELCOME TO PROVIDE THE REQUIRED INFORMATION ABOVE ON A SEPARATE PAGE IF YOU REQUIRE MORE SPACE

Proposed Kaipara District Plan

Submitter Contact List

for all other topics **(excluding the LIGHT topic)**

You must serve a copy of your further submission on the original submitter **within five (5) working days after it is served** on Kaipara District Council.

A list of original submitters contact details are available from www.kaipara.govt.nz/district-plan-review (go to submissions)

Or download from the link below

Download the Original Submitter Contact List

Additional pages which form part of the

Life Sciences Network further submission

Proposed Kaipara District Plan

The Life Sciences Network **opposes** the requests to insert policies and rules relating to Genetically Modified Organisms / Gene Technologies for the following reasons:

1. **Council chose not to insert GMO provisions**

    a. The LSN notes that there are no GMO provisions in the notified Proposed District Plan.
    b. Several councils (such as Invercargill, Queenstown, Timaru and Environment Canterbury) have rebuffed similar requests to insert GMO provisions into their plans or other documents. None of these decisions have been appealed.
    c. Because GMO provisions have been requested in primary submissions there is no relevant section 32 report.
    d. Submitters will not have the opportunity to submit on any provisions the council may subsequently decide to put in.
    e. Many potential submitters will be unaware that the issue of genetic modification is now before the decision makers for consideration.

    Thus, should the council change its mind on the need for GMO provisions in the District Plan, a separate plan change should be undertaken at a future time. A plan change to insert GMO Provisions could be sponsored by the proponents or by the Council itself.

2. **The "one size fits all" approach urged on the Council by some submitters is inappropriate**

    a. All living organisms vary in in type and risk.
        This applies to:
        i. organisms currently in New Zealand,
        ii. new organisms and
        iii. genetically modified organisms
    b. The GMO provisions sought by submitters are a 'one size fits all' approach to genetic modification which is simplistic, unworkable and in effect a prohibition on a useful technology.

3. **Unnecessary and inappropriate duplication of the Environmental Protection Authority under HSNO**

    a. The Environmental Protection Agency currently regulates the development and use of GMOs under the Hazardous Substances and New Organisms Act.
    b. Any development or use of a GMO must first obtain approval from the EPA.

c. Decisions are made on a case-by-case basis, dependent on an expert assessment of risks and both positive and adverse effects.
d. The EPA is the appropriate body with the necessary resources and expertise to properly and comprehensively consider and address the effects of GMOs, and not the Council.
e. Management of genetically modified organisms in New Zealand is considered one of the most conservative regulatory regimes in the world. Advice to government suggests that it is unnecessarily conservative. (see Attachment A)
   The Gene Technology Bill is progressing through the House but we understand that as this is not legislation is not for consideration by the council.

f. The EPA is required to (and does) exercise a precautionary approach in its decision making. (see Attachment B), for example:

> In 2015 the EPA considered an application to import for release the live genetically modified BoHV-1.1 strain (strain CEDDEL) contained within the veterinary vaccine Hiprabovis IBR Marker Live. This application was declined by the EPA decision committee as it was not satisfied that the vaccine would not combine with wild strains of the IBR cattle virus.

g. The issues which the EPA must consider are comprehensive and address the risks and effects of a physical, environmental, cultural, economic and spiritual nature. Therefore, it is unlikely there would be any residual risk which should be managed under the RMA.

h. Issues of safety (including environmental safety), adverse effects on areas such as markets, effects on Māori and local iwi, other adverse effects, risks (and risk mitigation) and management are comprehensively considered by the EPA.

i. Approval for field trials, conditional release and full release requires public consultation. Thus, there is plenty of opportunity for those wishing to oppose, or change the controls applied to, any field trial or release to make submissions and have their voice heard.

j. All matters which are raised by the submitters as a basis for seeking that the district plan control GMOs are those which must be considered by the EPA.

4. Jurisdiction and control of effects by the council

a. While the High Court has clarified that councils have legal jurisdiction to include provisions on organisms which are GMOs, the Court has said nothing about whether a council should include such provisions in any particular circumstance. Moreover, the Court has not said anything about whether it is appropriate for councils to prohibit or control GMOs as a class or put in place rules simply on the basis an organism is a GMO.

b. In addition to HSNO controls, other tools already exist (e.g. pest management strategies under the Biosecurity Act) for councils to manage any particular GMO which is economically useful but unwanted in the wrong place as it does with wilding pines, wilding kiwifruit, feral goats, deer and pigs.

c. The Council should not include provisions on GMOs in the district plan unless it can justify that the specific controls are necessary to address risks or effects which cannot be appropriately addressed by the EPA,.

d. International deregulation of some aspects of genetic modification and in particular gene editing, (as is presently occurring in the UK and the EU), and the inability to detect some GMOs will make regulation at the district level very difficult.

e. Prohibitive rules (such as those proposed by submitters) would require the council to incur unnecessary costs in plan enactment and oversight as well as a costly plan change to undo.

Thus it is more efficient:

i. To address any (unlikely) residual risk of an effect when that risk/effect is known
   - using current tools under the Biosecurity or Resource Management Acts.
   - and then, if necessary, consider specific objectives, policies and rules.

5. Paragraphs 6-10 below provide information on the developments, uses and record of the safe use of genetic modification. These paragraphs demonstrate the diverse issues the council would be faced with if it is to add another layer of regulation without jeopardising the district's ability to take advantage of the opportunities genetic technologies present.

Commented [WR1]: Re footnote. Suggest you delete as not considered by Council.

New Genetic Technologies and Gene Editing

a. Genetic technologies are developing rapidly.
    i. While the traditional methods of genetic modification involve the insertion of whole genes into an organism more recent techniques (often termed "gene editing"), allow changes to be made in a far more precise way. These techniques are explained in a series of information papers put out by the Royal Society of New Zealand. A simple analogy is that if the genetic code is a book, traditional GM is akin to inserting a sentence (possibly on an unrelated topic) randomly into the pages; gene editing is like using the find-and-replace function on a word processor. Some of these edits can be as small as a single letter.
    ii. The genetic code in an organism runs into billions of letters. Gene editing, where it changes only one or two letters of that genetic code in a precise and targeted way compares favourably with traditional (non-GM) methods such as mutagenesis where thousands of random mutations are created by exposing a plant or seed to radiation or chemicals in order to speed up the natural process of mutation.
    iii. Gene editing does, in fact, introduce fewer changes than either mutagenesis or traditional breeding using pollen crosses.
    iv. Mutagenesis is unregulated whereas gene editing is regulated in New Zealand as genetic modification. It is not possible to tell a gene edited organism from a non-GM organism produced through traditional breeding or mutagenesis making identification in breeding programmes or the market difficult. A number of countries have (USA, Brazil, Japan, Sweden, Australia) deregulated certain gene editing techniques where the outcome could have been achieved through traditional breeding. More recently, the United Kingdom has, and the European Union is in the process of also relaxing their legislation around Gene Technologies enabling the technology to be used in an appropriately regulated manner.

b. New genetic technologies are therefore more accessible to scientists outside multinational corporations such as those in our universities and national research institutions.
c. Gene editing technologies are now capable of making changes which are indistinguishable from traditional (non-regulated) breeding techniques.
d. Countries such as Australia, USA, Brazil, Japan, Sweden, and the United Kingdom no longer regulate some aspects of genetic modification, and the European Union is in the throes of passing similar legislation now.

6. The use of Genetic Modification in Modern Society

a. Genetically modified organisms (GMOs) are generally regarded as plants, animals, insects and microbes which have had their genetic structure changed using laboratory techniques.

b. Since 1982 GMOs have been used to produce enzymes for industry (e.g. for use in washing powders) and food manufacture (e.g. cheese making including in New Zealand); and for medicine (such as insulin for the treatment of diabetes; Keytruda for the treatment of breast cancer; heart drugs and drugs to treat inherited genetic disorders).
c. More recently live genetically modified organisms (principally viruses and *ex-vivo*[1] GM) have been used or are being developed to treat medical conditions such as cancer and blood and skin disorders (haemophilia, thalassemia and bullosa epidermolysis) as well as for vaccine use.
d. More recently live genetically modified organisms have been used in medicine including viruses for gene therapy and the treatment of cancers and the use of gene editing to reprogramme patient cells to fight cancer.
e. Since 1996 genetic modification has been used in agriculture in countries/regions such as Australia, the USA, South America, parts of Europe, India and Asia.
f. Where GM crops are approved, they are popular amongst farmers and GMOs now cover 10% of the world's arable land.
g. In its 2019 update on the *Global Status of Commercialized Biotech/GM Crops* [2](Attachment C) the International Service for the Acquisition of Agri-biotech Applications noted:
    - In 2019 up to 17 million farmers in 29 countries planted 190.4 million hectares of genetically modified crops
    - Since 1996 an accumulated area of 2.7 billion hectares have been planted, providing for a 112-fold increase in production in the 23-years making biotechnology the fastest adopted crop technology in the world.
    - Uptake by farmers in the top five growing countries is as high as 90-100%, with ISAAA reporting that adoption rates for these countries and the crops presently grown are 'close to saturation'.
    - The main biotech GM crops are cotton, soybeans, canola and corn
    - Other GM crops include alfalfa, sugar beets, papaya, squash, eggplant, potatoes, and apples
    - Crops under development include rice, banana, potato, wheat, chickpea, pigeon pea, rye grass, mustard, cassava, cowpea, and sweet potato
    - Economic gains from GM crops reached US$224.9 billion from 1996 to 2018

h. Internationally, approvals of genetic modification in the primary industry have moved beyond broad acre crops and into foods which are eaten unprocessed. In 2017 US regulators approved the production and consumption of GM salmon and apples.
i. The deregulation of some aspects of genetic modification (gene editing) in jurisdictions such as the USA and Australia means that the use of genetic modification in agriculture is likely to increase as those countries move to increase the quality and competitiveness of their products.
    i. Examples of gene editing being developed in agriculture include:
        - Non browning mushrooms – already approved in the USA as the

[1] ex-vivo is where cells (e.g. blood cells) are taken from a patient's body, genetically modified and then returned to the patient.
[2] https://www.isaaa.org/resources/publications/briefs/55/executivesummary/default.asp

USDA have decided not to regulate gene editing where the outcome could also be achieved through conventional breeding techniques.

- soybeans with healthier oil now being grown in the USA without GM regulatory constraints.
- Polled (hornless) cattle.

  Simulation of gene edited and conventional mating schemes indicates that gene editing will have positive outcomes for genetic improvement compared with conventional breeding.

- virus-resistant pigs.
- disease-resistant cassava.
- low-gluten wheat (that people with celiac disease could eat).
- low-fat pigs that better regulate heat (which would better protect piglets from cold weather, a common cause of death).
- oilseed crops with high levels of omega-3 fatty acids.
- disease-resistant rice.
- Wheat with a 27% increase in grain weight.
- New high-nutrient and flavoured tomatoes and their relatives.

7. Genetic Modification in the New Zealand Environment

a. New Zealand is not GMO free.

i. Between 2014 and 2018 genetically modified petunias were in sold without approval in New Zealand. MPI issued a recall when they realized certain varieties were likely to be genetically modified but do not appear to have undertaken any testing or surveillance work to understand the dispersal of this organism stating that it is neither a threat to health nor the environment. Nor to our knowledge have they (or any council with GMO prohibitions) undertaken any eradication perhaps reflecting, and demonstrating, that the regulators were unconcerned about risk and effect, notwithstanding the lack of approval.

ii. There have already been five GMO releases into the environment approved since the passing of the Hazardous Substances and New Organisms Act (Animal vaccines and human therapeutics). These releases have presented no issues.

Release of GMOs for medical use		
APP202371[3]	30/04/19	To import and release a genetically modified live attenuated vaccine that protects humans against Japanese encephalitis (Imojev) into New Zealand.
APP203530	23/04/18	To import a genetically modified live-attenuated oncolytic vaccinia virus for conditional release in a phase 1b clinical trial as an experimental therapy for renal cell carcinoma
APP202854	12/02/18	To import for release a genetically modified adenovirus (Telomelysin) for use in a Phase II clinical trial for patients with advanced melanoma

[3] Released without controls

APP202601	28/10/15	To import for release a genetically modified live-attenuated vaccinia virus (Pexa-Vec) for use in a Phase 3 clinical trial for patients with hepatocellular carcinoma
Release of GMOs for veterinary use		
GMR07001	19/11/08	To gain approval to import for release genetically modified vaccines (Proteqflu and Proteqflu Te) to protect horses against Equine Influenza

8. Field Trials in New Zealand

There is no evidence that field trials of GMOs in New Zealand have resulted in unacceptable risk, caused harm or have resulted in the establishment of a persistent population of GMOs in the New Zealand Environment.

a. AgResearch have been running GM field trials for many years without the need for separate and additional controls under the RMA by the Regional or District Council.

b. There have been 17 approvals for field trials under the HSNO Act 1996.

   i. In May 2002 the HSNO Act was amended by the then Labour government to include additional controls and considerations for field trials.

   ii. While a number of breaches of conditions have been reported we are unaware of any adverse effects resulting from these field trials or that any intervention by the local council was required.

9. Approved Use of Genetic Modification is Safe

a. The approved use of genetic modification has a history of safe use in medicine for 35 years and food production for 20-25 years. No scientifically credible incident of harm to human health or the environment is attributable to genetic modification.

b. Regulators and national scientific bodies around the world have concluded that the use of genetic modification poses no more risk that conventional agriculture.

   i. **The National Academy of Sciences** in the USA released a report in 2016 titled "Genetically Engineered Crops – Experiences and Prospects" (see Attachment D). In it they say:

      - The use of GM in agriculture has had an overall positive outcome for the environment.
      - Humans have been eating meals containing GM food for more than two decades resulting in the consumption of trillions of GM meals without any scientifically credible negative health effect.

   ii. In 2017 **131 Nobel Laureates** (1/3 of all those living) signed a letter written to Greenpeace in support of biotechnology (GMOs), stating that:

> "Scientific and regulatory agencies around the world have repeatedly and consistently found crops and foods improved through biotechnology to be as safe as, if not safer than those derived from any other method of production."

Commented [NM2]: Caps have been used here for 'Regional' and 'District Council', yet elsewhere council is in lower caps, consistency issue re formatting?

Commented [WR3R2]: Make them lower.

The letter also says:

> "WE CALL UPON GOVERNMENTS OF THE WORLD to reject Greenpeace's campaign against …..crops and foods improved through biotechnology …….; and to do everything in their power to oppose Greenpeace's actions and accelerate the access of farmers to all the tools of modern biology, especially seeds improved through biotechnology. Opposition based on emotion and dogma contradicted by data must be stopped."

iii. The **European Commission** after a decade of study made this statement in 2011:

> The main conclusion to be drawn from the efforts of more than 130 research projects, covering a period of more than 25 years of research, and involving more than 500 independent research groups, is that biotechnology, and in particular GMOs, are not per se more risky than e.g. conventional plant breeding technologies.

iv. Similar conclusions have been reached by more than 2**70 regulatory and national scientific and inquiry bodies** around the world including the U.S. National Academies; U.S. Institute of Medicine; American Medical Association; British Royal Society; Royal Society of Medicine; European Food Safety Authority; EU Economic Commission; World Health Organization; American Association for the Advancement of Science; American Dietetic Association and the International Seed Foundation. The list and links can be found in Attachment E.

v. New Zealand's peak science body, **The New Zealand Royal Society**, convened a panel of experts in 2019 to explore the risks, opportunities and implications for New Zealand of gene editing. The Gene Editing Panel was chaired by Professor Barry Scott, Professor of Molecular Genetics in the Institute of Fundamental Sciences at Massey University.

- The panel have published a number of information papers on gene editing including:
  - Gene Editing Evidence Update
  - Gene Editing in the Primary Industries
  - The use of Gene Editing to Create Gene Drives for Pest Control in New Zealand
  - Gene Editing in a Healthcare Context

  The first three technical papers are included in Attachments F-H.
- According to Professor Scott "gene editing techniques will allow more targeted and precise genetic changes than what has been possible before in crop and livestock breeding".

c. The strong scientific consensus on Climate Change and GMO safety is similar.
    i. Dan Ryder of the University of British Columbia-Okanagan has put together a table of views from seven of the most respected science organisations in the world comparing their statements on climate change and on the safety of GMOs. This table is contained in Attachment I.
    ii. A survey undertaken by the Pew Institute indicated that the scientific consensus on the safety of genetically modified foods (88%) was comparable to that on climate change (87%).
    iii. Just as we have seen with Climate Change, vaccination, the theory of evolution and fluoride not all scientists have to agree for there to be a strong scientific consensus.
        - There are reports and studies suggesting health risks from GM crops but these have not withstood scientific scrutiny and have been discounted by science-based regulators. Most famously a 2012 study published in Food and Chemical Toxicology by French biologist study Gilles-Éric Séralini claimed to show increased tumour development in rats through the consumption of GMO feed and/or the herbicide Roundup. This was retracted after criticism from the science community. It was later republished in a non-peer reviewed/low impact journal. Experts in this area do not publish in non-peer reviewed journals.
        - It is important to appreciate that studies do not gain legitimacy simply by being published. Critical for their credibility is repetition of the study by other science groups and critical analysis by the science community. It is our view that this study had critical flaws which have not been adequately addressed and we am not aware that this study has been repeated with the same outcomes.
        - Nonetheless a small group of vocal activists have continued to assert that the use of genetic modification is uncertain and presents significant safety risks. In in 2015 313 "scientists and experts" signed a declaration that "there is no scientific consensus on GMO safety". Of the five New Zealanders to sign this declaration were:
            a. Associate Professor Peter Wills of the group Physicians and Scientist for Global Responsibility,
            b. Professor Robert Mann of the Fluoride Action Network (which opposes the use of fluoride in community water schemes),
            c. Dr Kerry Grundy who chaired the Northland/Auckland region Inter-council Working Party on GMO Risk Evaluation and Management Options (IWPC) which commissioned the Terry and Associates reports referred to in primary submissions, and
            d. Canterbury University Professor Jack Heinemann.

10. Tolerance for GM food exists in the marketplace

a. Genetically modified crops and products (particularly food products) do face restrictions in some markets, are regulated by most countries and avoided by some consumers.
b. Where products have been approved as safe by regulators there is generally a tolerance level for the presence of a GMO in a food product before that food must

be labelled as genetically modified. For example, the European Union has a tolerance level of 0.9% (Regulation (EC) No 1829/2003) for the presence of GMOs in food before they must be labelled as GMOs.

c. Supermarkets and private certifiers (e.g. organic certifiers) generally have a level of tolerance or discretion for the presence of GMOs in a product. For example, the Non-GM Project in the USA (a non GM certification label used by Fonterra) allows up to 5% of animal feed inputs to be of GM origin while still meeting their non-GM standard.
d. The asserted problems concerning loss of premium by allowing GM are therefore overstated.
e. There are appropriate mechanisms under HSNO (and various certification schemes to address the issues of reliable claims as to GE Free or organic. The district plan need not try to second guess or duplicate those processes.

11. Inter Council Working Party reports are out of date and omit relevant information

a. Submitters have referred back to information and reports historically provided by the Inter Council Working Party on GMO Risk Evaluation and Management Options (ICWP).
b. The ICWP was formed by a number of Northland based councils to look into issues and management of genetically modified organisms. It was formed and led by Dr Kerry Grundy, an employee of the Whangarei District Council at that time.
c. Reports generated by the ICWP have been relied on in the implementation of GMO provisions in several District Plans in Northland, Auckland and Hastings.
d. The ICWP reports are based on outdated information and in particular omit information which would otherwise lead decision makers to conclusions contrary to those the report seeks.
e. In particular, the reports do not mention gene editing, nor do they provide a comprehensive and science-based view of the current safety record of GMOs.
f. In 2014, at the request of Federated Farmers, the Royal Society (New Zealand's peak science body), reviewed the validity of the scientific conclusions in the ICWP's key report *Managing Risks Associated with Outdoor Use of GMOs.* The Northland/Auckland section 32 reports draw heavily on this report. The Royal Society's review is critical of the scientific and technical assertion in the report. (see Attachment K)

12. Generic and prohibitive GMO provisions in the district plan are not appropriate

a. Implementing generic provisions (objectives, policies and rules) on GMOs as requested by the submitters would unnecessarily

limit the opportunity to use new genetic technologies such as gene editing to:

- address climate change, water quality and predator control;
- improve productivity;

- innovate to create new products, enhance the attributes and health outcomes of food; as well as
- remediate the environment, manage our biosecurity risks and incursions.

a. Genetic Modification is a tool which can be used alongside and complementary to other technologies and practices to address many of the issues we face in human health, primary production, conservation and the environment. Genetic modification, and its risks, benefits and effects, are fully controlled by, and subject to, the expert oversight and regulation by the EPA under HSNO. Provisions seeking to also regulate GMOs under the Kaipara District Plan fail the s32 tests of necessity and benefit.

While the Council has the legal power to include provisions on organisms which are GMOs in the district plan, the above comments demonstrate that there is no justification for doing so.

At the hearing LSN proposes to present expert evidence in support of the reasons set out in this submission.

Attachments

	Title	**Number of Pages**
A.	Gene Editing 2019 - Ministerial Briefing	17
B.	Anderson Lloyd Letter to Federated Farmers - GMO - precautionary approach liability and bonds	6
C.	ISAAA. 2019. Global Status of Commercialized Biotech/GM Crops in 2019: ISAAA Brief No. 55. Executive Summary ISAAA: Ithaca, NY.	606
D.	Genetically Engineered Crops – Experiences and Prospects https://www.nap.edu/catalog/23395/genetically-engineered-crops-experiences-and-prospects	153
E.	Scientific and Technical Institutions which Support the Safety of GM Crops	7
F.	Gene Editing Evidence Update Royal Society of New Zealand, Oct 2017	9
G.	The Use of Gene Editing to Create Gene Drives for Pest Control in New Zealand, Royal Society of New Zealand Technical Paper, Dec 2017	24
H.	Gene Editing in the Primary Industries Context Royal Society of New Zealand Technical Paper, Oct 2018	34
I.	Scientific Organisation Views on Climate Change and GMOs	1
J.	Waikato Tainui and Maniapoto Environmental Plans – New Organism/GMO extracts	2

K.	Royal Society Review-Managing-Risks-Associated-with-Outdoor-Use-of-GMOs	4

About the Life Sciences Network

The Life Sciences Network was formed in 2000 as an umbrella organization of national industry and science organisations to represent the interests of science, industry and agriculture in the public debates and regulation of genetic modification.

The LSN was considered by the Royal Commission on Genetic Modification to have an interest greater than the general public and was thus awarded interested person status.

Commented [WR4]: Change this to our new purpose.

5. Further Submissions on all remaining topics (excluding the LIGHT topic) on the Proposed Kaipara District Plan:

	Name of the original submitter	Original submitter number	Original submission point number	Support or Oppose	Reasons for supporting or opposing	I seek that the whole (or part [describe part]) of the submission be allowed (or disallowed) *Give precise details*
FS66.1	N Masters	31	31.10	**Oppose**	The LSN opposes this submission point for the reasons set out in the ensuing table which include: • GMOs are out of scope. • Claims of harm are not scientifically credible. • Successful coexistence between organic/conventional and farmers using Gene Technologies has occurred for over twenty years in countries which have both significant plantings of GE-Crops as well as large organic plantings, Australia and the USA, two of the best examples. • The issues raised in the submission are already considered (using a cautionary approach) by the Environmental Protection Authority under the HSNO Act. • In respect to comments regarding Tai Tokerau Iwi, LSN fully appreciates that Māori have a special interest and relationship with indigenous species, together with a desire to maintain kaitiakitanga and whakapapa of taonga species. • The EPA already considers effects and risks including cultural values.	**Disallow** this whole submission point.
FS66.2	Linda Grammer	131	131.10	**Oppose**	LSN's reasons for opposing this submission point are set out under 'submission point' 31.10 above.	**Disallow** this whole submission point.

	Name of the original submitter	Original submitter number	Original submission point number	Support or Oppose	Reasons for supporting or opposing	I seek that the whole (or part [describe part]) of the submission be allowed (or disallowed) *Give precise details*
FS66.3	Linda Grammer	131	131.20	**Oppose**	LSN's reasons for opposing this submission point are set out under 'submission point' 31.10 above.	**Disallow** this whole submission point.
FS66.4	J Sanderson	132	132.10	**Oppose**	LSN's reasons for opposing this submission point are set out under 'submission point' 31.10 above.	**Disallow** this whole submission point.
FS66.5	Auckland GE Free Coalition	154	154.10	**Oppose**	LSN's reasons for opposing this submission point are set out under 'submission point' 31.10 above.	**Disallow** this whole submission point.
FS66.6	Auckland GE Free Coalition	154	154.20	**Oppose**	LSN's reasons for opposing this submission point are set out under 'submission point' 31.10 above.	**Disallow** this whole submission point.
FS66.7	T Upperton	155	155.10	**Oppose**	LSN's reasons for opposing this submission point are set out under 'submission point' 31.10 above.	**Disallow** this whole submission point.
FS66.8	T Upperton	155	155.20	**Oppose**	LSN's reasons for opposing this submission point are set out under 'submission point' 31.10 above.	**Disallow** this whole submission point.
FS66.9	K Evans	157	157.10	**Oppose**	LSN's reasons for opposing this submission point are set out under 'submission point' 31.10 above.	**Disallow** this whole submission point.
FS66.10	GE Free New Zealand	159	159.10	**Oppose**	LSN's reasons for opposing this submission point are set out under 'submission point' 31.10 above.	**Disallow** this whole submission point.
FS66.11	G Mather	171	171.10	**Oppose**	LSN's reasons for opposing this submission point are set out under 'submission point' 31.10 above.	**Disallow** this whole submission point.
FS66.12	R Mueller-Glodde	194	194.10	**Oppose**	LSN's reasons for opposing this submission point are set out under 'submission point' 31.10 above.	**Disallow** this whole submission point.

	Name of the original submitter	Original submitter number	Original submission point number	Support or Oppose	Reasons for supporting or opposing	I seek that the whole (or part [describe part]) of the submission be allowed (or disallowed) *Give precise details*
FS66.13	I Bremner	196	196.10	**Oppose**	LSN's reasons for opposing this submission point are set out under 'submission point' 31.10 above.	**Disallow** this whole submission point.
FS66.14	I Cambourn	204	204.10	**Oppose**	LSN's reasons for opposing this submission point are set out under 'submission point' 31.10 above.	**Disallow** this whole submission point.
FS66.15	Kaipara District Council	222	222.17	**Support**	LSN's reasons for supporting this submission point are as follows: • LSN concurs that given the issue is handled nationally by way of the HSNO Act, and potentially the Gene Technology Bill, (if enacted); there is no point or value in addressing these points at a regional/district level.	**Allow** this whole submission point.
FS66.16	Kaipara District Council	222	222.18	**Support**	LSN's reasons for supporting this submission point are set out under 'submission point' 222.17 above.	**Allow** this whole submission point.
FS66.17	Kaipara District Council	222	222.19	**Support**	LSN's reasons for supporting this submission point are set out under 'submission point' 222.17 above.	**Allow** this whole submission point.
FS66.18	Kaipara District Council	222	222.20	**Support**	LSN's reasons for supporting this submission point are set out under 'submission point' 222.17 above.	**Allow** this whole submission point.
FS66.19	Kaipara District Council	222	222.21	**Support**	LSN's reasons for supporting this submission point are set out under 'submission point' 222.17 above.	**Allow** this whole submission point.
FS66.20	Kaipara District Council	222	222.22	**Support**	LSN's reasons for supporting this submission point are set out under 'submission point' 222.17 above.	**Allow** this whole submission point.

	Name of the original submitter	Original submitter number	Original submission point number	Support or Oppose	Reasons for supporting or opposing	I seek that the whole (or part [describe part]) of the submission be allowed (or disallowed) *Give precise details*
FS66.21	L Er	250	250.10	**Oppose**	LSN's reasons for opposing this submission point are set out under 'submission point' 31.10 above.	**Disallow** this whole submission point.
FS66.22	M Robinson	252	252.10	**Oppose**	LSN's reasons for opposing this submission point are set out under 'submission point' 31.10 above.	**Disallow** this whole submission point.
FS66.23	R Alspach	258	258.40	**Oppose**	LSN's reasons for opposing this submission point are set out under 'submission point' 31.10 above.	**Disallow** this whole submission point.
FS66.24	Ngunuguru Community Garden	264	264.10	**Oppose**	LSN's reasons for opposing this submission point are set out under 'submission point' 31.10 above.	**Disallow** this whole submission point.
FS66.25	S Sutherland	286	286.10	**Oppose**	LSN's reasons for opposing this submission point are set out under 'submission point' 31.10 above.	**Disallow** this whole submission point.
FS66.26	GE Free Northland	313	313.10	**Oppose**	LSN's reasons for opposing this submission point are set out under 'submission point' 31.10 above.	**Disallow** this whole submission point.
FS66.27	GE Free Northland	313	313.20	**Oppose**	LSN's reasons for opposing this submission point are set out under 'submission point' 31.10 above.	**Disallow** this whole submission point.
FS66.28	N Voot	327	327.10	**Oppose**	LSN's reasons for opposing this submission point are set out under 'submission point' 31.10 above.	**Disallow** this whole submission point.
FS66.29	Northland Regional Council	332	332.55	**Oppose**	LSN's reasons for opposing this submission point are set out under 'submission point' 31.10 above.	**Disallow** this whole submission point.
FS66.30	Te Runanga a Iwi o Ngapuhi	347	347.10	**Oppose**		**Disallow** this whole submission point.

Specific Issues Raised by Submitters

Many submitters made the same or similar requests and raised the same or similar issues. To avoid unnecessary duplication the table below has grouped the issues raised by submitters and provided a response, effectively responding to the two points set out in your draft table (originally attached to the preceding table) as follows:

- **"Reasons for supporting or opposing"**
- **"I seek that the whole (or part [describe part]) of the submission be allowed or disallowed) *Give precise details"***

These responses apply to each relevant submission. In addition, all of the general comments above apply to each of the specific submissions referred to below. The following tables should be read to include these general comments as they apply to each submission. Support or opposition to each submitter request is contained in the final table.

Issue Raised by Submitter(s)	LSN Response
Harm our clean green image	• This is not supported by cogent evidence. • Australia uses genetic modification in its agricultural systems yet its meat sells at a premium to New Zealand meat product. • Tasmania has declared itself GMO free yet its product (e.g. canola) does not command a premium over GM free product from mainland Australia. • Gene editing techniques have the potential to drive down our biological greenhouse gas emissions (e.g. AgResearch grass being trialled in the USA) and as a tool in our battle to save our birds (Predator Free 2050). Our clean green image would likely be harmed if we did not use these technologies should they be available and of benefit. • New Zealand's green future would benefit from planting more high value plants, many of which will be gene-edited • Economic effects, at both a local and national scale, must be considered by the EPA on a case-by-case basis. • The so-called 'Corngate' controversy where GM corn was discovered in the Hawke's Bay environment in 2002 had no impact on our sales of food products.
Lack of demand for GM products/Markets do not want GM products	• GM products are wanted by people when they perceive a benefit – for example cancer treatments such as Keytruda which have been the subject of protests demanding access in New Zealand. Insulin used by diabetics is also genetically modified. • The Impossible Burger, which is GMO food, sells at a premium over conventional meat.

Commented [NM5]: All points 'deleted' with 'Strikethrough' were made in Waikato submissions, so I've left them in here in the interim, even though I've struck them out.
I don't believe they're warranted in this submission because the original submitters haven't raised these points covered off to any significant degree at all.
I recommend they be deleted from this Submission.

Commented [WR6]: Why have you deleted this point?

Issue Raised by Submitter(s)	LSN Response
	• The "non-GM Project" commands less than 1% of the US food industry. • If there were no market for GM products (farmers or consumers) then these products would quickly disappear.
GM use in New Zealand could potentially bring an end to conventional agriculture	• This is not supported by the evidence. • Co-existence between organic, conventional and GM farming systems exists where GM technologies are allowed (e.g. USA which has thriving organic and GM agriculture) • Co-existence is best practice – an organic sector maximises its benefits from a point-of-difference only if the alternative is available • New Zealand imports GM free seed from the USA where over 90% of corn is genetically modified. If coexistence did not work this would not be possible.
Scientific uncertainty and precaution/ Insufficient research/Regulations not robust	• The EPA is responsible for considering scientific uncertainty. • The Royal Commission on Genetic Modification considered that "the basic regulatory framework is appropriate and that the key institutions, the [EPA] and the Australia New Zealand Food Authority (ANZFA), carry out their functions conscientiously and soundly. " • The EPA must also exercise a precautionary approach. (see Attachment B) • Decisions are more cautious where there is more uncertainty. • Zero risk and absolute certainty is an unrealistic requirement for any regulatory decision including decisions the WDC makes every day.
The risks are too great/health and environmental effects/there should be no risk	• Genetic modification has been used in agriculture and food production for more than two decades without any scientifically credible incident of harm attributable to the GM nature of its use. • The development and use of GM is assessed by the EPA on a case by case basis. • The EPA must take a precautionary approach to its decision making so if the "risks are too great" the EPA would not approve the development or use of that GMO. • Precision breeding using new GM techniques, such as gene editing, is more precise and more predictable than traditional breeding such as mutagenesis. • It is unrealistic to eliminate all risk even using conventional breeding.
Maori approach to GM/Adverse effects on	• The EPA considers effects and risks including cultural values.

Commented [NM5]: All points 'deleted' with 'Strikethrough' were made in Waikato submissions, so I've left them in here in the interim, even though I've struck them out.
I don't believe they're warranted in this submission because the original submitters haven't raised these points covered off to any significant degree at all.
I recommend they be deleted from this Submission.

Issue Raised by Submitter(s)	LSN Response
tangata whenua/cultural value	
Liability and bonds	• The Royal Commission on GM reported that "from a legal liability perspective we have not been persuaded there is anything so radically different in genetic modification as to require new or special remedies." • They also said that strict liability and bonds were a barrier to innovation and progress and could effectively prohibit an activity. • The EPA already have the power to impose bonds. • Strict liability already exists for GMO developers who breach their conditions. • Tort law still applies to GMOs/Gene Technologies enabling those who claim to be harmed can sue for damages.
Loss of markets and premiums/livelihood Reputational Damage	• These issues are considered by the EPA • Reputation is the result of many factors including our ability to address environmental issues such as water quality and climate change. Officials have advised the Government that our unnecessarily and overly strict regulations are an impediment to using genetic technologies to address these issues. (see Attachment A)
Cross contamination of crops Loss of organic/GE Free status	• It is an unrealistic demand to require zero risk of any cross pollination between sexually compatible crops. • Countries, markets and certifiers (e.g. organic and non-GMO certifiers) have a tolerance policy which allows coexistence. • Regimes to provide realistic and reasonable protection should be made on a case-by-case basis. This would be done by the EPA (under a conditional release), the industry or, if required, the council through the Biosecurity Act (pest management strategies as is the case for wild kiwifruit, wilding pines, feral goats, feral pigs and feral deer. • Seed purity is currently managed by the industry.
	•
	•
Irreversible Impacts of GMOs/eradication is impossible	• The same issues apply to new organisms. • Irreversibility must be considered by the EPA prior to any decision to use or release a GMO just as it is for the release of a new organism (e.g. Dung Beetle release). • GM Petunias have been sold in stores since 2014. MPI issued a recall in 2017. If irreversibility of GMOs were universal then GMO petunias would be still growing in the New Zealand/Waikato environment further voiding any claim to GM freedom. • In reality the ability to eradicate an unwanted GM (or new) organism will depend on the nature of the organism and the modifications made to it. Such consideration would be made by the EPA on a case by case basis before a decision would be made to release (or not release).

Commented [NM5]: All points 'deleted' with 'Strikethrough' were made in Waikato submissions, so I've left them in here in the interim, even though I've struck them out.
I don't believe they're warranted in this submission because the original submitters haven't raised these points covered off to any significant degree at all.
I recommend they be deleted from this Submission.

Commented [NM7]: Could stay in with some updating, Linda Grammer's submission briefly touches on Bonds/Strict Liability.

Commented [WR8R7]: What do you want to change?

Commented [NM9]: Should definitely stay in and needs to address the claim consistently made by submitters regarding "Northland, Naturally" branding as a primary point.

Issue Raised by Submitter(s)	LSN Response
Claims of benefits unsubstantiated	• This would be considered by the EPA • In countries where GM crops are available farmer uptake has been substantial (over 90% in many cases) suggesting that farmers see considerable benefit from using GM technology.
Provisions exist under the RMA to regulate GMOs/ GMOs are best managed through the RMA	• The legal jurisdiction of the RMA to control organisms which are GMOs is not in dispute. • The council is not obligated to put in place provisions related to GMOs. • Justification for putting in place rules (e.g. scientifically credible section 32 analysis) has not been provided and has not been tested in any other RMA process. • The EPA has the scientific and technical capability to assess the use of GMOs. • The EPA assesses the risks and benefits of GMO use on a case-by-case basis. • Conditional release allows the EPA to put in place requirements to manage any risk. • In the unlikely case that there are residual risks requiring management which have not been managed through the EPA hearing and decision making process the KDC would have the opportunity to put in place rules under the Biosecurity Act (Pest Management Strategy) or the RMA.

Prohibition	• The Royal Commission on Genetic Modification said we should proceed with caution while preserving our opportunities
	• "Strong precautionary" and "prohibitive" policies (a prohibitive approach) would:
	  ○ Reduce the opportunity to understand the environmental, social, cultural and economic opportunities for GM in New Zealand
	  ○ Reduce human capability as scientists move to other countries
	  ○ Means New Zealand would forego opportunities which may benefit the environment (e.g. mitigate wilding pines, reduce greenhouse gas emissions in agriculture, meet our ambition for predator free 2050) or animal welfare (e.g. hornless cattle).
	  ○ Erode the Waikato as a region in which science can flourish.

	•
New Zealand would lose its GM free status/	• New Zealand is not GM free now. • There have been five approvals for release of a GMO since the HSNO Act was enacted in 1996. Four human vaccines/therapeutics and one animal vaccine.

Commented [NM5]: All points 'deleted' with 'Strikethrough' were made in Waikato submissions, so I've left them in here in the interim, even though I've struck them out.
I don't believe they're warranted in this submission because the original submitters haven't raised these points covered off to any significant degree at all.
I recommend they be deleted from this Submission.

Issue Raised by Submitter(s)	LSN Response
New Zealand is GE Free in food production and/or the environment Waikato District is GM Free	○ The latest approval was the first release of a GMO into the New Zealand environment without controls (full release). • While there have been no GM crops or animals approved for release in New Zealand, GM is used/is legal in New Zealand's food production systems: ○ Genetically modified enzymes are used in cheese production ○ GM animal feed is imported and used in the meat, poultry and dairy industries.
	•

Commented [NM5]: All points 'deleted' with 'Strikethrough' were made in Waikato submissions, so I've left them in here in the interim, even though I've struck them out.
I don't believe they're warranted in this submission because the original submitters haven't raised these points covered off to any significant degree at all.
I recommend they be deleted from this Submission.

Attachment A

Ministerial Briefing

Gene Editing 2019

Life Sciences Network Inc

Further Submission

Proposed District Plan

Waikato District Council

15 July 2019

To Hon David Parker, Minister for the Environment			Tracking #: 2018-B-04195
Security Level	IN CONFIDENCE	Number of Attachments	0
Date Submitted:	07.06.2018	Response needed by:	06.07.2018
MfE Priority:	Non-Urgent	Action Sought:	Decision

Genetic Technology – Overview and Next Steps

Key Messages

1. This briefing provides a high-level overview of recent developments in genetic technologies occurring globally, how other jurisdictions are responding and why this matters for New Zealand. It is a platform for further advice to you as the Minister responsible for the regulation of genetic technologies under the Hazardous Substances and New Organisms Act 1996 (HSNO).
2. Our monitoring of developments shows that the rapid pace of technological change is testing regulatory definitions and has led to other countries beginning to clarify and/or review their regulatory position. The developments raise questions as to whether New Zealand's regulatory framework is still appropriate as HSNO is becoming outdated in light of developments. We believe a broad public conversation is required to ascertain New Zealanders' views on these developments. This input could led to future consultation on specific policy and/or regulatory changes to clarify New Zealand's position.

Development of new genetic technologies internationally

3. Recent and ongoing developments in genetic technologies are changing what is happening and what could be possible across a range of industries and sectors. The scale of change is already significant and technologies are still developing quickly. The technical advancements present new applications and methods for use in genetics that are accessible, easy to use, fast and have high success rates. It is becoming commonplace to use genetic technologies to make changes that are indistinguishable from natural genetic variation (changes that could occur naturally).
4. One key development is gene editing.[1] The distinguishing features of gene editing is the significantly increased precision of modification that can be made and the speed by which changes can occur, compared with earlier genetic modification (GM) tools. Gene editing can be used to make changes that:
   - are very small
   - leave no trace in an organisms genome
   - do not require the insertion of foreign DNA
   - could be indistinguishable from a naturally occurring organism
   - could be indistinguishable from changes made by a technique already exempt from regulation, or from naturally occurring mutations.

[1] Gene editing technologies use proteins, called enzymes, to cut a targeted area of DNA within the genome of a species. *Clustered Regularly Interspaced Short Palindromic Repeats* (CRISPR) is the most commonly mentioned gene editing approach.

5. These advances are challenging existing definitions of GM and what constitutes a genetically modified organism (GMO). Regulatory authorities globally are now considering questions about what is or should be regulated as a GMO. Currently, there is no clear international consensus on the best way to regulate the use of new genetic technologies, with countries taking a variety of different approaches.

6. There are jurisdictions choosing not to regulate some organisms made using new technologies (e.g. USA) and others that are reviewing how their regulatory frameworks apply in light of the developments (e.g. European Union). There are also countries doing both (e.g. Australia). Some countries have not made any changes and/or are unsure on what changes they will make. Despite the varying approaches, major players appear to be moving towards less regulation on some organisms created using new technologies. This is based on their country's own scientific risk assessment and regulatory framework concluding that these organisms do not pose added risks compared with organisms developed through conventional breeding.

New Zealand's regulation of GMOs

7. In New Zealand a GMO is defined as any organism containing or derived from genetic material that has been modified *in vitro*[2], this applies to plants, animals and microbes[3]. The HSNO (Organisms Not Genetically Modified) Regulations 1998 (Not-GM regulations) set out an exhaustive list of techniques that are captured by the GMO definition but are exempt from regulation. The list only contains techniques deemed safe and in use prior to 29 July 1998. Some of the technologies in this list have been used for more than 60 years and are generally considered to be conventional plant breeding techniques.

8. The Not-GM regulations were amended in 2016, in response to a 2014 court decision that adopted a strict interpretation of the regulations. This amendment clarified that no new mutagenesis technologies (such as gene editing) created after 1998 are captured by the Not-GM regulations. For new techniques to be added the Not-GM regulations would need to be reviewed and amended by Order in Council.

9. The strict interpretation of the regulations means organisms created using new technologies developed in recent years, e.g. gene editing, will be more highly regulated than organisms created using techniques listed in the Not-GM regulations or naturally occurring organisms, regardless of the level of risk they present.

10. Settings in the HSNO Act ensure New Zealand has a very robust assessment process and high threshold for the approval of GMOs (for research, field trials and commercial use). As a result there are no GMOs commercially available in New Zealand. We do allow food products with non-viable GMO ingredients into New Zealand (approximately 77 approvals currently) under the Food Standards Code, which is administered by Food Standards Australia New Zealand (FSANZ).

11. The HSNO Act has never had a full review and the legislation therefore has not evolved since 1998. The settings in the Act mean that transgenic technology[4] receives a high level of scrutiny. Organisms developed using new and more precise technologies receive the same level of scrutiny as earlier GM techniques as they are not listed in the Not-GM regulations. This may be an unnecessarily high threshold, particularly when new technologies are being used to create organisms that are not transgenic, are indistinguishable from organisms produced from a technique listed under the Not-GM regulations, and in some cases could occur through slower natural processes. This may

[2] *In vitro* means taking place in a test tube. This is in contrast to *in vivo* modification, which occurs inside an organism.

[3] The full statutory definition of a genetically modified organism is: "any organism in which any of the genes or other genetic material have been modified by *in vitro* techniques; or are inherited or otherwise derived, through any number of replications, from any genes or other genetic material which has been modified by *in vitro* techniques" (HSNO Act s2(1)).

[4] Transgenic organisms are those that have a gene or genetic material from a sexually incompatible species inserted to achieve a desirable trait. This was the common 1990s view of what GM entailed.

result in organisms being regulated at a level not proportionate to the risk they pose and New Zealand missing out on the benefits they could provide (such as medical treatments, crops, trees or forage with beneficial properties). Anecdotal evidence suggests the high level of regulation is discouraging potential applicants from submitting an application to the Environmental Protection Authority (EPA) for field trials in containment or a release of a GMO as the perception is they are unlikely to be successful or it will take too much time, effort and financial backing.

12. As genetic technologies continue to develop and international views and regulations evolve, the government may wish to consider how these could and/or should be used in New Zealand. Currently it is difficult to use the new technologies outside containment due to our stringent legislative regime. There will be a point when New Zealand should assess whether the policy settings in the HSNO Act are appropriate.

13. Maintaining our current position is becoming increasingly difficult for a variety of reasons:

    - Enforcement of the legislation has become difficult as products created using new technologies may arrive at our borders indistinguishable from products developed using unregulated techniques. There is not likely to be a mechanism to test how the product was created.
    - New Zealand developers test and sell products potentially beneficial to New Zealand overseas but their products cannot be used in New Zealand.
    - The definitional gap between what is considered GM under the Food Standards Code and the HSNO Act could widen, leading to different regulation of the same product.
    - New Zealand will not be able to receive the environmental benefits of some GMOs.
    - The high approval threshold could be a barrier to responding to major environmental concerns, such as kauri dieback, as New Zealand's research and reactive capacities may be suboptimal to develop/use tools to respond to threats and opportunities at a time when GM is becoming more widely used and the challenges it could help tackle are becoming more pressing.

New Zealand consideration of these issues

14. The broad application of the new technologies and the perception that New Zealand is 'GM-free' indicates that a national conversation will be helpful to find out New Zealanders views on new genetic technologies and their potential use. While such a conversation is likely to develop naturally in an ad hoc way, the complexity and wide reach of the new technologies suggests that it would be useful for government to take a lead on the most appropriate timing and scope of such a conversation. There are already some conversations occurring in New Zealand, e.g. the establishment of a gene editing panel by the Royal Society of New Zealand Te Apārangi to explore social, cultural, legal and economic implications of gene editing in New Zealand. There have also been some discussions on biotechnology and gene editing through iwi engagement, e.g. discussions on biotechnology occurring within the EPA's Te Herenga National Māori Network.

15. The current regulatory settings under HSNO are becoming quickly outdated, creating issues with the enforcement of the legislation. Regardless of whether New Zealand wishes to have a high threshold for the use of new genetic technologies or take a more permissive approach, we recommend updating the settings to clarify New Zealand's position. The Ministry for the Environment believes public input is required to decide on the approach New Zealand wishes to take before proposing any specific policy or regulatory changes. This approach (similar to that currently being undertaken in Australia) would allow for an open and transparent conversation without predetermining whether New Zealand should be using the technology or what regulation is appropriate for the technology. The outcome of such a conversation may then lead to specific policy and/or legislative changes with further public discussion.

16. We plan to investigate possible approaches to a future participatory public process to identify key issues and inform our policy analysis. There are several approaches to a public conversation; the specific method would be dependent on the purpose of such a conversation.

17. Some possible approaches are shown below and should not be considered an exhaustive list. The contentious nature of GM, complex issues involved, and the wide range of views on the topic mean that a public conversation will need to be carefully considered and the approach well planned to ensure it is effective and constructive. There is a risk that unless the conversation is done well the outcome could be worse than not having a conversation at all.

18. Possible options that government could explore include:

    - A high level conversation to gauge overall public views and identify key issues about the developments in genetic technologies and New Zealand's regulatory environment, without putting forward options for change. This approach is currently being used by the Australian Department of Health. Such a conversation could be done through e.g. another Royal Commission, the Prime Minister's Chief Science Advisor, the Productivity Commission, or the Ministry (supported by other departments).

    - Consultation on the primary legislation, through a general discussion document seeking feedback on the performance of the system, followed by proposing specific amendments. This approach was used in the development of the HSNO Act.

    - Consultation on the scope and risk settings of the Not-GM regulations through a discussion document and workshops, followed by a consultation document setting out specific proposals for amendment. This approach is being used by the Australian Office of the Gene Technology Regulator.

    - Structuring a public conversation around specific opportunities or challenges where GM organisms may provide a significant benefit e.g. health, environmental (kauri dieback, myrtle rust) or sterile pine trees.

19. The methods available for consultation have varying levels of formality. For example, a Royal Commission would be a more formal process whereas a Ministry or Prime Minister's Chief Science Advisor-led conversation would be able to use more interactive and flexible participatory processes to achieve great reach.

20. Policy thinking on the approach to a public conversation is still in its infancy. We will provide you with a briefing before the end of 2018 with an assessment of the feasible options and our recommendations going forward. We will include further analysis of both the risks of not having a conversation (such as potentially missed economic and environmental opportunities) and those that will arise in having a conversation (such as polarised public views, misinformation/lack of understanding on what the conversation is about). We will also consider who should lead such a conversation, such as whether government is best placed to lead, what other groups could possibly come on board, and exploring options for an external group to lead the conversation.

21. Our engagement to date has principally been with government agencies, Crown Research Institutes, and the Royal Society.

22. We recognise that we need to adequately acknowledge and integrate Mātauranga Māori and Māori perspectives. The Ministry has not yet engaged with Māori perspectives in relation to GMOs (although others have been engaged in this space). The Ministry for the Environment will work with existing contacts to build understanding on how to effectively understand perspectives in this area. We will undertake external engagement as required with appropriate stakeholders after we provide you with further advice in December.

23. We will be able to complete the necessary background work with current resource levels by the end of 2018.

24. Leaving a public conversation for too long (e.g. 2-3 years away) could mean that New Zealand risks missing opportunities, playing catch-up on the international stage, and facing increasing compliance issues from GMOs indistinguishable from conventionally developed organisms. It could also run the risk of having to narrow the conversation to specific legislative changes as a response to international positioning without gauging high level attitudes within New Zealand first.

25. There is also a risk that conversations will be informed by overseas models and practices, which may not be relevant to New Zealand, or by interest groups that do not have a good understanding of the science involved, which could result in misinformation and misunderstanding about what the new technologies are and can do.

Ministry for the Environment background work in 2018

26. We, with other agencies, will continue to monitor and analyse the following areas in 2018 to assist Ministers in developing New Zealand's response to international developments:

- analysis of the opportunities and challenges for New Zealand presented by:
  - developments in new genetic technologies and uses
  - international regulatory and policy responses to these developments
  - regulating rapidly-changing technology under our current framework
- monitoring of public views on the uses of genetic technologies in a range of applications (e.g. vaccines, pest control, plant breeding)
- exploration of possible approaches to a participatory public process to identify key issues and explore policy solutions.

27. We will provide you with updates during the year on any international developments.

28. We will also provide you with advice by the end of 2018 on options for a models of public engagement on new genetic technologies; including the benefits/ risks, trade-offs and cultural consideration of each option.

Recommendations

29. We recommend that you:

a. **Advise** if you would like to meet with Ministry for the Environment officials to discuss developments in genetic technologies and potential policy implications;

Yes/No

b. **Note** that the Ministry for the Environment, with other agencies, plans to continue its work over the next 6 months to:

- better understand the opportunities and challenges for New Zealand presented by:
    - developments in new genetic technologies and uses
    - international regulatory and policy responses to these developments
    - regulating rapidly-changing technology under our current framework
- monitor public views on the uses of genetic technologies in a range of applications (e.g. vaccines, pest control, plant breeding)
- explore possible approaches to a participatory public process to identify key issues and explore policy solutions.

c. **Note** that the Ministry for the Environment will provide updates on significant international developments in genetic technology during 2018.

d. **Note** that the Ministry for the Environment will provide you with a briefing on models of public engagement for undertaking a government-led conversation on new genetic technologies by the end of 2018.

e. **Refer** this briefing to other Ministers you consider appropriate. Refer to table two (page 16) for Ministers with a potential interest and/or responsibility in genetic technologies.

Yes/No

Signature

Glenn Wigley
Director Marine, Environmental Risk and Science **Date**

Hon David Parker
Minister for the Environment **Date**

Ministry for the Environment contacts

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Genetic Technology – Overview and Next Steps

Technology has moved beyond New Zealand's regulatory framework

1. Recent developments have meant that what is regulated as genetic modification is not clear-cut. Previously, 'transgenic' organisms were the focus of discussion and regulation.[5] The technology that is now available is capable of a range of processes and outcomes, which give increased precision and opportunities over what could previously be achieved and often do not result in a transgenic organism. These include:
   - speeding up a naturally-occurring process
   - producing organisms indistinguishable from those that occur naturally
   - mimicking what a technique exempt from regulations can do
   - turning genes 'on' or 'off' without adding any foreign DNA.
2. Technology that is now in use globally was not contemplated when the HSNO Act was passed in 1996 or during the Royal Commission on Genetic Modification in 2001. The current regime is inflexible and reflects a 1998 understanding of GM and the social priorities at the time. The Not-GM regulations exempt some techniques available in 1998 from being regulated as GM. The High Court has determined that this is an exhaustive list.[6] This means organisms created using new technologies developed in recent years will have to go through a full approval process, even if:
   - they pose a lower risk than naturally occurring organisms or organisms developed using techniques listed in the Not-GM regulations.
   - they are indistinguishable from naturally-occurring organisms or organisms developed using techniques listed in the Not-GM regulations..
3. Agencies consider that the original framework of the HSNO Act, and how it has been applied since the High Court decision, may be limiting New Zealand's ability to consider uptake of appropriate new technology and therefore preventing the benefits and advancements that new technologies could provide. It is also providing increasing challenges to agencies enforcing regulations when organisms defined as GM and conventionally bred organisms cannot be differentiated.

[5] Transgenic organisms are those that have a gene or genetic material from a sexually incompatible species inserted to achieve a desirable trait.

[6] *Sustainability Council v Environmental Protection Authority* [2014] NZHC 1067. This High Court case established that only techniques specifically listed in the HSNO (Organisms Not Genetically Modified) Regulations are, or can be made, exempt. Similar techniques or techniques that do the same thing are not exempt unless expressly stated in the regulations.

International Responses

4. The international context of genetic technology regulation is complex. There is no universal definition of GM or GMO.[7] There is no consensus on the best way to regulate genetic technologies, with countries taking a variety of approaches. How jurisdictions regulate is dependent on the level of flexibility and interpretation within their domestic legislation, the existing use of GM in their jurisdictions, and willingness to review their current policies.

5. Different regulatory schemes use different methods for determining what falls inside and outside the scope of regulation. A common approach is to use triggers; that is, to specify which factors will trigger or make the regulations apply. New Zealand, like many other countries, operates a process trigger, which means that any organism that has been developed using a particular genetic technology is subject to the regulatory requirements of the HSNO Act, regardless of the actual level of risk presented by the final product. In other countries regulation is based on the risk presented by the final product (a 'product trigger'), regardless of technique used. The USA uses a product trigger. Others, such as the EU and Canada, use a combination of both approaches.

6. Jurisdictions around the world are at varying stages of determining how to deal with new technologies. The questions policy makers and regulators around the world are now asking include:

    - whether organisms with genetic changes indistinguishable from naturally occurring organisms should be regulated (e.g., a flower genetically edited to be white, which is exactly the same as a white flower created through unregulated cross-breeding)
    - whether organisms produced by a technique with results indistinguishable from those produced by an already exempt technique should be regulated (e.g. using gene editing to get the exact same result as radiation treatment listed in the not-GM regulations)
    - whether regulatory frameworks generally triggered by process used to create the product rather than the product itself, are commensurate with risk.

7. There is a range of approaches emerging internationally. Countries appear to be leaning towards not regulating organisms as GMOs when:

    - they could have occurred naturally or produced by conventional plant breeding techniques;
    - do not contain any foreign DNA;
    - are null segregants.[8]

    We set out some country examples below

United States of America (USA)

[7] Countries, including New Zealand, that are party to the Cartagena Protocol on Biosafety have agreed on a definition of a 'living modified organism'. However, countries such as Australia, Canada and the United States are not party to the Protocol and do not use this definition. Some countries have incorporated the definition verbatim while others have alternative, but similar, wording in domestic legislation. In New Zealand the HSNO Act predates the Cartagena Protocol but still has similar wording and gives effect to the Protocol.

[8] Null segregants are organisms that used GM as an intermediate step in development but the final organism does not contain any foreign or intentionally altered DNA.

8. The USA is one of the leading countries in the uptake of genetic technologies. What happens in the USA has considerable influence on global responses.
9. The USA's Co-ordinated Framework for the Regulation of Biotechnology 1986 covers a range of legislation. At least one agency is involved in the approval process, depending on the classification given to an organism and its intended use.[9]
10. On 28 March 2018 the United States Department of Agriculture (USDA) clarified that there is no regulation for plants created using new technologies, provided that they:
    - could otherwise have been developed through traditional breeding techniques
    - are not plant pests (such as viruses or bacteria)
    - have not been developed using plant pests.
11. There are some crops that require risk assessment as they could not have occurred naturally or through traditional breeding techniques. Several of these crops have been given regulatory approval and are commercially available, including potatoes with reduced acrylamide[10] and apples that do not go brown.
12. It is likely that more products created using new technologies with altered traits will be commercialised, as there is a clear path to market for such products. The USDA announcement is likely to open the way for more products.
13. The USA uses new genetic technologies in other sectors such as health and pest control. Several clinical trials that use CRISPR gene-editing technology are underway (e.g., for editing of human T cells to target tumours) as well as studies to target mosquitoes that carry malaria.
14. There has also been the development of disease-resistant American chestnut trees with the intention of reintroducing them to areas from which they have disappeared[11]. This technology has been raised as having potential to help combat the presence of kauri dieback and myrtle rust in New Zealand.

European Union

15. The EU has a conservative approach to the environmental release of GMOs. Despite this there is a lot of research and design investment in Europe.
16. It is ambiguous how some applications of the new technologies (such as CRISPR) currently fall under the EU regulatory framework.
17. The European Court of Justice (ECJ) is actively considering how new genetic techniques should be regulated after an application from the French court requested a ruling. A decision is expected soon. In January 2018, an advisory legal opinion from the Advocate General to the ECJ concluded that new techniques should be considered GM, but should be exempt from regulation under EU law. This opinion is non-binding; however it carries considerable weight and will be looked at by the ECJ in its decision-making process.
18. If the Advocate General's opinion is adopted by the ECJ, the EU regulatory regime will have taken the opposite position to New Zealand. The EU regime would consider many

[9] The agencies that could be involved are the US Environmental Protection Authority, US Food and Drug Agency and the US Department of Agriculture.

[10] Acrylamide is a chemical that potatoes heated to high temperatures in the presence of certain sugars can express. One variety is already approved for food use in New Zealand and five more similar varieties will soon be allowed as FSANZ approved them on 7 December 2017. These are only available in processed potatoes such as frozen chips.

[11] https://www.acf.org/our-community/news/new-genetically-engineered-american-chestnut-will-help-restore-decimated-iconic-tree/.

new techniques exempt from regulation whereas in New Zealand the list of techniques exempt from regulation is limited to those listed in the Not-GM regulations.[12]

19. If the Advocate General's opinion is affirmed, EU foodstuffs and pharmaceuticals derived from organisms made with techniques that are exempt from regulation as GMOs in the EU could still be considered GM products in New Zealand (if they are also a viable organism e.g. it can reproduce) and subject to restrictions under the HSNO Act. They would also be subjected to approval processes (e.g. from FSANZ for food products or Medsafe for pharmaceuticals). Enforceability will be difficult as it may not be possible to detect what technique was used to make a product. It will also make labelling requirements under the Food Standards Code difficult. These difficulties will be common with any countries that do not regulate products from new technologies as GMOs. The Ministry will undertake further analysis of the impact on New Zealand when a final ECJ decision is released and we will provide you with a briefing. There are no immediate effects as a result of the Advocate General's opinion.

Australia

20. Australia is actively reviewing its policy and regulatory frameworks, with three reviews being undertaken by the Department of Health, the Office of the Gene Technology Regulator, and Food Standards Australia New Zealand.

The Department of Health (DoH)

21. The Australia Gene Technology Scheme was introduced in 2001 and has been reviewed twice since its commencement (2006, 2011). The current third review of the scheme is again focused on the ongoing achievement of the policy objectives, but it is doing this with a future-focused lens, taking into account the rapidly developing and innovative area of gene technology.

22. The current review includes a discussion on whether to change the process-based system to, for example, a product-based approach with tiered levels of risk.

23. After three rounds of consultation, the DoH has produced a preliminary for comment. The report has 33 findings that include a recognition that the scheme has not kept up to date with technological advances. The DoH expects to present recommendations to all state governments later this year. We will brief you on their findings at this point.

The Office of the Gene Technology Regulator (OGTR)

24. The OGTR performs technical reviews (separate to reviews of the overall Gene Technology Scheme). It is currently undertaking a technical review of the Gene Technology Regulations to provide clarity about whether organisms developed using a range of new technologies are subject to regulation as GMOs, and to ensure that new technologies are regulated commensurate with the risk they pose. The technical review is intended to provide an interim solution while broader policy considerations associated with new technologies are being progressed through the overall policy review of the scheme.

25. An exposure draft with proposed amendments was made publically available for comment from November 2017 to February 2018. The OGTR is now considering the issues raised in submissions and finalising the draft amendments. The Regulator will then propose the amendments to the Commonwealth, State and Territory governments for agreement.

26. The OGTR's current proposal, if accepted, will mean that null segregants and some forms of gene editing techniques, generally referred to as Site Directed Nucleases-1

[12] As established in *Sustainability Council v Environmental Protection Authority* [2014] NZHC 1067.

(SDN-1)[13] are not regulated as GM (both of these types of organisms are regulated as GM in New Zealand). SDN-1 techniques do not introduce DNA from another species and make changes that are within the bounds of normal genetic variation. They can speed up the process and produce fewer unintended effects. The decision on null segregants will put into regulation what is already occurring in practice.

Food Standards Australia New Zealand (FSANZ)

27. FSANZ is consulting with the Australian and New Zealand public to consider whether, and how, food derived from new technologies should be captured for pre-market approval, and whether the definitions for 'food produced using gene technology' and 'gene technology' should be changed to improve clarity about which foods require pre-market approval.

28. FSANZ's discussion document considers a range of options from treating new techniques like conventional breeding techniques ('given a green light once a technique has been proved safe') or like current GMOs (which would mean that each application requires a rigorous safety assessment).

29. The review will not directly result in changes to the Food Standards Code (which governs food safety in both Australia and New Zealand). After completing the review FSANZ will decide whether to prepare a proposal to amend the Code, which would involve further public consultation. There is no timeframe for preparing a proposal, although it is unlikely to be this year.

30. If FSANZ decides that amendments to the Code are necessary, this might result in a situation where the HSNO Act and the Food Code are not consistent. For example, a food import could potentially be given market approval for New Zealand through FSANZ, but under the HSNO Act it would still be considered a GMO and could not be imported or produced in New Zealand without going through a rigorous assessment process.

31. The Ministry for Primary Industries (MPI) has made a submission to this review, with input from the Ministry for the Environment. MPI considers foods that are identical to those developed through conventional breeding or could occur naturally should be exempt from requiring a pre-market assessment and approval as a GM food. The submission also acknowledges the potential definitional inconsistencies between the Food Standards Code and the HSNO Act, and implications of such gaps.

Interest for New Zealand

Opportunities

32. New Zealand has an opportunity to position itself on current GM technologies before new products start reaching our shores. This includes consideration of the workability of the regulatory system, such as enforcement, and whether the high thresholds in the Act create a disincentive for New Zealand-specific solutions. For example, AgResearch is currently under taking field trials on a drought-tolerant ryegrass in the USA – it chose not to apply for approval to test this in New Zealand.

33. There are possible opportunities for new technologies in a number of sectors, as set out in an illustrative list in Table 1 below. These opportunities have the potential to assist in areas that have been indicated as current Government priorities (e.g. climate change mitigation/adaptation and predator control/conservation).

[13] SDN-1techniques involve the use of gene editing that does not use a template to repair the cut that has been made in DNA. The cut is repaired by natural repair mechanisms that join the two 'cut' ends back together without using a template (guide DNA sequence). No foreign or additional DNA is added to the organism.

34. While there are indications of the potential new technologies may have for predator control (such as the use of gene drives), these uses are still a long way off. They would require significant development before their possible use should be considered. There is still uncertainty as to whether such methods would be successful or should be used and significant background research that would be required before testing could even occur. For that reason we do not believe the use of genetic technologies for predator control should be the instigator for a public conversation on genetic technologies.

Table 1: Examples of potential uses of new genetic technologies beneficial for New Zealand

Environment	Forestry	Industrial
• Climate mitigation such as stock with reduced methane emissions and drought-tolerant pasture species • Animal and plant pest control • Use of genetic tools to breed kauri and pohutukawas resistant to diseases (e.g. such as kauri dieback and myrtle rust) • Potential treatment of diseases for horticultural crops	• Improved growth and disease tolerance • Modified traits such as sterility to reduce risk of wilding pine spread • Improved wood density and quality	• Microbes and other organisms used in the production of biofuels and other products • Microbes used for environmental mitigation (e.g. to degrade harmful/wasteful plastic) • Enhanced ability of plants and/or bacteria to bind heavy metals
Food	**Farming Forage**	**Health**
• Improved traits such as non-browning apples, milk free from allergenic protein, 'tearless' onions • Improved nutritional benefits such as low-acrylamide potatoes • Entirely new food production platforms such as synthe ic or plant based alternatives to meat and dairy	• Higher-yielding crops • Grass with more efficient use of nitrogen and phosphorus, which will reduce fertiliser needs and result in less run-off	• Medical treatments that target disease-causing genes • Medical treatments that modify and reintroduce a patient's cells • Vaccines using modified viruses • Pharmaceuticals – producing drugs using GM microbes or animals

Challenges

35. It w ll become increasingly difficult to enforce current regulations as some organisms developed using new technologies are indistinguishable, both visually and by DNA esting, from non-GM organisms or organisms produced using an exempt technique. Attempting to regulate one but not the other will be virtually impossible in practice and will result in disproportionate regulation where the risks from an organism produced in either way are the same.

36. New Zealand-based companies may decide to go offshore to avoid New Zealand's rigorous controls. This could result in New Zealand missing out on the benefits from products designed for the New Zealand environment.

New Zealand's regulatory framework

37. The Ministry for the Environment's current focus is to keep abreast of developments in genetic technologies internationally and monitor how other jurisdictions respond. This will aid us to understand the broader environment in which New Zealand's regulatory framework operates. Our policy work this year will consider the impact of regulation in other countries on New Zealand's system, and the benefits and risks of our system.

New Zealand's GM legislation is over 20 years old

38. GM is regulated under the HSNO Act, which has been in place for 22 years. The HSNO Act emphasises precaution in the regulation of organisms that meet the definition of a GMO as specified in the Act and do not have an exemption under the Not-GM regulations. Over this time genetic science has also advanced substantially and has challenged existing regulatory frameworks.

39. The Act has never been fully reviewed, though some amendments to the Act were made following the Royal Commission in 2001.

Definitions under HSNO do not align controls to risk

40. Legislation can be based on technique (process) or product (outcome). The HSNO Act sets regulatory requirements and provides a risk-assessment framework based on the technique used to create an organism. Technique is not correlated with risk, so the framework can result in organisms being regulated disproportionately to the risk they actually pose. For example, gene editing can be used to more swiftly produce an organism that could have occurred naturally or produced through traditional plant breeding – yet the gene edited organism would be highly regulated whilst the naturally-occurring one or the one from traditional plant breeding would have no regulation at all. As the use of new technology becomes more widespread this issue will become more prevalent.

Approval process

41. The use of any new organism requires approval under the HSNO Act from the EPA. If an application for the contained use, development or release of a new organism is submitted, the EPA undertakes a risk/benefit assessment of the new organism under the provisions of the HSNO Act on a case-by-case basis.

42. The HSNO Act sets out a specific methodology for the assessment and decision-making process, including considering effects on native species, biodiversity, and natural habitats. If any of the Act's minimum standards cannot be met, or cannot be *shown* to be met, then the EPA must decline the application.

43. This risk assessment framework sets a very high threshold for the release of a new organism, including GMOs. People can apply for a GMO field trial (in containment) or a full release; however the high threshold for either of these approval options appears to discourage would-be applicants. Anecdotal feedback from stakeholders and EPA is that the high thresholds make it essentially impossible to obtain a release approval for virtually any GMO in pastoral and horticultural species, and that there is no clear path to market, which discourages commercial development.

44. The system has ensured that 1998-era transgenic technology has been given a high level of scrutiny, while other techniques that mimic natural processes and techniques that were well understood at the time were exempted in the Not-GM Regulations. As the legislation has not evolved, new technologies receive the same level of scrutiny as older transgenic techniques when this may be an unnecessarily high threshold.

How we got to where we are

45. In 2001–2002 a Royal Commission investigated a way forward for GM in New Zealand. The Royal Commission's recommendation was to "proceed with caution". It did not advocate for a complete ban on GM technology, however the interpretation of the Commission's recommendation has contributed to the current cautious approach. This coupled with the perception that something will not get approved, has led to a very conservative operation of the Act's settings.

46. To date only three GMOs have been approved for conditional release in New Zealand:

    - *Proteqflu*, an equine influenza vaccine
    - *Pexa-Vec*, used in a clinical trial for patients with liver cancer
    - *Telomelysin,* used in a clinical trial for patients with advanced and inoperable melanoma.

47. No GM organisms are commercially available and no application for a full environmental release has ever been received by the EPA. Some GMOs are approved for research in containment. New Zealand maintains a certain level of capability with genetic technologies. The majority of MBIE-funded research is in genomics or uses GM technologies as part of a research project that is not primarily about GMOs. There is currently relatively little research into developing GM products or GMOs for eventual commercial application. Research in this space appears to be exploratory rather than close-to-market.

International obligations

48. The Cartagena Protocol on Biosafety (the Protocol) to the Convention on Biological Diversity (CBD) aims to ensure the safe handling, transport and use of living modified organisms (LMOs) between countries. The Protocol has been in force since 2003.

49. New Zealand is one of 171 parties to the Protocol and has implemented its obligations under the HSNO Act and other legislation and regulations. New Zealand actively contributes to Parties' discussions about improving risk assessment and risk management practices.

50. For several years, the CBD has been considering developments in genetic technologies and impacts on biodiversity. Its November Conference of the Parties (COP) will again discuss this topic. The Ministry of Foreign Affairs and Trade will lead advice to Ministers to prepare for the November COP.

Public conversations occurring now

51. The Royal Society Te Apārangi has convened a multidisciplinary panel on gene editing to discuss the potential use of gene editing in different sectors. The Royal Society has said that the aim of the Panel is not to come to a view on the merits or otherwise of these technologies, but to inform the inevitable and necessary societal debate.

52. In December 2017 the Panel released two technical papers and two general discussion documents on the current and potential uses of gene editing in pest control and healthcare. It is developing further papers on gene editing in agriculture, legislation and regulation, and Māori perspectives, for release in 2018. These papers follow on from resources produced last year to explain gene editing technology.[14] The Society is holding a number of stakeholder forums this year to discuss their findings. Last year the Society also hosted a series of panel discussions hosted by Kim Hill.

[14] royalsociety.org.nz/gene-editing-technologies

53. We are supportive of the Royal Society's efforts in raising awareness and encouraging discussion of genetic technology.

The Ministry for the Environment is preparing to respond to international developments

54. We want to be prepared for New Zealand to respond to international developments. We are continuing to do background analysis on the policy settings of the HSNO Act to be in a good position to advise you about the policy and regulatory issues arising from international developments in genetic technologies.

55. We are monitoring:

    a. developments in new genetic technologies

    b. international regulatory and policy responses to these developments

    c. potential impacts on New Zealand of these international developments.

56. This information will help us to assess:

    a. the enforceability of our regulatory regime when products developing using a new technology arrive at our border

    b. opportunities and impacts for New Zealand if we were to choose to use (or not) new technologies

    c. whether the HSNO Act is fit for purpose to regulate the developments.

57. This work is a desk-based exercise. At this stage we are seeking input from other agencies, including the Departmental Science Advisors (DSA) network. We are also tapping into existing conversations and analysis, including the Royal Society's panels.

58. The contentious nature of GM and the wide range of views on the topic mean that any decisions about the policy settings and regulatory framework should include public input. However, a public conversation needs to be carefully considered and planned to ensure it is effective and constructive. The Ministry for the Environment believes this should involve an open and transparent process, entered into without preconceived ideas about whether New Zealand should be using the technology or any potential policy and/or legislative changes. We will provide you with advice by the end of 2018 on possible approaches to seeking input from stakeholders and the public in future policy work.

Consultation and Collaboration

59. The Ministry for the Environment has consulted with the Ministries of Business, Innovation and Employment, Foreign Affairs and Trade and Health, the Ministry for Primary Industries, the Department of Conservation, the Environmental Protection Authority and the Treasury in the drafting of this briefing.

60. The Ministry for the Environment has convened a cross agency group of the above agencies that meets every few months to keep in contact about the latest developments, and to contribute to the Ministry's work programme.

61. We have provided the table (Table 2) below as a guide to the broad range of portfolios with either an interest and/or responsibility in addressing GM issues in New Zealand.

Table 2: An overview of portfolios (and relevant Minister) with an interest or responsibility relating to genetic modification in New Zealand

Portfolio (and relevant Minister)	Interest/Responsibility
Agriculture (Minister O'Connor)	Opportunities to: • Use GM forage with improved food value, decreased nutrient requirements, and resistance to drought • Speed up the breeding of new fruit tree varieties
Biosecurity (Minister O'Connor)	Opportunities to: • Develop fruit trees resistant to pests and diseases • Possible solutions to control pests and diseases Responsible for: • Enforcing compliance of use of GM organisms approved by the EPA • Enforcing requirements relating to imports of GMOs • Enforcing containment requirements of laboratories holding new organisms, including GMOs
Food Safety (Minister O'Connor)	Responsible for: • Oversight of New Zealand's involvement with Food Standards Australia New Zealand • FSANZ approving GM food products • Labelling of GM foods
Forestry (Minister Jones)	Opportunities to: • Use sterile plantation trees which do not cause wilding problems • Use trees with GM developed resistance to pests and diseases
Foreign Affairs (Minister Peters)	Responsible for: • New Zealand's obligations under the Convention for Biological Diversity and its Cartagena Protocol on Biosafety (governs the movement of living modified organisms between countries)
Research, Science and Innovation (Minister Woods)	Responsible for: • New Zealand's science and research investment
Local Government (Minister Mahuta)	Responsible for: • Local government GM decision making under the Resource Management Act
Climate Change (Minister Shaw)	Opportunities to: • Use GM technology for climate mitigation such as stock with reduced methane emissions and drought-tolerant pasture species
Conservation (Minister Sage)	Opportunities for:

	• Possible solutions for pest control
Associate Minister for the Environment (Minister Sage)	Responsible for: • Oversight of the EPA who is responsible for making decisions on new organism applications
Health (Minister Clark)	Responsible for: • GM medical medicines and therapies Opportunities for: • GM medical treatments that target disease-causing genes • Medical treatments that modify and reintroduce a patient's cells • Vaccines using modified viruses • Pharmaceutical drugs using GM microbes or animals

Next Steps

62. We recommend that you meet with Ministry for the Environment officials to discuss the developments in genetic technology and its potential risk and benefits for New Zealand.

63. We will brief you on developments as they arise. We will provide you with a briefing on international developments as they occur and a briefing in November about further steps towards a participatory process for a possible public conversation.

Attachment B

Anderson Lloyd Letter

To

Federated Farmers

GMO - precautionary approach liability and bonds

Life Sciences Network Inc

Further Submission

Proposed District Plan

Waikato District Council

15 July 2019

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12 October 2018

Federated Farmers of New Zealand
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Dear Gavin

Genetically Modified Organisms – precautionary approach, bonds and liability

Introduction

1 Federated Farmers has further submitted on Northland Regional Council's (**Council**) Proposed Regional Plan (**PRP**) opposing primary submissions that seek the inclusion of provisions relating to genetically modified organism (**GMO**) in the PRP.

2 In support of Federated Farmers' case against GMO provisions being introduced in the PRP, you have asked us to identify existing mechanisms for liability as a result of a GMO activity. There are a wider range of existing statutory and legal avenues in existing that manage GMOs. This letter addresses:

(a) an explanation of the precautionary approach in the Hazardous Substances and New Organisms Act 1996 (**HSNO**) and how this is applied;

(b) the ability to require bonds under HSNO;

(c) liability provisions in HSNO;

(d) liability provisions in the Resource Management Act 1991 (**RMA**);

(e) liability provisions in the Biosecurity Act 1993; and

(f) other liability mechanisms under common law.

Precautionary approach

3 Section 7 of HSNO provides for a precautionary approach:

> All persons exercising functions, powers, and duties under this Act including, but not limited to, functions, powers, and duties under sections 28A, 29, 32, 38, 45, and 48, shall take into account the need for caution in managing adverse effects where there is scientific and technical uncertainty about those effects.

4 In *Bleakley v Environmental Risk Management Authority*[1] the High Court considered several points of appeal alleging failure to apply the s 7 requirement for caution. The Court accepted that

[1] *Bleakley v Environmental Risk Management Authority* [2001] 3 NZLR 213.

the s 7 direction is to take into account the need for caution in managing adverse effects. It also noted that this obligation arises only where there is scientific and technical uncertainty as to those effects, not where there is for example ethical or social uncertainty.[2] The Court's approach to the application of s 7 does not contemplate that this is optional.

5 In considering the meaning of section 7, the Court found it "should be construed in its own language and in light of s 4 purposes, one of which is declared to be "preventing or managing the adverse effects of… new organisms"".[3] McGechan J went on to state[4]:

> …I construe s 7 reference to "managing adverse effects" as including managing by reduction of risk such effects will ever arise. "Management" of effects goes to risk reduction as well as damage control. I do not see the inclusion of both concepts of management and prevention within s 4 purposes as intended to produce sharp differentiation. That would not be in accordance with the overall policy of the Act, which aims generally at effective protection.

6 McGechan J also concluded that, in the context of a containment application, s 7 requires caution in management of effects if they occur, a matter which goes beyond mere caution over the risk of occurrence.[5]

Bonds

7 Approval from the Environment Protection Authority (**EPA**) must be obtained under HSNO to import, develop, field test or release any new organism.[6] Approval can be granted for full release or conditional release.[7] Conditional release allows the EPA to approve release with conditions or controls. The EPA has a wide discretion to set controls on conditional release approvals,[8] as well as for field test approvals.[9]

8 Section 38D(1) identifies a range of controls that the Authority may impose on a conditional release approval, while subsection (2) confirms that subsection (1) does not limit the type of controls the Authority may impose on a conditional release approval.

9 Controls are defined in HSNO as:

> any obligations or restrictions imposed on any hazardous substance or new organism, or on any person in relation to any hazardous substance or new organism, by this or any other Act or any regulations, rules, EPA notices, codes, or other instruments or documents made in accordance with the provisions of this or any other Act for the purposes of controlling the adverse effects of that substance or organism on people or the environment

10 The EPA has previsouly considered bonds as a type of control. Application Decision ERMA200479, which relates to conducting field trials on *Pinus radiata*, records that the Committee took account of the containment regime, likelihood of a self-sustaining population and

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[2] At paragraph [153].

[3] At paragraph [154].

[4] At paragraph [157].

[5] At paragraph [164].

[6] Section 25, HSNO.

[7] Section 27, HSNO.

[8] Section 38C, HSNO.

[9] Section 45, HSNO.

the existing laibility provision, before deciding not to impose a control requiring that a bond be provided by the approval holder. The decision therefore contemplates that a bond was an available control in appropriate circumstances.

HSNO liability

11 Section 109 of HSNO identify a range of breaches of HSNO which constitue offences, including developing, field testing, importing or releasing a new organism in contravention of the Act, or failing to comply with controls or regulations imposed. Where a person is convicted, HSNO prescribes maximum penalties for imprisonment or fines.

12 Part 7A of HSNO provides for pecuniary penalties and civil liability on breach of the Act.

13 Pecuniary penalty orders may be made in favour of the Crown where the Court is satisfied that the person acted in breach of the Act in possessing, disposing of, developing, field testing, importing or releasing a new organism, or failing to comply with controls imposed in an approval or specified in regulations. Maximum penalties are prescribed. The Court must not make the order if the person satisfies the Court that the person did not know, and could not have reasonably known, of the breach.[10] The Court may, instead of or in addition to a pecuniary order, order the person to mitigate or remedy any adverse effect on people or the environment, or make an order to pay the costs of mitigating or remedying adverse effects.[11]

14 A person is civilly liable whether or not the person intended the act, omission or breach, or the person was taking reasonable care when the act, omission or breach occurred. Limited defences are provided, and relate to necessity, reasonableness, steps taken to mitigate or remedy the effects of the breach after it occurred, or the breach being due to an event beyond the control of the defendant (for example, natural disaster).

RMA liability

15 Section 314 of the RMA provides for enforcement orders, which are civil proceedings where a party applies for an order to the Environment Court. The scope of enforcement orders is wide. The Court of Appeal has noted that:[12]

> s 314 with its reference to 'adverse effects on the environment' encompasses [an] intrinsically very wide … horizon of damage.

16 Enforcement orders may require a person to cease an activity that has already begun, or prohibit a person from commencing an activity. Enforcement orders are not limited to activities that are directly in breach of a RMA provision, a plan, or consent[13], but can also be made where a person is carrying out an activity that is, or is likely to be, "noxious, dangerous, offensive or objectionable to such an extent that it has or is likely to have an adverse effect on the environment".[14] Accordingly, GMOs may be captured by the latter.

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[10] Section 124B, HSNO.

[11] Section 124D, HSNO.

[12] *Canterbury Regional Council v Newman* [2002] 1 NZLR 289.

[13] Section 314(1)(a)(i), RMA

[14] Section 314(1)(a)(ii), RMA.

17 The test for what is "offensive" or "objectionable" involves the Court undertaking a four-step inquiry:[15]

(a) Whether the assertion of the person seeking an enforcement order is honestly made; and

(b) If so, whether in the opinion of the Court, it is or is likely to be noxious, dangerous, offensive or objectionable; and

(c) If so, whether it is of such extent that it is likely to have an adverse effect on the environment;[16] and

(d) Whether in all the circumstances the Court's discretion should be exercised and an enforcement order made.

18 While the scope of section 314 is broad, there are some limited strict liability offences under section 341 of the RMA.[17] Of most relevance to GMOs, is the strict liability offence of discharging contaminants into the environment under section 15. GMOs may be considered a "contaminant", which is defined as:

> ***contaminant*** includes any substance (including gases, odorous compounds, liquids, solids, and micro-organisms) or energy (excluding noise) or heat, that either by itself or in combination with the same, similar, or other substances, energy, or heat—
>
> (a) when discharged into water, changes or is likely to change the physical, chemical, or biological condition of water; or
>
> (b) when discharged onto or into land or into air, changes or is likely to change the physical, chemical, or biological condition of the land or air onto or into which it is discharged

19 Whether a GMO is a contaminant is likely to be case dependent.

20 Under the RMA, there are only two defences to strict liability available.[18] The first is a "due diligence" offence, where the action was necessary for the purpose of saving or protecting life or health or preventing serious damage to property or avoiding an actual or likely adverse effect on the environment. The second is an "act of god" defence, where the event was beyond the control of the defendant, including natural disaster, mechanical failure, or sabotage.

Biosecurity Act Liability

21 Part 5 of the Biosecurity Act 1993 provides that a Minister of the Crown or regional council to make certain pest management plans. These include national and regional pest management plans and national and regional pathway management plans. In most circumstances, where pest management plans are inconsistent with other rules or regulations the management plan will prevail.

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[15] *Watercare Services Ltd v Minhinnick* [1998] 1 NZLR 294 (CA)

[16] The environment referred to in step (c) is a complex entity which includes people and the social, economic, aesthetic, and cultural conditions which affect people.

[17] Section 341(1) , RMA "In any prosecution for an offence of contravening or permitting a contravention of any of sections 9, 11, 12, 13, 14, and 15, it is not necessary to prove that the defendant intended to commit the offence".

[18] Section 341(2), RMA.

22 Under the Biosecurity Act, any breach of a pest management plan may result in enforcement action. Section 154 allows an authorised person to make a compliance order against a person for an breach of a pest management plan. Additional offences under the BA may also apply, and these include section 154H which allows the Director-General to apply to the High Court for a pecuniary penalty order, strict liability offences under sections 154M and 154N, and non-strict liability offences under sections 154NA and 154O.

Common law liability

23 The remedies available at common law will depend on the particular facts in question. Possible causes of action include nuisance, negligence and the rule in *Rylands v Fletcher*[19]. These potential causes of action were addressed in a background paper by Professor Todd[20] for the Royal Commission on Genetic Modification, summarised in the Royal Commission's Report[21], and are further summarised below.

Negligence

24 A claimant may bring a negligence action for damage to property or for economic loss caused by genetic modification techniques or products. The claimant must show that there was a foreseeable risk of damage, that the defendant was negligent (assessed against a standard of care reasonably and objectively to be expected of persons holding themselves out as possessing the relevant skill and experience), and that on the balance of probabilities the negligence caused the harm.

Nuisance

25 A claimant may bring a nuisance action where a neighbour has used land it is in possession and control to carry out an activity and that causes damage or interferes with the enjoyment of the claimant's land. Liability depends on whether the interference is reasonable or unreasonable. Interference becomes unreasonable and actionable where it exceeds what an ordinary neighbour could reasonably be expected to tolerate.

Rylands v Fletcher

26 The Report of the Royal Commission on Genetic Modification summarised the rule in *Rylands v Fletcher* as follows (footnotes omitted):

> 37. This rule has been regarded as an extension of the law of nuisance to cases of an isolated event. The rule applies to the "escape" from the defendant's land of something likely to cause damage. Liability applies even if the defendant was not at fault or took all reasonable precautions to prevent the escape; the defendant must be in possession or control of the land from which the "harm" came and be making a "non-natural" use of the land; and the possibility of escape and the consequent harm must have been foreseeable, although the manner or immediate cause of the escape need not have been foreseeable. The effect of the rule is to impose a higher standard of responsibility for activities with inherent risks. Since, however, such activities generally have utility for the community, they should not be subjected to the kind of disincentive a rule of absolute liability would impose.

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[19] (1868) LR 3 HL 330 (HL).

[20] Professor Stephen Todd. *Liability issues involved, or likely to be involved now or in the future, in relation to the use, in New Zealand, of genetically modified organisms or products.* 27 April 2001.

[21] Report of the Royal Commission on Genetic Modification, July 2001.

> 38. Courts have applied the forms of action discussed above (nuisance, and *Rylands v Fletcher*) to many different factual situations. Those having some analogy to present subject matter include damage caused by water, weeds, and sprays. If faced with a novel situation, such as a claim by a farmer for damage to a crop caused by contamination from a neighbour's genetically modified canola, the courts would deal with the issues by drawing on principles established by earlier cases.

Application to GMOs

27 At present there are no judicial decisions in New Zealand which have dealt with harm caused by new organisms or GMOs. The common law regime will apply, but whether a tort is established will depend on the facts of the case. In considering whether specific statutory liabilities should be established to address harm resulting from the release of a genetically modified organism, the Royal Commission concluded[22]:

> As technology advanced with ever-increasing pace throughout the 20th century, the common law (that is, law based on court decisions, as distinct from statute law) showed it was well able to mould new remedies for novel situations. Parliamentary intervention has rarely been needed in this area. From a legal liability perspective we have not been persuaded there is anything so radically different in genetic modification as to required new or special remedies.

Yours faithfully
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[22] Chapter 12, paragraph 80, at page 328.

https://www.isaaa.org/resources/publications/briefs/55/executivesummary/default.asp, accessed Monday 15th December 2025

ISAAA Brief 55-2019: Executive Summary

Biotech Crops Drive Socio-Economic Development and Sustainable Environment in the New Frontier

Introduction

Safeguarding food security and nutrition is critical in order for countries to overcome problems of hunger and malnutrition. The United Nations estimates that the interplay of current various challenges of high population rate, political instability, degradation of natural resources, forced migration (from farms to urban communities), and the ongoing COVID 19 pandemic will make a significant impact on food security that could raise the hunger and malnutrition problems globally. Actions to be undertaken should be bolder and stronger in terms of multisectoral collaboration involving agriculture, food, health, water and sanitation, accompanied by policy domains on social protection, development planning, and economic policy.

Socio-economic benefits of biotech crops have been documented in the last 23 years (1996-2018) showing that biotech crops have contributed to:

- increasing productivity that contributes to global food, feed, and fiber security;
- supporting self-sufficiency on a nation's arable land;
- conserving biodiversity, precluding deforestation and protecting biodiversity sanctuaries;
- mitigating the challenges associated with climate change; and
- improving economic, health, and social benefits.

These economic benefits, health improvement, and social gains obtained through biotech crop adoption must be made known to the global community so that farmers and consumers can make informed choices on what crops to grow and consume, respectively; to the policymakers and regulators to craft enabling biosafety guidelines for commercialization and adoption of biotech crops; and to the science communicators and the media to facilitate correct and effective dissemination of the benefits and potentials of the technology.

The International Service for the Acquisition of Agri-biotech Applications strongly espouses the scientific truths behind them with the publication of ISAAA review of biotech/GM crop commercialization, Brief 55. This publication documents the latest information on the subject, the global database on the adoption and distribution of biotech crops since the first year of commercialization in 1996, country situations, and future prospects of the technology. Termed as the ISAAA Briefs, the annual reports from 1997 to 2015 were authored by Dr. Clive James, and the 1996 report was co-authored with Dr. Anatole Krattiger.

ISAAA dedicates this Brief to Dr. Clive James, Founder and Emeritus Chair of ISAAA, who has painstakingly authored the 20 Annual Reports making it the most credible source of information on biotech crops in the last two decades. We also dedicate this Brief to the late Dr. Randy A. Hautea, former Global Coordinator and *SEAsia*Center Director for more than two decades. They

have been great advocates of biotechnology and biotech products and believe that ISAAA can make a difference in enhancing the knowledge and capacities of the global community in order to benefit from the technology, especially the poor and marginalized people of the world.

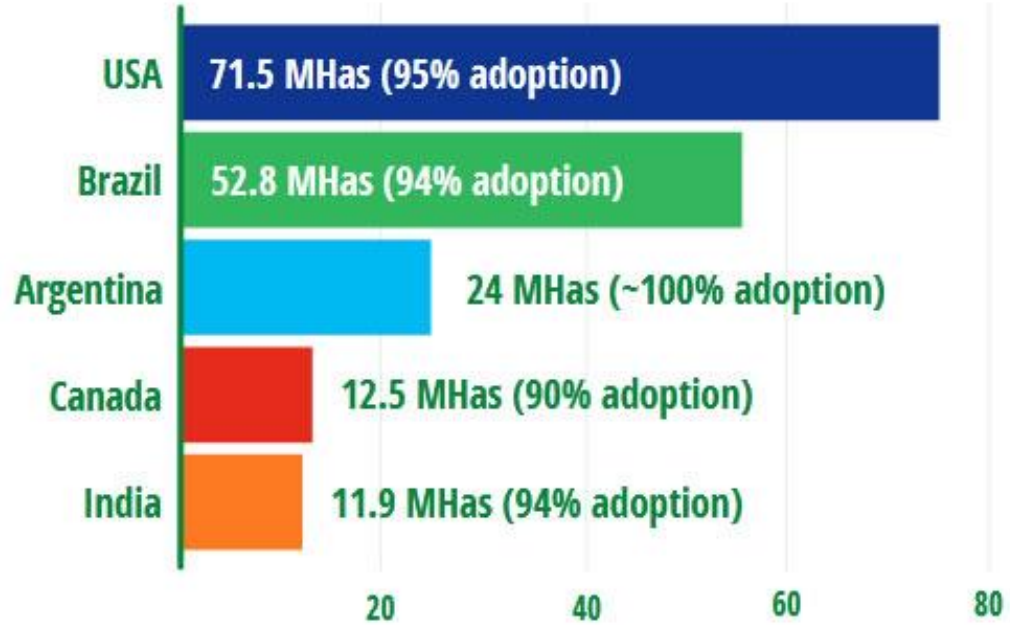
HIGHLIGHTS OF THE 2019 ADOPTION OF BIOTECH CROPS

- **Adoption of biotech crops declined slightly in 2019 at 190.4 million hectares worldwide.**

In the 24th year of commercialization of biotech/GM crops in 2019, 29 countries grew 190.4 million hectares of biotech crops – a slight decline of 1.3 million hectares (3.2 million acres) or 0.7% from 191.7 million hectares in 2018.

- **The adoption rates of the top five biotech crop-growing countries reached close to saturation.**

The average biotech crop adoption rate in the top five biotech crop-growing countries increased anew in 2019 to reach close to saturation, with the USA at 95% (average for soybeans, maize, and canola adoption), Brazil (94%), Argentina (~100%), Canada (90%), and India (94%). Expansion of biotech crop areas in these countries would be through immediate approval and commercialization of new biotech crops and traits for increased production of nutritious food, mitigate problems related to climate change accompanied with the emergence of new pests and diseases.



TOP 5 COUNTRIES THAT PLANTED BIOTECH CROPS IN 2019 (AREA AND ADOPTION RATE)

Source: ISAAA, 2019

- **Biotech crops increased ~112-fold from 1996, with an accumulated biotech area of 2.7 billion hectares making biotechnology the fastest adopted crop technology in the world.**

The global area of biotech crops has increased ~112-fold from 1.7 million hectares in 1996 to 190.4 million hectares in 2019 – this makes biotech crops the fastest adopted crop technology in recent times. An accumulated 2.7 billion hectares or 6.7 billion acres were achieved in 24 years (1996-2019) of biotech crop commercialization

- **A total of 72 countries adopted biotech crops – 29 countries planted and 43 additional countries imported.**

The 190.4 million hectares of biotech crops were grown by 29 countries – 24 developing and 5 industrial countries. Developing countries grew 56% of the global biotech crop area compared to 44% for industrial countries. An additional 42 countries (16 plus 26 EU countries) imported biotech crops for food, feed, and processing. Thus, a total of 72 countries have adopted biotech crops.

- **Biotech soybeans covered 48% of the global biotech crop area.**

The most adopted biotech crops by the 29 countries were soybeans, maize, cotton, and canola. Soybean was the leading biotech crop with 91.9 million hectares that occupied 48% of the global biotech crop area, with a 4% reduction from 2018. This is followed by maize (60.9 million hectares), cotton (25.7 million hectares), and canola (10.1 million hectares). Based on the global crop area for individual crops, 79% of cotton, 74% of soybeans, 31% of maize, and 27% of canola were biotech crops in 2019.

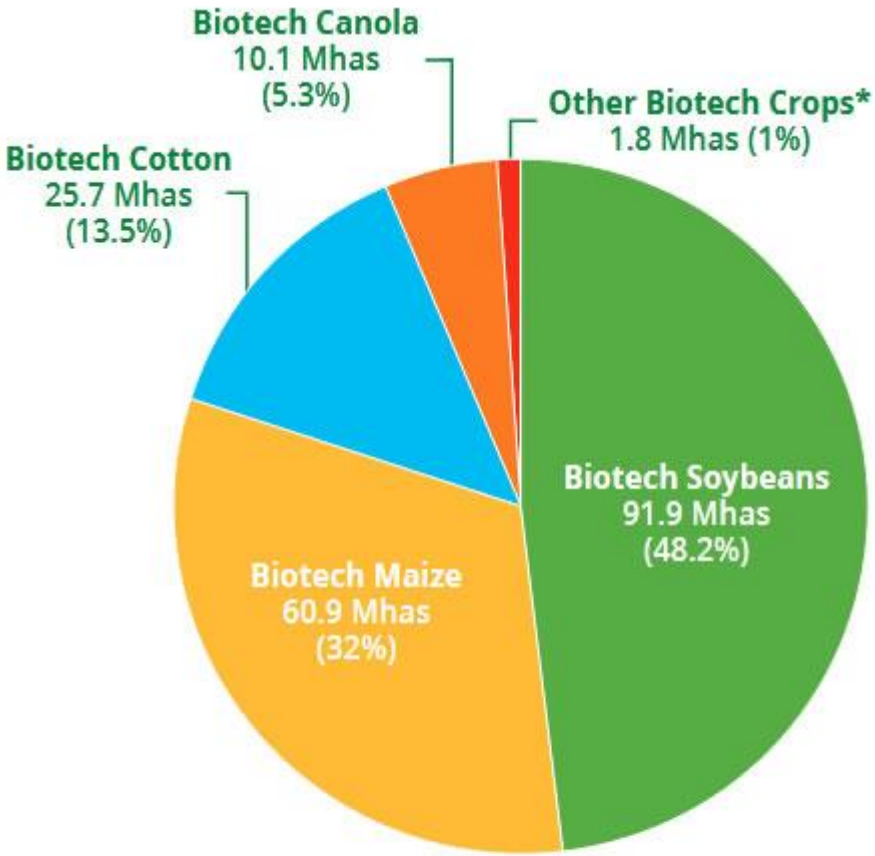
- **Biotech crops provided more diverse offerings to consumers in 2019.**

Biotech crops have expanded beyond the big four (maize, soybeans, cotton, and canola) to give more choices for many of the world's consumers and food producers. These biotech crops include alfalfa (1.3 million hectares), sugar beets (473,000 hectares), sugarcane (20,000 hectares), papaya (12,000 hectares), safflower (3,500 hectares), potatoes (2,265 hectares), eggplant (1,931 hectares), and less than 1,000 hectares of squash, apples, and pineapple. Additionally, biotech crop researches conducted by public sector institutions involve rice, banana, potato, wheat, chickpea, pigeon pea, and mustard with various economically-important and nutritional quality traits beneficial to food producers and consumers in developing countries.

- **Stacked IR/HT traits increased by 6%, occupied 45% of the global biotech crop area, and surpassed the area planted to herbicide tolerant traits.**

Stacked traits with insect resistance and herbicide tolerance increased by 6% equivalent to 85.1 million hectares and covered 45% of the global area, proof of farmers' preference for smart farming with no-till and reduced insecticide use. Herbicide tolerance in soybeans, canola, maize, alfalfa, and cotton, has consistently been the dominant trait till 2018. In 2019, the area planted to herbicide tolerant crops was reduced to 81.5 million hectares or 43%. Some 12% of the global area was planted to insect tolerant traits. New traits approved for 2019 for import and/or cultivation include: the stacked IR/HT/HT cotton with glyphosate and isofluxatole, IR/pyramided HT (glyphosate, glufosinate, dicamba, 2,4-D) and intermediates in maize, IR pyramided (for coleopteran, hemipteran, and lepidopteran)/HT (glyphosate, glufosinate) and intermediates in maize, salt tolerant and herbicide tolerant soybean, and insect

resistant sugarcane, all in Brazil; Argentine canola with HT and modified oils and low gossypol cotton in the USA.



** Biotech sugar beets, potatoes, apples, squash, papaya, and brinjal/ eggplant.*

BIOTECH CROPS IN 2019 (AREA AND ADOPTION RATE)

Source: ISAAA, 2019

- **The top five countries (USA, Brazil, Argentina, Canada, and India) planted 91% of the global biotech crop area of 190.4 million hectares.**

The USA led the biotech crop planting in 2019 at 71.5 million hectares, followed by Brazil (52.8 million hectares), Argentina (24 million hectares), Canada (12.5 million hectares), and India (11.9 million hectares) (Table 1) for a total of 172.7 million hectares, representing 91% of the global area. Thus, biotechnology benefited more than 1.95 billion people in the 5 countries or 26% of the current world population of 7.6 billion.

Table 1. Global Area of Biotech Crops in 2019: by Country (Million Hectares)**

Rank	Country	Area (million hectares)	Biotech Crops
1	***USA****	**71.5**	Maize, soybeans, cotton, alfalfa, canola, sugar beets, potatoes, papaya, squash, apples
2	**Brazil***	**52.8**	Soybeans, maize, cotton, sugarcane
3	**Argentina***	**24.0**	Soybean, maize, cotton, alfalfa
4	***Canada****	**12.5**	Canola, soybeans, maize sugar beets, alfalfa, potatoes
5	**India***	**11.9**	Cotton
6	**Paraguay***	**4.1**	Soybeans, maize, cotton
7	**China***	**3.2**	Cotton, papaya
8	**South Africa***	**2.7**	Maize, soybeans, cotton
9	**Pakistan***	**2.5**	Cotton
10	**Bolivia***	**1.4**	Soybeans,
11	**Uruguay***	**1.2**	Soybeans, maize
12	**Philippines***	**0.9**	Maize
13	***Australia****	**0.6**	Cotton, canola, safflower
14	**Myanmar***	**0.3**	Cotton
15	**Sudan***	**0.2**	Cotton
16	**Mexico***	**0.2**	Cotton
17	***Spain****	**0.1**	Maize
18	**Colombia***	**0.1**	Maize, cotton
19	**Vietnam***	**0.1**	Maize
20	**Honduras**	**<0.1**	Maize
21	**Chile**	**<0.1**	Maize, canola
22	**Malawi**	**<0.1**	Cotton

23	***Portugal***	**<0.1**	Maize
24	**Indonesia**	**<0.1**	Sugarcane
25	**Bangladesh**	**<0.1**	Brinjal/Eggplant
26	**Nigeria**	**<0.1**	Cotton
27	**Eswatini**	**<0.1**	Cotton
28	**Ethiopia**	**<0.1**	Cotton
29	**Costa Rica**	**<0.1**	Cotton, pineapple
	Total	190.4	

*19 biotech mega-countries growing 50,000 hectares, or more, of biotech crops

**Rounded-off to the nearest hundred thousand.

Figure 1. Global Map of Biotech Crop Countries and Mega Countries in 2019

The US reached an average 95% adoption rate for planting biotech soybeans, maize, and cotton

In 2019, the biotech area in the USA was 71.5 million hectares, covering 38% of the global biotech area, with an average adoption rate of 94% for principal crops, similar to 2018. Biotech crops planted were soybeans (30.43 million hectares, a 3.6 million hectare reduction from 2018), maize (33.17 million hectares), cotton (5.31 million hectares), canola (800,000 hectares), sugar beets (454,100 hectares), alfalfa (1.28 million hectares), potatoes (1,780 hectares), some 1,000 hectares each of papaya and squash, and 265 hectares apples.

New approvals for biotech crops and traits in the US include USDA commercialization approval for Argentina's HB4 drought tolerant soybeans, following approvals in Argentina in 2018 and Brazil in 2019. Biotech cotton with low gossypol content event TAM66274 received a non-regulated status from USDA APHIS and an FDA approval in 2019, for commercialization and use for human food and animal feed within the USA. Another variety of apple, Arctic®Gala with non-browning trait was approved for commercialization. The non-browning trait has also been successfully introduced to GreenVenusTM Romaine lettuce by Intrexon.

Brazil expanded biotech crop area to reach 52.8 million hectares

Brazil maintains its standing as the second country, after the USA, with the largest biotech crop area planted in 2019. The 52.8 million hectares of biotech crops include 35.1 million hectares soybeans (surpassing the US biotech soybean area for the first time), 16.3 million hectares maize, 1.4 million hectares cotton, and some 18,000 hectares insect resistant sugarcane. The 52.8 million hectares was an increase of ~1.6 million hectares or 3% in 2019, at an adoption rate of 94% (1% higher than 2018). Brazil has systematized the process for GM authorization. The procedures were modernized and increased the deadline for decisions by CNTBio. This will allow applicants to submit any additional information on new data to ensure that application complies with the new conditions.

Argentina maintains 100% adoption rate of biotech crops

Argentina ranked third in the top ten countries planting biotech crops in 2019. A minimal increase of 110,000 hectares of biotech crops were planted in Argentina in 2019 at 23.9 (24) million hectares, compared to 23.8 million hectares in 2018 which is 13% of the global total of 190.4 million hectares. The biotech crop area consisted of 17.5 million hectares soybeans, 5.9 million hectares maize, 485,000 hectares cotton, and more than 1,000 hectares of biotech alfalfa (planted for the first time in Argentina), at an average adoption rate of close to 100%. The Argentinian government through the Argentine National Advisory Committee on Agricultural Biotechnology (CONABIA) approved nine biotech applications in 2019: six maize events, two cotton events, and one soybean event. A wheat event containing the HB4 gene that confers drought resistance received full technical approval but awaits commercial approval by the National Direction of Agricultural Food Markets (DNMA) under the Ministry of Agro-Industry.

Canada had a 23% increase in biotech sugar beets area

Biotech crop area in Canada declined slightly in 2019 by ~2% from 12.75 million hectares in 2018 to 12.46 million hectares due to reduction in planted areas of total and biotech soybeans. The decrease in soybean area was due to the unstable weather conditions during the planting season. Areas planted to biotech maize, canola, and alfalfa had marginal increases, while sugar beets reached its highest increase of 23%. Innate® potato was planted in only 40 hectares in 2019. The average adoption rate of 90% in 2019 was a decrease of 2% from 2018. New and upcoming biotech crops and events in Canada include: (a) Roundup Ready tolerant Truflex™ canola launched on 404,000 hectares; and (b) approval of two varieties of high oleic acid soybeans. Biotech Golden Rice with provitamin A Event GR2E was given approval by Health Canada in 2019. This decision coincides with the approval from Food Standards Australia New Zealand (FSANZ) in 2017. The Canadian Food Inspection Agency (CFIA) and Health Canada (HC) approved the use for feedstock of one Bayer CropScience cotton product.

India hit 94% adoption rate of IR (Bt) cotton

The IR (Bt) cotton adoption rate in India has almost stabilized in the past five years at more or less 95%. The 94% adoption rate in 2019 by more than 6 million farmers who planted 11.9 million hectares of biotech cotton reflects the continuing confidence of the farmers and the benefits they obtain from the technology. Thus, they are in need of other biotech crops that will provide them profit and help improve their living status. This caused some farmer groups to plant unauthorized stacked trait IR(Bt)/HT cotton in major cotton growing areas in Central and Southern zones in Kharif 2017 and numerous protests to push for the approval of the stacked trait cotton event. In addition, the widening spread of fall armyworm infestations prompted the government to strategize on its control, which can be solved by pyramided insect resistant crops.

- **Ten countries in Latin America grew 83.9 million hectares of biotech crops.**

Ten countries in Latin America planted biotech crops in 2019 including Brazil (52.8 million hectares), Argentina (24 million hectares,), Paraguay (4.1 million hectares), Bolivia (1.4 million hectares), Uruguay (1.2 million hectares), Mexico (223,000 hectares), Colombia (101,188 hectares), Chile (41,093 hectares), Honduras (37,386), and Costa Rica (297 hectares) for a total of 83.9 million hectares, covering 44% of the 190.4 million hectare global biotech areas. The increases in biotech crop area in most of the Latin American countries compensated for the losses from the extensive drought incidence of 2017 and 2018. In addition, enabling regulations; profitability, high prices, and high market demand in the local and international market; availability of new seed technologies for maize, soybeans, and cotton; subsidized credit for farmers and foreign investments from the industry; favorable weather; and improved agronomic practices with efficient fertilizer applications encouraged the farmers in Brazil, Argentina, Paraguay, Mexico, Colombia, and Honduras to plant biotech crops. In Bolivia, the increase in biotech soybean area was due to favorable conditions in 2019, after two years of extreme drought. Moreover, the Bolivian government gave its support to soybean producers by granting the approval to cultivate two new genetically engineered soybean events to boost their biofuel production. In the future, the adoption of drought tolerant soybeans will be useful to overcome the drought incidences in the Latin American countries.

- **Nine countries in Asia and the Pacific grew 19.5 million hectares of biotech crops**

Biotech countries in the Asia and Pacific region were led by India with the largest area of biotech crops at 11.9 million hectares cotton, followed by China (3.2 million hectares cotton and papaya), Pakistan (2.5 million hectares cotton), Philippines (875,000 hectares biotech maize), Australia (614,446 hectares cotton, canola, and safflower), Myanmar (300,000 hectares cotton), Vietnam (92,000 hectares maize), Indonesia (2,000 hectares drought tolerant sugarcane), and Bangladesh (1,931 hectares eggplant). This region planted 19.5 million hectares in 2019, which indicates a 2% increase from 19.1 million hectares in 2018. This area also covered 10.2% of the 190.4 million hectares global biotech crops. The favorable global cotton price has positively impacted biotech cotton adoption in India and China, while public acceptance of clean and hazard free production of biotech eggplant motivated more farmers in Bangladesh. In Vietnam, the high price of imported maize and increasing fall army worm incidence increased the biotech maize area. The planting of drought tolerant sugarcane in Indonesia is only limited to government-owned farms, thus limiting its potential to contribute to the country's sugar industry. Australia's extended extreme drought during the growing season in 2019 affected canola and cotton (biotech and total) area. Australia's cotton planted area was the smallest on

record, but the adoption rate of biotech canola went up due to better weed control and higher profit. There was a minimal decrease in Bt cotton area planted in Myanmar. New biotech cotton varieties and the approval of the new Biosafety Framework could increase the area planted in the future.

- **Africa had a 100% increase in biotech crop planting-countries.**

The African continent remains the region with the biggest potential to reap from the benefits associated with modern agricultural biotechnology. There has been increased awareness and appreciation of GM crops among African farmers in 2019. Thus, the African continent doubled the number of countries planting biotech crops from three in 2018 to six in 2019. The countries in descending order of biotech crop area were South Africa (2.7 million hectares for maize, soybeans, and cotton), IR/Bt cotton in Sudan (236,200 hectares), Malawi (6,000 hectares), Nigeria (700 hectares), Eswatini (401 hectares), and Ethiopia (311 hectares) for a total of 2.9 million hectares, 1.54% of the global biotech crop area of 190.4 million hectares. The approval of Nigeria's Bt cowpea resistant to pod borers was a major milestone in 2019. Moreover, Kenya approved the commercialization of biotech cotton in 2019 for cultivation in 2020. Other African countries continued to transition from confined field trials to the environmental release phase: Mozambique for drought tolerant maize and Kenya for Bt maize and cassava brown streak disease resistant cassava. The countries that improved their biosafety regulation to facilitate biotech crop development and adoption are Ghana and Niger. A number of countries also endorsed the trade of biotech crops and vouched for their food safety including Zambia.

- **Two countries in the European Union continued to plant biotech maize at 111,883 hectares**

The acceptance of biotech crops for cultivation in the EU has not improved in the last 24 years. Two countries planted biotech maize, because of the infestation brought by the European corn borer. Since 2016, only Spain and Portugal planted biotech Bt maize. In 2019, 107,130 hectares and 4,753 hectares were planted by Spain and Portugal, respectively, for a total of 111,883 hectares, 7.5% less than the biotech maize area of 120,980 hectares in 2018. There was less motivation to plant biotech maize since the market calls for non-biotech raw materials. Imports of feedstocks from Argentina, Brazil, and the United States were mostly biotech. There were imports of more than 30 million metric tons (MT) of soybeans and soybean products (90-95% biotech), 10 to 20 million MT of maize products (20 to 25% biotech), and 2.5 to 5 million MT of rapeseed products (close to 25% biotech) per year, mainly for feed. This situation is expected to continue as there is no change in the EU regulation, there is no approval for cultivation in sight, and movement against biotech crops is still strong. At the beginning of 2018, six biotech crops were authorized for entry into the EU for food and feed uses including four soybean events, one oilseed rape, and one renewal for maize. Before the end of 2019, two new varieties of maize and renewal of three existing authorizations for maize and sugar beets were approved for food and feed uses.

STATUS OF APPROVED EVENTS FOR BIOTECH CROPS USED IN FOOD, FEED, PROCESSING, AND CULTIVATION

A total of 72 countries (29 planting and 43 non-planting + EU 26, counted as one) have issued regulatory approvals for genetically modified or biotech crops for consumption either as human food, animal feed, as well as for commercial cultivation. Since 1992, there have been 4,485

approvals granted by regulatory authorities to 403 biotech events from 29 biotech crops, excluding carnation, rose, and petunia.

Of these approvals, 2,115 were for food, either for direct use or for processing, 1,514 were for feed use, for direct use or processing, while 856 were for environmental release or cultivation. The USA had the highest number of GM events approved (single traits only) followed by Japan (not including intermediate events from approved stacked and pyramided events), Canada, Brazil, and South Korea in the top five.

Maize still has the most number of approved events (146 events in 35 countries), followed by cotton (66 events in 27 countries), potato (49 events in 13 countries), soybeans (38 events in 31 countries), and canola (38 events in 15 countries).

The top ten events with the highest number of approvals in different countries include: herbicide tolerant maize event NK603 (61 approvals in 28 countries + EU 28 as one) still has the highest number of approvals. It is followed by herbicide tolerant soybean GTS 40-3-2 (57 approvals in 28 countries + EU 28 as one), insect resistant maize MON810 (55 approvals in 27 countries + EU 28), herbicide tolerant and insect resistant maize TC1507 (55 approvals in 27 countries + EU 28), herbicide tolerant and insect resistant maize Bt11 (54 approvals in 26 countries + EU 28), insect resistant maize MON89034 (51 approvals in 25 countries + EU 28), herbicide tolerant maize GA21 (50 approvals in 24 countries + EU 28), herbicide and insect resistant maize MON88017 (45 approvals in 24 countries + EU 28), herbicide tolerant soybean A2704-12 (45 approvals in 25 countries + EU 28).

Table 2. top ten Countries which Granted Food, Feed and Cultivation/Environment Approvals*

Rank	**Country**	**Food**	**Feed**	**Cultivation**	**Total**
1	United States	183	178	178	539
2	Japan*	186	177	130	493
3	Canada	147	138	144	429
4	Brazil	111	111	106	328
5	South Korea	157	148	0	305
6	Philippines	116	114	14	244
7	Mexico	188	29	14	231
8	Argentina	77	69	75	221
9	European Union	100	101	4	205
10	Australia	118	18	39	175
	Others	732	431	152	1315

	TOTAL	2115	1514	856	4485

*For Japan, data is collected from Japan Biosafety Clearing House (JBCH, English and Japanese) as well as the website of the Ministry of Health, Labor and Welfare (MHLW). However, intermediate events derived from an approved pyramided event recorded in JBCH are not included in our database if they do not appear in MHLW. Also, expired approvals are included in our database from 1992 while JBCH's records starts in 2004.
**USA only approves individual events.
***While cultivation approvals are granted in Japan, there are no current GM planting done.

Contribution of biotech crops to food security, sustainability, and climate change solutions

Biotech crops are being adopted globally because of the enormous benefits to the environment, health of humans and animals, and contributions to the improvement of socio-economic conditions of farmers and the general public. Global economic gains contributed by biotech crops in the last 23 years (1996-2018) have amounted to US$224.9 billion economic benefits to more than 16 to 17 million farmers, 95% of whom come from developing countries.

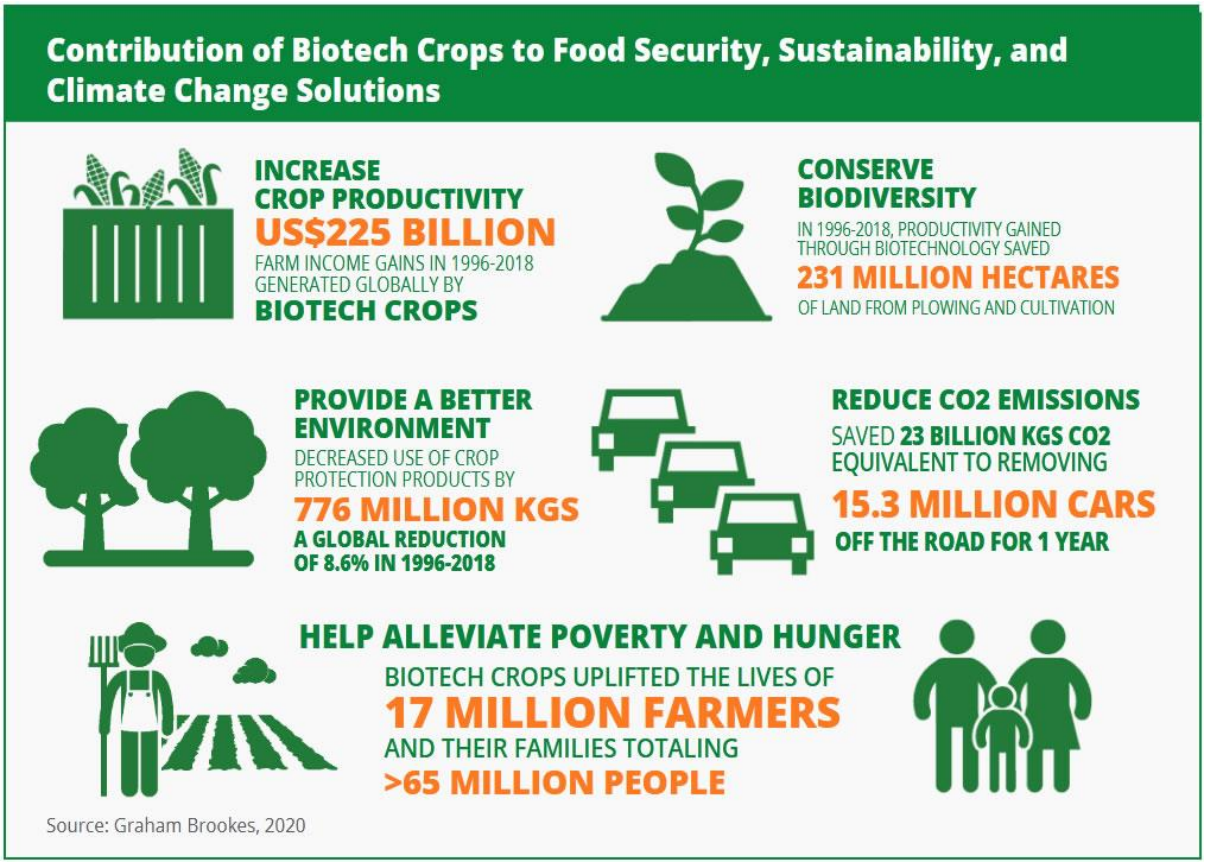
Biotech crops contributed to food security, sustainability, and climate change solutions by:
- **increasing crop productivity** by 822 million tons valued at US$224.9 billion in 1996-2018; and 86.9 million tons valued at US$18.9 billion in 2018 alone;
- **conserving biodiversity** in 1996 to 2018 by saving 231 million hectares of land and 24.3 million hectares of land in 2018 alone;
- **providing a safer environment**
  – by saving on 776 million kg. a.i. of pesticides in 1996-2018 and by 51.7 million kg in 2018 alone from being released into the environment;
  – by saving on pesticide use by 8.3% in 1996-2018, and by 8.6% in 2018 alone;
  – by reducing EIQ (Environmental Impact Quotient) by 18.3 % in 1996-2018, and by 19% in 2018 alone.
- **reducing CO2 emissions** in 2018 by 23 billion kg, equivalent to taking 15.3 million cars off the road for one year; and
- **helping alleviate poverty through uplifting the economic situation** of 16-17 million small farmers, and their families totaling >65 million people, who are some of the poorest people in the world (Brookes and Barfoot, 2020).

Thus, biotech crops can contribute to a "sustainable intensification" strategy favored by many science academies worldwide, which allows productivity and production to be increased on the current 1.5 billion hectares only of global cropland, thereby saving forests and biodiversity. Biotech crops are essential but are not a panacea, and adherence to good farming practices such as rotations and resistance management, are a must for biotech crops as they are for conventional crops.

Economic gains from biotech crops reached US$225 billion from 1996 to 2018

A total of US$224.9 billion economic benefits was gained by countries planting biotech crops from 1996 to 2018. The highest gain was obtained by the USA (US$95.9 billion), Argentina (US$28.1 billion), Brazil (US$26.6 billion), India (US$24.3billion), China (US$23.2 billion), Canada (US$9.7 billion), and others (US$23.2 billion) for a total of US$224.9 billion. For 2018

alone, six countries gained the most economically from biotech crops, they were the USA (US$ 7.8 billion), Brazil, (US$3.8 billion), Argentina (US$2.4 billion), India (US$1.5 billion), China (US$1.5 billion), Canada (US$ 0.9 billion), and others (US$1 billion) for a total of US$18.9 billion (Brookes and Barfoot, 2020).



CONCLUSION

The Global Food Insecurity Report of 2019 revealed that the targets of the United Nations (UN) Millennium Development Goals (MDG) that ended in 2015 were not achieved, and that more than 820 million people in the world were still hungry in 2018 which makes it difficult to achieve the Zero Hunger target by 2030. The State of Food Security and Nutrition in the World 2019 also showed that the decline in hunger the world had enjoyed for over a decade was at an end, and that hunger is again on the rise. The global level of the prevalence of undernourishment has stabilized; unfortunately, the absolute number of undernourished people continues to slowly rise.

Regional details show that in almost all African subregions, the highest prevalence of undernourishment is close to 20%, This is followed by Asia especially the Western Asian region which shows a continuous increase since 2010 of more than 12% of its population. Hunger is also slowly rising in Latin America and the Caribbean at close to 7%. It is discouraging to note that over 2 billion people do not have regular access to safe, nutritious, and sufficient food, including 8% of the population in Northern America and Europe. The economic slowdowns and downturns have greatly impacted the likelihood of severe food insecurity and undernutrition, and this effect is 20% higher for low-income countries. Moreover, climate change is heavily affecting food production globally. Overall, year-to-year changes in climate factors during the

growing season of maize, rice, soybeans, and spring wheat could account for 20%-49% of yield fluctuations.

Thus, in the 24th year of biotech crop commercialization (cultivation and import for food, feed, and processing), the 190.4 million hectares could contribute to the alleviation of these problems. The accumulated biotech crop area from 1996 to 2019 of 2.7 billion hectares (6.7 million acres) continues to provide food, feed, and shelter to the 7.7 billion global population. Moreover, there were accumulated (1996-2018) economic benefits of US$229.4 billion to 18 million farmers and their families, 95% of whom are small farmers. New biotech crops and traits were made available for consumers to sustain ample and nutritious food and for farmers with agronomic traits to mitigate climate change related-biotic and abiotic agricultural problems.

Public acceptance and enabling policies in the government are key for agricultural, socio-economic, and environmental benefits of biotech crops to reach the poor and the hungry. More importantly, a regional regulatory harmonization that facilitate data transportability would expedite biosafety decision-making. Ensuring that these benefits will continue now and in the future depends also on the diligence and forward-looking regulatory steps based on science, critically looking at the benefits instead of risks, agricultural productivity with a sense of environmental conservation and sustainability, and most importantly taking into consideration the millions of hungry and impoverished populace in need of resources.

To purchase an electronic copy of full Brief 55, send an e-mail to publications@isaaa.org. You can also request for a sample report.

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Attachment D

Genetically Engineered Crops – Experiences and Prospects

Download from

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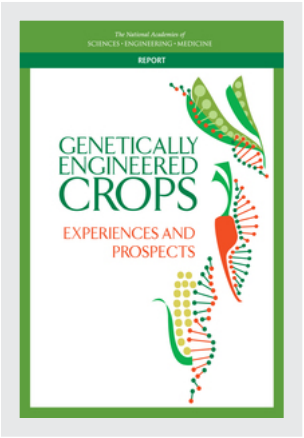
Life Sciences Network Inc

Further Submission

Proposed District Plan

Waikato District Council

15 July 2019



Genetically Engineered Crops: Experiences and Prospects

DETAILS

606 pages | 6 x 9 | PAPERBACK
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CONTRIBUTORS

Committee on Genetically Engineered Crops: Past Experience and Future Prospects; Board on Agriculture and Natural Resources; Division on Earth and Life Studies; National Academies of Sciences, Engineering, and Medicine

GENETICALLY ENGINEERED CROPS

EXPERIENCES AND PROSPECTS

Committee on Genetically Engineered Crops:
Past Experience and Future Prospects

Board on Agriculture and Natural Resources

Division on Earth and Life Studies

The National Academies of
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Attachment E

Scientific and Technical Institutions which Support the Safety of GM Crops

Life Sciences Network Inc

Further Submission

Proposed District Plan

Waikato District Council

15 July 2019

Attachment E

Scientific and Technical Institutions which Support the Safety of Genetically Modified Crops

Africa (14)

South Africa	Academy of Science of South Africa	GMOs for African Agriculture: Challenges and Opportunities (2010)
Continent	Academies of Sciences from Cameroon, Ethiopia, Ghana, Kenya, Mozambique, Nigeria, Senegal, South Africa, Sudan, Tanzania, Uganda and Zimbabwe.	Declaration of the 9th Annual Meeting of African Science Academies (2013)
Continent	International Society of African Scientists	Potential Benefits of Biotechnology to Agriculture in Africa and the Caribbean (2001)
South Africa	AfricaBio	Food and Feed Safety Assessment (2017)

Asia (5)

China	Chinese Academy of Sciences	Transgenic Plants and World Agriculture (2000)
India	Indian National Academy of Sciences	Transgenic Plants and World Agriculture (2000)
India	Indian National Academy of Agricultural Sciences	GM Crops for Nutritional Security (2014)
Japan	Agricultural Academy of Japan	Agricultural Academy of Japan proposes conduct of confined field trial of GM crops (2017)
Philippines	National Academy of Science and Technology (NAST)	Filipino Scientists in Support of Biotechnology (2001)

Europe (89)

Czech Republic	Biology Centre of the Academy of Sciences of the Czech Republic	White Book: Genetically Modified Crops (2009)
France	French Academy of Agriculture	Conclusions du groupe de réflexion et de proposition de l'Academie d'Agriculture de France sur les Plantes Génétiquement Modifiées (2012)
France	French Academy of Agriculture, French Academy of Science, National Academy of technologies of Frances	French Academies call for freedom of research on Genetically Modified Plants (GMPs) to be restored (2014)
France	French Academy of Sciences	Genetically Modified Plants (2002)
Germany	National Academy of Sciences (Leopoldina) | German Academy of Science and Engineering (acatech) | Berlin-Brandenburg Academy of Sciences and Humanities	In support of a new policy on Green Genetic Engineering (2009)
Germany	Union of the German Academies of Science and Humanities (8 academies)	Are There Health Hazards for the Consumer from Eating Genetically Modified Food? (2006)
Germany	Federal Ministry of Education and Research	BMBF Research Programme: Biological safety research on genetically modified organisms (2014)
Italy	National Academy of Science | Lincean Academy	Plant biotechnology and GMO variety (2007)
Italy	Joint statement of 14 scientific intitutions of Italy	Food safety and GMOs. Consensus Document (2004)
Italy	Joint statement of 21 scientific intitutions of Italy	Coexistence of Traditional, Organic and Genetically Modified Crops (2006)
Netherlands	Plant Research International – Wageningen UR	Sustainability of current GM crop cultivaton (2011)
Spain	Declaration promoted by the Spanish Bioindustry Association (ASEBIO) and signed by more than 150 Spanish scientists from different universities and research institutes.	Science, progress and environment (2007)
Spain	Declaration promoted by the National Association of Plant Breeders (ANOVE) and signed by 14 Spanish institutions	Press release (2010)

United Kingdom	Royal Society of London	Transgenic Plants and World Agriculture (2000) | Genetically modified plants for food use and human health—an update (2002) | Reaping the benefits: Science and the sustainable intensification of global agriculture (2009) | GM Plants: Questions and Answers (2016)
United Kingdom	Royal Society of Medicine	Genetically modified plants and human health (2008)
United Kingdom	Royal Society of Edinburgh	RSE Calls for a Rational GM Debate (2015)
United Kingdom	Biochemical Society UK	Genetically Modified Crops, Feed and Food: A Biochemical Society position statement (2011)
United Kingdom	British Medical Association	Genetically modified foods and health: a second interim statement (2004)
United Kingdon	Letter signed by 32 scientific and agricultural institutions	Letter to Scottish Government from research organisations (2015)
United Kingdon	Science and Technology Committee – House of Commons (UK)	EU regulation on GM Organisms not 'fit for purpose' (2015)
Vatican	Pontifical Academy of Sciences	Transgenic Plants for Food Security in the Context of Development (2010)
European Union	European Commission	*A Decade of EU Funded GMO Research (2010)*
European Union	European Academies Science Advisory Council (EASAC)	Planting the future: opportunities and challenges for using crop genetic improvement technologies for sustainable agriculture (2013)
European Union	European Food Safety Authority (EFSA)	FAQ on genetically modified organisms (2012) | Safety and nutritional assessment of GM plants and derived food and feed: The role of animal feeding trials (2008)

** In this table the academies of Germany are 10, in the case of United Kingdom there are 33 institutions; 22 institutions from Italy, 14 from Spain, and 3 from France.*

** The European Academies Science Advisory Council (EASAC) currently has **29 members**: one representative each from the 25 national science academies of EU member states, the Academia Europaea, ALLEA, and also representatives of the Norwegian and Swiss national academies of sciences.*

Latin America (9)

Argentina	Nutrition Society of Argentina (SAN)	Transgenic Food: SAN Position (2012) | Biotechnology and genetically modified food: Answers to frequently asked questions (Undated)
Argentina	International Life Sciences Institute (ILSI)	Safety of Genetically Modified Organisms: The case of GM soy in Argentina (2004) Pages 22-27 | Biotechnology and genetically modified food: Answers to frequently asked questions (Undated)
Brazil	Brazilian Academy of Sciences	Transgenic Plants and World Agriculture (2000)
Brazil	Brazilian Association of Nutrition*	ABRAN supports the development of GMOs with better nutritional properties* (2005)
Chile	Chilean Academy of Sciences	Declaration of the Chilean Academy of Sciences on GM crops (2004)
Chile	Chilean Academy of Agricultural Sciences	Position of the Chilean Academy of Agricultural Sciences on GMOs (2013)
Mexico	Mexican Academy of Sciences	Transgenic Plants and World Agriculture (2000) | For the responsible use of GMOs (2011) | Transgenic: Great Benefits, Absence of damage and Myths (2017)
Peru	Peruvian Association for the Development of Biotechnology (PeruBiotec)	PeruBiotec takes up the challenge (2009)
Continent	REDBIO (600 scientists from 21 countries)	Viña del Mar Declaration: RedBio participants express support for agrobiotechnology (2007)

* *The source is an interview where is mentioned the support of "Brazilian Association of Nutrition" to biofortified GM crops. A public statement should be corroborated.*

North America (28)

Canada	Canadian Cancer Society	Food Issues: Genetically modified foods (2016)
Canada	Royal Society of Canada	Elements of Precaution: Recommendations for the Regulation of Food Biotechnology in Canada (2001)
Canada	Health Canada	Safety Assessment of Genetically Modified Foods (2016)
USA	National Academy of Sciences (NAS)	Transgenic Plants and World Agriculture (2000) | Impact of Genetically Engineered Crops on Farm Sustainability in the United States (2010)
USA	Institute of Medicine (IOM) & National Research Council (NRC) of the National Academies.	Safety of Genetically Engineered Foods: Approaches to Assessing Unintended Health Effects (2004)
USA	National Academies (NRC, NAS, NAM)	Genetically Engineered Crops: Experiences and Prospects (2016)
USA	American Medical Association (AMA)	Council on Science and Public Health Report (2012)
USA	American Association for the Advancement of Science (AAAS)	Statement by the AAAS Board of Directors On Labeling of Genetically Modified Foods (2012)
USA	American Council of Science and Health (ACSH)	Biotechnology and Food (Second Edition) (2000)
USA	Society of Toxicology (SOT)	The Safety of Genetically Modified Foods Produced through Biotechnology (2003) | Food and Feed Safety of Genetically Engineered Food Crops (2017)
USA	American Dietetic Association	Position of the American Dietetic Association: Agricultural and food biotechnology (2006)
USA	Genetics Society of America	Assessing Benefits and Risks of Genetically Modified Organisms (2001)
USA	American Society for Cell Biology (ASCB)	ASCB Statement in Support of Research on Genetically Modified Organisms (2009)
USA	American Society of Plant Biology (ASPB)	Statement on Plant Genetic Engineering (2006) Plant scientists: GM technology is safe (2016)
USA	American Society for Microbiology (ASM)	Statement of the American Society for Microbiology on Genetically Modified Organisms (2000)
USA	American Phytopathological Society (APS)	APS Statement on Biotechnology and its Application to Plant Pathology (2001)
USA	Society for In Vitro Biology (SIVB)	Position Statement on Crop Engineering (Undated)
USA	Crop Science Society of America	CSSA Perspective on Biotechnology (2001)

USA	Council for Agricultural Science and Technology (CAST)	Crop Biotechnology and the Future of Food: A Scientific Assessment (2005)
USA	Federation of Animal Sciences Societies (FASS) – *representing the American Dairy Science Association (ADSA), American Society of Animal Science (ASAS) and the Poultry Science Association (PSA).*	FASS Facts On Biotech Crops – Impact on Meat, Milk and Eggs (2001) | Biotechnology as a Tool to Enhance Sustainability for Animal Production (2011)
USA	Food and Drug Administration (FDA)	Questions & Answers on Food from Genetically Engineered Plants (2015)
USA	Entomological Society of America	ESA Position Statement on Transgenic Insect-Resistant Crops (2001)
USA	American Cancer Society	Common questions about diet and cancer: Genetically modified foods (2016)
USA	American Veterinary Medical Association	AVMA supports safety of GMO and GE foods (2017)

* *The American Dietetic Association (ADA) has become The Academy of Nutrition and Dietetics (AND). While the above statement reflected the ADA's position the president of AND has stated that AND is currently neutral and has no position on GMOs.*

Oceania (7)

Australia	Australian Academy of Science	Submission to the Inquiry into Primary Producer Access to Gene Technology (1999) Statement gene technology and plants (2007)
Australia	Biotechnology Ministerial Council	Australian Biotechnology: A National Strategy (2000)
Australia	Commonwealth Scientific and Industrial Research Organization (CSIRO)	Biotechnology Strategy (2002)
Australia	National Farmers' Federation (NFF)	Biotechnology Position Statement (Undated)
Australia	Australia's Biotechnology Organization (AusBiotech)	Backing innovation: The way forward for Australian agriculture (2004)
Australia & New Zealand	Food Standards Australia – New Zealand	Review of genetically modified food safety assessments (2009)
New Zealand	New Zealand Royal Commission	Report of the Royal Commission on Genetic Modification (2000)

International Organizations (14)

World Health Organization (WHO)	Modern food biotechnology, human health and development: an evidence-based study (2005) Frequently asked questions on genetically modified foods (2014)
Food and Agriculture Organization of the United Nations (FAO)	FAO Statement on Biotechnology (2001) | Frequently Asked Questions about FAO and Agricultural Biotechnology (2011)
Thirld Word Academy of Sciences (TWAS)	Transgenic Plants and World Agriculture (2000)
International Council for Science (ICSU)*	New Genetics, Food and Agriculture: Scientific Discoveries – Societal Dilemmas (2003)
International Union of Food Science and Technology (IUFoST)	IUFoST Scientific Bulletin on Biotechnology and Food (2005)
International Seed Federation (ISF)	Position Paper on Genetically Modified Crops and Plant Breeding (2005)
International Union of Nutritional Sciences (IUNS)	Statement on Benefits and Risks of Genetically Modified Foods for Human Health and Nutrition (Undated)
Consultative Group for International Agricultural Research (CGIAR)	Agricultural Biotechnology and the Poor: Promethean Science (2000)
United Nations Development Programme (UNDP)	UNDP Report Supports Biotechnology (2001)
AgBioWorld Foundation [*Declaration signed by 25 Nobel Prize winners and more than 3,400 scientists*]	Scientists In Support Of Agricultural Biotechnology (2011)
Organisation for Economic Co-operation and Development (OECD)	The OECD Edinburgh Conference on the Scientific and Health Aspects of Genetically Modified Foods (2000)
International Society for Plant Pathology.	Genetic modification for disease resistance: a position paper (2016)
International Congress on Poverty, hunger and emerging food (Catholic University of Valencia, Spain)	Press: The World Congress against hunger concludes that GM doesn't affect health (2016)
123 Nobel Prize Laureates Supporting Precision Agriculture (GMOs)**	Laureates Letter Supporting Precision Agriculture (GMOs) (2017)
Asian Development Bank	Agricultural Biotechnology, Poverty Reduction, and Food Security (2001)

* The document from the International Council for Science (ICSU) was signed in 2003 by **101 science academies and 27 scientific unions**. ICSU currently has **31** Scientific Union Members and **121** National Scientific Members.

** The statement from Nobel prizes is included by the importance of the document, but it is not counted as an institution.

Source : http://www.siquierotransgenicos.cl/2015/06/13/more-than-240-organizations-and-scientific-institutions-support-the-safety-of-gm-crops/

Attachment F

Gene Editing Evidence Update

Royal Society of New Zealand

Oct 2017

Life Sciences Network Inc

Further Submission

Proposed District Plan

Waikato District Council

15 July 2019

Gene Editing

Evidence Update

the ROYAL SOCIETY of NEW ZEALAND
TE APĀRANGI

Summary

- **Gene editing involves the insertion, deletion or replacement of genetic material called DNA.**
- **New gene-editing technologies have been developed which have increased the speed, ease and accuracy of making changes to DNA in cells, and their use is increasing rapidly.**
- **These technologies are beginning to be used for new approaches in a variety of areas including research, medicine, agriculture, biotechnology and have the potential to be used in pest control.**
- **The three most widely used new gene-editing tools use bacterial proteins to find, cut, edit, add or replace genes, and are known as Zinc Fingers (ZFNs), TALENs, and CRISPR.**
- **Gene-editing technologies open up new opportunities and potential risks from new uses which may challenge people's views on what is acceptable.**
- **These new technologies pose challenges for regulators who will find it harder to distinguish between genetic changes in organisms generated by conventional breeding, gene editing, or natural mutation.**

What is a genome?

The characteristics of all living organisms are determined by their genetic material and their interaction with the environment. An organism's complete set of genetic material is called its genome which, in all plants, animals and microbes, is made of long molecules of DNA (deoxyribonucleic acid). The genome contains all the genetic information needed to build that organism and allow it to grow and develop.

Within the genome are regions of DNA called 'genes'. These 'genes' can carry instructions for making proteins, which in turn give the organism its characteristics or 'traits' [1]. For example, the red colour of a pōhutukawa flower is determined by the plant's genes, which carry the instructions for colour production within the flower. While every cell in an organism will have essentially the same genome, the differences between cells are determined by how and when different sets of genes are turned on or off. For example, genes in specialised cells in the eye are turned on to make proteins that detect light, while genes in red blood cells are turned on to make proteins for carrying oxygen.

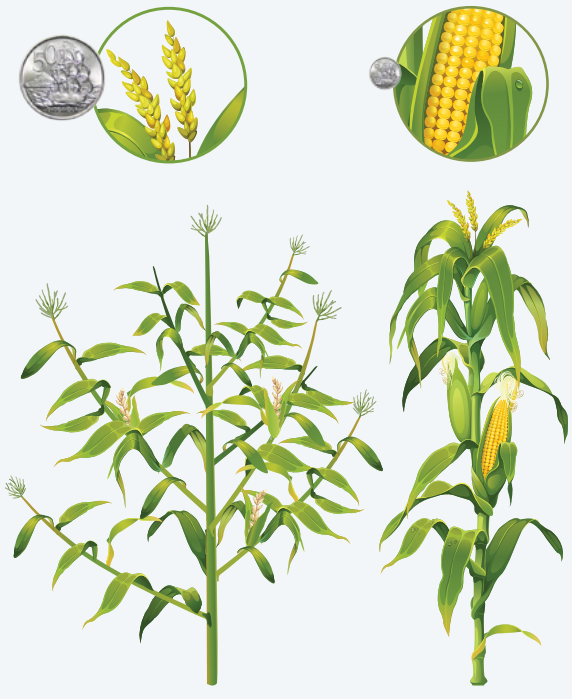
Occasionally, changes to DNA in cells can occur that create a new and different version of a gene which can then be carried by that organism's offspring. These changes are known as mutations and mean different individuals can carry different versions of that particular gene, which can result in differences in the trait within populations, for example for individual eye colour.

Identifying and using these different versions of genes, and the traits they create, has been an important part of agriculture for thousands of years. By cross-breeding plants with different versions of genes, and repeatedly selecting preferred plants from their offspring to serve as new parent lines [2], agricultural plants have been created over time with more desirable traits, such as higher yields, reduced toxicity, and improved flavour (see BOX 1). Much the same is true of livestock animals [6].

BOX 1

HISTORIC SELECTION IN AGRICULTURAL CROPS

Some 6,000 – 10,000 years ago, Meso-American farmers began the drastic changes to a grass species called teosinte to become what is now known as maize. Through selecting and growing plants based on very rare, desirable attributes caused by naturally occurring mutations, a plant was created with a single stalk and a cob with dozens or even hundreds of large seeds that were encased in husks, resulting in the maize that is grown today [3 – 5].



History of genetic engineering

Since the 1930s, chemical methods or ionizing radiation [7] have been used to change (or mutate) genomes, and to introduce new traits. This is a random process and breeders do not know what changes had actually occurred in the DNA. These methods are considered established tools of conventional plant breeding, along with 'marker-assisted selection' in the last 15 years. This latter process involves the genetic screening of agricultural plants and animals to see which individuals have useful versions of specific genes, and then selectively breeding from them. This selective breeding, however, would still introduce thousands of 'unwanted' genetic variations alongside any desired genes identified.

The introduction of genetic engineering in the 1970s and 80s enabled the possibility of moving beyond the conventional sources of random genetic variation, described above, by allowing researchers to introduce a specific single new or altered gene, or to disrupt or enhance an existing gene. While more targeted systems were available for some organisms, in many cases (such as in plants) the first set of tools provided little control over where new engineered DNA could be integrated into the organisms' genome. Two of these techniques used bacteria or viruses to transfer the DNA, and a third method involved coating small metal particles with the DNA, and then 'shooting' the particles into cells [2].

The impact on the biological sciences since these first tools were developed has been profound. However, in the past 10 years, researchers have developed tools to enable the manipulation of specific genes within a genome with greater and greater precision in the modification process, and fewer and fewer unintended changes elsewhere in the genome [8]. With their wide availability and simplicity, these gene-editing technologies are now being used to significantly accelerate research, and offer new treatments for a range of genetic diseases, while new agricultural products are beginning to be commercialised.

Alongside the development of the technology, the concept of genetic engineering, or genetic modification, has raised ethical and values-based questions in many societies [9, 10]. New Zealand has adopted a regulatory framework under the Hazardous Substances and New Organisms Act 1996 (HSNO Act[a]) to manage adverse effects on the environment and health and safety of people associated with the technology, which takes into account both benefits and risks. This act is based on the assumption that genetically modified organisms are different from unmodified organisms and can be distinguished from them. Food which has been derived or developed from an organism that has been modified by gene technology must also meet the Australia New Zealand Food Standards Code[b]. With the arrival of new gene-editing technologies, there are now increasing challenges to New Zealand's national regulatory system's ability to distinguish between genetically modified and conventionally produced products and organisms (see BOX 2).

BOX 2

WHAT IS CLASSIFIED AS A GENETICALLY MODIFIED ORGANISM?

In New Zealand, the HSNO Act defines genetically modified organisms as:
'any organism in which any of the genes or other genetic material have been modified by in vitro[c] techniques; or are inherited or otherwise derived, through any number of replications, from any genes or other genetic material which has been modified by in vitro techniques', and the Australia New Zealand Food Standards Code defines food produced using gene technology as **'a food which has been derived or developed from an organism which has been modified by gene technology'.**

However, the organisms, resulting from modern gene-editing techniques may show no direct trace of a genetic modification, and therefore it will be harder to distinguish from a fully conventionally produced organism [11]. For example, accelerated plant breeding. This process involves an intermediate generation of GM plants where a new gene is inserted to shorten the time to flowering of a plant, speeding up the breeding process [12]. The inserted gene is then removed later by conventional crossing with other non-GM plants, so that no foreign genetic material remains in the resulting crop [13, 14].

In New Zealand, this example would still be considered a genetically modified organism, however in other countries there may be no legislative requirement to record the genetic modification step as part of the process [15]. For example, in the US, the Department of Agriculture has ruled that commercial production of CRISPR gene-edited mushrooms [16] and waxy corn[d] do not need regulation, while in Europe, the Swedish Board of Agriculture have ruled that plants mutated by CRISPR, which do not contain any foreign DNA sequences, are exempted from GM legislation[e].

What are the new gene-editing technologies?

Gene-editing technologies use proteins, called enzymes, to cut targeted areas of DNA within a genome. Cells repair these cuts but if no instructions are provided for the repair, the repair process can make mistakes, resulting in altered DNA sequences. If specific DNA repair information is provided, however, the cell will use this to repair the cut in the way it is instructed. The use of this process provides an opportunity for researchers to modify the genome, by providing slightly different repair information from what was there before. In this way, it is possible to use gene editing to change a version of a gene from one that causes disease to one that does not (for example gene variants that contribute to Parkinson's disease [17] or genetic metabolic disorders [18]), or choose the version of a gene that confers better resistance to disease in agricultural plants and animals (for example resistance to powdery mildew in wheat [19]).

It is also possible to use the technique to modify genes without introducing foreign DNA sequences. For example, gene editing can be used to switch off genes [20] in laboratory-grown cells to identify their function [21], or to switch off genes that are causing disease, such as in animal models of Huntington's disease [106]. Alternatively, a DNA template could be provided for a whole new gene based on a gene found within the same species, or from a different species, providing a new set of traits such as new disease resistance or hornlessness in dairy cows [23 – 25].

While technologies to make cuts in DNA have been known since the 1970s, using them in a controlled and accurate way, and in organisms whose genome is poorly understood, has been a major hurdle. However, in the last 10 years, researchers have identified, or created, proteins that permit gene-editing technologies to make gene edits in specific areas of DNA, rather than introducing these changes randomly into the genome. Also, advances in very rapid genome sequencing now mean that genome DNA sequence information for any species can be quickly assembled [26], opening up the way for widespread use of gene editing approaches.

The three main new gene-editing technologies [27] which have been developed to do this (see FIG. 1) are:

- **Zinc-finger nucleases** [28, 29]
- **TALENs** [30]
- **CRISPR** [31]

Zinc-finger nucleases (ZFNs)

ZFNs use a bacterial DNA cutting enzyme [32] that has been combined with proteins called 'zinc fingers', which can be customized to recognise a specific section of DNA [27]. In 2005, this technology was first used to edit DNA in human cells [33]. ZFNs are small (one-third of the size of TALENs and much smaller than CRISPR) so they are easier to package inside delivery vehicles, such as viruses, to enable them to reach their targets in cells for genome-editing-based therapies [34].

TALENs

TALENs (transcription activator-like effector nucleases) again use a DNA-cutting enzyme combined with proteins from bacteria [35] that target areas of DNA, in a similar way to the zinc finger proteins. TALENs can be designed with long DNA recognition sections, and therefore tend to have lower unintended off-target cut sites, which can occur when parts of a genome have an identical or near-identical sequence to the target site [36, 37].

CRISPR

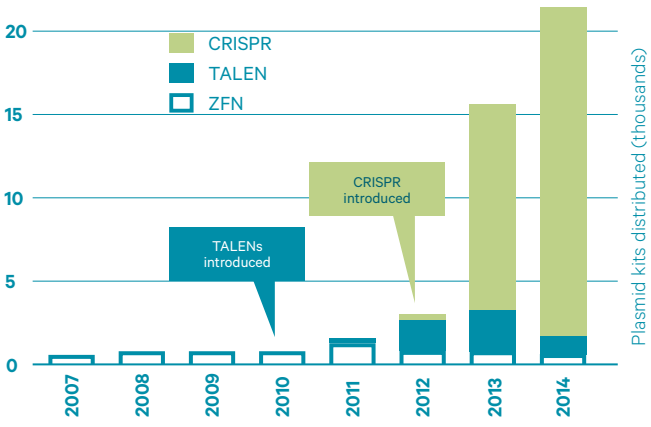
Bacteria possess an immune system which recognises invading viral DNA and cuts it up, making the invading virus DNA inactive. This type of immune system is known as CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats) [38]. In 2012, it was discovered that by modifying this mechanism, it was possible to target and cut any DNA sequence and edit genomes [39]. In 2013, this technology was modified further so that the target DNA is bound and blocked, rather than cut, allowing a gene to be turned off without altering the DNA sequence [40 – 42]. In 2014, a further advance allowed the blocking enzyme to be reactivated, enabling a way to turn genes on and off using chemical triggers, or blue light [43]. In 2016, researchers further improved on the performance of CRISPR by allowing for editing of single DNA letters [44].

CRISPR, unlike ZFNs and TALENs allows for many DNA sites to be edited simultaneously and easily [45]. It is also the most affordable and programmable genome editing technology. While much more accurate than earlier genetic modification technologies, there can still be unintended off-target effects, although these are detectable and new research is rapidly improving the technology's accuracy [46 – 50].

FIG. 1

POPULARITY OF GENOME-EDITING KITS

Popularity of genome-editing kits. The ease of use of CRISPR has seen a rise in the number of orders for genome-editing kits from Addgene, in the US.



How are these new technologies being used and applied?

New gene-editing technologies are enabling a broad range of applications from basic biological research to biotechnology and medicine [51] (see FIG. 2).

Medical applications in treatments and research

Of the approximately 25,000 identified genes in the human genome so far, mutations in over 3,000 have been linked to disease [52]. Gene-editing tools are now being used to understand how gene variants are linked to disease in mammalian cells and whole animal models, indicating the potential for this technology to be used to understand and treat human disease [20, 53–57] (see FIG. 3 [20]).

For example, CRISPR has been used in research mouse models to correct a mutation in genes responsible for Hepatitis B [58], haemophilia [53], severe combined immunodeficiency [59], cataracts [60], cystic fibrosis [61], hereditary tyrosinemia [62] and inherited Duchenne muscular dystrophy [22].

Clinical trials with patients are underway in the US using ZFN to modify the genes of immune-system cells to treat HIV [63]. HIV infects and destroys immune system cells and key genes within these cells have been modified using ZFN to make them resistant to HIV, and the cells then transplanted back into patients.

The Great Ormond Street Hospital in the UK has used TALENs for gene editing in donated blood cells to disable the gene which the immune system uses to recognise 'foreign' cells. This allowed a patient to receive donated blood cells, without the donor cells attacking the patients' healthy cells [64, 65]. In June 2016, a federal biosafety and ethics panel in the US approved a clinical study in patients using CRISPR-based genome-editing to create genetically altered immune cells to attack three kinds of cancer[f].

Gene editing is also being used by researchers to try to overcome allergic reactions to chicken eggs, which prevents about 2% of children worldwide from receiving many routine vaccinations. Researchers at Deakin University in Australia are working with gene modifications using CRISPR to produce hypoallergenic eggs [66].

The use of gene-editing technologies in the early stage embryo allows modifications which can be passed on to future generations. In the UK, the Human Fertilisation and Embryology Authority (HFEA) has approved an application for the use of CRISPR in healthy human embryos to help researchers to investigate the genes involved in early embryo development. This could lead to improvements in assisted reproductive technologies used to treat infertility, although the CRISPR technology itself will not form the basis of a therapy [67]. In China, researchers have used CRISPR in non-viable human embryos to genetically modify genes responsible for ß-thalassemia, a potentially fatal blood disorder [68], and to modify genes in immune cells to develop increased HIV resistance [69].

FIG. 2

APPLICATION OF GENOME EDITING
(Modified from Hsu et al. 2014)

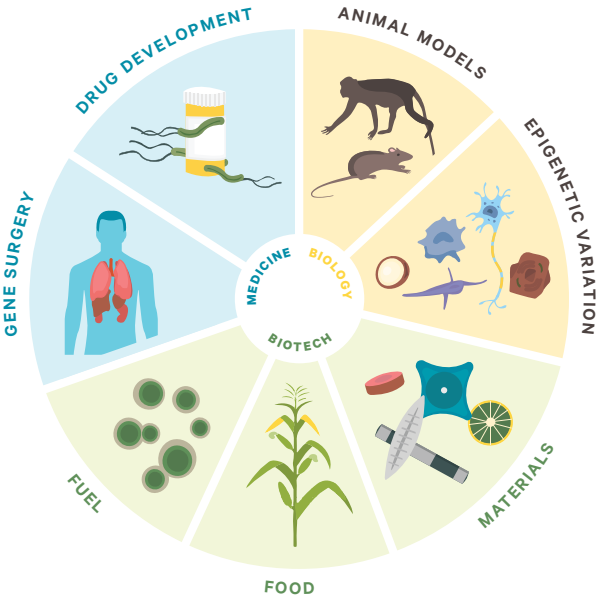
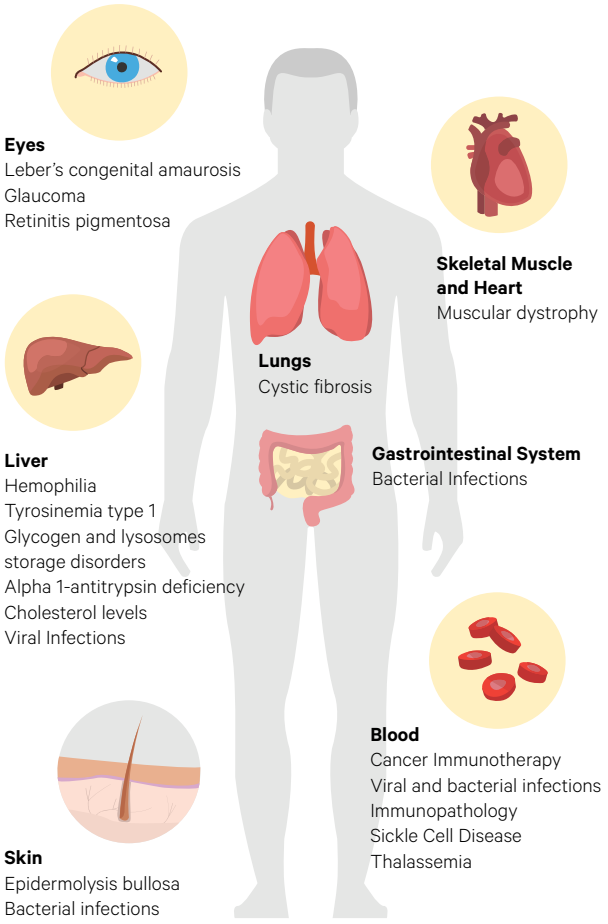


FIG. 3

DIVERSITY OF TARGETS FOR THERAPEUTIC GENOME EDITING (Maeder & Gersbach 2016)



Agricultural applications

In agriculture, the new gene-editing technologies make it possible to modify a range of agriculturally-important organisms easily, cheaply, and if desired, without introducing foreign DNA sequences [13, 70].

Food production

In the US, researchers have used gene-editing technologies on agricultural crops such as maize [29], soybean [71], sorghum [72], and developed a rice resistant to bacterial blight [73]. In commercial development, the common white button mushroom has been modified by CRISPR at Penn State University to prevent them from becoming off-colour by targeting a gene that produces an enzyme that causes browning [16]. Further, DuPont Pioneer have used CRISPR to produce a higher-yielding waxy corn variety [74] and Calyxt Plant Sciences Inc. have produced soybean lines that are low in polyunsaturated fats, using TALENs [75].

Chinese researchers have similarly used TALENs and CRISPR to modify a range of agriculturally important plants and animals, including maize [76], rice [77, 78], and wheat [79]. They have also used the techniques to develop goats with longer coats (for Angora) and more muscle (for increased meat yield) [80]. Elsewhere in the world, researchers have used the techniques to modify barley (Denmark) [81]; wheat (India) [82]; and to study allergenic milk protein production in cow embryos cultured in the laboratory (New Zealand) [83].

Animal health and welfare

In the US, hornless dairy cattle have been produced using gene editing to avoid the need for painful de-horning and to prevent animals injuring each other during transport. Using TALENs, the genetic code that makes dairy cattle have horns has been substituted for the one that makes Angus beef cattle have none [24]. The University of Missouri has also bred the first pigs resistant to Porcine Reproductive and Respiratory Syndrome by suppressing the production of a protein within the pigs that the virus uses to help it spread [84].

African swine fever is a highly contagious disease that kills up to two-thirds of infected animals. In Scotland, ZFN has been used by the University of Edinburgh to modify a gene in pigs to the version of the gene found in warthogs, to produce pigs that are potentially resilient to the disease [25]. The university has also used gene editing to modify chicken genes so they don't spread bird flu by introducing a gene that produces a 'decoy' molecule that interrupts the replication cycle of the bird flu virus, thereby restricting its transmission [85].

In China, TALENs have been used to add a gene that is found in mice into cattle to improve tuberculosis (TB)-resistance. The modified cattle have immune cells that are better at slowing the growth of the disease and are less susceptible to developing the internal symptoms of TB [86].

Pets

In China, CRISPR has been used to create micro-pigs which are approximately half the size of their non-modified counterparts, which can be sold as pets [87].

Biocompound production

By using gene-editing technology to manipulate biological pathways, new materials are being developed, such as algae-derived porous silica-based particles for drug delivery [88], CRISPR modified silkworms to produce spider silk, algae-derived lipids for biofuels [89], and microbial production of pharmaceuticals and commodity chemicals such as ß-carotene [90], L-lysine [91], and mevalonate [92].

Environmental applications

Gene-editing tools have not been used to date in the conservation of wildlife [93], but their use in the control of non-native invasive organisms is being explored with the use of gene drives.

Gene drives

In 2015, researchers demonstrated the use of CRISPR to develop 'gene drives', a genetic system named for the ability to 'drive' themselves and nearby genes through populations of organisms over many generations [94].

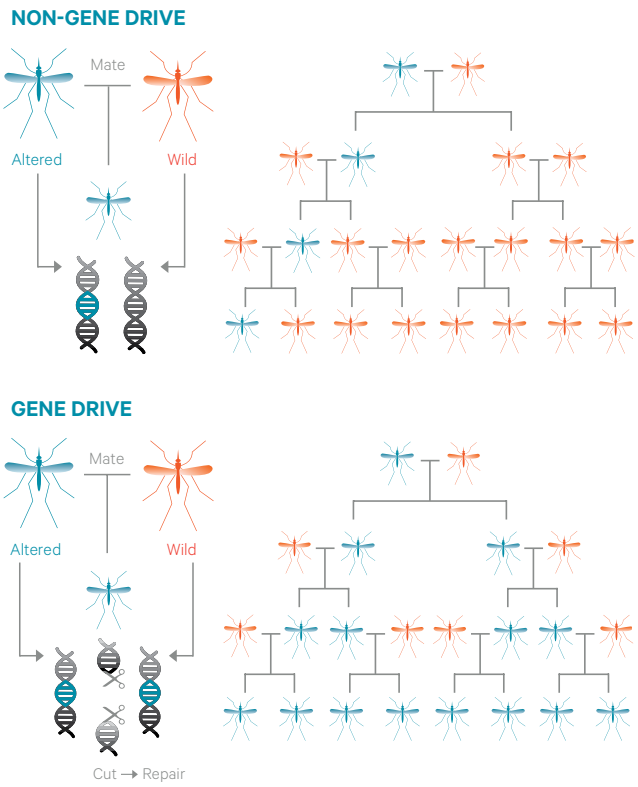
In sexual reproduction, offspring inherit two versions of every gene, one from each parent. Each parent carries two versions of the gene as well, so chance (50:50) normally governs which particular variant of the gene that will be passed on.

But 'gene drives' ensure that the genetic modification will almost always be passed on, allowing that variant to spread rapidly through a population (see FIG. 4). So far, 'gene drives' have been developed in yeast [95], the fruit fly [96], and two mosquito species.

One of the mosquito gene drives, developed in the US by researchers at the University of California, causes a malaria-resistance gene to be passed on to the mosquitoes' offspring, meaning they are unable to transmit malaria in mice [97]. The other mosquito gene drive strategy, developed by Imperial College in the UK, propagates a gene that sterilizes all female mosquitoes (which could suppress specific mosquito populations to levels that will not support malaria transmission) [98].

FIG. 4

CRISPR gene editing can be used to propagate a genetic modification rapidly through generations, using a gene drive which cuts the partner chromosome and copies the modification to this chromosome through the repair process.



Changing research approaches

In biological research, gene editing can increase the speed and ease of creating new animal-based or cellular models for disease, and it is proving to be an important tool in the study of cell development.

Rapid generation of cellular and animal models

Many human illnesses, including heart disease, diabetes, cancer and various neurological conditions, are affected by numerous variants in genes. Working out the impact of these variants on the illness with the help of animal models has been a slow process. To create these animal models, mutations need to be introduced into multiple genes. But using conventional tools to create a mouse with a single mutation can take up to a year and cost US$20,000 to produce [99]. If a scientist wants an animal with multiple mutations, the genetic changes must be made sequentially, and the timeline for one experiment can extend into years. In contrast, CRISPR has allowed the creation of a strain of mice with multiple mutations in a few weeks [100], with the CRISPR tools costing as little as US$30 [101].

Functional genomic screens

Cultures of cells developed from a single cell, which has a uniform genetic make-up, are used to examine the contribution of genes to biological processes. CRISPR can now be used to rapidly generate thousands of these different cell lines, with each cell line having a different gene switched off, to speed up the search for DNA sequences linked to specific biological processes [102].

Exploring gene expression

Almost every cell in the human body has roughly the same DNA sequence but cells use their DNA code in different ways, depending on where they are located in the body. One way that genes are controlled is by DNA-packaging proteins called histones [103]. In 2015 it was reported how CRISPR could be used to attach to and switch on these proteins, to determine whether they cause changes to the growth and development of the organism [104].

Tracing cells during development

In 2016 it was discovered that CRISPR can be used to mark cells whenever they divide based on a specific pattern (or barcode) of deletions and insertions. This technology now allows researchers to re-construct a 'family tree' of the cells that compose an animal's body, revealing which cells spawned others [105]. The use of this technique is now also being considered to record a cell's history in response to environmental signals, or to trace the evolution of tumours.

Implications of these technologies for New Zealand

With the falling cost and increasing simplicity and availability of these techniques, their application is increasing around the world, offering new opportunities and risks with legal and ethical implications. For example, gene editing poses challenges for regulators who will find it harder to distinguish between genetic changes generated by conventional breeding, gene editing, or natural mutation. The use of these techniques in human genome editing in particular has led to a global summit being held in December 2015 to consider human gene editing and the implications of these emerging technologies[g].

To explore these issues for New Zealand, the Royal Society of New Zealand has established an expert panel in 2016 to consider the implications of gene-editing technologies for New Zealand society, including the ethical, social, legal, environmental and economic considerations that reflect current and future trends in New Zealand's population and community diversity. The intention of the Panel will be to raise public awareness of the technologies and their uses, and provide insight and advice on the future implications associated with the application of these new technologies for New Zealand.

For further information

This paper was authored by the Royal Society of New Zealand, under the guidance of the following expert reference group: Professor Barry Scott FRSNZ, Professor Peter Dearden, Associate Professor Peter Fineran, Professor Neil Gemmell, Professor Emily Parker, and Professor Andrew Allan.

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For further information, please contact info@royalsociety.org.nz or go to the Royal Society of New Zealand web page: **www.royalsociety.org.nz/gene-editing**

Endnotes

[a] http://www.legislation.govt.nz/act/public/1996/0030/latest/DLM381222.html. The Act also implements New Zealand's obligations under the Convention on Biological Diversity and its Cartagena Protocol on Biosafety, which regulates living modified organisms resulting from modern biotechnology.

[b] http://www.foodstandards.govt.nz/code/Pages/default.aspx To date foods derived from 88 lines of genetically modified canola, corn, Lucerne (alfalfa), potato, rice, soybean and sugar beet are approved for use in foods in Australia and New Zealand. None of these have been derived from gene editing, [c] https://www.pioneer.com/CMRoot/Pioneer/About_Global/Non_Searchable/15-352-01_air_response_signed.pdf

[c] *In vitro* techniques are those that occur in a laboratory vessel or other controlled experimental environment rather than within a living organism.

[d] https://www.pioneer.com/CMRoot/Pioneer/About_Global/Non_Searchable/15-352-01_air_response_signed.pdf

[e] http://www.upsc.se/documents/Information_on_interpretation_on_CRISPR_Cas9_mutated_plants_Final.pdf

[f] https://www.statnews.com/2016/06/21/crispr-human-trials/

[g] http://www.nationalacademies.org/gene-editing/Gene-Edit-Summit/index.htm

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TE APĀRANGI

Attachment G

The Use of Gene Editing to Create Gene Drives for Pest Control in New Zealand

Royal Society of New Zealand

Technical Paper, Dec 2017

Life Sciences Network Inc

Further Submission

Proposed District Plan

Waikato District Council

15 July 2019

December 2017

The use of gene editing to create gene drives for pest control in New Zealand

Royal Society Te Apārangi Gene Editing Panel

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Background

The revolution in gene editing technologies is making it easier to change genetic material with huge potential benefits in many sectors including healthcare, agriculture and conservation. However, the technology to carry out gene editing and the ideas about how it might be applied are, in many cases, moving well ahead of the knowledge about how to safely effect the desired changes. For example, in conservation applications, gene editing could be used to make a native species resistant to disease, but this might accidentally make it more susceptible to drought.

As a technology, gene editing is rapidly moving ahead of any consensus on the rights and wrongs of how it should be used. So to explore the implications of gene editing technology for New Zealand, the Royal Society Te Apārangi has convened a multidisciplinary panel of some of New Zealand's leading experts to consider the social, cultural, legal and economic implications of revolutionary gene-editing technologies for New Zealand to:

- Raise awareness of the scientific possibilities and associated public issues of new gene-editing technologies to inform debate
- Provide information and guidance for policy makers to address current and new issues needing to be clarified or resolved
- Show where gene-editing applications are covered by established policies and regulations and where changes are needed
- Provide a New Zealand perspective to the global discussion on this technology and identify where global consensus is important

This paper is one of a series[1] considering the implications of the technology in health, pest control, and agricultural situations, and is accompanied by a companion discussion paper inviting public feedback, and a fact sheet on how these technologies work and are being used and applied [1].

To help consider the implications for pest control in New Zealand, this paper[2] highlights three scenarios which raise specific considerations for three different types of pest. In particular, these case studies consider:

- The range of scientific complexities of developing a gene drive for different organisms
- The implications for the spread of animals with the gene drive to different countries.

[1] https://royalsociety.org.nz/gene-editing/

[2] derived from [2.] Dearden, P.K., et al., *The potential for the use of gene drives for pest control in New Zealand: a perspective.* Journal of the Royal Society of New Zealand, 2017: p. 1-20.

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Introduction

The last two decades have seen a substantial increase in our knowledge and ability in genetics. Researchers have now developed tools, chief among them being CRISPR[3], to enable the manipulation of specific genes within an organism's genetic material with greater and greater precision in the modification process, and fewer and fewer unintended changes elsewhere in the genome (see box 1). With their wide availability and simplicity, these gene-editing technologies are now being used to significantly accelerate research, and offer new treatments for a range of genetic diseases, while new agricultural products are beginning to be commercialized. However, alongside the development of the technology, the concept of genetic engineering, or genetic modification, has raised ethical and values-based questions in many societies.

Box 1: Gene editing with CRISPR

Bacteria possess an immune system that recognises invading viral DNA and cuts it up, making the invading virus DNA inactive. This type of immune system is known as CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats) [3]. In 2012, it was discovered that by modifying this mechanism, it was possible to target and cut any DNA sequence and edit genomes [4]. Cells which have their DNA cut by CRISPR, will repair these cuts as 'instructed' if specific DNA repair information is provided. By altering this repair information, it is possible to change a gene of interest, for example, from one that causes disease to one that does not [5, 6].

Modern advances in gene-editing technologies now provide potential novel solutions for the challenges of pest control through the development of gene drives [7-10]. Much of the research on gene editing of pests published to date has concentrated on species that cause human diseases [11-15]. However as researchers begin to understand and consider the use of gene-editing techniques in pest control, more and more species are being considered as potential targets, from agricultural pests [16] to unwanted predators.

New Zealand has unique requirements when it comes to pest control [17]. New Zealand's natural and agricultural environments are beset with pest species, imported deliberately or accidentally. Pests range from mammalian omnivores such as the Brushtail Possum [18-21], that impact our native birds and their food sources, through to a wide assortment of predators such as rats, cats, stoats and ferrets, and insect predators such as *vespulid* wasps [22]. Weeds increasingly impact our ecosystem structure and integrity [23] and the recent discovery of the fungal disease myrtle rust threatens many native and valued plant species. Our marine and freshwater ecosystems are also threatened by pests such as sea squirts [24], koi carp [25] and invasive algae [26]. Our agricultural production ecosystems are threatened by crop and pasture pests such as leafroller moths and Argentine stem weevil [17], and weeds such as ragwort and dock. New Zealand also actively maintains a biosecurity cordon to inhibit the colonisation of our islands from new pest threats. Major biosecurity threats from pests include fruit flies (e.g. Queensland fruit fly and the Mediterranean fruitfly), the brown marmorated stink bug and lymantrid moths such as the gypsy moth.

Within our native ecosystems, intensive poisoning and trapping has been undertaken for many mammalian pests. As a result of their control, it is now known that these ecosystems rebound well after key pest suppression and removal [27-30]. In many places in New Zealand, including offshore islands [28, 29], isolatable peninsulas and predator-proofed ecosanctuaries, predators have been eradicated. The benefits of control to native wildlife have been immense, even extending outside

[3] CRISPR in this paper is being used to refer to the CRSIPR-Cas9 gene editing technique.

such sanctuaries. The Zealandia ecosanctuary in Wellington has increased native bird life in the surrounding city to the point that a rare native parrot, the kākā, is considered by some to be becoming a local pest species itself [31]. New Zealand agencies have cleared many offshore islands of pests, including the removal of Norway rats from the 11,000 hectares of Campbell Island. New Zealand's expertise in this area is well recognised internationally [32].

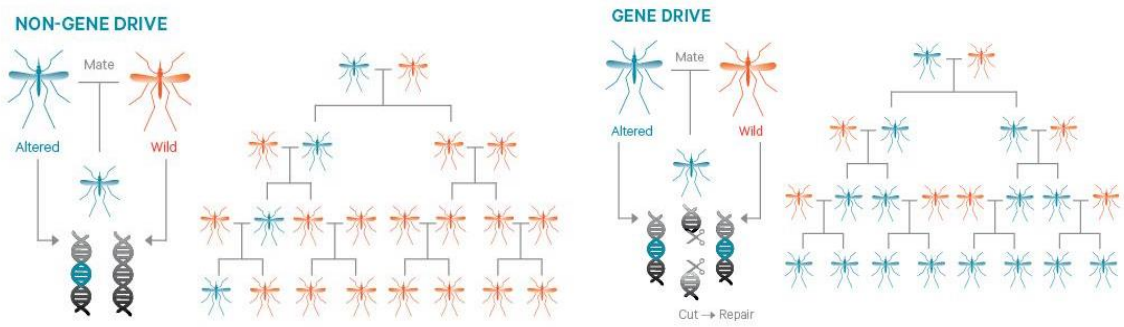
New Zealand has led the way internationally in pest management, incorporating significant biological control. However, ongoing improvement in existing pest management methodologies and novel approaches are required as various classes of pesticides are being withdrawn for ecological and public health reasons [17]. While classical biocontrol has had success in pastoral ecosystems, there now appear to be emerging issues around possible pest resistance and limitation of further opportunities based on regulatory and social requirements [17].

New Zealanders understand the risks they face from invasive species, both economically and environmentally. To achieve significantly reduced impacts, greater diversity will be needed in available management tools. This has been accentuated by the recently announced goal to make New Zealand predator-free by 2050, with a focus on mammalian pests in natural ecosystems where the challenge is to achieve landscape level eradication. New Zealand is already at the forefront of developing new pesticides, trapping technologies, and biological control technologies, as well as using Trojan females and sterile insect techniques [33-35] (described below). A gene edited gene drive may offer a further opportunity to expand our arsenal for pest control in New Zealand, although the development of gene drives is still very much in its infancy, and possible implementation of a gene drive approach in New Zealand is still a long way off.

What are gene drives?

CRISPR gene editing can be used to create a 'gene drive' to spread a gene rapidly through generations. In sexual reproduction, one set of chromosomes is provided from each parent and combined in their offspring. If one set of chromosomes contains a 'gene drive' it will cut the partner chromosome that lacks the gene drive and copy itself onto this chromosome. In this way gene drives are a genetic system with the ability to 'drive' themselves and nearby genes through populations of organisms over many generations [1]. For example, in normal sexual reproduction, offspring inherit two versions of every gene, one from each parent. Each parent carries two versions of the gene as well, so chance (50:50) normally governs which particular variant of the gene will be passed on. But 'gene drives' ensure that a certain gene will almost always be passed on, allowing that variant to spread rapidly through a population (see Figure 1). In this way it would be possible, for example, to spread a gene that suppresses fertility in females in a pest species population.

Figure 1. Example of a gene drive in a mosquito population [1]



The science behind gene drives

In 2003, Austin Burt described how gene drive systems could be an efficient means for population suppression of pest insects [36]. A gene drive is a gene which creates an enzyme which cuts both strands of DNA within a targeted area of the genome and is copied across because of a DNA repair system. This DNA repair system is a 'rescue process', whereby an organism with a double-stranded break in its DNA will try and repair that break by copying any similar sequence it can find in the cell [37]. In the case of the gene drive cut, this leads to the gene drive being copied into the gap made by the gene drive itself. This then leads to guaranteed inheritance of the gene drive to all offspring and is the basis for the gene drive mechanism [36]. To be useful for population suppression, the targeted area for the gene drive should be within a gene essential for viability or fertility of the pest insect. Modelling has shown that suppression is particularly efficient if the gene drive is targeted to a gene essential for females but not males, or a gene required for germ-cell development or reproduction in one sex [36, 38].

The implementation of this system in the past has been hampered by the difficulty in modifying the gene drive to recognize a specified site within a specific genome [39] using previous genetic modification technologies. However, the advent of CRISPR technologies [40] has given new life to the gene drive idea. CRISPR makes use of a bacterial system that allows cells to cut invasive DNA that has been encountered previously [41]. The system consists of a cutting enzyme that can be targeted to any sequence using a small RNA sequence, called a guide RNA [41]. The combination of the DNA cutting enzyme and specific guide RNA that guides the enzyme to a particular sequence, provides the technology to cut and target the sequence required [42, 43]. In bacteria, the guide sequence is derived from an invading virus or other organism. However, the guide sequence can be almost any sequence at all. Using a guide RNA to target a specific sequence in a pest genome, a gene drive mechanism using CRISPR is easily able to target and modify recognition sites [44].

To illustrate a gene drive system, consider the situation of a release of a few genetically modified insects that carry a dominant fluorescent protein marker gene. All the offspring from mating between the fluorescent genetically modified insects and wild type (non-fluorescent) insects will be fluorescent as the fluorescence gene is a dominant one. Most likely these insects will mate with the numerous wildtype insects in the environment. From these matings, in the absence of a gene-drive, only half of the offspring will show fluorescence because of normal patterns of inheritance. In the following generation, even fewer of the population will show fluorescence because crossing with non-fluorescent wild type insects again only result in half the offspring carrying the fluorescence gene (represented in Figure 1). Now consider a release of a few insects carrying the fluorescent protein marker gene linked to a gene drive. As for the original non-gene-drive release, all the offspring from matings with wild type insects will be fluorescent as they will carry the dominant fluorescence gene. In the genome of this first generation, the gene drive will cause a cut in the chromosome that does not contain the fluorescence gene and the insertion of a copy of the gene drive with the fluorescence gene. This repair process is likely to be near 100% efficient; all the gametes will contain a chromosome with the gene drive and the linked fluorescence gene. Thus, when the first-generation insects mate with wild type insects, all the offspring in this second generation will also be fluorescent. Further generations will continue to lead to the marker gene being driven into all offspring (see Figure 1).

Assuming that carrying the gene drive and marker gene have no negative effects on the animal's reproductive fitness in being able to pass its genes to the next generation, a 1% release could theoretically lead to 99% of the local population carrying the marker gene after just 9 generations [36, 38]. For population suppression, the gene drive would alter an essential gene, perhaps a gene essential for, for example, female development or fertility [36].

Scenarios for the use of gene drives for pest control in New Zealand

In view of the challenges around economically sustainable, effective nationwide pest eradication, the potential of genetic technologies, such as gene drive systems could be evaluated. In this review, a series of scenarios is used to examine the potential from such approaches for the control of three key pests in New Zealand. All three scenarios, outlined in Table 1, are discussed in terms of the pest control opportunities they present, along with technical, social and legal ramifications.

Table 1. Three gene edited gene drive scenarios for pest control in New Zealand

	Scenario 1: Insect	***Scenario 2: Possums***	***Scenario 3: Stoats & Rats***
Species	*Vespine wasps, Argentine stem weevil, Australian sheep blowfly*	*Brushtail possums*	*Stoats & rats*
Aim	*Eradication*	*Eradication*	*Eradication*
Justification: Conservation, Agriculture or other	*Conservation & Agriculture. Wasps attack native birds and insects and deplete critical food resources.*	*Conservation & Agriculture: Predator on native birds & invertebrates, eats native plants, carrier for bovine TB*	*Conservation & Agriculture: Predator on native birds & invertebrates, eats native plants, carrier for diseases*
Genetic target	*Fertility or sex ratio*	*Fertility*	*Fertility or sex ratio*
Nature of gene editing	Inactivation of gene	Inactivation of gene? (not yet known)	Insertion of new gene? (not yet known)
Affects target individuals or passed on to future generations	Passed on to future generations	Passed on to future generations	Passed on to future generations
Method of transmission of CRISPR gene edit: Virus, bacteria, compound, other.	Direct injection into embryo	Direct injection into egg cell	Direct injection into egg cell
Are non-naturally arising genes introduced into the genome?	No	No	No

Scenario 1: Insect pests in New Zealand

Invasive wasps

Environmental rationale for control

Two colony-living social wasp species in the genus *Vespula* were accidentally imported into New Zealand and became established here. These colony-living wasps are different from the many solitary species of wasps native to New Zealand, which have evolved here with other insects and plants over thousands of years, and have never been considered a nuisance. The common wasp (*V. vulgaris* (L.)), however, was first recorded from New Zealand in 1921 and became abundant in the 1970s [22]. The German wasp, *V. germanica* (F.), became widespread and abundant in New Zealand after an incursion in 1945 [45]. These Vespine wasps are both now distributed throughout New Zealand, with the common wasp as the dominant social wasp in beech forests [46]. They are especially abundant wherever there are large quantities of honeydew produced by scale insects. This honeydew provides considerable carbohydrate food resources and is plentiful in approximately a million hectares of native beech forest [47]. The world's highest recorded *Vepsula* densities are observed in New Zealand, with up to 40 nests per hectare [48] and numbers exceeding 370 wasps per square metre of tree trunk [49]. The biomass of *Vespula* in honeydew beech forests has been estimated as similar to, or greater than, the combined biomasses of birds, rodents and stoats [50].

The extreme abundance and effects of both these wasps has resulted in them being listed amongst '100 of the World's Worst Invasive Alien Species' [51]and as a 'critical issue' for New Zealand entomology [52]. Their large densities exert intense predation pressure on native invertebrates. For example, vulnerable species of native caterpillars were observed to have almost no chance of surviving to become adults during times of peak wasp population densities [53]. Similarly, the probability of an orb web spider surviving until the end of a wasp season is

effectively nil [54]. They are strong competitors with native predators [55], and these competitive effects over a short evolutionary period may have even altered the morphology of native species [56].

Economically, a recent analysis suggested these wasps annually cost approximately $133 million to the New Zealand economy [57]. The direct economic impacts of wasps are largely associated with their predation on bees, with flow-on effects associated with impacts on pollination (in 2015 approximately 20% of beehive losses in the North Island were due to wasp attack [58]). This economic review also suggested wasps have substantial impacts on animal health, forestry, arable farming, horticulture, tourism, human health and even traffic crashes [57]. Wasps are one of the most dangerous and lethal animals for humans, and they periodically kill New Zealanders; approximately 1,300 people per year are estimated to seek medical attention as a result of wasp stings throughout New Zealand [59, 60].

Current control options

Effective wasp control options are currently limited to small-scale operations involving pesticides or other chemicals (e.g. petrol). These pesticides may be effective on relatively small scales but the use of toxins over large areas such as the 1 million hectares of beech forest currently overwhelmed with high wasp numbers is impractical. Prior attempts at self-sustaining options that would be suitable for such large area, such as biological control, have been unsuccessful [46, 61].

Potential future approaches

A variety of additional and 'next-generation' pest control approaches have been proposed and are being developed for wasps, funded through New Zealand's Biological Heritage National Science Challenge. These approaches include the use of the Trojan female technique, which utilizes the release of females with naturally occurring mitochondrial DNA defects that cause male infertility, and is seen as a novel and humane approach for pest population control [33]. Other approaches in the National Science Challenge include gene silencing[4] technologies, the use of pheromones for mating disruption, which require annual replacement and use at each site, or biological control options [59]. These can all form part of a 'toolbox' approach that can be used in combination. The individual limitations of each approach highlight the need to expand the 'toolbox' to discover and refine new technologies based on a good biological understanding [17].

Another potential approach is the sterile insect technique, which involves the release of large numbers of sterile insects that mate with an established insect population, leading to an effective reduction in that population. In these techniques, some of which use genetic modification to create the sterile insects, a huge number of insects must be released to ensure that matings with sterile insects are more common than those between unmodified fertile insects. The sterile insect technique has been an effective approach for eliminating screw-worm, medfly and the Mexican fruit fly [62], and has recently been used to control mosquito populations in Brazil [63]. This technology has not been used broadly in New Zealand [64], perhaps because of the large number of insects needed for release, and the large cost associated with their production. In addition, social insects have only one reproductive individual per colony and so the impact for wasps of introducing a large number of sterile males in the region is uncertain.

Technical/scientific considerations of gene drives

The development of a gene drive system in wasps using CRISPR faces a number of challenges. Current gene drive methods would require genetic modification of the Common or German wasp genome, a technology not previously developed. Genetic modification of honeybees [65, 66] using CRISPR based approaches has been carried out, and given the similarities of social wasps and bees, it seems likely that this technical barrier will be able to be overcome. In both cases, microinjection of honeybee eggs or larvae was required to achieve transformation [65, 66]. Some understanding of the basic biology of wasp embryos will also be required for transformation to be achieved.

Another set of barriers to the development of gene drives in wasps is the nature of wasp genetics and their social organisation. Vespine wasps genetically are quite unlike other pest species already targeted by gene drive systems. These wasps, like many wasp species, have haplodiploid sex determining systems, meaning males are haploid (have one copy of their genome) and females are diploid (have two copies). Males develop, like clones, from unfertilised eggs laid by the queen. The alternative haploid and diploid generations may have significant, unknown consequences for the inheritance of a gene drive system.

The social organisation of the wasp hive, with a single queen and non-reproductive workers is also a critical factor in the development of gene-drive for these species. Rather than the approach used in mosquitoes of trying to spread a

[4] A gene silencing pesticide uses double stranded RNA to prevent the operation of targeted genes, and is applied as a pesticide.

gene drive that damages reproductive fitness in a population [11, 14], a gene drive system might fail if queens made defective by a gene drive system do not spread their genes, ensuring the gene drive will be rapidly removed from the population with little pest-control benefit.

Containing complex eusocial insect species (i.e. those with different worker castes, overlapping generations, and cooperative care for their young) is challenging and so it seems likely that computer modelling will be required to assess the potential impact of a gene drive system in a vespine wasp species, and to determine the optimum efficiency of a gene-drive approach in achieving wasp extinction. Computer modelling will also be required to understand how many modified wasps might need to be released, and where, to have the most significant effect.

International considerations
While *Vespula* wasps in New Zealand are a critical pest, in their native European range they are valued and important components of the ecosystem. Social wasps were not introduced deliberately to New Zealand, but have hitchhiked here [45], presumably in import cargo. Given this route of introduction, the use of any gene drive system must take into account the possibility that modified wasps might be transported to regions where these wasps are valued. While New Zealand would greatly benefit from eradication of these pests, their extinction here must not mean global extinction of the entire species.

Regulatory considerations
Genetically modified animals are defined as new organisms under the HSNO Act, and therefore wasps containing gene drive systems would be classified as 'new organisms'. Risk assessments of organisms produced through gene drive systems would be carried out under the provisions of the HSNO Act on a case-by-case basis by the Environmental Protection Authority. Importation of wasps with gene drives would also be regulated under the Biosecurity Act 1993.

Other possible insects of focus

Argentine Stem Weevil
Arthropod pests include such species as the Argentine Stem Weevil (*Listronotus bonariensis*). The Argentine Stem Weevil is native to Brazil, Uruguay, Argentina, Bolivia and Chile, and is a pernicious pest of pasture grasses that costs NZ up to $250 million p.a. [67]. Biocontrol combined with endophyte-based plant resistance[5] has kept the pest in check [68], but the effectiveness of the biocontrol agent (the parasitoid wasp *Mictroctonus hyperodae)* is decreasing, probably though genetic resistance arising from continual selection pressure [69, 70]. This is a critical problem, as it is possible that the full cost of the Argentine Stem Weevil may fall on New Zealand's pastoral industries. Thus, there is good reason to consider the use of genetic technologies.

Australian sheep blowfly
Despite its name the Australian sheep blowfly is native to Africa and North America. The blowfly causes large lesions on sheep and, left untreated, can prove fatal to the animal. It has huge animal welfare implications in NZ and Australia. The Australian blowfly is expected to have an increasing impact, both in incidence and in geographical spread, as a result of climate change. In contrast to wasps and weevils, development of a gene drive for genetic control of the Australian sheep blowfly *Lucilia cuprina* should be relatively straightforward. This is because the technology for germline (or hereditary) modification has already been developed [71, 72]. The technology, first developed in New Zealand, has since been adapted to the New World Screwworm, a blowfly that is a major pest of livestock in the Americas [73]. Further, the *transformer* gene has been shown to be essential for female but not male development [74] and thus would be a good target for a gene drive. Genetically modified strains of *L. cuprina* have been developed that produce only males, which could be used for a genetic control program [75, 76]. However, these strains have not been adopted by the sheep industry in New Zealand or Australia because of the rearing and distribution costs of their use in an eradication campaign, and the perceived difficulty in obtaining regulatory approval. A gene drive for population suppression would be much more economical as at least 100 fold fewer flies would need to be released [77].

New pests
Important arthropod incursion threats exist overseas that are still not present in New Zealand, but which could arrive. Species such as the Queensland fruit fly (*Bactrocera tryoni*), the brown marmorated stink bug (*Halyomorpha halys*),

[5] An endophyte is a bacterium or fungus that lives with in a plant without causing disease. These endophytes can enhance resistance of host plant against insect herbivores by production of defensive compounds in the plant

and the glassy winged sharp shooter (*Homalodisca vitripennis*), would have major impacts on our predominantly agricultural economy if they became established here, attacking grapes, kiwifruit, apples, citrus and stone fruit, corn and many other valuable crops. Gene drives, because of the research needed to develop them, are unlikely to be useful as first-responses to a biosecurity incursion, but given that many pest species present biosecurity risks overseas, it may be possible in the future to utilise a gene drive developed for control elsewhere. For example, gene drive systems are being developed for spotted wing *Drosophila*, a fruit fly that is a major invasive pest of soft skinned fruits such as blueberries[6].

Scenario 2: The brushtail possum

Environmental rationale for control

Perhaps New Zealand's most significant mammalian pest is the brushtail possum (*Trichosurus vulpecula*). This marsupial was first brought to New Zealand from Australia with the aim of establishing a fur industry in 1837 [78]. The possum, as it is known in New Zealand, found an environment with few of the challenges of Australia and grew to plague proportions in New Zealand forests. Along with eating native trees [20] and predating native birds [79] and invertebrates [80], the possum is also a carrier for bovine tuberculosis [81], and thus possum control is carried out for conservation and agricultural purposes. It is indeed this latter problem that has driven most of the current program of possum control in New Zealand. The ecology of possums in New Zealand is also well known, and has fed into computer models for exploring possum population dynamics under different control scenarios [82]. Consequently, it is possible to model the impacts of a gene drive in controlling possum populations in New Zealand.

Current control options

Possum control costs the New Zealand government approximately $110 million /year [83], much of which is spent on aerial distribution of poison baits. Other approaches, such as traps and bait stations, are also used. These technologies are effective when animals are at high densities but become less effective as densities drop [84]. Gene drives and other genetic solutions may provide an opportunity to add to the 'toolbox' of approaches to achieve national eradication.

Technical/scientific considerations of gene drives

Although valued in their native range in Australia, possums are a pest unique to New Zealand and, as such, little work has gone into the development of novel methods of possum control beyond our shores. Over about twenty years, major projects were run in New Zealand, focused on establishing immunocontraception as a tool for possum control, which uses an animal's immune system to prevent it from fertilizing offspring [85]. While these projects were ultimately wound up, they did provide knowledge of possum reproduction and genetics [21] that may be useful in the era of gene editing and gene drives.

One key barrier that needs to be solved in possums, and is necessary for a gene drive, is the ability to genetically modify the organism, a feat never achieved in a marsupial. To do so would require the generation of reasonable quantities (100-1000s) of oocytes. Techniques for superovulation, and implanting embryos [86, 87] into possums have been developed as part of a reproductive control approach to possums [88], and could be used to generate oocytes for manipulation.

If genetic modification of possums is possible, there will be a need to identify what genes or processes should be targeted for a gene drive system. In comparison to the mouse, little is known about functional genetics in marsupials, mainly due to the lack of a well-established model system. Several marsupial genomes have been sequenced [89], providing a resource for further genetic work, but understanding the function of marsupial genes is only making slow progress. Some potential vulnerabilities are known, particularly around reproduction, milk production, and water balance, but there is still a lot of work to do to determine the viability of such targets.

With no well-established marsupial model system, the best option may be to adapt gene drives developed in mice that target genes or processes that are similar in possums. To this end, sequencing the possum genome, now underway as part of the Biological Heritage National Science challenge, is an important and necessary first step in developing a potential gene drive.

[6] https://swdmanagement.org/

The use of possums with gene drives to control wild possum populations would require very large numbers of altered animals to be bred and released (1-10% of the wild population). Taking an average density of around one possum per hectare [90, 91], it would require a quarter of a million altered possums to be distributed throughout the country for a 1% release. This would involve successfully putting one altered possum into every 100 ha, including rugged back country.

International considerations
One area of concern is around the control and containment of a possum gene drive. As envisaged the gene drive would be specific to possums, likely targeted to a specific vulnerability such as fertility, with the only organisms affected being the offspring of those possums that mate with a possum possessing the gene drive. The spread of the gene drive would occur through the possum population as large numbers of gene drive possums were distributed throughout the country, and the possums disperse. This would be effective for the goal of widespread control and eradication in New Zealand. However, there would likely be an issue for Australia if a gene drive possum were to find its way or be deliberately released there, because in Australia brushtail possums are a protected species and an important part of many Australian ecosystems. While the likelihood of release may be extremely small, even the prospect of such an incident suggests the need for a means to turn off a gene drive. Currently, the only mechanism available to deliberately switch off a gene drive is to use another gene drive. However, recent work suggests that, over time, evolution will work to thwart gene drives (see below), so the issue of rare escapees may be less of an issue than anticipated. Nonetheless mechanisms to switch off a gene drive need to be thoroughly explored.

Regulatory considerations
As for wasps, genetically modified possums are defined as new organisms under the HSNO Act, and therefore possums containing gene drive systems would be classified as 'new organisms'. As with wasps, risk assessments of organisms produced through gene drive systems are carried out under the provisions of the HSNO Act on a case-by-case basis by the Environmental Protection Authority. In addition, the Animal Welfare Amendment Act (No 2) 2015 has amended the meaning of *manipulation* and includes reference to *genetic modification* and *killing*. The implications of this Act for this scenario are unclear for its use in pest management/control/ eradication, as 'genetic modification' and 'biological product' are not defined in the Animal Welfare Act.

Scenario 3: Rodents and stoats

Environmental rationale for control
Environmental rationale for control like possums, stoats are a predominantly New Zealand problem, with the Orkney and Shetland Islands the only other place on the globe that shares the problem of invasive stoats [92]. Stoats (*Mustela erminea)* are ferocious predators that do significant damage to many of our native bird populations and have contributed to the extinction of five native species [93]. Rats are also a very serious pest problem. In New Zealand there are three rat species: the ship or common rat (*Rattus rattus*), the Norway or brown rat (*Rattus norvegicus*) and the Polynesian rat or kiore (*Rattus exulans*). Of the three, the ship rat is of greatest conservation concern, but all prey on native species [94].

Current control options
These pests in New Zealand are currently controlled in many different ways depending on the target species, including the widespread use of biodegradable 1080 poison (sodium fluoroacetate), a naturally occurring metabolic poison most effective against mammalian pests [95]. 1080 is a cost-effective and safe pest control tool [96], especially when distributed by air in rugged, heavily forested terrain where trapping is not viable. However, its use remains controversial in some sections of the community [97]. Other pest control measures include innovative new approaches to trapping, including the development of self-resetting traps [98]. Technologies for identification of pests, and targeted removal have also improved [99] and many of these technologies are now available to the general public.

Current pest control measures, as demonstrated by the removal of pests from large offshore islands, are effective; but they are relatively expensive and take a lot of planning [17, 100]. Given the alternatives of a broad-range poison dropped from the air, and expensive and intensive trapping campaigns, gene-drive solutions could provide another avenue for pest control [44].

Technical/scientific considerations of gene drives
While New Zealand researchers have spent decades understanding the ecology, reproduction and, more recently, the genetics of possums, researchers are less well informed about many of these key issues for stoats [101]. One

potentially promising avenue to explore is to harness the significant efforts made in understanding the reproduction and genetics of mink, a related species valued for its fur that is farmed in parts of the Northern hemisphere [102, 103].

Unlike possums and stoats, rats are global pests that are implicated in food spoilage, the spread of diseases of global concern e.g. bubonic plague, and are a key conservation threat around the globe [104]. Thus, New Zealand might not have to solve the problem alone and active efforts are underway to tap into international initiatives now aimed at establishing gene drives for the control of invasive rodents [105]. Rats are also among the best-studied mammals, so there is no shortage of knowledge on reproduction or genomics, although most of this knowledge comes from the Norway rat, a well-established lab model that was among the first mammal to have its complete genome sequenced [106]. Less is known about the ship rat, although it has just had its genome sequenced by a New Zealand team, as a legacy project from the Allan Wilson Centre, which should provide an important stepping stone towards the challenge of establishing a gene drive for rats [107].

While establishing gene drives in rats will be less challenging than for stoats and possums, there are still significant practical barriers to establishing such a system. One of these is that rats are surprisingly hard to genetically manipulate [108]. Huge efforts have gone into solving this issue, with some progress made in recent years [109, 110]. However, this may be a major challenge to the use of gene drives for controlling rodents in New Zealand, and that mice (also a significant pest) might be the easiest species to target in the first instance.

Several international groups are looking to develop gene drive solutions for mice. One of the most advanced is a project that aims to link a sex determining factor to a naturally occurring gene drive to produce mice that produce predominantly male offspring [111]. While feasible in theory, there are multiple questions, as yet unanswered, that may thwart the efforts to use these in the wild to achieve population control [112]. For example, researchers do not yet know if the health, survival and reproductive success of mammalian species carrying such modifications might be impaired and how frequently mutations might arise in the gene drive or its cargo gene that could disable them. Robust modelling to explore the possibilities by which gene drives may fail, need to be undertaken in a similar way to those for insect systems [8].

As with possums, the use of gene drives to control wild populations of rodents and stoats would likely require the breeding and repeated release of very large numbers of altered animals over large areas.

International considerations
Globally, while rats are pests in many contexts, they are also important providers of ecosystem services e.g. pollination or critical elements of ecosystem food webs. Eradicating rats in New Zealand, where our ecosystems were free of rodents up until human arrival around 800 years ago, may have few knock-on effects. However, in other parts of the globe the effects on natural systems might be very different. Rats are very good invaders, disperse well, and hybridise with closely related species, making the accidental release and spread of gene drive modified rats a serious consideration. Stoats are less likely to be inadvertently spread, but they are an important animal in northern European ecosystems, so even the prospect of dispersal from New Zealand will mean the need for a means to turn off the gene drive.

Regulatory considerations
As for wasps and possums, genetically modified animals are defined as new organisms under the HSNO Act, and therefore stoats and rats containing gene drive systems would be classified as 'new organisms'. Risk assessment of organisms produced through gene drive systems are carried out under the provisions of the HSNO Act on a case-by-case basis by the Environmental Protection Authority. As with the use of a gene drive in possums, the implications of Animal Welfare Amendment Act (No 2) 2015 for this scenario are unclear for its use in pest management/control/ eradication, as 'genetic modification', 'biological compound' and 'management' are not defined in the Animal Welfare Act.

Social considerations

Social license to operate

Relational trust and communication between the public, government, and scientists will need to be healthy for new genetic technologies to be accepted. The idea of releasing a genetically modified organism that leads to the extinction of a species speaks to the darkest fears expressed about GM technology. That leading conservationists have expressed

similar fears[7] only reinforces such concerns. The need to control invasive predators and pests is known, what is problematic is the way it is done and the unknown consequences on an ecosystem. While trapping and shooting are seen as acceptable by some, the use of poisons is more controversial, with protests about the use of 1080, in particular, occurring. In this environment, gene drive technologies might have a place because of their species specificity. Alongside this, there is jurisdiction under the Resource Management Act for local councils to control the use of genetically modified organisms via regional policy instruments[8] and there may be implications of this on the use of gene drive pest control techniques.

Māori cultural considerations

From a Māori perspective, there are concerns that genetic modification, including gene editing, is at odds with Māori tikanga, in that it may interfere with natural processes pertaining to whakapapa and violate the tapu of different species. Māori communities will need to be well informed about the implications, benefits and risks associated with gene editing in pest control. Education and consultation will be central to empowering whānau, communities, hapū and iwi to assess the social, moral, ethical and health considerations of gene editing within different contexts and scenarios.

For the three scenarios, in Māori terms, the ethical considerations relate to whakapapa (of the organism, as well as the relationship/kinship between humans and other species), tika (what is right or correct), manaakitanga (cultural and social responsibility/accountability, e.g. to other nations who value wasps), and mana (justice and equity) [113]. Other relevant Māori values include tapu (restrictions), tiakitanga (guardianship), and whānaungatanga (support of relatives). Implicit in those considerations would be the question of who stands to benefit from the introduction of a gene drive in this scenario; what are the risks to the ecosystems of other nations; and where do Māori accountabilities lie in terms of the outcomes [114]. In addition, broader impacts on Māori also need consideration, including any negative financial impacts on whānau that may arise, and the assurance of Māori participation in decision making regarding use of these technologies.

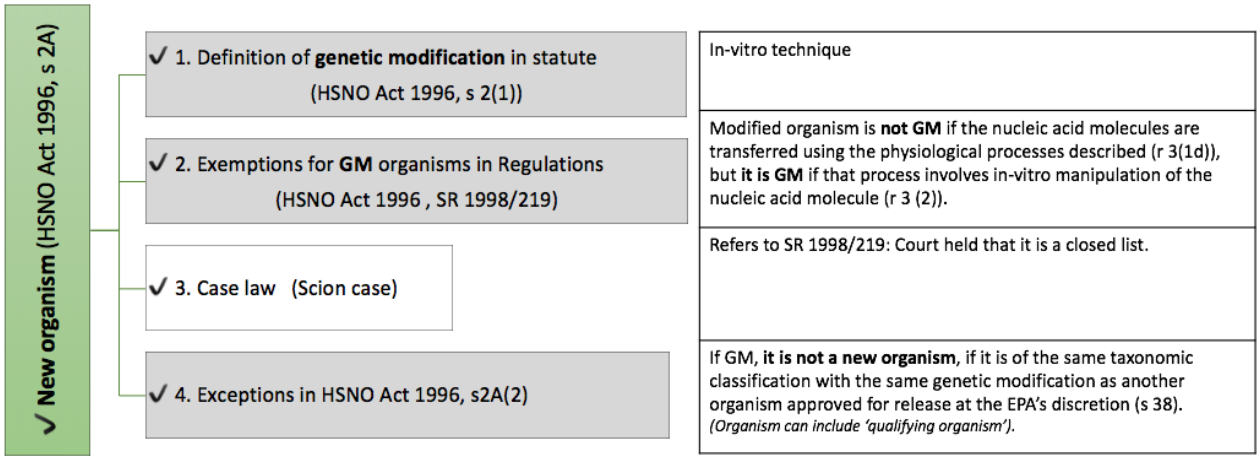
As part of this project, Māori perspectives and broader cultural contexts are being sought by the Panel in a parallel process.

New Zealand regulation of the use of genetic modification for pest control

Genetic modification in New Zealand, such as using gene editing on a pest to include a gene drive, is regulated primarily by central government through the Hazardous Substances and New Organisms Act (1996) (HSNO Act). Gene drives will be regulated by the HSNO Act if they come within the definition of an 'organism' and 'new organism' in this Act. 'Organism' is defined in the HSNO Act and includes a genetic structure (other than a human cell) that is capable of replicating itself, whether that structure comprises all or part of the entity[9]. The definition of 'new organism' includes genetically modified organisms (GMOs) and organisms belonging to species that were not present in New Zealand prior to July 1998[10]. The definition of a GMO is expressly defined in supporting regulations[11], but otherwise the HSNO Act defines GMOs as 'any organism in which any of the genes or other genetic material have been modified by in vitro techniques; or are inherited or otherwise derived, through any number of replications, from any genes or other genetic material which has been modified by in vitro techniques' (see Figure 2). The EPA can make a rapid assessment for 'low risk genetic modification'[12].

[7] http://www.etcgroup.org/files/files/final_gene_drive_letter.pdf
[8] http://www.mfe.govt.nz/more/hazards/risks-new-organisms/what-are-new-organisms
[9] HSNO Act, s2(1)
[10] HSNO Act, s2A
[11] HNSO Act, SR 1998/219
[12] HSNO Act s 41(c) and SR 2003/152 r 4

Figure 2. Summary of the process determining a new organism according to the HSNO Act



It is unlawful to import, develop, field-test and release any 'new organism' without approval from the Environmental Protection Authority. If there is uncertainty about whether an entity is a GMO (or even an 'organism' or 'new organism'), there is a formal determination the Environmental Protection Authority can undertake pursuant to the HSNO Act (s 26). The HSNO Act is enforced at the New Zealand border under section 28 of the Biosecurity Act 1993.

The case studies evaluated in this paper highlight a complicated regulatory framework with many 'grey' areas. The current regulatory framework may permit gene editing for pest control in containment and for release, as each application is assessed on a case by case basis. An application would need to be made to the Environmental Protection Authority (EPA) for approval under the HSNO Act for development and field testing in containment. Further applications would be required for release from containment, and controls may be imposed by the EPA. The HSNO Act further prescribes the mandatory assessment and decision-making process for applications, including a risk assessment of the new organism's effect on native species, biodiversity, and natural habitats[13]. The EPA will decline the application if the minimum standards cannot be met.

The following legislation and associated amendments require evaluation alongside the Hazardous Substances and New Organisms Act 1996, for pest control using gene editing technologies (See Figure 3):

- Animal Welfare Act 1999 and the Animal Welfare Amendment Act (No 2) 2015 (Animal Welfare Act)
- Agricultural Compounds and Veterinary Medicines Act 1997(ACVM Act)
- Biosecurity Act 1993 (Biosecurity Act) Conservation Act 1987 (Conservation Act)

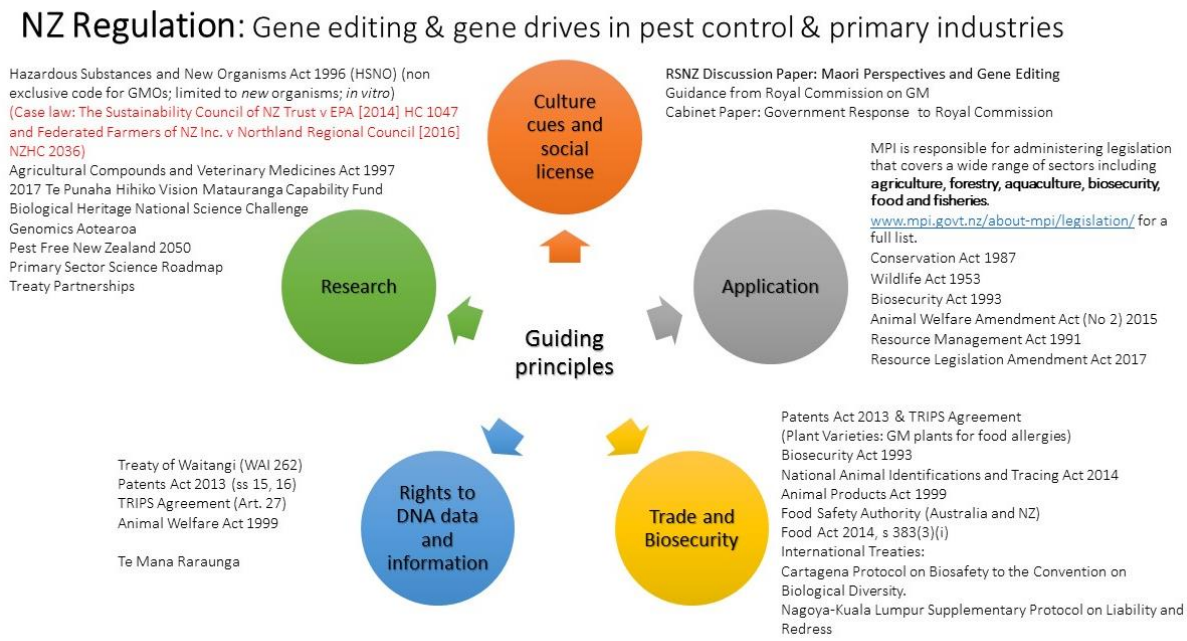
[13] HSNO Act, section 36. Minimum standards:

The Authority shall decline the application, if the new organism is likely to—
(a) cause any significant displacement of any native species within its natural habitat; or
(b) cause any significant deterioration of natural habitats; or
(c) cause any significant adverse effects on human health and safety; or
(d) cause any significant adverse effect to New Zealand's inherent genetic diversity; or
(e) cause disease, be parasitic, or become a vector for human, animal, or plant disease, unless the purpose of that importation or release is to import or release an organism to cause disease, be a parasite, or a vector for disease.

HSNO Act, section 37. Additional matters to be considered:

The Authority, when making a decision under section 38, shall have regard to—
(a) the ability of the organism to establish an undesirable self-sustaining population; and
(b) the ease with which the organism could be eradicated if it established an undesirable self-sustaining population.

Figure 3. New Zealand legislation influencing gene editing technologies in animals and organisms



Regulatory process

There is, however, no clear regulatory framework for specifically evaluating gene drive technologies as a method for controlling pests

HSNO Act

The HSNO Act has been described as a comprehensive, strict and rigorous code [115] and additional amendments sought to increase restrictions following release of the organism, including reassessment (section 63), conditional release (section 38) and clarifying the meaning of genetically modified organism (Statutory Regulation 1998/219, r 3(ba)).

Regulation of genetically modified organism under the HSNO and Resource Management Acts have been challenged in the New Zealand courts. Most notable was the Scion case[14], which clarified the classification of gene edited organisms as 'genetically modified organisms' for the purposes of the HSNO Act[15]. The Northland Regional Council case clarified that Regional Councils control the use of genetic modification through their regional policies and district plans under the Resource Management Act[16]. Both of these cases have wide ranging implications for New Zealand and are not limited to genetically modified crops. Central government consequently amended regulations to clarify the exemptions to the HSNO Act (EPA, HSNO Act SR 1998/219). Central government has also amended legislation (Resource Legislation Amendment Act 2017) introducing a new regulation making power to prohibit or remove specified rules or types of rules by Territorial Authorities that would duplicate, overlap, or deal with the same subject matter that is included in other legislation. Rules that regulate the growing of GM crops do not apply[17].

[14] *The Sustainability Council of New Zealand Trust v The Environmental Protection Authority* [2014] NZHC 1067.

[15] The High Court Judge ruled that the exemption list in the Regulations is a closed list. The conclusion was based on an interpretation of the language of the Regulation and that the regulations did not prescribe factors for the EPA to add other techniques to the list. The Judge interpreted the HSNO Act and the regulations as not implicitly giving the EPA discretionary power to add to the exemption list and ruled that the EPA could not expand the exemption list to include techniques similar to chemical mutagenesis and adding to the exemption list was a political decision, not an administrative decision.

[16] *Federated Farmers of New Zealand v Northland Regional Council* [2015] NZEnvC 89.

[17] Resource Legislation Amendment Act 2017, s 360D.

New Zealand has a network of legal instruments and treaties that require consideration alongside review of the HSNO Act, when introducing new biotechnologies. These include the Treaty of Waitangi[18] (the Waitangi Tribunal Report recommending that Māori have a greater interest in genetic modification[19]) and the Resource Management Act 1991 (the ability of regional councils to control the use of genetically modified organisms through regional policy statements or district plans). A recent amendment to the Resource Management Act has introduced a new provision that allows the prohibition or removal of certain rules that would duplicate, overlap with, or deal with the same subject matter that is included in other legislation[20].

Agricultural Compounds and Veterinary Medicines Act 1997 (ACVM Act)

In addition to the HSNO Act, the Agricultural Compounds and Veterinary Medicines Act 1997 (ACVM Act) has possibly the greatest effect on this technology. Depending on the interpretation of 'veterinary medicine', a gene drive intervention could be regulated under the ACVM Act and thereby assessed under the Conditional Release and Release statutory provisions in the HSNO Act (potentially bypassing the Containment provision).

A veterinary medicine, according to the ACVM Act (s 2(1)), means any substance, mixture of substances, or biological compound used or intended for use in the direct management of an animal.

- Note that direct management is not defined in the Act.

The HSNO Act defines a 'qualifying veterinary medicine' as a veterinary medicine that is, or contains, a new organism and meets the criteria set out in section 38I(3) of the HSNO Act.

- A new organism has the same meaning in the ACVM Act and in section 2A of the HSNO Act.
- A qualifying organism means a new organism that is or is contained in a qualifying veterinary medicine (HSNO Act, s 2(1)).

Royal Commission on Genetic Modification

The 2001 Royal Commission on Genetic Modification report concluded that, 'New Zealand should preserve its opportunities by allowing the development of genetic modification whilst minimising and managing the risks involved.' The Royal Commission's overall strategy was supported by the Government. However, the Government required that research practices adhere to strict safety guidelines, including secure containment, thereby limiting discretion when determining the conditions of the research. Government also required a precautionary approach to be exercised in the operation of the HSNO Act (s 7): '*All persons exercising functions, powers and duties under this Act including, but not limited to, functions, powers, duties under sections 28A, 29, 32, 38, 45, and 48, shall take into account the need for caution in managing adverse effects where there is scientific and technical uncertainty about those effects'*.

International governance

The Cartagena Protocol on Biosafety (the Biosafety Protocol) is designed to address the biosafety risks presented by GMOs when these move across borders. Established under the Convention on Biodiversity, this international treaty is founded on the principle of prior informed consent with respect to the transboundary movement of living modified organisms (LMOs). It puts a duty on an exporting party to seek prior informed consent from the destination country (Article 7). However, the procedures only work for intended movements across the border of a single nation. The protocol does not define best practice guidelines, for example, for standards for assessing effects, estimating damages, or mitigating harms [75]. While these may be seen as 'gaps', it could also be argued that best practice

[18] NZ Law Commission (2002). *Liability for loss resulting from the development, supply, or use of genetically modified organisms.* Study Paper 14.The Law Commission looked into the issue of liability for loss resulting from GMOs and described the adverse cultural effects of GM on Maori: "*Concerns have also been raised by Maori, which arise from a different belief structure, Although the basis for many of the Maori cultural objections to genetic modification vary among iwi, they are usually based around impacts on whakapapa, mauri, kaitiakitanga and rangatiratanga. The traditional Maori worldview considers all parts of the natural world to be related through whakapapa. Genetic modification risks interfering with such relationships, and threatens the sanctity of mauri (life principle) and wairua (spirit) of living things. Concluding that genetic modification may affect Maori's ability to be kaitiaki (guardians) of their taonga and particularly their ability to care for valued flora and fauna*".

[19] Anna Kingsbury (2011). Intellectual Property. WAI 262. *NZ Law Journal*, September 2011, 273.

[20] Resource Legislation Amendment Act 2017

guidelines are best left out of such rigid instruments. The related Nagoya-Kuala Lumpur Supplementary Protocol on Liability and Redress identifies response measures in the event of damage to the conservation and sustainable use of biological diversity resulting from living modified organisms that result from transboundary movements. It does not define rules governing liability and redress for damage, but requires Parties to either apply their existing general law on civil liability or develop specific legislation that addresses (as appropriate): damage; standard of liability (including strict or fault-based liability); channelling of liability where appropriate; and the right to bring claims.

Concerns around the potential unintended impacts of gene drives were highlighted in a US National Academies of Science review of gene drives [116] which noted:

"Gene drives do not fit well within the existing regulatory logic of confinement and containment because they are designed to spread a genotype through a population, making confinement and containment much more difficult (or even irrelevant) and the environmental changes introduced by release potentially irreversible.... Research on gene drives is global. Responsible governance will need to be international and inclusive, with clearly-defined global regulatory frameworks, policies, and best practice standards for implementation."

This will have implications for New Zealand's international social license to develop gene drives that could potentially threaten other countries' native species.

Safety mechanisms for gene drives

In their 2014 article, Esvelt and colleagues outlined a variety of uses for CRISPR gene drives in human health, agriculture and the environment [44]. Importantly, the authors noted that the potential efficiency of CRISPR gene drive systems posed a requirement for a high certainty of laboratory containment before they are deemed safe to move out of the laboratory. They suggested parallel development of a 'reversal' gene drive that would restore the original gene, but with a slightly different sequence that would not be targeted by the original guide RNA.

Although Esvelt *et al.* [44] had highlighted the need for safeguards, the ease and efficiency of the CRISPR-mediated gene drive in the fruit fly *Drosophila melanogaster* [7] was a surprise to many. These results have led to wide discussion of the risks of gene drives. Recently, scientists working on CRISPR [117] recommended a number of safeguards, including:

1. Perform gene drive experiments outside the ecological range of the organism (e.g. *Anopheles* mosquito in Boston). Consequently, if any individuals do escape the laboratory they would likely perish and/or have no potential mates.
2. Use a laboratory strain that cannot reproduce with wild organisms.
3. Have a high level of laboratory containment, using multiple substantial physical barriers. In practice, this could be a higher level of containment than is currently recommended for transgenic strains of the species of interest (i.e. for organisms containing genetic material into which DNA from an unrelated organism has been artificially introduced). For example, using air blast fans and higher precautions to prevent escape (e.g. sealing possible escape routes).

In 2016, another safety mechanism was developed, called the 'daisy-chain' gene drives [118], which gradually vanish after 50-100 generations. To create these gene drives that don't spread indefinitely, the gene drive is split into three or more parts to create a 'daisy chain'. Each part contains a genetic element that drives the next element in the chain so that element A can only copy and paste itself if element B is present. Element B can only copy and paste itself if element C is present. And element C, crucially, cannot copy and paste itself at all – it can only spread by normal breeding, to half of offspring. When the gene drive animals are released, they carry all three elements. Then, when they mate with their wild counterparts, all the offspring will inherit element A and B, but only half will inherit element C. In the following generations, element B will spread rapidly and A will spread even more rapidly, but C will gradually die out. Once it does, B will start to disappear, and finally A will too. By adding more elements to the daisy chain, the gene drive could be made to persist longer in the wild. This could allow the use of gene drives locally without the worry about the risk of worldwide spread.

Evolutionary resistance to gene drives

The promise of gene drives lies in their inherent ability to rapidly move target alleles to fixation in a very short period of time to generate a desired effect on a population. If all individuals within a population are susceptible to the gene drive linked gene, then it is predicted that the gene drive version of the gene will rapidly spread. However,

substitutions, insertions or deletions within the DNA adjacent to the gene drive that occur through natural mutational processes or during gene-drive mediated DNA cutting are expected to lead to a resistant version of the gene [8]. Most cells also have an alternative pathway for repairing double-stranded breaks, known as non-homologous end joining (NHEJ) [119]. With NHEJ, the broken ends of DNA are fused together without regard to matching similar sequences. Errors during this repair process can lead to small deletions or insertions in the genetic code, called mutations. In many cell types, this type of repair can outnumber repairs that try to copy similar sequences in the cell. A NHEJ mutation of the gene drive recognition site would suppress its targeting accuracy [36].

Because many resistant versions of the gene will have greater Darwinian fitness than the gene drive gene, population level resistance to the gene drive is expected to appear [8]. In fact this is what was observed in the laboratory-based gene drive experiments on *Anopheles gambiae* mosquitos [14] and *Drosophila* [120].

In addition to the gene drive process generating resistant versions of the gene, it is also predicted that many pest species will harbour genetic variations resistant to the gene drive construct. While gene drive approaches have not been used in the field, many species targeted for control via gene drives harbour significant levels of genetic variation, especially insects which are likely early targets for gene drive. In these cases, under known mutation rates and with large population sizes, mutations in the DNA adjacent to the gene drive sequence are inevitable. If these variants lie within the target region of the gene drive then, as with the mutant gene versions generated though NHEJ, it is expected that these gene versions will be selected for and subsequently lead to individuals resistant to the gene drive. For example, [121] measurements of genetic variation in *Anopheles gambiae* across Africa through whole genome resequencing found that approximately half of the potential gene drive target sites had variants in the wild that would disrupt targeting by the gene drive construct.

How can resistance be overcome? Detailed population genomic surveys of the target pest species would need to be employed to assess variation across all potential gene drive target sites. Ideally, this would include whole genome resequencing to detect the presence of variants across potential target sites. These data would also yield information to guide the identification of alternative target sites in the same gene or alternative genes. This approach would also have the advantage in aiding the prediction of off-target effects. Large numbers of individuals would need to be assayed as resistant versions of genes are expected to be strongly selected for, even from very low initial frequencies [8]. Based on the population genomics results from *An. gambiae* [121], gene drives are unlikely to work unless multiple genes and multiple target sites within those genes are targeted. Increasing the number of target sites in the genome leads to a corresponding increase in the probability of off-target effects with the associated safety and ethical concerns. The use of multiple guide RNAs could also be used to target a wide range of gene variants [14]. Again, this approach requires detailed knowledge of gene variation. A further approach could be to target a conserved region of a biologically essential gene [44].

Another implication of this resistance is that intentionally releasing a resistant gene into a population could be an effective means of reversing the effects of a gene drive [122].

For further information

For more information and resources about gene editing, visit the Society's web pages: https://royalsociety.org.nz/gene-editing/, or contact info@royalsociety.org.nz.

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Attachment H

Gene Editing in the Primary Industries Context

Royal Society of New Zealand

Technical Paper, Oct 2018

Life Sciences Network Inc

Further Submission

Proposed District Plan

Waikato District Council

15 July 2019

October 2018

Gene editing in the primary industries

Technical Paper

Royal Society Te Apārangi Gene Editing Panel

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ROYAL SOCIETY TE APĀRANGI

Background

A revolution in gene editing technologies is making it easier to change genetic material. This has implications for many sectors including healthcare, agriculture and conservation. However, the technology to carry out gene editing and the ideas about how it might be applied are, in many cases, moving ahead of our understanding and regulatory frameworks, and any consensus on the rights and wrongs of how it should be used.

To explore the implications of gene editing technology for New Zealand, Royal Society Te Apārangi has convened a multidisciplinary panel of some of New Zealand's leading experts to consider the implications of gene-editing technologies for New Zealand to:

- Raise awareness of the scientific possibilities and associated public issues of gene-editing technologies to inform debate;
- Provide information and guidance for policy makers to address current and new issues needing to be clarified or resolved;
- Show where gene-editing applications are covered by established policies and regulations and where changes are needed;
- Provide a New Zealand perspective to the global discussion on this technology and identify where global consensus is important.

This paper is one of a series produced by the panel considering the implications of the technology in health, pest control, agriculture and forestry, and is accompanied by a companion discussion paper inviting public feedback, and a fact sheet on how these technologies work and are being used and applied [1].

To help consider the implications for primary production in New Zealand, five scenarios in which gene editing might be used are highlighted, and the implications that might arise are identified. These case studies consider:

- Uses of the technology within and outside the human food chain
- Use of the technology in agricultural plants and animals
- What the potential harms and benefits are.

Contents

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Primary industries in New Zealand

New Zealand, unlike many OECD countries, has an economy and self-image that are closely linked to land and sea-based managed ecosystems and the natural environment. New Zealand's productive capacity has flourished through the introduction of plants and animals, and the managed ecosystems they create are critical to our economy. Nearly 60% of the mainland is used, at least in part, for agricultural production.

In 2016, agriculture, forestry and their respective products contributed $23 billion to the New Zealand economy, almost 10% of GDP[1]. Of New Zealand's top 25 exports in 2017, 12 were agricultural and forestry products, representing 19% of all New Zealand exports, with 48% of these to China, 19% to the EU, 15% to the US, 9% to Australia, 6% to Algeria, and 4% to Malaysia[2]. However, New Zealand's primary industries are under pressure from a changing climate, impacts on the environment, new pests and pathogens, innovations in synthetic foods, competition from other countries' exports and changing market access.

History of genetic selection in agriculture

The success of our agriculture, horticulture, aquaculture and forestry industries has been helped, and will continue to be helped, by our ability to identify, select and breed desirable traits into commercial species. New traits generally arise within a population through spontaneous mutation of genes within the genome of the organism. By selecting for those desirable traits, animal and plant breeders are able to concentrate these traits within the population; a process known as *selective breeding* [1]. This process of selective breeding started as early as the Neolithic period, when early farmers started selecting individual plants and animals with superior traits or performance [2, 3].

In the absence of any knowledge of genetics this would have been a very time consuming and laborious process. Nevertheless, some of the results from this selective breeding were spectacular, such as the selection of maize and wheat. In the case of maize, it is now known that as few as five genetic changes account for the major differences in the size of the flower head (or ear/cob) in comparison with that of its ancient ancestor, teosinte [4], while we know that wheat is a complex hybrid of three different species [5]. Current breeding approaches of crop plants and animals[3] involve a variety of methods to accelerate and refine the selective breeding process. These include selection based on appearance, the use of mutagenic agents, the use of DNA markers in approaches such as genomic selection, marker assisted selection and backcrossing[4] and, in the last 35 years, genetic modification involving the insertion of genes from related and unrelated species.

The discovery of X- and gamma-rays and, in the 1920s the demonstration that they were highly mutagenic, provided a new tool (*radiation induced mutagenesis*) for plant breeders to generate mutations at a higher rate and so create a wider range of variants from which to select for new traits. However, because of the random nature of the changes, generating mutants with desirable traits, or without undesirable ones, remained a challenge.

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[1] Statistics New Zealand. National accounts (industry production and investment): Year ended March 2016. Table 2 (Agriculture, Forestry & Logging, Food manufacturing, Wood & paper manufacturing).

[2] Statistics New Zealand. Goods and Services Trade by Country: Year ended June 2017. Table 4.

[3] https://www.mpi.govt.nz/funding-and-programmes/primary-growth-partnership/completed-pgp-programmes/the-new-zealand-sheep-industry-transformation-project-nzstx/

[4] Screening for genetic markers to identify whether offspring contain a gene of interest

Likewise, experiments in the 1940s demonstrated how certain chemicals such as ethylmethanesulfonate could be used as mutagenic agents (*chemical induced mutagenesis*) to increase the mutation rate to generate random variation in the population from which new plant cultivars could be selected. While the radiation and chemical induced mutagenesis techniques used over the last 75 years [6] have been useful tools for generating variation within a genome, the position and number of induced changes cannot be controlled. Mutagenesis results in many, mostly deleterious, genetic changes requiring sophisticated, and time consuming, screening and selection processes to identify those few organisms which carry beneficial mutations.

Early DNA modification methods were developed in the 1970's, and by the 1980's gene delivery systems such as *Agrobacterium*, enabled the transfer of novel genes into plants. However, the ability to target the gene to a specific site in the genome or to modify specific genes remained very difficult.

Genetically modified (GM) plant crops, made using these DNA modification and gene insertion methods, are now used in production systems for some of the major commodity crops including soybean, corn, canola, cotton, potato, squash, alfalfa, papaya, and sugar beet [7]. This generation of GM crops typically involves the introduction of genes from another species that, for example, confer resistance to insect pests or resistance to specific herbicides to manage weeds. The production area of GM crops is significant and growing (10% of the world's arable land, covering 189 million hectares [7, 8]). Currently, 24 countries grow GM crops. While there are many examples of GM technology being used to generate transgenic animals for research and commercial developmental purposes, there is currently only one example of a genetically modified farm animal in commercial food production (GM salmon[5]).

Te Ao Māori

Like many other cultures, pre-European Māori practiced selective breeding, as evidenced by cold-adapted kumara varieties and tribal narratives. This history of food harvesting and production in Aotearoa New Zealand and their holdings in land and fish-quota have led Māori, in the modern era, to have significant interests in New Zealand's primary sector and, in some cases, direct interests in commercial plant and animal breeding programmes. One example of Māori involvement in plant breeding is the Ngai Tahu-owned company ProSeed, which produces commercial quantities of seed from radiata pine and other tree species. Indirectly, virtually all of the commercially grown non-indigenous species are of interest to Māori entities involved in primary production. Moreover, because Māori have kaitiaki rights under the Article 2 of the Treaty of Waitangi, commercial production systems are of interest to Māori on land over which Mana Whenua iwi ostensibly have rights. Māori also assert kaitiaki rights over indigenous species, including genetic resources, although this is not currently recognised in New Zealand law. The long histories of interaction with indigenous species that have led to specialised knowledge of many indigenous species, in addition to the emotional and spiritual connections with indigenous biota within a broader whakapapa context, further underpin the significance of indigenous species to Māori.

Use of modern gene editing techniques

The recent development of gene editing tools such as CRISPR[6] that enable a broad scope of highly precise changes in the genome are enabling rapid advances in microbe, plant and animal research and

[5] https://www.fda.gov/downloads/AnimalVeterinary/DevelopmentApprovalProcess/GeneticEngineering/GeneticallyEngineeredAnimals/UCM466215.pdf

[6] CRISPR in this paper is being used to refer to the CRISPR-Cas9 gene editing technique.

breeding. These techniques use gene repair mechanisms to insert, remove, replace or modify genes at predetermined sites in the genome [9] (See Box 1). The precision of gene editing technologies has been improving over the last 10 years, substantially reducing the frequency of inserting a replacement gene in an unintended location and in most cases not using, or leaving behind, foreign gene sequences following manipulation [10-15]. In plants, this has resulted in a significant improvement over past genetic engineering technologies [10], which either used bacteria or viruses to randomly transfer the DNA, or involved coating small metal particles with the DNA, and then 'shooting' the particles into cells [16]. In animals, gene editing technology has also resulted in major improvements in accuracy [17, 18], although unintended changes can still occur [19]. With modern gene sequencing, any unintended insertions can be identified and, if undesirable, can be eliminated from the breeding programme.

There are now a number of research examples of the effectiveness of this approach in improving plant traits (e.g. drought tolerance, disease resistance, fruit ripening, grain number and size within the major crop species [23-29]) and animal traits (e.g. angora coat length, increased meat yield, lack of horns and disease resistance [30-34]). This new technology can use existing variation within the plant or animal or introduce gene sequences equivalent to those in related species. Such an approach has an advantage over traditional breeding methods by enabling continuous improvement of elite cultivars and breeds without potentially introducing deleterious versions of genes from crossing and recombination or requiring time-consuming plant and animal breeding to restore the original elite genetic background. In a plant breeding context, gene editing can rapidly generate improved cultivars with no trace of foreign DNA. There is also considerable potential for domestication of new crops that are better adapted to more extreme climate, soil and nutrient conditions [23]. Gene editing is a powerful new breeding tool: it relies on information about the genome of the species; requires bioinformatics tools to interrogate the DNA sequence of the genome; as well as an understanding of the impact that gene editing-induced modifications have on the target gene and other genes and characteristics.

Box 1: Gene editing with CRISPR

Bacteria possess an immune system that recognises invading viral DNA and cuts it up, making the invading virus DNA inactive. This type of natural microbial immune system is known as CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats)[20]. In 2012, it was discovered that, by modifying this mechanism, it was possible to target and cut any DNA sequence and edit genomes in a very precise manner [21]. Cells which have their DNA cut by CRISPR will repair these cuts as 'instructed' if specific DNA repair information is provided. By altering this repair information, it is possible to change a gene of interest, for example, from one that causes disease susceptibility to one that does not [22].

Genomics research in New Zealand

Several New Zealand Crown Research Institutes (CRIs) have been involved in programmes to sequence and improve our knowledge of the genomes of crop plants and domesticated animals of importance to New Zealand's primary production systems. Examples include AgResearch's involvement in sequencing the sheep genome [35] and improving ryegrass genetics [36], Plant & Food Research in sequencing the genomes of apple, pear and kiwifruit [37-39], and Scion's ongoing efforts in sequencing the very large genome of radiata pine[7]. Further, functional genomics research is also being undertaken to identify the genes that underpin important traits in these plants and animals.

The new MBIE advanced genomics platform, "Genomics Aotearoa"[8], is providing advanced genome sequencing and bioinformatics capabilities across New Zealand's universities and CRIs, to keep New

[7] https://www.scionresearch.com/about-us/news-and-events/news/2017/radiata-pine-genome-draft-assembly-completed

[8] http://www.otago.ac.nz/genetics/news/otago659624.html

Zealand crop and animal production at the forefront of technology and land efficiency, respond to pests and diseases, and improve human health. These capabilities are likely to be applied to a range of New Zealand grown species such as cattle, sheep, radiata pine, ryegrass, apples and kiwifruit and, while this information will be critical for conventional breeding scenarios, it will provide some of the underpinning information, such as genome sequences and annotation, needed to implement gene editing.

Genomics Aotearoa is working with Māori to ensure work in this area takes into account Treaty of Waitangi obligations, and to develop culturally informed guidelines for the application of genomics in indigenous species.

Genomics and agriculture internationally

Table 1 lists the crop plant species used for food for which genome sequences are available [37, 39-44]. This number is growing as the cost of genome sequencing reduces, and the speed with which it can be accomplished accelerates.

Table 1: List of agricultural crops that have had their genome sequenced

Scientific name	Common name	Economic importance
Actinidia chinensis	Kiwifruit	Food (fruit)
Beta vulgaris	Sugar beet	Sugar production
Brassica napus	Rapeseed	Oil, animal feed, biodiesel
Brassica oleracea var. capitata	Cabbage	Food (vegetable)
Brassica rapa	Chinese cabbage	Food (vegetable)
Cajanus cajan	Pigeon pea	Food (grain/pulse/bean)
Carica papaya	Papaya	Food (fruit, vegetable)
Capsicum annuum	Hot pepper	Spice
Cicer arietinum	Chickpea	Food (grain/pulse/bean)
Citrullus lanatus	Water melon	Food (fruit)
Citrus clementina	Clementine mandarin	Food (fruit)
Citrus sinensis	Sweet orange	Food (fruit)
Coffea canephora	Robusta coffee	Food (grain/pulse/bean)
Cucumis melo	Melon	Food (fruit)
Cucumis sativus	Cucumber	Food (vegetable)
Elaeis guineensis	Oil palm	Edible oil
Fragaria vesca	Strawberry	Food (fruit)
Glycine max	Soybean	Food (grain/pulse/bean)
Leptospermum scoparium	Mānuka	Food (honey)
Malus x domestica	Apple	Food (fruit)
Musa acuminata	Banana	Food (fruit)
Oryza sativa subsp. indica	Rice	Food (grain/pulse/bean)
Phaseolus vulgaris	Common bean	Food (grain/pulse/bean)
Phoenix dactylifera	Date palm	Food (fruit)
Prunus mume	Chinese plum/Mei	Food (fruit)
Prunus persica	Peach	Food (fruit)
Pyrus bretschneideri	Asian pear	Food (fruit)
Pyrus communis	European pear	Food (fruit)

Scientific name	Common name	Economic importance
Rubus occidentalis	Raspberry	Food (fruit)
Solanum lycopersicum	Tomato	Food (vegetable)
Solanum melongena	Eggplant	Food (vegetable)
Solanum tuberosum	Potato	Food (vegetable)
Sorghum bicolor	Sorghum	Food (grain/pulse/bean)
Theobroma cacao	Cocoa	Food (grain/pulse/bean)
Triticum aestivum	Bread wheat	Food (grain/pulse/bean)
Vaccinium corymbosum	Blueberry	Food (fruit)
Vaccinium macrocarpon	Cranberry	Food (fruit)
Vigna radiata	Mungbean	Food (grain/pulse/bean)
Vitis vinifera	Grape	Food (fruit), beverage
Zea mays	Maize	Food (grain/pulse/bean)

Regulation of gene editing in New Zealand and internationally

Gene editing is considered genetic modification under current law and regulation in New Zealand. That means all uses of the technology must be approved by the Environmental Protection Authority and any releases into the environment are subject to public consultation through a series of hearings. Experience has shown that these hearings can be protracted and expensive.

Many other countries are also grappling with how to define and regulate gene-edited plants and animals, given that many gene-edited organisms will be indistinguishable from those generated by traditional plant and animal breeding processes [45]. For instance, accelerated plant breeding using gene editing, involves an intermediate generation of GM plants where a new gene is inserted to shorten the time to flowering of a plant, speeding up the breeding process (see the apple breeding scenario). The inserted gene is later removed by conventional crossing with other non-GM plants, so that no foreign genetic material remains in the resulting crop [15, 46]. In addition, not all countries are subject to the same international obligations, which has a bearing on the kinds of domestic regulations they have in place[9].

The USA chose to use existing regulatory frameworks to manage genetically modified plants and animals; principally the USDA for plants, the EPA for environmental releases and the FDA for food and animals. The FDA has, for example, co-opted its regulations designed for animal drugs to regulate GM animals. In 2016, USDA approved the cultivation and sale of a gene-edited mushroom and waxy corn[10] without regulation [47]. More recently, the USDA stated that under its biotechnology regulations, it will not regulate, nor has any plans to regulate, plants that could otherwise have been developed through traditional breeding techniques, as long as they are developed without the use of a plant pest as the donor or vector and they are not themselves a plant pest [48, 49]. The FDA on the other hand has indicated in draft guidance released in 2017 that animals with "intentionally altered DNA" (i.e. which are gene edited) would likely continue to be considered and regulated as GMOs[11].

[9] Neither Canada, Australia nor the US are bound by the Cartagena Protocol as the US is not a party to the Protocol, and Canada and Australia have not ratified the agreement. The EU, New Zealand, China and Japan have ratified the agreement.

[10] https://www.pioneer.com/CMRoot/Pioneer/About_Global/Non_Searchable/15-352-01_air_response_signed.pdf

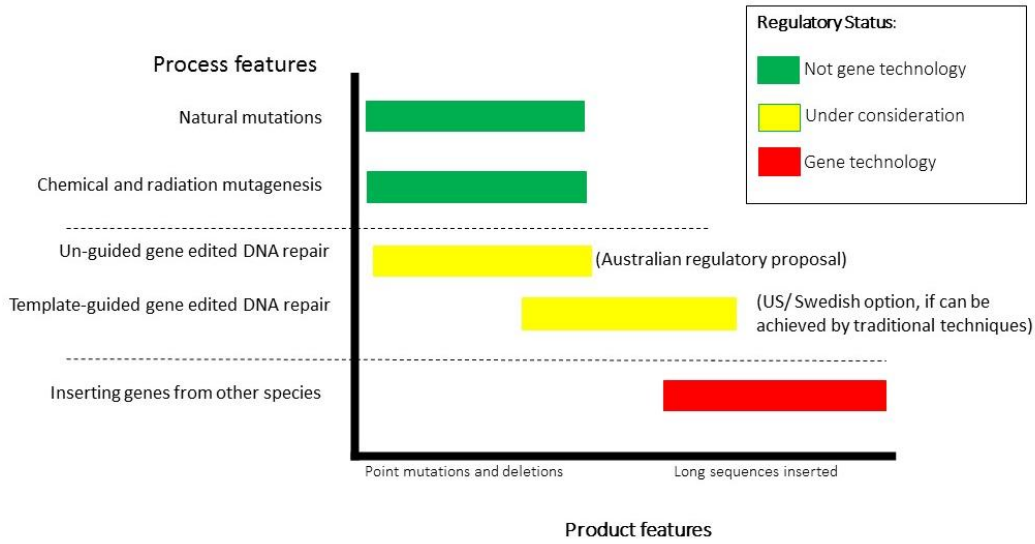
[11] https://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/UCM113903.pdf

In August 2018, an expert committee in Japan has recommended that only gene editing which involves foreign genes should be regulated and that gene editing that involves switching off or deleting genes already present in the genetic code of organisms should not require government approval[12].

Coming to a similar conclusion, the Swedish Board of Agriculture have decided that plants mutated by CRISPR that do not contain any foreign DNA sequences, are exempted from GM legislation[13]. Canada has also decided to regulate on a case-by-case basis focusing on the risks associated with the outcome of the modification (new traits) rather than the process used to generate the change [50]. This trait-based approach is in line with their regulation of other forms of genetic modification and is analogous to the regulation of new medical products, in that it takes into account the context in which the product will be applied [51].

An opinion recently issued by the Advocate General of the European Court of Justice in March 2018 considered that EU GMO regulations were not applicable to certain gene edited plants and animals [52, 53]. European regulations exempt traditional 'mutagenesis' from GM regulations, thereby plants and animals possessing novel traits produced by nuclear radiation or chemical mutagens are not regulated as GMOs. The European Advocate General suggested that the mutagenesis exemption should not be confined to mutagenesis techniques such as radiation and chemical mutagens, as they were understood in 2001 when the original European GMO Directive was drafted, but should also include new techniques that induce mutagenesis, such as the gene editing tools Zinc finger nucleases, TALENs and CRISPR [48, 54]. However, in July 2018, the Court of Justice of the European Union provided its judgement that organisms created through new gene editing techniques are not covered by the Directive's 'mutagenesis exemption' and are thereby subject to the same rigorous risk assessment, product development and trade requirements as transgenic plant varieties [55].

In Australia, a technical review of the Australian Gene Technology Regulations 2001 was initiated in October 2016 [56]. Under proposed recommendations, gene editing, without introduced templates to guide genome repair, would not be regulated as GMOs as the repairs would be guided by the cell's normal repair processes. Similarly, organisms modified by introduced RNA that blocks gene expression (RNAi) would not be deemed GMOs provided the RNA does not give rise to any change in the genome sequence. Figure 1 outlines these different approaches.



[12] https://mainichi.jp/english/articles/20180821/p2a/00m/0na/033000c

[13] http://www.upsc.se/documents/Information_on_interpretation_on_CRISPR_Cas9_mutated_plants_Final.pdf

Figure 1: Comparison of international regulatory scenarios for gene editing[14]

GM Free Districts

At the time of writing several councils (Far North[15], Whangarei[16], Auckland[17] and Hastings[18]) have, or are consulting on, restrictions on the use of genetic modification in the environment while exempting medical and veterinary uses. This restriction would include those organisms that may have been approved for release by the EPA.

Regulation of gene edited food and food products in New Zealand

Half of New Zealand's domestic food supply in 2013 was imported[19]. Food standards for regulation of food and food products sold in Australia and New Zealand are set by the independent regulatory agency, Food Standards Australia New Zealand (FSANZ). The current policy is that all food produced using gene technology cannot be sold unless it has been assessed and listed in Schedule 26 of Section 1.1.1-10 of the New Zealand (Australia New Zealand Food Standards Code) Food Standards 2002.

To date, 88 varieties of genetically modified canola, corn, potato, rice, soybean, sugar beet, and lucerne (alfalfa) are approved for use in foods in Australia and New Zealand. None of these have been derived from gene editing, and none are currently grown in New Zealand[20].

However, in response to the development and application of a number of new breeding techniques, including gene editing, FSANZ is undertaking a review of the Food Standards Code to assess its application to food products of new breeding techniques, and to consider the definitions of "*food produced using gene technology*" and "*gene technology*" [57].

Ethical questions

As noted by the Nuffield Council of Bioethics [2], food production is one of the necessities of human life, and is also a matter of deep social significance, often rooted in cultural, ethnic, religious and social practices, such as fairness, freedom, harm/benefit, and sanctity or purity [58]. Many of the resulting questions relating to genomic manipulation of foods that we eat are common to both plants and animals and involve complex ethical, political and scientific considerations.

Opinions on genetic modification are often dependent on an individual's broader worldview [59]. For some, genetic modification of plants and animals is not wrong according to their ethical principles. This could perhaps be because they see gene editing as a logical continuation of selective breeding; an ethically permissible practice that humans have been carrying out for years; or because of views that human life is more important than animal/plant life. There can also be a belief that if, for example, gene editing creates animals or plants that help to develop new human medicines or which have

[14] http://www.ogtr.gov.au/internet/ogtr/publishing.nsf/Content/reviewdiscussionpaper-htm
[15] https://www.fndc.govt.nz/services/the-far-north-district-plan
[16] http://www.wdc.govt.nz/PlansPoliciesandBylaws/Plans/DistrictPlan/Documents/District-Plan-Part-E-District-Wide/GMO-Genetically-Modified-Organisms.pdf
[17] https://www.aucklandcouncil.govt.nz/plans-projects-policies-reports-bylaws/our-plans-strategies/unitary-plan/history-unitary-plan/ihp-designations-reports-recommendations/Documents/ihp024gmos.pdf
[18] https://www.hastingsdc.govt.nz/our-council/news/latest-news/press-releases/article/1038
[19] FAOSTAT, Commodity Balances -Livestock and Fish Primary Equivalent & Commodity Balances – Crops Primary Equivalent. Food and Agriculture Organization of the United Nations, Rome, Italy. http://www.fao.org/faostat/en/#data
[20] http://www.foodstandards.govt.nz/code/Pages/default.aspx

positive outcomes for the environment, then we may have an ethical obligation to create and use them.

For others, genetic modification of animals and plants may go against their ethical principles in a variety of ways [60]. For example, costs may be seen to outweigh benefits because the ultimate cost is the violation of species integrity and disregard for the inherent value of plants and animals. Some may view a plant or animal's whakapapa as something that cannot or should not be altered, and therefore altering the whakapapa would be ethically wrong. Others may simply see genetic modification as wrongfully exaggerating an imbalance of power between humans and nature, in effect 'playing god'. In addition, there may be those who feel strongly opposed to certain applications of genetic modification, but more accepting of others. For example, recent evidence suggests that some individuals may be more accepting of biomedical applications than those relating to food production [61, 62].

In a recent UK study on the potential uses for genetic technologies [63], the contexts that moderated public acceptability of developing UK research into genetic technologies included applications that:

- Promote equitable access to genetic technologies as they are developed
- Prioritise collective welfare
- Enable the science to develop further and knowledge of future applications to be extended
- Provide cheaper health interventions
- Prioritise positive and reduce negative environmental impacts
- Have benefits to society that outweigh risks to human health, animal welfare and the environment
- Alleviate suffering
- Use transparent processes.

Applications that were unacceptable to many were those which:

- Edit out difference and create a monoculture
- Prioritise individual and/or corporate wealth
- Drain currently over-stretched healthcare resources
- Enable humans, plants or animals to be weaponised
- Are introduced with insufficient safety monitoring or measures
- Restrict freedom to choose whether they should be applied or not, e.g. enforced genetic screening
- Reduce biodiversity or harm the ecosystem and related food chains
- Contaminate plants or animals not grown or reared using genetic technologies
- Are not sufficiently regulated and equally are so over-regulated as to stifle scientific progress.

There is also an entanglement between technology and big business in agriculture. The opposition to the use of these genetic technologies is often associated with the concern around ownership of food resources.

Genetic modification, branding and economic returns

Successful branding depends on consumer beliefs and responses rather than on analysis [64, 65]. For example, consumer food choice is more strongly influenced by branding and price than by nutritional quality. While consumer choice may change in response to information, the process of informing can be a very long one [66].

There are a range of views about the desirability of genetically modified (GM) crops and animals in New Zealand [67-69], which may have relevance to gene editing. Social science and public policy research

suggests that if the choices of individuals are independent, the choice over the use of GM crops and animals can be left to individuals in the relevant market. However, when the actions of one producer constrain the reasonable choices of other producers, there might be a case for public intervention [70-72]. This would be the case if there is a feasible intervention, and the intended consequences of the intervention generate an increase in public welfare [73]. Clearly, these balances need to be considered with gene edited crops and animals, at least at a national level.

An important characteristic of New Zealand foods is that they generally aim for "premium" status[21] in export markets, often with a focus on naturalness. If the presence of genetic modification affects acceptability as a premium product, there might be a case for public intervention to protect certain producers from the actions of others, around the use of genetically modified organisms. This is especially relevant in the case of genetic modification because while export markets might vary in their reactions to genetic modification [74], it is unlikely that geographic regions of New Zealand could be differentiated in international markets. This is particularly true for New Zealand products as government agencies and exporters promote the country's products in some respects using New Zealand as a brand.

To be in New Zealand's economic interests, a market premium is required for "GM-free" produce, however that might be defined, and this should be weighed against any applications of GM which may have to be foregone. Furthermore, even if all these links were substantiated, the appropriate policy response is not obvious. That requires further analysis of the options of "GM-free" and "not GM-free", with the inclusion of GM produce not resulting in the exclusion of New Zealand from major markets. If GM products are also able to command premiums for their qualities, such as nutritive and health values or environmental benefits, and retain access to major markets, the attractiveness of a GM-free brand is diminished [75]. But gene-editing technology may cause reconsideration of the concept of "GM-free". For example, small CRISPR-directed edits could produce outcomes both possible by, and indistinguishable from, those achieved with conventional breeding (albeit faster and more cheaply).

While there is no systematic analysis of being GM-free, the overall position could be considered similar to organic produce which has attracted a minority of producers [76] who can co-exist with other producers, even if not always entirely harmoniously [77], with concerns around contamination from herbicides and pesticides from nearby fields. The biggest differences with GM are probably in the extent to which producers are interdependent, and some entrenched philosophical differences between some producers who want to use GM and their opponents. For New Zealand to remain innovative in the primary sector, the loss of the advantages provided by gene editing technology may be a risk.

Scenarios for the use of gene editing in primary industries in New Zealand

The sustainability of global primary production systems faces many challenges from issues such as climate change, invasive pests, diseases and weeds, and increasing and ever-changing consumer demands. Because New Zealand's economy is strongly linked to primary production, we have been at the forefront in addressing these challenges through improving management systems, biosecurity measures and being responsive to changing consumer attitudes. Genetic selection and breeding have also been important approaches, but the relative imprecision and long time frames slow uptake and create a lag in the realisation of benefits. Gene editing technologies, such as CRISPR, have the potential to increase precision while reducing the risk of societal concerns about previous approaches to genetic modification.

[21] https://www.mpi.govt.nz/exporting/food/

Five scenarios have been selected to illustrate the potential benefits from using gene editing to reduce environmental impacts, improve productivity, protect taonga species, help animal welfare and improve human health. The five scenarios, outlined in Table 2, are discussed in terms of potential opportunities, risks and concerns, along with possible agricultural, environmental, ethical, societal and legal ramifications.

Table 2: Five primary industries' gene editing scenarios and associated issues

	1: Reducing environmental impact	*2: Responding to pests & stress*	*3: Speeding up innovation*	*4: Protecting taonga species*	*5: Providing new health benefits*
Species	Douglas fir	Ryegrass	Apple	Mānuka	Dairy cows
Aim	Reduce weediness in agricultural and conservation land	Provide field persistence to ryegrass by protection from pest herbivory and environmental stress	Speed up breeding of high value plant cultivars	Provide disease resistance	Remove allergen from milk
Estimated economic impact	Government currently spends $15M/yr on wilding pine control	Currently, endophytes in ryegrass contribute about $200M/ yr	Rapid breeding of high value cultivars	Potentially high if mānuka is susceptible to new disease	Potential new markets for milk in Asia
Potential implications for trade	Export logs may be considered genetically modified in some markets, with conditions on exports	New endophyte may be considered genetically modified in some markets, with conditions on exports, but new qualities could be attractive to customers	New varieties would be considered a GM crop in New Zealand, but might not be in other markets	New varieties could be perceived as GM honey	New milk could reach new markets overseas, but could be considered GM by some consumers
'Degrees of separation' from human food consumption	Not consumed by humans or any other animal	Consumed by animals, that are then consumed by humans	Cultivar of apple without transgene, but from gene-edited parents, consumed by humans	Honey derived from plant with gene edited genome consumed by humans	Milk and meat from gene-edited cows consumed by humans

Scenario 1: Reducing environmental impact

Wilding conifers are derived from the seeds of exotic species such as *Pseudotsuga menziesii* (Douglas fir) and are an unintended consequence of plantation forestry, agriculture (shelter belts) or erosion control plantings in New Zealand. Wildings currently occupy large tracts of conservation land in New Zealand because they are difficult and costly to control [78]. It is critical that management of new plantings of wilding-prone species includes strategies to prevent the generation of new wilding populations in the conservation estate.

A gene editing approach that modifies genes involved in the sexual reproductive process of conifers is an option to prevent the production of wildings. Targets include genes essential for cone initiation or development that would be deactivated (modified) to produce sterile trees [79]. There are promising candidate target genes but these would require research and testing to establish their role in conifer reproduction [80-84]. Once identified, gene editing could be used to target and inactivate these genes, to prevent reproduction [85].

Increasingly, conifers that are planted are not derived from seeds, but are reproduced via tissue culture. In this clonal forestry route, clones for planting are derived from a single embryo taken from cones that were produced by crossing two trees with desirable traits. These embryogenic cells can be preserved by cryopreservation and can also be propagated to ultimately produce huge numbers of trees [86]. To identify the best clones, cells are recovered from cryopreservation and the trees produced can be tested for their properties. The best performing ones, the "production" clones, can then be mass-produced from the cells remaining in cryopreservation.

Once good clonal lines are identified, it would be intended to gene-edit cells recovered from cryopreservation and then use the same tissue culture techniques as used in clonal forestry. Each original "production" clone would need to be edited independently, but this would fit in with the current production programme, where each clone is propagated independently by tissue culture and not via crossing. While the production method would be the same as is currently being used for clonal forestry, there would be an extra gene editing step early in the process. The additional costs are thus mainly associated with developing the gene editing and sterility technology, rather than production of the edited trees.

As per current practice, there would need to be a number of different production clones to mitigate the dangers of planting a monoculture [87]. The number required would be decided by the forestry company using already established procedures.

Agricultural/environmental considerations

When wilding conifers become established outside the plantation areas, they overwhelm native landscapes, compete with native plants, and reduce native insect and bird populations [88, 89]. They also have a huge impact on our economy by removing valuable water out of catchments, adding costs to farming and conservation, and impacting on tourism and recreational opportunities. In 2016, the government declared wildings to be "the most significant weed problem New Zealand faces"[22] and added a further $4M per year to the existing $11M spent annually on their control. There are also economic and regulatory barriers in place to prevent planting of wilding-prone species in potentially productive areas where there is a risk of spread. However, because wood derived from Douglas fir is economically important, the complete removal of Douglas fir is not ideal, so moves to minimise harmful effects from wilding are critical.

Ethical/social considerations

Forests have an emotive and aesthetic value for many people and a place in history, mythology and identity [90]. Forests, unlike agricultural fields and paddocks, may be seen as 'uncultivated' – even though they are, in fact, in many cases both cultivated and intensively managed. Concerns about genetic modification may be rooted in concerns about the purity, or freedom, of wilderness, and a belief that wild nature needs to be free of human influence [91].

There could, however, be a kaitiaki obligation to reduce the environmental impact of wilding pines, which this technology could support, and intergenerational fairness considerations to prevent the impact of wilding conifers falling on future generations to remedy. Prevention of wilding conifers would also protect the purity of surrounding wilderness from human influence.

[22] https://www.beehive.govt.nz/release/16m-new-funding-tackle-wilding-conifers

Legal considerations

Gene editing wilding-prone species is a hypothetical example that aims to target the germline cells using an *in vivo* cell application gene editing technique to inactivate genes and thus enabling male and female plant sterility. Genetically modified organisms are *new organisms* under the Hazardous Substances and New Organisms Act 1996 (HSNO Act). The CRISPR gene editing system is initiated *in vitro*, thereby classifying it as an *in vitro* technique for the purposes of genetically modified organisms. Thereby, gene editing wilding-prone conifer species would be deemed to be genetic modification in statute (HSNO Act, section 2(1) and section 2A(2)(b)) and by regulation and case law (SR 1998/219 and Scion Case[23]). The Environmental Protection Authority (EPA) may, on application by any person, determine whether any organism is a new organism (HSNO Act, section 26) and the determination must be issued by notice in the *Gazette*.

Wilding-prone conifer species that are new organisms must be developed and field tested in containment (HSNO Act, section 27). Subsequent approvals need to be sought for release from containment and conditional release. The EPA can decline the application if the organism fails to meet the minimum standards (HSNO Act section 36), or the adverse effects outweigh the benefits, or insufficient information is available to enable the EPA to assess the adverse effects of the organism (HSNO Act, sections 37 and 38).

The National Parks Act 1980, the Reserves Act 1977 and the Resource Management Act 1991 (RMA) would need to be considered and applied as these statutes legislate for the introduction of biological organisms using ministerial authority. Douglas fir is not native to New Zealand and therefore is not to be preserved according to section 5 of the National Parks Act 1980. Tools or mechanisms to reduce the population of wilding pines will promote the protection of indigenous flora and fauna (RMA, section 6).

New Zealand logs and conifer products are exported. The role of the Agricultural Compounds and Veterinary Medicines Act 1997 (ACVM Act) is to prevent or manage risks associated with the use of agricultural compounds in primary produce, as they may pose a risk to trade or to agricultural security (ACVM Act, sections 4(a)(i) and (iii)). The CRISPR gene editing system may be deemed an agricultural compound for the purposes of the ACVM Act (sections 2(1)(i) and (ii)) if it meets the definition for a biological compound (section 2(1)) or a biological compound declared to be an agricultural compound for the purposes of the ACVM Act by Order in Council (section 2(1)(b)(iii)). The scheme of the ACVM Act (section 4a) enables integration with the Biosecurity Act (regulation of unwanted organisms) and HSNO Acts (regulation of new organisms).

The Cartagena Protocol to the Convention on Biological Diversity is an international agreement that aims to ensure an adequate level of protection in the field of safe transfer handling and use of *living modified organisms* (LMOs). Article 1 of the Protocol states that this is in accordance with the precautionary approach contained in Principle 15 of the Rio Declaration on Environment and Development. According to the definition of a living modified organism in the Cartagena Protocol, gene edited wilding-prone conifers or seeds (but not logs or sawn timber) would be considered living organisms and gene edited wilding-prone conifer species would likely meet the definition of a living modified organism resulting from modern biotechnology if it possessed a novel combination of genetic material. This would result in the requirement for seed or sapling export to comply with the procedures for transboundary movement of LMOs intended for direct use as food or feed, or for

[23] The HC Judge ruled that the exemption list is a closed list; that plants created with genetic techniques ZFN-1 and TALENs are genetically modified organisms.

processing (Article 11)[24]. New Zealand importers and exporters are legally bound by the Imports and Exports (Living Modified Organisms) Prohibition Order 2005 (SR 2005/12).

Risks and potential benefits

The primary benefits derived from using gene-edited conifers in plantation forestry would be through prevention of environmental, social and economic damage caused by new wildings, but this would not address existing wildings. The ability to plant stock that does not generate wildings would remove the risk from future commercial forestry plantings and allow control operations to focus on existing wildings.

Prevention of pollen production would mitigate problems associated with pollen allergy and the seasonal nuisance created by large pollen clouds from planted forests.

It is predicted that preventing cone development will boost growth and increase wood production by redirecting energy and nutrients to increased vegetative growth [92]. This would have a substantial economic impact as it is estimated that 10-15% of a tree's energy is used for cone production [93, 94].

The gene-edited trees would be sterile and would not contain foreign DNA, but the availability and cost of the new trees could be more restrictive and expensive than conventional varieties, and some argue that using gene edited trees is a risk to our national brand. Of New Zealand's 1.71 million hectares of planted plantation forest[25], 1.24 million hectares was certified by the Forest Stewardship Council in 2016[26], which prohibit the use of GM trees[27].

Scenario 2: Responding to insect pests and environmental stress

Perennial ryegrass (*Lolium perenne*) is the most important crop grown in New Zealand, being the dominant pasture grass in livestock production [95]. Important to the persistence of this crop in the field is the presence of a beneficial fungus (*Epichloë festucae*) that lives inside the grass [96] and is therefore known as an endophyte ('living inside'). These fungi produce a range of secondary metabolites that provide bioprotective benefits for the grass host in natural ecosystems such as protection from insect and mammalian herbivory, as well as providing protection to environmental stresses such as drought [97]. However, some of the chemicals that the fungi produce, including alkaloids (e.g. ergovaline) and indole-diterpenes (e.g. lolitrem B), are detrimental to grazing livestock under certain environmental conditions, resulting in welfare, production and financial losses to the farmer [98]. To overcome issues of mammalian toxicity, a number of novel beneficial fungi have been selected which retain the beneficial ability to protect the grasses from insect herbivory but have also lost the ability to synthesise the mammalian toxins [99]. Molecular analysis of these strains show that the loss of this capability is due to deletion or inactivation of key genes in the biosynthetic pathways for these compounds [100]. While the selection and transfer of these 'novel' fungi into the most productive ryegrass cultivars has brought significant benefits to the farmer and the forage industry in New Zealand, further advances are limited by identification of and selection for natural variation of the fungi found in seed collections [101].

[24] http://www.mfe.govt.nz/more/hazards/new-organisms/genetic-modification-new-zealand/exporting-living-modified-organisms
[25] http://www.mpi.govt.nz/news-and-resources/open-data-and-forecasting/forestry/new-zealands-forests/
[26] https://www.nzfoa.org.nz/images/stories/pdfs/Facts_Figures_2016_%C6%92a_web_version_v3.pdf
[27] https://nz.fsc.org/preview.national-standard-for-certification-of-plantation-forest-management-in-new-zealand-version-3-5-for-2nd-consultation.a-1341.pdf

Identification of the genes required for the synthesis of fungal alkaloid toxins, combined with an understanding of the individual steps in the biosynthetic pathways, has created the opportunity to breed these fungi through various genetic techniques [102-105]. With the advent of gene editing technology it is now possible to selectively delete single or multiple genes in these alkaloid toxin biosynthetic pathways to generate strains that either completely lack the ability to synthesise mammalian toxins or accumulate intermediates with unique bioprotective properties [95]. There is also the potential to introduce genes sourced from other organisms that confer new protective properties, such as drought tolerance, alter the herbage quality and/or provide health benefits to the grazing livestock.

In this scenario there is no genetic alteration of the grass, only of the fungus that lives within it. While the fungi colonise the grass seed and pass from generation to generation they do not colonise pollen so are not wind dispersed [106]. Foreign genes may be present or absent in the final edited strain depending on the nature of gene editing carried out. Such genetic manipulations have the potential to generate beneficial fungal strains with novel protective properties thereby enhancing persistence in the field as well as conferring animal welfare benefits. These novel beneficial fungi could be readily developed either in New Zealand or overseas.

Agricultural/environmental considerations

Most proprietary ryegrass seed currently sold in New Zealand contains endophyte because of the added protection the presence of this endophyte confers on the host in the field. Ryegrass and other introduced grasses (non-native) to this country are very widely distributed throughout the country. Many grass species are highly adapted to a range of environmental conditions. Persistence of temperate grasses in the field will be dependent on both grass and endophyte genotypes.

Grass cultivars containing these 'novel' fungi have been estimated to contribute around $200M per year to the New Zealand economy [99].

Ethical/social considerations

The main social consideration would be acceptability of using forage seed in agriculture containing gene-edited endophytes, and the perceptions of risks from the chemicals from the new gene edited fungi. There would be reduced risk from the endophyte's chemicals for the grazing animals, with resulting animal welfare benefits.

Legal considerations

Gene editing *Epichloë festucae* is a hypothetical example that aims to inactivate the toxicity genes using an *in vivo* cell application technique. Genetically modified organisms are *new organisms* under the HSNO Act. The CRISPR gene editing system is initiated *in vitro*, thereby classifying it as an *in vitro* technique for the purposes of genetically modified organisms[28]. Consequently, gene edited *Epichloë festucae* would be deemed genetically modified in statute (HSNO Act, section 2(1) and section 2A(2)(b)) and by regulation and case law (SR 1998/219 and Scion Case[29]).

According to the HSNO Act (section 25(1)) no new organism shall be imported, developed, field tested, or released otherwise than in accordance with an approval issued under the HSNO Act. Importation of non-genetically modified ryegrass seed with a new endophyte into New Zealand also needs to meet

[28] HSNO Act, section 2(1).

[29] The HC Judge ruled that the exemption list is a closed list; that plants created with genetic techniques ZFN-1 and TALENs are genetically modified organisms.

the Import Health Standard, Seeds for Sowing (155.02.05) and may require a phytosanitary certificate to meet biosecurity requirements[30]

Perennial ryegrass (*L. perenne*) containing new organisms (gene-edited *Epichloë festucae*) must be developed and field tested in containment (HSNO Act, section 27), in a Ministry for Primary Industries' approved[31] facility. Subsequent approvals need to be sought for release from containment and conditional release. Where the EPA receives an application under section 40 of the HSNO Act to develop a genetically modified organism in containment, the EPA may make a rapid assessment of the adverse effects of developing that organism (HSNO Act, section 42(1) and 42A). The EPA can decline the application if the organism fails to meet the minimum standards in section 36, or the adverse effects outweigh the benefits, or insufficient information is available to enable the EPA to assess the adverse effects of the organism (HSNO Act, sections 37 and 38).

The purpose of the proposed gene editing scenario is to improve animal welfare and animal production by removing endophyte mammalian toxicity of the fungi and improving drought tolerance of the grass. Gene-edited *Epichloë festucae* will likely be deemed an *agricultural compound* if it meets the definition for a *biological compound* used in the direct management of plants and animals as a feed for animals (ACVM Act, subsections 2(1)(ii),(iii) and (vi)). The ACVM Act's role is to prevent or manage risks to animal welfare associated with the use of agricultural compounds (ACVM Act, section 4(a)(ii)). The scheme of the ACVM Act (section 4a) enables integration with the Animal Welfare Act 1999 and HSNO Acts (regulation of new organisms).

Gene-edited endophytes of exported perennial ryegrass species would meet the definition of a living organism in the Cartagena Protocol to the Convention on Biological Diversity. However, it may not meet the definition of a *living modified organism* (LMO) if the endophyte does not possess a novel combination of genetic material, for example, if the CRISPR technique is used to delete a nucleotide using a sequence that is already present in the species' population. If it is deemed an LMO, it would need to comply with the procedure for transboundary movement of LMOs intended for direct use as food or feed, or for processing (Article 11)[32]. New Zealand importers and exporters are legally bound by the Imports and Exports (Living Modified Organisms) Prohibition Order 2005 (SR 2005/12). If ryegrass products such as hay, silage or nuts to be used as animal feed were to contain viable endophytes, the product would be deemed a living modified organism and therefore would be subject to the Cartagena Protocol and gene editing regulation in the import country. If the endophytes were not viable, the product would be subject to the importing country's laws and regulations on gene-edited animal feed products.

Risks and potential benefits

Introduction of edited endophytes with novel bioprotective benefits into forage grasses will provide protection to the host from various environmental and biological stresses, leading to greater persistence in the field and potential benefits to the forage industry. Endophytes that have been edited to prevent the synthesis of harmful toxins provide welfare benefits and production benefits to the grazing livestock.

Forage seed is widely traded both within and external to New Zealand. While there are good tracking systems in place it would be difficult to control movement of all seed. This would lead to the risk of inadvertent movement of seed containing modified endophyte to a region or country where it is

[30] https://www.mpi.govt.nz/importing/plants/seeds-for-sowing/steps-to-importing/
[31] https://www.epa.govt.nz/assets/Uploads/Documents/New-Organisms/Policies/155-04-09-MAF-ERMA-Std-2007.pdf
[32] http://www.mfe.govt.nz/more/hazards/new-organisms/genetic-modification-new-zealand/exporting-living-modified-organisms

regulated differently to the source of origin. Seed containing endophyte with minor edits would be difficult to distinguish from naturally occurring strains.

If we were to handle or export seed considered GM in other countries, consideration would need to be given to the implication for seed exports to countries with a purity threshold of zero for GM contamination. Approval would need to be sought around the level of possible contamination risks for exports of non-GM seed.

Scenario 3: Speeding up innovation

The speed with which new apple varieties with high value traits can be generated is limited by the long juvenile period in apple, often up to 5 years before the plants are able to flower and then fruit [107]. Thus, plant breeding, which typically involves multiple cycles of sexual crossing and selection to produce improved varieties with desirable fruit characteristics, is a very slow process. New Zealand has benefited from long-term selection and breeding programmes but increasing threats from pests and diseases and rising consumer expectations for new varieties means that much of the research effort in breeding new fruit tree varieties is focused on reducing breeding cycle time. Even small improvements in breeding speed can deliver significant returns sooner or can provide a timely solution to the industry if a new disease or pathogen strikes, or with changing conditions due to climate change [108].

In apples, previous research has demonstrated substantial reductions in the time to flowering are possible through gene editing technology. Initial research using the overexpression of a gene from silver birch (*BpMADS4*) has been able to reduce the breeding cycle in apple to a single year [109-111]. Using this technology, researchers were able to integrate fire blight resistance into an elite cultivar through five crosses within seven years to generate a plant that, while carrying the desirable fire blight resistance trait, no longer carried the *BpMADS4* transgene [109]. A similar reduction in the juvenile period in apple has been achieved using antisense technology[33] to reduce the expression of the flowering gene *MdTFL1,* thus bringing the plants into flower and fruit much more rapidly [112, 113]. Therefore, rather than over-expressing a foreign gene, a similar outcome was achieved by turning an apple gene off.

Gene editing could be used to obtain the same rapid flowering phenotype for use in rapid breeding, with a guide RNA targeting and knocking out the gene that represses flowering using CRISPR technology [114]. This would result in an apple that flowers almost constantly and is able to be crossed every eight months. Once the desirable characteristics have been combined through rapid crossing, the modified flowering gene and gene editing machinery could be removed by conventional plant crossing, restoring the typical flowering pattern and leaving no modifications in the final plant [115] (See Figure 2).

[33] Antisense technology uses synthetic single stranded strings of nucleic acids that bind to RNA and thereby alter or reduce expression of the target RNA.

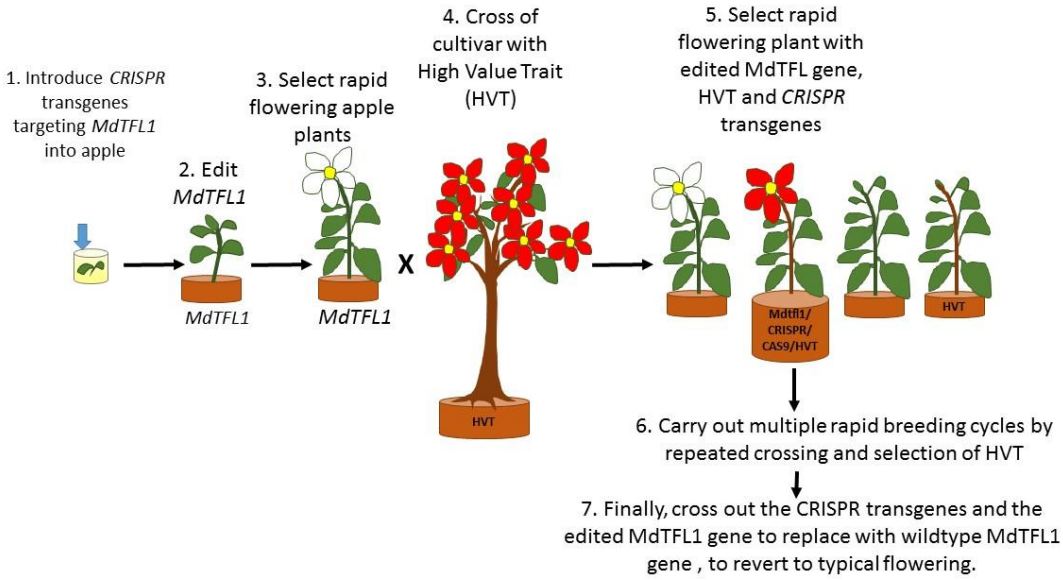


Figure 2: Using CRISPR and flowering gene MdTFL1 in rapid breeding (Fast-track breeding approach)

Horticultural considerations

The proposed scenario speeds up the apple breeding cycle with the resulting plants not containing any transgene or even the gene edited version of the new flowering gene. Potentially, crosses using the edited flowering gene line could be developed and field tested in containment, and permission then sought to release from containment the subsequently produced plant that would no longer contain the modified gene. This would have implications for horticulture producer boards, to ensure the GM status is known for New Zealand and international consumers.

Ethical/social considerations

As noted by the Nuffield Council on Bioethics [2], although gene-edited plants might be analytically indistinguishable from traditionally bred plants, the fact that a technical procedure, which might be perceived as unnatural, or affecting the apple's purity, is involved in producing these new plants, may be of concern to some people [116]. This is arguably a matter for the consumers rather than producers, since it allows consumers to exercise choices about the kinds of producers and production systems they wish to support through their purchasing. For consumers to have the freedom to make such a choice, labelling (either voluntary or compulsory) may be particularly important. Consequently, tracing through an auditable chain of custody becomes imperative for that purpose. The fact that it is only the tree flowering that is being altered using gene editing, rather than the apple, and that this edit will not be present in the cropping variety, may change people's views.

Legal considerations

Gene editing the apple *MdTFL1* gene is a hypothetical example that aims to enable continuous flowering using an *in vivo* cell application and clonal propagation techniques. Out-crossing breeding techniques are then used to remove the edited version of the *MdTFL1* apple gene along with the CRISPR machinery, to restore normal flowering. The primary purpose of gene-edited apple trees is to rapidly breed high value cultivars to increase production and develop new varieties for consumers.

Genetically modified organisms are *new organisms* under the HSNO Act. The CRISPR gene editing system is initiated *in vitro*, thereby classifying it as an *in vitro* technique for the purposes of genetically

modified organisms[34]. Thereby, fast flowering gene-edited apple trees would be deemed *genetic modification* in statute (HSNO Act, section 2(1) and section 2A(2)(b)) and by regulation and case law (SR 1998/219 and Scion Case[35]). It is unclear whether the out-crossed apple tree for release to orchardists, with the fast flowering gene removed by conventional plant crossing, would meet the definition of genetic modification according to section 2(1)(b) of the HSNO Act. The EPA may, on application by any person, determine whether or not the out-crossed apple tree is a *new organism* and the determination must be issued by notice in the *Gazette* (HSNO Act, section 26). The EPA may revoke or reissue a determination issued by it under section 26(6) if it receives further information. According to the HSNO Act (section 25(1)) no new organism shall be imported, developed, field tested, or released otherwise than in accordance with an approval issued under the HSNO Act.

The gene-edited apple tree would be developed and field tested in containment and, following out-crossing, the progeny lacking the edited gene may be released. Release would allow the new organism to move within New Zealand free of any restrictions other than those imposed by the RMA, Biosecurity and Conservation Acts. Evaluation by the EPA under the provisions of the HSNO Act would determine whether the new organism would be released free of any restrictions, released with controls (conditional release), restricted to containment or released under special emergency conditions. Gene edited apple trees must be developed and field tested in containment (HSNO Act, section 40). The EPA can decline the application if the organism fails to meet the minimum standards in section 36, or the adverse effects outweigh the benefits, or insufficient information is available to enable the EPA to assess the adverse effects of the organism (HSNO Act, sections 37 and 38). Note that the restriction on the importation of a new organism in New Zealand does not apply to biological material of the organism that cannot, without human intervention, be used to reproduce the organism (HSNO Act, section 25(5)), for example apple juice.

The ACVM Act's role is to prevent or manage risks to trade in *primary produce* and risks to public health associated with the use of agricultural compounds (ACVM Act, subsections 4(a)(i) and 4(a)(ia)). The gene edited *apple tree* may be deemed an *agricultural compound* for the purposes of the ACVM Act (sections 2(1)(ii) and (vii)) if the CRISPR system meets the definition for a *biological compound (*section 2(1)) *and* the biological compound is declared to be an agricultural compound for the purposes of the ACVM Act by Order in Council (section 2(1)(b)(iii)). The scheme of the ACVM Act (section 4A) enables integration with the Biosecurity and HSNO Acts (regulation of new organisms).

Since gene-edited apples contain viable seeds, gene edited apples would meet the definition of a living modified organism (LMO) resulting from modern biotechnology in the Cartagena Protocol on Biological Diversity if it possessed a novel combination of genetic material. This would result in the requirement to comply with the procedure for transboundary movement of LMOs intended for direct use as food or feed, or for processing (Article 11)[36]. New Zealand importers and exporters are legally bound by the Imports and Exports (Living Modified Organisms) Prohibition Order 2005.

Risks and potential benefits

The primary beneficiaries of the proposed scenario would be apple breeders as they would be able to rapidly introduce traits into elite cultivars through more rapid breeding cycles. Indirectly, this could benefit growers and consumers, both directly and indirectly, depending on the traits incorporated. As the resulting cultivars no longer contain the edited flowering gene, the risks would be "off target effects", that is genetic changes that might occur in other parts of the genome as a result of the gene-

[34] HSNO Act, section 2(1).

[35] The HC Judge ruled that the exemption list is a closed list; that plants created with genetic techniques ZFN-1 and TALENs are genetically modified organisms.

[36] http://www.mfe.govt.nz/more/hazards/new-organisms/genetic-modification-new-zealand/exporting-living-modified-organisms

editing and might have negative effects. Genome sequencing would, however, be able to identify if any on target effects had occurred.

Scenario 4: Protecting taonga species used in the primary industries

Mānuka (*Leptospermum scoparium*), which Captain Cook called the tea tree, has a rather variable form ranging from flat creeping varieties and small shrubs to tall trees. Extracts of leaves and bark were traditionally prepared and used by Māori, and are still used in modern day medicine, for healing purposes for a wide range of ailments. Mānuka is found throughout New Zealand and grows in many different habitats. It is an early coloniser of ecosystems and fulfils an important role in stabilising soils on steep erosion-prone hillsides. Mānuka is bee pollinated and has very small wind-blown seeds, which ensure widespread dispersal. Recently a burgeoning business has developed from the harvesting and niche marketing of mānuka honey, which in 2016 could command prices of $148 per kilogram [117]. However, the arrival of new plant diseases, such as myrtle rust, raises considerable concern about the threat to mānuka and other members of the Myrtaceae family (e.g. kānuka, pōhutukawa and rātā)[118, 119]. While there is uncertainty about the impact of a new disease on this group of highly valued native species, plans are in place to collect seed to deposit in germplasm collections and research is underway to find ways to mitigate the impact of diseases should they become established in our forests.

At present little is known about natural resistance to pathogens within mānuka. Plant & Food Research have established populations of mānuka that could be used to map genes that confer tolerance/resistance to different pathogens. In addition, the mānuka genome has been sequenced, providing a crucial resource for identifying putative susceptibility and/or resistance genes to inform future breeding programs and conservation efforts across mānuka provenances as well as to provide potential targets for gene editing[37]. One of the first challenges to overcome in order to gene edit mānuka would be development of a delivery system to introduce the CRISPR machinery. A very common method that is used in plants is *Agrobacterium*-mediated transfer, but this methodology has yet to be developed in mānuka. Two possible approaches of gene editing that might provide resistance to disease in mānuka include:

- the deletion of a susceptibility gene, or
- the introduction of a resistance gene from another species.

In the former, the resulting organism would not contain any foreign genes whereas in the latter it would.

These scenarios involves gene editing of a valued indigenous species and would therefore require active engagement, participation by, and ongoing consultation with, Māori collectives on whether this approach is appropriate and useful for Māori as kaitiaki. Māori worldview perspectives, Māori cultural norms and other holistic considerations, including environmental, social and economic benefits and risks, would be considered during these decision making processes to ensure adequate protections are adhered to and to maintain balances and protocols. Ultimately, Māori would consider whether the whakapapa, mauri, and mana of the mānuka, and of Māori themselves, are not adversely impacted or irreversibly destroyed [120].

Agricultural and environmental considerations

If only a limited range of mānuka ecotypes/provenances are gene-edited, then there is the potential that these disease resistant types will have increased fitness and may spread throughout the country.

[37] https://www.plantandfood.co.nz/page/news/media-release/story/cracking-manukas-genetic-code-to-mitigate-myrtle-rust/

This spread could potentially affect the genetic diversity of the species in New Zealand. One solution would be to cross breed disease-resistant, gene-edited, mānuka from a wide range of provenances before releasing.

Gene-edited mānuka could result in resistance to many microbes, including beneficial ones [121,122]. This can be managed by research on the growth of resulting gene edited mānuka lines, under differing environmental conditions, prior to field release.

Ethical/social considerations

Products derived from gene-edited disease resistant mānuka could preserve jobs in regions such as East Cape and Northland, due to the maintenance of a thriving and resilient mānuka honey and oils industry. Māori communities would be able to be actively involved in leading and being part of the research efforts.

For some, gene-edited, disease resistant mānuka will be seen as enabling the responsibilities of kaitiakitanga by contributing to long term conservation of the species and maintaining ecosystems where mānuka is an integral species. It could be seen to have a positive impact by conserving species interconnected with other species (human, game animals, bees, beneficial fungi). However, for others, there may be opposition to the use of the technique, as gene edited mānuka may alter, or impact, the mauri or essential life force of mānuka, or its natural properties [123]. Some may also argue that there is a special value in processes and organisms that live without the influence of human agency – nature is wild and should exist without human influence. Thus, even though it seems like mānuka is helped through use of this technology, and other species too, potentially, this is in fact their replacement with a cultural artefact, which does not have the natural value of the original [124, 125]. Others argue that humans and nature cannot be separated in this way, and that efforts in restoring nature is valuable for nature itself, as well as any benefits for humans [126]. Moreover, the alternative of not doing anything to help mānuka survive disease challenge, may risk losing mānuka completely.

The economic interests of Māori and other producers are also likely to be negatively impacted if gene editing is poorly perceived by consumers of mānuka honey products.

Legal considerations

Mānuka are taonga species, are native to Aotearoa New Zealand and therefore a matter of national importance to be preserved, sustainably managed and protected (RMA sections 5 and 6, National Parks Act 1980 (section 5), Biosecurity Act section 54, the Wai 262 Claim and Article 2 of the Treaty of Waitangi). The purpose of the gene editing would be to provide mānuka with disease resistance to aid in their preservation and support a growing export honey industry.

Gene-edited mānuka trees would be deemed *genetic modification* in statute (HSNO Act, section 2(1) and section 2A(2)(b)) and by regulation and case law (SR 1998/219 and Scion Case). Genetically modified organisms are *new organisms* under the HSNO Act, and therefore a gene edited mānuka tree would likely be deemed a new organism for the purposes of the HSNO Act[38]. According to the HSNO Act (s 25(1)) no new organism shall be imported, developed, field tested, or released otherwise than in accordance with an approval issued under the HSNO Act.

Gene-edited mānuka would have to be developed and field tested in containment (HSNO Act, section 27), but to achieve their purpose, the gene-edited trees would need to be released. Approval for release would need to be sought from the EPA (sections 34, 34A and 38A). Release would allow the

[38] Refer to HSNO Act section 2A. Please note the exceptions in section 2A(2).

new organism to move within New Zealand free of any restrictions other than those imposed by the Biosecurity and Conservations Acts (HSNO Act, section 2(1)).

Evaluation by the EPA under the provisions of the HSNO Act would determine whether the new organism (gene edited mānuka tree) will be released free of any restrictions, released with controls (conditional release), restricted to containment or released under special emergency conditions. The EPA would decline the application if the organism fails to meet the minimum standards in section 36, or the adverse effects outweigh the benefits, or insufficient information is available to enable the EPA to assess the adverse effects of the organism (HSNO Act, sections 37 and 38).

The ACVM Act's role is to prevent or manage risks to trade in primary produce and risks to agricultural security associated with the use of agricultural compounds (ACVM Act, section 4(a)(i)). Primary produce is defined as 'a*ny plant or animal, or any derivative of any plant or animal, intended for sale' (ACVM Act, section 2(1)).* Mānuka honey would likely be deemed *primary produce* and therefore subject to risk assessment by MPI in relation to trade. Gene-edited mānuka may be deemed an agricultural compound for the purposes of the ACVM Act (subsections 2(1)(ii) and (vii)) if the gene edited product meets the definition for a *biological compound* (section 2(1)) *and* the biological compound is declared to be an agricultural compound for the purposes of the ACVM Act by Order in Council (section 2(1)(b)(iii)). The scheme of the ACVM Act (section 4A) enables integration with the Biosecurity (regulation of unwanted organisms) and HSNO Acts (regulation of new organisms).

Gene-edited mānuka would meet the definition of a *living modified organism* (LMO) resulting from modern biotechnology under the Cartagena Protocol on Biological Diversity if it possessed a novel combination of genetic material, but the honey from the mānuka would not be classified in this way.

Risk and potential benefits

The economic benefits of protecting mānuka in this way would be to allow continued production of mānuka-derived product, such as oils and honey, should a new pathogen become established, and to protect mānuka plants from new pathogens. Economic risks may include the perception by some of gene-edited mānuka as unnatural, which could negatively affect the New Zealand honey industry. Such campaigns could be triggered nationally and globally by competitors to the mānuka honey industry.

There is a risk that the disease resistance conferred by the gene edit may be short lived especially if the gene edit takes the form of targeting a single gene whose product may be negatively affecting the pathogen (a resistance gene). For example, selection pressure may favour pathogens with mutations that can get around the resistance afforded by this single gene. This might necessitate ongoing selection and breeding. However, a significant advantage of gene editing is that it is possible to target susceptibility genes. These would be genes that are required for pathogens to establish disease in the mānuka plant. Studying resistant mānuka lines can lead to the discovery of such genes and editing them would likely result in durable on-going resistance [127].

Scenario 5: Providing new human health benefits

Cows have evolved to provide milk as a balanced source of nutrition to support the early life of calves. Recognising its high nutritional value and potential for a safe and secure food supply, humans have embraced cows' milk as a major source of nutrition to promote human health and wellbeing. But the consumption of cows' milk is not universally tolerated and can cause allergic reactions, ranging from mild to life-threatening symptoms, particularly in infants. Cows' milk contains the milk protein beta-lactoglobulin that has no equivalent in human milk or anywhere else in the human body, and constitutes a major cows' milk allergen. It can raise a strong immune reaction resulting in high levels

of anti-beta-lactoglobulin antibody in people with allergies against this protein. Different processing technologies, including enzymatic hydrolysis, are current strategies to mitigate the allergenic properties of milk proteins. Besides being expensive, such processing also risks exposing previously hidden parts of proteins that may be novel triggers for allergic reactions or that cause the milk to taste bitter. Elimination of beta-lactoglobulin from cows' milk could be a safe option to minimise the allergenic potential and produce a milk that could provide a valuable source of nutrition for those consumers that currently cannot eat or drink dairy products from cows due to an allergic immune response against this protein [128].

The precision and efficiency of gene editing makes it now possible to simply eliminate the allergy-causing protein from cows' milk by disrupting the gene responsible for its production in cows [129]. This can be achieved by designing gene editing tools that target the gene for beta-lactoglobulin to introduce a small deletion that disrupts the reading frame of the encoded milk protein. In cows, this can be done by introducing the beta-lactoglobulin-specific gene editor into one-cell cow embryos [130, 131]. In this approach, the embryos are cultured *in vitro* for seven days until they reach an early embryonic stage called a blastocyst. Typically, a small biopsy will be taken from the embryos and used to confirm the intended edit before the embryos are transferred to recipient cows for development to term and production of live gene edited calves. The only change to the genome will be the small deletion in the beta-lactoglobulin gene, allowing the direct introduction of specific desirable traits within a single generation.

Agricultural considerations

The Nuffield Council of Bioethics [2] has identified that, unlike for plants, gene editing of animals has not merely accelerated research, but made research possible that was previously unfeasible [132]. Because the breeding interval in most commercial animals is long (typically many months) and their reproductive rates are often low (for example, one offspring per generation in cattle, although as many as 15 in pigs), the backcrossing strategies that are used so effectively in crop breeding are considerably less productive in most livestock. On the other hand, the embryo transfer mode of animal reproduction enables embryological micromanipulation, makes animals more responsive to certain forms of editing, and can be applied to traits already known [133].

The New Zealand dairy industry is presently based around bulk production. The beta-lactoglobulin-free milk would be a high value, specialty product with health benefits for only a defined group of people. It would, therefore, require separation from the supply/value chain. It is important to note that meat from gene-edited dairy cows would also enter the food chain. Beta-lactoglobulin free milk would have a benefit of improved processing efficiency in milk factories as beta-lactoglobulin fouls the heat exchanges in milk processing plants [134, 135].

In terms of beta-lactoglobulin's function in dairy cows, the whey protein may be an important source of amino acids for calves [136], so there may be a need to ensure that the gene-edited calves' diets are sufficiently supplemented to replace the missing protein.

Ethical/social considerations

People's interactions with food and being able to choose what they eat is important. There will be social and ethical issues around people's views on genetic modification of animals and the milk produced from such animals, which will need to be weighed against the advantages of reduced allergenicity. Some people may have ethical concerns around the disruption of species boundaries, or the nature, or mauri, of the animals modified, and the welfare of animals modified, including during the research and development for the modification process [137].

Legal considerations

Gene-editing of the bovine beta-lactoglobulin gene would be done by introducing a beta-lactoglobulin-specific gene editor into single-cell embryos.

Gene edited beta-lactoglobulin dairy cow embryos, and the milk producing adult cows resulting from the gene edited embryos, would be deemed *genetically modified* in statute (HSNO Act, section 2(1)) and section 2A(2)(b)) and by regulation and case law (SR 1998/219 and Scion Case[39]). The progeny of adult gene-edited dairy cows also meet the definition of genetic modification according to section 2(1)(b), as they 'are inherited or otherwise derived, through any number of replications, from any genes or other genetic material which has been modified by *in vitro* techniques'.

The gene-edited and *genetically modified* embryo and adult dairy cow will likely be deemed a *new organism* for the purposes of the HSNO Act (section 2A). According to the HSNO Act (section 25(1)) no new organism shall be imported, developed, field tested, or released otherwise than in accordance with an approval issued under the HSNO Act (HSNO Act, section 27). Gene-edited beta-lactoglobulin dairy cows would have to be developed and field tested in containment (HSNO Act, section 39), and released to the wider dairy industry as part of the conventional farming production system. Approval for release would need to be sought from the EPA (sections 34, 34A and 38A). Release would allow the new organism to move within New Zealand free of any restrictions other than those imposed by the Biosecurity and Conservations Acts (HSNO Act, section 2(1)).

Evaluation under the provisions of the HSNO Act would determine whether the *new organism* (gene edited dairy cows) will be released free of any restrictions, released with controls (conditional release), restricted to containment or released under special emergency conditions. The EPA would decline the application if the organism fails to meet the minimum standards in section 36, or the adverse effects outweigh the benefits, or insufficient information is available to enable the EPA to assess the adverse effects of the organism (HSNO Act, sections 37 and 38).

Animals used in gene-edited beta-lactoglobulin dairy cow research are subject to Part 6 of the Animal Welfare Act, which legislates the use of animals in research, testing and teaching and provides the circumstances under which animals can be manipulated. The purpose of Part 6 is to ensure that the use of animals for research purposes is confined to cases in which there is good reason to believe that the findings of the research or testing will enhance the maintenance or protection of human health and welfare (Section 80(1)(a)(ii)); or the production and productivity of animals (section 80(1)(a)(iv)). Research, testing and teaching must only occur when, along with other conditions, the anticipated benefits of the research outweigh the likely harm to animals (section 80(1)(b)). There are restrictions on who can *manipulate* animals (section 82). The term manipulation includes the breeding or production of an animal using any breeding technique (including genetic modification) that may result in the birth or production of an animal that is more susceptible to, or at greater risk of pain or distress during its life as a result of the breeding or production (section 3(1B)). In this scenario, the association of the gene edited beta-lactoglobulin gene on other genes in the cattle genome may not be known. There are also restrictions on carrying out research (section 83) whereby no person may carry out any research unless it has been first approved by an animal ethics committee appointed by the code holder.

To eventually make beta-lactoglobulin-free milk available for people affected by milk protein allergies, the milk would require both regulatory approval according to the Food Standards Australia New Zealand (FSANZ) standard for 'Food produced using gene technology', which would include evidence that the product is safe to eat. Meat products from the gene edited animals and their progeny would

[39] The HC Judge ruled that the exemption list is a closed list; that plants created with genetic techniques ZFN-1 and TALENs are genetically modified organisms.

also need to be approved for human consumption by FSANZ and would have to be labelled as a food derived from genetic modification. Food sold in a café, restaurant or takeaway is exempt from the labelling requirements.

The ACVM Act's role is to prevent or manage risks to public health, risks to trade in primary produce and risks to animal welfare associated with the use of agricultural compounds and veterinary medicines (ACVM Act, subsections 4(a) (i), (ii) and (iii)). The scheme of the ACVM Act (section 4A) enables integration with the Animal Welfare Act, Animal Products Act, Food Act and HSNO Acts (regulation of new organisms). The gene editing system used to eliminate beta-lactoglobulin from cow's milk may be deemed an *agricultural compound* for the purposes of the ACVM Act (subsections 4(a)(i),(ii) and (iii)) if it meets the definition for a *biological compound* (section 2(1)(a)(ii); intended for use in the direct management of animals for the purposes of promoting animal productivity and performance) and the biological compound is declared to be an agricultural compound for the purposes of the ACVM Act by Order in Council (section 2(1)(b)(iii)).

Gene-edited cows, gametes (sperm) and embryos (but not milk or meat) would meet the definition of a living organism and a *living modified organism* (LMO) resulting from modern biotechnology under the Cartagena Protocol on Biological Diversity. This would result in the requirement to comply with the procedure for transboundary movement of LMOs intended for direct use as food or feed, or for processing (Article 11)[40]. New Zealand importers and exporters are legally bound by the Imports and Exports (Living Modified Organisms) Prohibition Order 2005 (SR 2005/12).

Risk and potential benefits

The benefit of this milk would be to provide a high-quality protein source to sufferers of milk allergies and in particular infants, who are otherwise unable to consume cows' milk.

Some consumers, however, may prefer alternative milks that don't contain the allergy causing milk proteins from dairy animals, but which aren't a product of gene editing, such as those from other ruminant species, or plants or nut 'milks'. While beta-lactoglobulin is a major cows' milk allergen, some people will have allergic reactions not only to beta-lactoglobulin but to other milk proteins such as α-lactalbumin [138] and α-casein [139]. Lactose intolerance is another, unrelated, reason for adverse reactions associated with milk consumption. Where there is allergy or intolerance to cows' milk, care is needed, and tolerance to any substitute milk must be appropriately assessed [140]. There is a risk that people with milk allergies not solely caused by beta-lactoglobulin might suffer adverse health effects from other allergens when drinking a beta-lactoglobulin free milk. Hence, labelling would need to say "beta-lactoglobulin free" to avoid risks of legal liability associated with any claims around a product being "less allergenic", if this doesn't prove to be the case.

Implications for New Zealand

Royal Society Te Apārangi is encouraging New Zealanders to consider and share their views on some potential uses of gene editing in New Zealand. To assist the public discussion, it is publishing a number of papers that outline scenarios for the use of gene editing in pest management and healthcare, alongside this one on the primary industries. The Society will be running a number of stakeholder forums to discuss the technology later in the year.

[40] http://www.mfe.govt.nz/more/hazards/new-organisms/genetic-modification-new-zealand/exporting-living-modified-organisms

For further information

For more information and resources about gene editing, visit the Society's web pages: https://royalsociety.org.nz/gene-editing/, or contact info@royalsociety.org.nz.

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Staff from the Environmental Protection Authority, National Animal Ethics Advisory Committee, Ministry for the Environment, Ministry for Primary Industries, Ministry of Foreign Affairs and Trade, and the Office of the Prime Minister's Chief Scientific Advisor were also consulted in developing this paper.

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Attachment I

Scientific Organisation Views

on

Climate Change and GMOs

Life Sciences Network Inc

Further Submission

Proposed District Plan

Waikato District Council

15 July 2019

GMO: What is the independent scientific consensus?

The organizations you trust on climate science state that GMOs are safe and beneficial:

Organization	Statement on Climate Change	Statement on GMOs
American Association for the Advancement of Science	"The scientific evidence is clear: global climate change caused by human activities is occurring now, and it is a growing threat to society." (AAAS Board Statement on Climate Change, 2006)	"The science is quite clear: crop improvement by the modern molecular techniques of biotechnology is safe." (AAAS Board Statement on Labeling of Genetically Modified Foods, 2012)
American Medical Association	"Our AMA ... supports the findings of the Intergovernmental Panel on Climate Change's fourth assessment report and concurs with the scientific consensus that the Earth is undergoing adverse global climate change and that anthropogenic contributions are significant." (Global Climate Change and Human Health, 2013)	"Our AMA recognizes that there is no evidence that unique hazards exist either in the use of rDNA (GE) techniques or in the movement of genes between unrelated organisms." "Bioengineered foods have been consumed for close to 20 years, and during that time, no overt consequences on human health have been reported and/or substantiated in the peer-reviewed literature." (Report of the Council on Science and Public Health, 2012)
National Academies of Science (USA)	"The scientific understanding of climate change is now sufficiently clear to justify taking steps to reduce the amount of greenhouse gases in the atmosphere." (Understanding and Responding to Climate Change, 2005)	"Genetic engineering is one of the newer technologies available to produce desired traits in plants and animals used for food, but it poses no health risks that cannot also arise from conventional breeding and other methods used to create new foods." (Expert Consensus Report: Safety of Genetically Modified Foods, 2004) "An analysis of the U.S. experience with genetically engineered crops shows that they offer substantial net environmental and economic benefits compared to conventional crops." "Generally, GE crops have had fewer adverse effects on the environment than non-GE crops produced conventionally." (Impact of Genetically Engineered Crops on Farm Sustainability in the United States, 2010)
World Health Organization	"There is now widespread agreement that the Earth is warming, due to emissions of greenhouse gases caused by human activity. It is also clear that current trends in energy use, development, and population growth will lead to continuing – and more severe – climate change." (Protecting Health from Climate Change, 2008)	"GM foods currently available on the international market have passed risk assessments and are not likely to present risks for human health. In addition, no effects on human health have been shown as a result of the consumption of such foods by the general population in the countries where they have been approved." (20 questions on genetically modified foods, 2013)
European Commission	"There is unequivocal evidence that the Earth's climate is warming…. The consensus among climate experts is that it is extremely likely that the main cause of recent warming is the 'greenhouse' gases (GHGs) emitted by human activities, in particular the burning of fossil fuels – coal, oil and gas – and the destruction of forests." (Climate Change Fact Sheet, 2012)	"The main conclusion to be drawn from the efforts of more than 130 research projects, covering a period of more than 25 years of research, and involving more than 500 independent research groups, is that biotechnology, and in particular GMOs, are no more risky than conventional plant breeding technologies." (A decade of EU-funded GMO research, 2010)
The Royal Society (UK)	"There is strong evidence that the warming of the Earth over the last half-century has been caused largely by human activity, such as the burning of fossil fuels and changes in land use, including agriculture and deforestation." (Climate Change: A summary of the science, 2010)	"A previous Royal Society report (2002) and the Government's GM Science Review (2003/2004) assessed the possibilities of health impacts from GM crops and found no evidence of harm. Since then no significant new evidence has appeared. There is therefore no reason to suspect that the process of genetic modification of crops should per se present new allergic or toxic reactions." (Reaping the benefits: Science and the sustainable intensification of global agriculture, 2009)
International Science Academies: Joint Statement	"Climate change is real… there is now strong evidence that significant global warming is occurring. The evidence comes from direct measurements of rising surface air temperatures and subsurface ocean temperatures and from phenomena such as increases in average global sea levels, retreating glaciers, and changes to many physical and biological systems. It is likely that most of the warming in recent decades can be attributed to human activities." (The Science of Climate Change, 2001)	"GM technology has shown its potential to address micro-nutrient deficiencies [in developing nations]." "GM technology, coupled with important developments in other areas, should be used to increase the production of main food staples, improve the efficiency of production, reduce the environmental impact of agriculture, and provide access to food for small-scale farmers." "Decisions regarding safety should be based on the nature of the product, rather than on the method by which it was modified. It is important to bear in mind that many of the crop plants we use contain natural toxins and allergens." (Transgenic Plants and World Agriculture, 2000)

Attachment J

Waikato Tainui and Maniapoto Environmental Plans –

New Organism/GMO extracts

Life Sciences Network Inc

Further Submission

Proposed District Plan

Waikato District Council

15 July 2019

15.1.9 Genetic modification (GM) remains a controversial issue both globally and nationally. It is vital that Waikato-Tainui views and policies on the potential adverse consequences of GM are clearly outlined and recognised. Most importantly, Waikato-Tainui wants to avoid any disruption caused by Genetically Modified Organisms to the balance of indigenous ecosystems and/or to cultural beliefs and the whakapapa of taonga species.

New organisms and Genetically Modified Organisms

15.2.13 New organisms continue to be introduced, either intentionally or unintentionally, or developed through genetic manipulation (GMO's). Until proven otherwise, Waikato-Tainui remains concerned about the potential of these new organisms to attack, compete with, interbreed, or otherwise harm native and taonga species.

15.2.14 Waikato-Tainui also has a vested interest in protecting the economic sustainability of tribal members and/or tribal lands within the primary production sector, and the negative impacts on productivity which can be caused by the introduction of new organisms – whether GMO or otherwise. PSA (kiwifruit), varroa bee mite, and oyster herpes virus are examples of devastating biological outbreaks that risk creating severe economic loss and reduced capability.

Methods

(a) Applicants will engage with Waikato-Tainui prior to the submission of applications to the Environmental Protection Authority and/or other regulatory agency.

(b) The relevant authorities will work with Waikato-Tainui to ensure that all cultural and spiritual beliefs are appropriately recognised, respected and thoroughly considered.

(c) All efforts must be made by the relevant authorities to ensure that the effects of current and future introduced pests, new organisms, and Genetically Modified Organisms are minimised on taonga species, areas of significant indigenous vegetation, spiritual and/or cultural significance, and on the ecosystems in which these species and areas of significance occur.

Objective – new organisms and Genetically Modified Organisms

15.3.5 A precautionary approach to the introduction of new organisms and GMO's shall be adopted.

Policy – Protection of natural heritage from risk of new organisms

15.3.5.1 Applications for new organisms and GMO's must demonstrate that there are no risks to humans, indigenous ecosystems, indigenous species, or primary production.

19.2.1.4 New or genetically modified organisms (GMO) – The application of new or genetically modified organisms to address environmental issues has the potential to impact on indigenous species and habitats. Refer to Chapter 24 Biosecurity for objectives, policies and actions.

PART 25.0 - BIOSECURITY

25.1 INTRODUCTION

25.1.1 In this section, biosecurity refers to the use and management of plant and animal pests, control agents, hazardous substances as well as new and GMOs.

25.2.3 New organisms and genetically modified organisms

25.2.3.1 The term GMOs refers to new organisms created in a laboratory by the transfer of genes between different species. The use and application of new organisms and genetically modified organisms for medicines and food in currently on the increase. Maniapoto are concerned about the effects of GMOs on the mauri and whakapapa of indigenous species, the costs and benefits to Maniapoto and the risk to natural resources and the environment.

25.2.3.2 Maniapoto promote transparent information and processes on the development and use of GMOs and/or the introduction of new organisms. This includes considering the risks and threats, including outcomes and benefits and trade-offs between economic benefit and environmental integrity. Recent examples of PSA (Kiwifruit), varroa bee mite and oyster herpes virus highlight biological outbreaks that pose risks to businesses and communities. In many cases, such outbreaks are not through intentional introduction of organisms.

25.3.4 Objective: New or genetically modified organisms

To adopt a precautionary approach to the introduction and use of new organisms and GMOs in recognition of Maniapoto tikanga and kawa.

25.3.4.1 ***Policy***

Applications for new organisms and GMOs must demonstrate that there are no unacceptable risks to humans, indigenous ecosystems, indigenous species or primary production.

Action

(a) Ensure resource users, resource managers, applicants and decision makers give effect to Maniapoto values and interests in any proposal to develop or introduce new or genetically modified organisms.

(b) Require relevant agencies engage and consult with Maniapoto to ensure that Maniapoto values and interests are explicitly considered in decision-making criteria.

(c) Require relevant agencies to demonstrate that the effects of new organisms, and GMOs are negligible or minimised on taonga species, areas of significant indigenous vegetation, and on the ecosystems in which these species and areas of significance occur.

(d) New organisms and GMOs demonstrate no unanticipated effect, and no-effect on non-target species, or a minimal effect that may be acceptable to Maniapoto, before new organisms and GMOs are introduced into the Maniapoto rohe.

(e) Increase Maniapoto participation in decision-making on applications to introduce or develop a new and/or genetically modified organism.

Attachment K

Royal Society Review

Managing Risks Associated with

Outdoor Use of GMOs

Life Sciences Network Inc

Further Submission

Proposed District Plan

Waikato District Council

15 July 2019

Commissioned Review | July 2014

Managing Risks Associated with Outdoor Use of Genetically Modified Organisms

Professor Barry Scott FRSNZ
Professor Clive Ronson FRSNZ

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.