Papers for Technical Advisory Group meeting 4 April 2024 (excerpts – topics 3 and 5)

2. Paper title	Legislative purpose, key definitions, and regulation of specific technologies
Meeting date	4 April, 9-11 am
Approved by	Simon Rae

Item purpose and summary
This paper covers topics 1-5 on the agenda: 1. Legislative purpose 2. Key definitions 3. Regulation of specific technologies 4. Synthetic nucleic acid screening 5. Streamlining field trials, releases and medical use
Discussion questions
Set out following each topic background and discussion

Topic 3: Regulation of specific technologies

GENE EDITING

Questions for members of the Technical Advisory Group:

- In general, what exemptions could provide New Zealand with a regulatory system that delivers the benefits of gene editing technology while appropriately considering risks?
- From your perspective, what risks need to be provided for or considered when determining exempt gene editing techniques for a New Zealand context?
- Several countries base their exemptions on 'equivalence to what can be achieved through conventional breeding techniques'. What would you deem to be natural variation, considering genetic variability for an entire population may not be captured in current data sets (such as existing reference genomes)?
- Are off-target effects a significant issue specific to gene-editing techniques? Would you consider this a reason to not exempt gene-editing techniques under new legislation?
- What organisms would you consider it to be inappropriate or risky to include within the scope of any gene-editing exemptions? What organisms would you consider appropriate or not risky?

New Zealand's current regulatory approach for GMOs is referred to as 'process-based', as the HSNO Act focuses on the technology used to produce a GMO to determine what is and is not regulated. Internationally, there are alternative approaches to regulation including outcome-based and hybrid approaches. A hybrid approach, which has been adopted by the likes of Australia, Japan and England, combine a process-based approach while exempting certain gene-editing techniques from regulation.

There are several international examples of different levels of permissiveness to these regulatory exemptions. Outlined below is a comparison of jurisdictions including New Zealand, Australia, the recent EU proposal and Argentina. For the purpose of this discussion, the range of gene editing techniques are defined below, and international examples of their regulation are further explored.

Site Directed Nuclease Modifications

Site Directed Nuclease (SDN) genome editing involves the use of different DNA-cutting enzymes (nucleases) that are directed to cut the DNA at a predetermined location by a range of different DNA binding systems, creating a double stranded DNA break. These breaks can be repaired by one of two major cellular mechanisms;

- Nonhomologous end joining (NHEJ) – no template DNA is provided.
- Homology-directed repair (HDR) – template DNA is provided.

The range of applications of these repair mechanisms for gene editing purposes can be categorised as below.

SDN1: The position of the DNA break is precisely selected, but the DNA repair by the host cell is **random** and results in small nucleotide deletions, additions, or substitutions (NHEJ).

SDN2: The position of the DNA break is precisely selected, and a short template identical to the target site except for one or a few nucleotide changes is used to repair the break. The outcome is a targeted and predetermined **point mutation** in the desired gene of interest.

SDN3: The position of the DNA break is precisely selected, and a DNA repair template that contains new DNA sequence (e.g., gene) is used to repair the break. The donor organism of this DNA repair template further breaks SDN3 into sub-categories.

- **SDN3 cisgenics and intragenics:** The DNA repair template is sourced from a sexually compatible donor organism.
- **SDN3 transgenics:** The DNA repair template is sourced from a non-sexually compatible donor organism.

Modification	New Zealand	Australia	EU	England	Argentina
SDN 1			*Plants only*	*Plants + Animals*	
SDN 2			*Plants only*	*Plants + Animals*	
SDN 3 – cisgenesis and intragenesis			*Plants only*	*Plants + Animals*	
SDN 3 - transgenesis					

Regulated as GMO Organism specific exemptions Exempt

New Zealand

Process based regulatory approach

No modern gene technology techniques or modifications are exempt from regulation. All organisms modified with gene-editing techniques are regulated as GMOs.

Australia

Hybrid regulatory approach

Australia has a process-based trigger while exempting certain modifications (SDN-1) from regulation, resulting in a hybrid approach. In 2019, the Office of the Gene Technology Regulator clarified that SDN-1 edited organisms were not considered to be GMOs, based on the similarity of the technique to other non-regulated random mutagenesis techniques. This clarification was not based on equivalency to conventional breeding nor did it relate to the risk of the technique *per se*.

Under Australian legislation, SDN-1 edited organisms are not considered to be GMOs provided that:

- No nucleic acid template was added to the cells to guide genome repair following site directed nuclease application.
- The organism has no other traits from gene technology (e.g., a cas9 transgene, or an expressed SDN protein) in the final product.

Further to this, SDN1 edited plants are exempt from regulation provided they meet the above criteria.

European Union

Currently process-based regulatory approach – the new proposal (if agreed to by Member States) will establish a hybrid regulatory approach.

Under current EU legislation, all plants derived from New Genomic Techniques' (NGTs) face stringent regulations akin to traditional GMOs. Compliance involves navigating existing GMO approval processes and traceability and labelling requirements.

A new proposal from the EU Commission would create two new categories of NGT plant, each with their own regulations.

- **NGT1** – includes techniques that the EU Commission considered produce results equivalent to those that could result from conventional breeding. Subject to a verification procedure, based on the criteria in the proposal. NGT plants that meet these criteria would be treated like conventional plants and exempted from the requirements of the GMO legislation. This includes SDN1, SDN2, and SDN3 (cisgenesis and intragenesis).
- **NGT2** – the requirements of the current GMO legislation would apply. This includes SDN3 (transgenesis) techniques.

In February 2024, the EU Environment Committee voted in favour of the EU Commission's proposals for new rules on plants obtained through NGTs. The proposal will now go to Member States for their approval.

England

Hybrid regulatory approach

Precision Bred Organisms (PBOs) where the genetic changes could have occurred naturally or through traditional breeding methods are exempt from GMO regulation. GMOs organisms containing genes from a sexually incompatible species that could not occur through natural

breeding are still subject to regulation. These exemptions include SDN1, SDN2, and SDN3 (cisgenesis and intragenesis).

They intend to utilise two notification systems; one for PBOs used for research purposes, and the other for marketing purposes. They are also in the process of setting up a proportionate regulatory system for precision bred animals to ensure animal welfare is safeguarded.

Argentina

Outcome based regulatory approach

The Argentine regulations consists of only regulating genome-edited organisms with permanent insertion of foreign DNA. All gene-edited products are examined on a case-by-case basis by the Argentine Biosafety Commission.

If the final product is *not a combination of new genetic material* and *does not contain any temporary transgenes,* then it is not regulated as a GMO (i.e., exempt from regulation). This applies to all organisms (plants, animals and microorganisms). These exemptions include SDN1, SDN2, and SDN3 (cisgenesis and intragenesis). When an organism contains a combination of new genetic material or any temporary transgenes then the product is regulated as a GMO.

Considerations for New Zealand

We consider that a successful regulatory framework for New Zealand should, among a number of considerations, proportionately manage the risks that gene technologies pose and flexibly accommodate future technological developments. Should we consider a hybrid approach, a key decision will be determining which gene-editing techniques (and/or organisms) are exempted and how this would be updated as technology advances.

Our initial thinking is that we may consider a system that goes further than the current Australian settings by exempting gene editing modifications that are indistinguishable from conventional breeding techniques for plants, in a manner similar to the EU proposal. If we were to implement a regulatory approach of this nature, there are several aspects that we think we would need to take into consideration. Some of these are explored below.

Equivalence to what can be achieved through conventional breeding techniques

Some genome edits (including SDN-1 and SDN-2) produce changes that can be identical to those that are, or could be, produced in nature (i.e., naturally) and can be indistinguishable from conventional or other techniques that have been excluded from regulation due to a history of safe use. This is commonly the basis behind exemptions of gene editing techniques internationally, as seen above for the EU, England and Argentina.

However, through our targeted engagement it was been brought to our attention that there is complexity in determining the reference point for what is ‘natural’, given it is not a static state.

Off target effects

Common international justification for exempting SDN-1 is because changes brought about through SDN-1, including off target effects, are no different to natural mutations that occur with DNA breakage (unguided repair). The repair of off-target DNA breaks leads to the same range of DNA changes that are possible through repair of naturally occurring DNA breaks. Because the

changes brought about through SDN-1 are no different to natural mutations, they do not give rise to any different risks to natural mutations.

For further SDN genome edits, the importance of off target effects differs based on the application. For example, if an SDN2 introduced point mutation is replicated outside of the target site during the development of an edited crop, further breeding cycles can segregate for this resulting in a product that only contains the intended edit. In contrast, for a therapeutic application of an SDN2 point mutation this segregation could not easily occur and subsequently it may present a higher risk.

We are interested in your views on how a regulatory approach could control for a range of unintended effects, across a range of organisms.

Organisms

In relation to gene-editing techniques that are exempt, thought will need to be given to which organisms these exemptions do and do not apply to. Countries have taken a range of positions on this, as noted above. Below is a non-exhaustive list of organisms that may have relevance to the question of what organisms these exemptions apply to. In particular, we will need to appropriately manage any risks associated with gene editing that may be specific to certain organisms. We will also need to take into account a Māori perspective on the applications of these technologies.

- Microorganisms
- Fungi
- Plants
- Animals
- Human somatic cells
- Taonga species e.g., tuatara, kauri, mānuka

Other considerations

There are several further aspects that may need to be taken into consideration when we consider exempted techniques for New Zealand. These might include the stability of genome edits, traceability, reversibility and containability of gene-edited organisms. We would be interested in hearing your thoughts on these considerations.

NON-REGULATED TECHNOLOGIES

Questions for members of the Technical Advisory Group:

- Are there specific aspects of the Australia list of non-regulated technologies/organisms (Annex 2) that you think are better than the New Zealand list (Annex 1)? Any aspects that you think the New Zealand list does better than the Australian?
- Are there non-regulated technologies that you would add or remove from the Australian list? If so, why? How would you define those technologies?
- Is the Australian list and its definitions clear? Are there improvements you would make to it to make it clearer for researchers and industry?

Annex 1 lists technologies not regulated by the HSNO Act, as listed under the Not-GM regulations and confirmed via statutory determination.

Annex 2 lists technologies not regulated under the Australian Gene Technology Act.

Notable differences between the technologies that are not regulated under the Australian and New Zealand systems are:

- As noted above, SDN-1 gene-editing techniques[1] are not regulated under Australian legislation whereas in New Zealand they are;
- The EPA has determined that replication-defective viral vectors are not GMOs[2], whereas under Australian legislation these are still considered to be GMOs.

Additionally, Australian legislation has codified that null segregants, RNA interference, and nucleic acid vaccines are not GMOs or do not result in GMOs, whereas under the New Zealand system these have only been clarified via statutory determinations.

[1] *An organism modified by repair of single-strand or double-strand breaks of genomic DNA induced by a site-directed nuclease, if a nucleic acid template was not added to guide homology-directed repair.*

[2] Application number: APP202444. Year of decision: 2016. More information: https://www.epa.govt.nz/database-search/hsno-application-register/view/APP202444

REGULATED TECHNOLOGIES

Questions for members of the Technical Advisory Group:

- We are interested in whether there are technologies that you would consider should definitely be regulated under legislation (i.e., and we need to ensure that they are not inadvertently exempted)?
- Examples of technologies we would be interested to hear your views on include, but are not limited to:
    - Gene drives
    - Base editing
    - DNA methylation
- Are there any other technologies on the horizon that we should be aware of and that chould be potentially captured in the scope of legislation, so that the legislation is future proof?
- Do you have any views on how the technologies listed above, and others, chould be regulated?

Topic 5: Streamlining field trials, releases and medical use

Questions for members of the Technical Advisory Group:

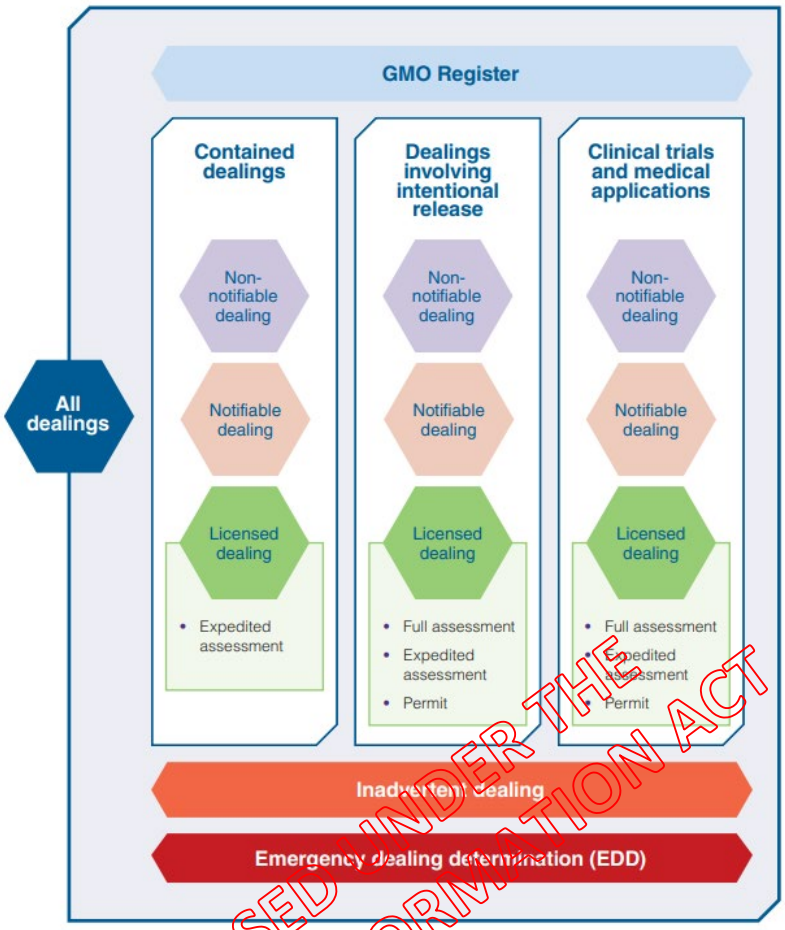
- Do you see any issues with the proposed risk-matrix, either operationally or in terms of risk?
- Do you think that the proposed risk-matrix will deliver benefits and risk-proportionate regulatory settings for field trials, environmental releases and medical uses?
- What are your views on better enabling the use of information from international regulators and enabling joint reviews with other international regulators?
    - What New Zealand-specific factors would it be good for the Regulator to give specific consideration to in their final assessment of a joint review?

Annex 4 contains a high-level description of the current regulatory requirements for field trials, full environmental releases and medical use of GMOs under Australia's regulatory regime.

Modification 1: A risk-matrix for contained, non-contained, and medical dealings

As part of the Third Review of Australia's National Gene Technology Scheme, a number of changes to the regulatory requirements for contained and non-contained 'dealings' were proposed. We would like to test with the TAG one of the options proposed under the Third Review, Option C, which is outlined in the explanatory paper *Modernising and future-proofing the National Gene Technology Scheme*. Below is a summary of the explanatory paper's outline of Option C, adapted to refer to a new proposed New Zealand Regulator, for clarity.

The Australian National Gene Technology Scheme's Option C matrix differentiates between three categories of dealings with GMOs: contained dealings, dealings involving the intentional release of a GMO into the environment, and clinical trials and medical applications. Within each category, there are several authorization types based on risk level. A visual representation of this matrix can be seen here:



Non-notifiable dealings would cover those dealings that are very low risk and can be commenced without prior notification to the Regulator, provided specific requirements are met and the dealing does not involve an intentional release of a GMO into the environment. These dealings are not exempt from regulation, as SDN-1 is under Australia legislation for instance, as these dealings must still meet certain requirement.

Notifiable dealings would cover those dealings that are low risk. The requirements attached to these dealings are that they would need to be reported to the Regulator annually, and for contained dealings that they would need to be undertaken in Physical Containment facility appropriate for the research in question. One change that we propose to make to this framework is that the requirement for assessment by an Institutional Biosafety Committee would be removed, and the responsibility to ensure dealings meet the criteria and requirements would lie with the organization or person(s) responsible for the relevant containment facility.

Licensed dealings would cover medium to high-risk dealings or dealings where there is substantial uncertainty. While all licensed dealings would be assessed by a proposed new Regulator before the dealing commences, the level of assessment and regulatory oversight applied to the dealing would be graduated on the basis of indicative risk. Risk management measures, reporting requirements, and monitoring and enforcement would apply.

Permits would be required for medium risk dealings that do not require case-by-case risk analysis, for instance where a Regulator has extensive experience and defined management conditions. Examples include certain field trials of GM plants and clinical trials using previously authorized viral vectors.

Expedited assessments could be used for medium-high risk dealings requiring case-by-case risk analysis and tailored licence conditions. This applies when some risks are well understood, such as variations on permit-eligible dealings, dealings with familiar parent species but unfamiliar traits, previously licensed GMOs, or GMOs authorized by reputable overseas agencies. A Regulator would perform a risk analysis and may consult if warranted.

Full assessments are required for high-risk dealings or where there is substantial uncertainty, involving case-by-case risk analysis and full consultation. This applies when the Regulator has limited or no experience. It is only necessary for intentional release and clinical trials/medical applications categories, not for contained dealings. The assessment involves applicant suitability checks, risk assessment and management plan, and consultation with government agencies, advisory committees (if established), and the public. The timeframe depends on the breadth of consultations needed.

For non-notifiable dealings, notifiable dealings, permits, the new Regulator could determine and then publish in a secondary legislative instrument (within the parameters set by the primary legislation and following public consultation) the types of dealings that are covered by these authorisations. Additionally, as each of the three categories would have non-notifiable and notifiable dealings, this would mean establishing what are very low risk and low risk dealings for the purposes of all three categories.

This framework could provide a risk-based, graduated approach to regulating dealings with GMOs, with streamlined processes for lower risk activities and more comprehensive assessments for higher risk or uncertain activities.

For a detailed description of this framework, please see **Annex 5**.

Modification 2: Enable the regulator to make use of information from other 'recognised' international regulators

Consider adding the ability for the regulator to make use of information from other 'recognised' international regulators for the purpose of assessing licensed dealings. This would be similar to the 'trusted regulator' provisions under the hazardous substances provisions of the HSNO Act.[3]

Instead of the proposed new Regulator having to consider, review and verify information from international regulators, potentially repeating technical work already done overseas, this additional provision would allow the regulator to use their discretion to apply reliable information from recognised regulators, saving resources and time for both the regulator and applicants.

In order to use information from international regulators for licensed dealings, the proposed new Regulator would have to recognise a specific regulator in advance through a Gazette Notice. The regulator would be able to recognise other international regulators if:

- they operate in a manner comparable to the New Zealand Regulator,
- their legislative regime is comparable to New Zealand's gene technology legislative regime,

[3] For more information, see Hazardous substances assessments: Improving decision-making – Discussion document and section 76E of the Hazardous Substances and New Organisms Act 1996.

- information from the international regulator is readily accessible by the New Zealand Regulator.

Modification 3: Enable joint reviews of licensed dealings

The third modification that we consider could be made to the Australian legislation is adding the ability for the new Regulator to collaborate with other comparable overseas regulators in the assessment of applications for licensed dealings under two categories: dealings involving the intentional release of a GMO into the environment, and clinical trials and medical applications. An *enabling* provision would be added to the new primary legislation for gene technology, such that the new Regulator could form joint assessment agreements with other regulators in advance, but the new Regulator would not be required to enter into joint assessment agreements.

Joint reviews of veterinary medicines by New Zealand and other countries

New Zealand and the following overseas jurisdictions have put in place guidance documents to allow joint reviews for the registration of a veterinary medicine product:

- New Zealand, Australia, and Canada
- New Zealand and United Kingdom.[4]

Under these veterinary medicine joint reviews each regulator is assigned a technical section of the submission, and each review report is peer-reviewed by the other countries' regulators. The aggregation of the review reports constitutes the basis for the regulatory decision of all regulators in their respective countries. At the end of the joint review process, **each partner regulator makes its own sovereign decision based on recommendations contained in the review reports and its own legislative and regulatory context.**

Agreement between Argentina and Brazil on joint evaluation and authorisations

In October 2022, a memorandum of understanding was agreed between the regulatory agencies of Argentina and Brazil to allow the joint evaluation and authorisations of products of agricultural biotechnology. The agreement commits Argentina and Brazil to start working together and to build the necessary mechanisms and procedures for the joint evaluation and authorisations of products of agricultural biotechnology.

GM safety assessment sharing arrangement between FSANZ and Health Canada

FSANZ and Health Canada have been collaborating on GM safety assessment sharing since 2013. Under the arrangement, where approval for a GM food is being sought from both FSANZ and Health Canada, companies may request to have their product assessed under a safety assessment sharing arrangement.[5] Under this arrangement, and in line with agreed protocols, an application is submitted to both agencies, but only one food safety assessment is prepared (either by FSANZ or Health Canada). The assessment is then referred to the other agency for review and input to ensure it meets the requirements of both agencies. The joint food safety

[4] More information on joint reviews for veterinary medicines can be found here: Registering a veterinary medicine | NZ Government (mpi.govt.nz)

[5] For more information see: https://www.foodstandards.gov.au/science/international/Pages/gm-food-safety.aspx

assessment is then used by both FSANZ and Health Canada for their own separate and independent decision-making process.

Potential benefits of joint reviews

Joint reviews for dealings under the new legislation would offer the following benefits without compromising domestic standards and scientific rigour:

- Reduces administrative burden for industry by harmonizing data requirements, and offering transparent and predictable regulatory processes
- Simultaneous access to multiple major markets
- Consistent and robust regulatory decisions
- More and better choices for users and patients by supporting faster access and expanding the number of product and treatment options available
- Maximizes efficiency for partner regulators by sharing the work
- Builds a stronger global review community that allows partner regulators to work across jurisdictions to share knowledge and expertise
- Independent, sovereign decision-making by each partner regulator while striving for harmonization.

A potential issue with joint reviews might include:

- Factors specific to the New Zealand context may not be given sufficient weight in the assessment, despite the New Zealand regulator being able to make its own final assessment of the full assessment report.

Annex 1: Technologies not regulated by the HSNO Act, as listed under the Not-GM regulations and confirmed via statutory determination

Hazardous Substances and New Organisms (Organisms Not Genetically Modified) Regulations 1998
For the purposes of the HSNO Act, the following organisms are not to be regarded as genetically modified: (a) organisms that result solely from selection or natural regeneration, hand pollination, or other managed, controlled pollination: (b) organisms that are regenerated from organs, tissues, or cell culture, including those produced through selection and propagation of somaclonal variants, embryo rescue, and cell fusion (including protoplast fusion): (ba) organisms that result from mutagenesis that uses chemical or radiation treatments that were in use on or before 29 July 1998: (c) organisms that result solely from artificial insemination, superovulation, embryo transfer, or embryo splitting: (d) organisms modified solely by— (i) the movement of nucleic acids using physiological processes, including conjugation, transduction, and transformation; and (ii) plasmid loss or spontaneous deletion: (e) organisms resulting from spontaneous deletions, rearrangements, and amplifications within a single genome, including its extrachromosomal elements. Despite anything in subclause (1)(d), if nucleic acid molecules produced using *in vitro* manipulation are transferred using any of the techniques referred to in subparagraph (i) or subparagraph (ii) of subclause (1)(d), the resulting organism is a genetically modified organism for the purposes of the Act.

Techniques determined to not result in a GMO / organisms determined not to be GMOs
Eukaryotic cells treated with double-stranded RNA[6]
Null segregants (eukaryotic) [7]
Epigenetics[8]
Replication-defective viral vectors[9]
Non-germline transformed vertebrates (APP202122) [10]

[6] Application number: APP203395. Year of decision: 2021. More information: https://www.epa.govt.nz/database-search/hsno-application-register/view/APP203395
[7] Application number: APP204173. Year of decision: 2024. More information: https://www.epa.govt.nz/database-search/hsno-application-register/view/APP204173
[8] Application number: APP203395. Year of decision: 2021. More information: https://www.epa.govt.nz/database-search/hsno-application-register/view/APP203395
[9] Application number: APP202444. Year of decision: 2016. More information: https://www.epa.govt.nz/database-search/hsno-application-register/view/APP202444
[10] Application number: *APP202122. Year of decision: 2015. More information: https://www.epa.govt.nz/database-search/hsno-application-register/view/APP202122*

Annex 2: Technologies not regulated under the Australian Gene Technology Act

Techniques that are not gene technology

Somatic cell nuclear transfer, if the transfer does not involve genetically modified material.

Electromagnetic radiation-induced mutagenesis.

Particle radiation-induced mutagenesis.

Chemical-induced mutagenesis.

Fusion of animal cells, or human cells, if the fused cells are unable to form a viable whole animal or human.

Protoplast fusion, including fusion of plant protoplasts.

Embryo rescue.

In vitro fertilisation.

Zygote implantation.

A natural process, if the process does not involve genetically modified material. Examples of natural processes include conjugation, transduction, transformation and transposon mutagenesis.

Introduction of RNA into an organism, if:

(a) the RNA cannot be translated into a polypeptide; and
(b) the introduction of the RNA cannot result in an alteration of the organism's genome sequence; and
(c) the introduction of the RNA cannot give rise to an infectious agent.

Organisms that are genetically modified organisms

An organism that has had its genome modified by oligonucleotide-directed mutagenesis

An organism modified by repair of single-strand or double-strand breaks of genomic DNA induced by a site-directed nuclease, if a nucleic acid template was added to guide homology-directed repair

Organisms that are not genetically modified organisms

A whole animal, or a human being, modified by the introduction of naked recombinant nucleic acid (such as a DNA vaccine) into its somatic cells, if the introduced nucleic acid is incapable of giving rise to infectious agents.

Naked plasmid DNA that is incapable of giving rise to infectious agents when introduced into a host cell.

An organism modified by repair of single-strand or double-strand breaks of genomic DNA induced by a site-directed nuclease, if a nucleic acid template was not added to guide homology-directed repair.

An organism that results from an exchange of DNA if:
(a) the donor species is also the host species; and
(b) the vector DNA does not contain any heterologous DNA.

An organism that results from an exchange of DNA between the donor species and the host species if:

(a) such exchange can occur by naturally occurring processes; and
(b) the donor species and the host species are micro-organisms that:
    (i) satisfy the criteria in AS/NZS 2243.3:2010 for classification as Risk Group 1; and
    (ii) are known to exchange nucleic acid by a natural physiological process; and
(c) the vector used in the exchange does not contain heterologous DNA from any organism other than an organism that is involved in the exchange.

An organism that is descended from a genetically modified organism (the initial organism), if none of the traits it has inherited from the initial organism are traits that occurred in the initial organism because of gene technology.

An organism that has inherited particular traits from an organism (the initial organism), being traits that occurred in the initial organism because of gene technology, if:

(a) the initial organism was not a genetically modified organism (because of the application of regulation 5); or
(b) all such inherited traits are traits that occurred in the initial organism as a result of a modification described in an item in this Schedule.

An organism that was modified by gene technology but in which the modification, and any traits that occurred because of gene technology, are no longer present.

Agrobacterium radiobacter strain K1026.

Pasteurella multocida strain PMP1.

Annex 3: Current members of the International Gene Synthesis Consortium

Aclid	Ginkgo Bioworks
Aldevron	Genome Project-write (GP-write)
Ansa Biotechnologies	iBioFAB
Atum (formerly DNA2.0)	IDT
Azenta Life Sciences (formerly GENEWIZ)	Molecular Assemblies
Battelle	Nuclera
BGI	Raytheon BBN Technologies
Bioneer Corp.	Ribbon Biolabs
Blue Heron Biotech	Switchback Systems
Camena Bioscience	Synbio Technologies
The DAMP Lab	Synplogen
DNA Script	Telesis Bio
Edinburgh Genome Foundry	Thermo Fisher Scientific
Elegen Bio	Touchlight
Emerald Cloud Lab	Tsingke Biotechnology
Evonetix	Twist Bioscience
GenScript USA	

Further information:

Diggans, J., & Leproust, E. (2019). Next steps for access to safe, secure DNA synthesis. *Frontiers in bioengineering and biotechnology*, *7*, 86.

Hoffmann, S. A., Diggans, J., Densmore, D., Dai, J., Knight, T., Leproust, E., ... & Cai, Y. (2023). Safety by design: Biosafety and biosecurity in the age of synthetic genomics. *Iscience*, *26*(3).

Kobokovich, A., West, R., Montague, M., Inglesby, T., & Gronvall, G. K. (2019). Strengthening security for gene synthesis: recommendations for governance. *Health security*, *17*(6), 419-429.

Rose, S., Alexanian, T., Langenkamp, M., Cozzarini, H., & Diggans, J. (2024). Practical Questions for Securing Nucleic Acid Synthesis. *Applied Biosafety*.

Sophie Rose and Cassidy Nelson (November 2023). *Synthetic Nucleic Acid Screening: Overcoming challenges with implementation*. The Centre for Long-Term Resilience.

Tucker, J. B. (2010). Double-edged DNA: preventing the misuse of gene synthesis. *Issues in Science and Technology*, *26*(3), 23-32.

World Economic Forum, Nuclear Threat Initiative (2020). *Biosecurity Innovation and Risk Reduction: A global Framework for Accessible, Safe and Secure DNA Synthesis*.

Annex 4: Description of the regulatory requirements for non-contained 'dealings' in Australia (taken, and amended for clarity, from the Final report of the Third Review of the National Gene Technology Scheme)

Under Australia's legislative system for gene technology and genetically modified organisms, all dealings with GMOs are prohibited unless they are authorised by the Office of the Gene Technology Regulator (OGTR) under the Gene Technology Act 2001. The Act requires that dealings with GMOs are authorised as:

- an exempt dealing;
- a Notifiable Low Risk Dealing (NLRD);
- a licensed dealing;
- a dealing included on the GMO Register; or
- specified in an emergency dealing determination.

Australia has a risk-based regulatory scheme for GMOs. Each of the above authorisation categories (or 'tiers') impose different regulatory requirements depending on the level of risk posed by the GMOs in that particular category. For example, some categories impose specific containment requirements, while others require case-by-case assessment.

For the purposes of this workstream, the relevant *current* authorisations are: licensed dealings and dealings included on the GMO Register. Exempt dealings and Notifiable Low Risk Dealings will be discussed under the *Contained dealings* workstream document, while authorisations specified in an emergency dealing determination will be covered under the *Regulator* workstream document.

Licensed dealings

The Gene Technology Act 2000 (the Act) provides a licensing system under which a person can apply to the OGTR for a licence authorising dealings with GMOs. Licence application forms issued by the OGTR specify the information required to support an application. The OGTR may provide advice to individuals and organisations to aid in the preparation of licence applications, including identifying specific data that would be required to inform the Regulator's risk assessment.

Each application for a licence to work with a GMO is subject to a comprehensive, science-based, case-by-case analysis process and the preparation of a Risk Assessment and Risk Management Plan (RARMP), as outlined in the Regulator's Risk Analysis Framework 2013. The RARMP informs the Regulator's decision on whether to issue a licence, and which specific licence conditions to apply in order to manage risks.

There are three types of licences that can be issued by the Regulator:

- Dealings involving Intentional Release (DIR) licences;
- Dealings Not involving Intentional Release (DNIR) licences; and
- Inadvertent Dealings licences.

Depending on the type of licence, application assessments may involve consultation with a range of relevant parties. For example, the Act requires the Regulator to invite written submissions from the public on RARMPs prepared for DIR applications. The Regulator must also seek advice from states and territories, Gene Technology Technical Advisory Committee

(GTTAC), prescribed Commonwealth authorities and agencies, the Environment Minister and any local council that the Regulator considers appropriate.

The majority of DIR licences issued to date have been for experimental field trials (limited and controlled releases) or general/commercial releases of genetically modified (GM) plants. A small number of DIR licences have also been issued for GM vaccines for human or veterinary use, either for trial (limited and controlled release) or general/ commercial release. The release of GM animals would also require a DIR licence.

DNIR licences authorise dealings with GMOs which do not meet the criteria for classification as exempt dealings, NLRDs or DIRs. The majority of DNIRs involve work with GM pathogenic (disease-causing) organisms, or GMOs containing genes from pathogens or genes that encode toxins. DNIRs can also be used to authorise clinical trials with non-transmissible GMOs. As with exempt dealings and NLRDs, work authorised under a DNIR licence must not involve the release of the GMO into the environment.

Inadvertent Dealings licences are temporary licences (no longer than 12 months) intended to allow people who have unintentionally come into possession of a GMO to dispose of it in a manner which protects the health and safety of people and the environment. Inadvertent Dealings licences can only be issued when the Regulator is satisfied that a person has come into possession of a GMO inadvertently. Consideration of Inadvertent Dealings applications follows a simpler process than required for other application types.

Managing risks which may be associated with licensable dealings is achieved by imposing licence conditions that specify when, where and how certain activities with the GMO may be carried out. A number of licence conditions are specified in the Act and apply to all GMO licences. The Regulator may also impose additional licence conditions specific to each application. Failure to comply with the conditions of a licence is an offence under the Act.

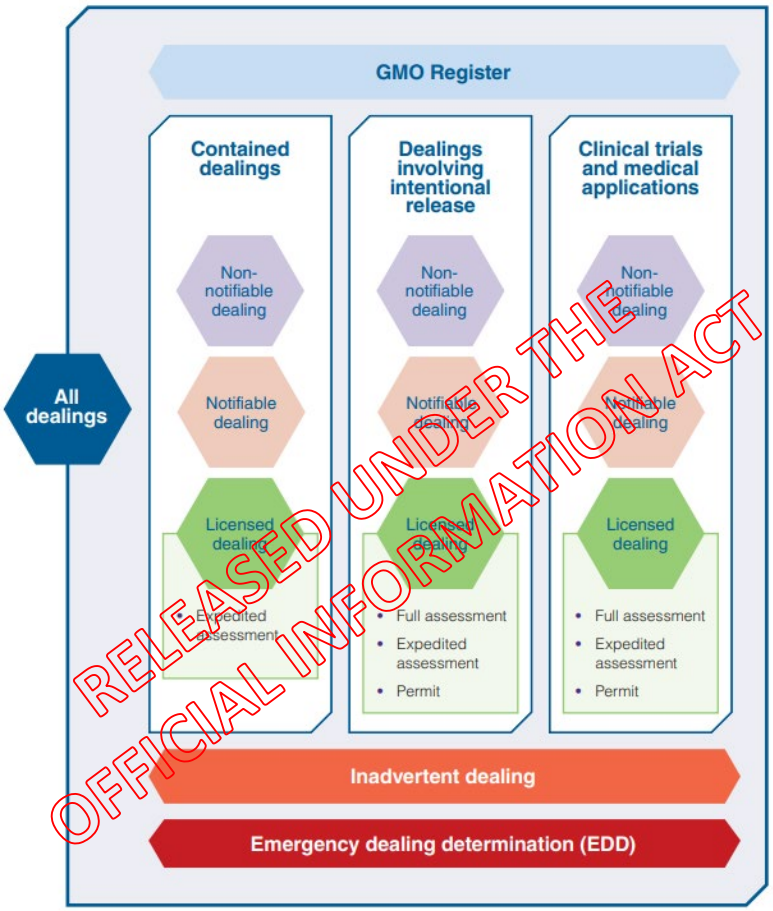
GMO Register

The GMO Register (the Register) provides an alternative mechanism for dealings with certain GMOs to be authorised. The Register is a list of dealings that the Regulator has determined pose minimal risk, and do not require those conducting the dealing to be covered by a licence in order to adequately protect the health and safety of people or the environment. Once a dealing has been entered on the Register anyone can conduct the dealing, in accordance with any conditions specified in the Register.

To date, only one dealing has been entered on the Register – the commercial scale release of four lines of colour modified GM carnations.

Annex 5: Detailed description of Option C

We would like to test with the TAG the Option C matrix taken from the explanatory paper *Modernising and future-proofing the National Gene Technology Scheme: Proposed regulatory framework to support implementation of the Third Review of the Scheme*. This matrix differentiates between three broad categories of dealings: contained dealings, dealings involving the intentional release of a GMO into the environment, and clinical trials and medical applications. Within each of these three broad categories would be a number of authorisation types, as shown here:



Non-notifiable dealings (very low risk dealings)

Dealings currently classified as exempt dealings (specified in Schedule 2 of Australia's *Gene Technology Regulations 2001*) would come under the new 'non-notifiable dealings' pathway. This is currently dealings that do not involve an intentional release of a GMO into the environment nor involve a genetic modification other than a modification that has been described as exempt by the Gene Technology Regulations. For example, contained research into very well understood organisms using well established processes for creating and studying GMOs.

For these dealings:

- the primary legislation (the Gene Technology Act) would describe the considerations required for categorisation of a dealing with a GMO as non-notifiable

- the new Regulator would be enabled to determine (within the parameters set by the primary legislation and following public consultation) the types of dealings that are non-notifiable. These would be published in a non-legislative regulatory instrument (examples in the New Zealand context include EPA notices) to provide transparency, accountability and certainty for industry and other stakeholders.

As each of the three categories would have non-notifiable dealings, this would mean establishing what are very low risk dealings for the purposes of all three categories.

While the legislation could specify relevant dealings (i.e. through legislative lists) that would be non-notifiable dealings for the purpose of each category, where features of the dealing are relevant to two or more categories, it would be necessary for the person undertaking the dealing to establish and provide evidence to support the relevant authorisation type.

Regulatory process for non-notifiable dealings

As with the current regulatory requirements for exempt dealings, dealings would meet the criteria for non-notifiable dealings on the basis of risk could be commenced without prior notification to the new Regulator, provided the requirements for those dealings are met.

Notifiable dealings (low risk dealings)

Under Australia's current legislation, Notifiable Low Risk Dealings (NLRDs) are activities with GMOs undertaken in containment (i.e. not released into the environment and suitable for Regulator-approved physical containment facilities, levels 1 to 3) that have been assessed as posing low risk to the health and safety of people and the environment provided certain risk management conditions are met. These are described under Parts 1 and 2 of Schedule 3 of Australia's *Gene Technology Regulations 2001*. Under the Australian system currently, an NLRD may only be undertaken after it has been assessed as being an NLRD by an Institutional Biosafety Committee.

Under the new model it is considered that, for notifiable dealings, that the new primary legislation for gene technology in New Zealand could:

- describe the considerations that influence whether a dealing with a GMO is low risk such that it can be classified as a notifiable dealing
    - For example, considerations that are currently required for listing GMO dealings as NLRDs under the Australian legislation, such as whether the dealing with the GMO would involve any risk to the health and safety of people, or to the environment taking into account the properties of the GMO as a pathogen or a pest, and the toxicity of any proteins produced by the GMO, and any related risk management measures, would likely also be relevant to notifiable dealings.
- enable the Regulator to determine (within the parameters set by the primary legislation and following public consultation) the types of dealings that are notifiable. As for non-notifiable dealings, these would be published in a non-legislative regulatory instrument (examples in the New Zealand context include EPA notices) to provide transparency, accountability and certainty for industry and other stakeholders.

Regulatory process for notifiable dealings

The authorisation process to undertake a notifiable dealing could be similar to that of the existing NLRD process under the Australian system, in that notifiable dealings would need to be reported to the Regulator annually (using the online reporting form). Notifiable dealings reported to the Regulator would be published on the Regulator's website as part of the Record of GMO Dealings.

One significant modification to the Australian system would be the removal of the requirement that a notifiable dealing may only be undertaken if it has been assessed as being a notifiable dealing by an Institutional Biosafety Committee. We consider that replacing this current requirement with the requirement that the organisation, entity or person(s) responsible for the containment facility must ensure that the dealing to be undertaken is a notifiable dealing able to be undertaken in that facility.[11] We consider that this modification would remove the potential for disproportionate costs on small organisations that may not have the resources to stand-up an Institutional Biosafety Committee while still ensuring an appropriate level of accountability.

Requirements applicable to notifiable dealings would include:

- compliance with any conditions or restrictions placed on the dealing including any containment conditions (where applicable)
    - For example, it would be conducted within a facility certified to either physical containment level 1 (PC1), PC2 or PC3 (as appropriate), or another facility specifically approved in writing by the new Regulator, and in accordance with any conditions imposed on the facility.
- reporting to the new Regulator and participation in audits conducted by the Regulator
- adverse event reporting to the Regulator
- that the dealing be conducted only as provided for in the non-legislation regulatory instrument
- that the dealing be conducted by people with appropriate training and/or experience
- that the GMO be transported, stored and disposed of according to the new Regulator's Guidelines for the Transport, Storage and Disposal of GMOs, or alternative conditions specifically approved by the Regulator
- that changes to the dealing involve reassessment as per any conditions or requirements specified in new secondary legislation for gene technology
- compliance with any requests from the new Regulator to provide further information about the dealing and with any directions given by the new Regulator.

As each of the three categories would have notifiable dealings, this would mean establishing what are low risk dealings for the purposes of all three categories.

While the legislation could specify relevant dealings (i.e. through legislative lists) that would be notifiable dealings for the purpose of each category, where features of the dealing are relevant

[11] This could potentially be prescribed as: "The organisation, entity or person(s) responsible for the ownership, control and management of the containment facility where the notifiable dealing is to be undertaken must ensure that the dealing is a notifiable dealing able to be undertaken in that containment facility."

to two or more categories, it would be necessary for the person undertaking the dealing to establish and provide evidence to support the relevant authorisation type.

Licensed dealings

A licence would be required for GMO dealings for which the indicative risk is medium or high, or for which there may be substantial uncertainty as to risk level.

While all licensed dealings must be assessed by the new Regulator before the dealing commences, the level of assessment and regulatory oversight applied to the dealing would be graduated on the basis of indicative risk (to enable further streamlining of lower risk applications). For example, where regulatory experience and scientific information establish that the risk for a particular dealing is at the lower end of the medium to high indicative risk categorisation, then the assessment of that application would be streamlined and involve reduced data requirements in line with the permit or expedited licence requirements described below.

All licensed dealings would share common post-commencement processes and safeguards. This would include:

- Risk management measures – If the risks associated with the activity can be managed, then the Regulator may allow the activity (by issuing a permit or licence) and may also impose risk management measures and/or conditions.
- Reporting and notification requirements (including through routine reporting, trigger-based notification and in response to the Regulator's information gathering powers).
- Iterative information exchange with regulated stakeholders to ensure the risk management conditions of a licence have the right settings.
- Monitoring and enforcement – Having commenced the dealing under the authority of a permit or licence, permit/licence holders would be subject to compliance audits and targeted post-commencement assessments. This would include monitoring of compliance with risk management conditions and enforcement through the application of offence provisions in the legislation.

Permit

A type of licence known as a permit would be required for dealings that are medium indicative risk and do not require a case-by-case risk analysis.

This licence type would include GMO dealings with which the new Regulator has extensive regulatory experience. Dealings would only be added to this licence type if a risk analysis undertaken by the new Regulator determined that any risks posed by the dealings could be managed with a specific set of defined management conditions that have already been used in New Zealand and are confirmed to be effective in managing risk and, for field trials, effective in containing the GMO.

In addition, dealings with GMOs developed with new technologies could be authorised under permits if the risks posed by the dealings can be managed by an identified 'universal' set of licence conditions (again where such conditions have been clearly established as effectively managing risk).

The new primary legislation for gene technology would describe the relevant considerations that must be taken into account in determining whether a dealing with a GMO may be subject to a permit, the new Regulator would consult publicly on the dealings that could be so authorised

(and any relevant risk management conditions) and the dealings able to be authorised in this way would be published in a tertiary legislation instrument.

Examples of dealings that could be included in this licence type are:

- Dealings for which the Regulator has extensive regulatory experience regarding management measures that are effective in confining GMOs and mitigating any risks posed by certain GMO dealings, such as field trials of certain GM plants that apply limits and controls used in the past to effectively prevent the dispersal and the persistence of the GMO in the environment.
    - An example of this under the Australian system could be a field trial of cotton genetically modified for herbicide tolerance. Most licences issued by the Australian Office of the Gene Technology Regulator (OGTR) authorising field trials of this type of GM cotton contain the same or very similar conditions. On the basis of a risk analysis, the Australian regulator could identify a set of standard permit conditions that could manage the risks of any given field trial of herbicide tolerant GM cotton, taking into account the scale of the trial.
- Dealings for a clinical trial involving a GM virus based on a viral vector backbone that has been authorised in the past by the new Regulator, expressing a transgene or class of transgenes and/or displaying a modified trait that has been previously assessed by the Regulator.
    - For example, the OGTR has approved multiple licences for clinical trials using Adeno-associated virus based vectors expressing different clotting factor proteins for treatment of different types of haemophilia.
- Dealings with GMO therapeutics authorised through particular medical approvals, where the number of patients to receive the therapeutic are limited.

It is considered that a permit (for medium indicative risk dealings) could be available across two of the three categories, that is 'dealings involving intentional release' and 'clinical trials and medical applications'.

Permits would not be available for contained dealings because the three current contained dealings authorisation types under the Australian system have already been found to provide graduated and proportionate levels of oversight for contained dealings.

Regulatory process for permits

Applicants would apply to the new Regulator for a permit prior to commencing the dealing.

Applications for permits would be assessed in the shortest timeframe, as the new Regulator would only make administrative, financial and compliance checks regarding the applicant (i.e. applicant suitability checks).

Following assessment, a permit would either be issued with standard conditions (as required), or the new Regulator may refuse to issue the permit, or the application would be reallocated to a more appropriate licence type. Permits would only be issued if applicants certify that standard conditions can be met.

The common post-commencement processes and safeguards described above would apply.

Expedited assessment

An expedited assessment could be used for GMO dealings with a medium-high indicative risk that require a case-by-case risk analysis and tailored licence conditions.

The appropriateness of an expedited (or reduced) assessment under this category reflects that some risks are already well understood by the Regulator, such that only some components of the dealing could require assessment.

For example, an expedited assessment could be sought if:

- the dealing involves a variation on matters that would otherwise make it eligible for the permit category
    - For example, an open-ended timeframe in which to undertake a clinical trial or a field trial that is larger scale or has different containment measures than one which would otherwise meet the criteria for a permit.
- it is for a GMO dealing for which the new Regulator has extensive regulatory experience with the species that has been genetically modified (parent species) but that requires a case-by-case risk analysis due to unfamiliarity with the introduced trait or the type of dealings. For example:
    - a clinical trial of a GMO therapeutic based on adeno-associated virus, expressing a new transgene or class of transgene and/or displaying a new modified trait.
- it is for a GMO dealing that occurs in a certified containment facility but requires a case-by-case risk analysis due to the parent organism and the introduced trait – For example, dealings currently authorised under DNIR and described in Part 3 of Schedule 3 to the GT Regulations.
- = GMO dealings have been previously licensed by the Regulator and the risk analysis undertaken in the past would significantly inform assessment of the new application
    - For example, a new field trial of a GM plant that has been authorised in the past under a full assessment licence or is a new transformation event of a construct previously assessed for a field trial licence.
    - For example, a field trial of a plant obtained by crossing GMO X and GMO Y if field trials of GMO X and GMO Y have been previously authorised under a full assessment licence and standard permit criteria are not suitable.
    - For example, the commercial release of a GM vaccine if it has been commercially released in the past under a full assessment licence. For instance, if an organisation sought authorisation for the commercial release of a GM cholera vaccine similar to one previously authorised under a licence that was surrendered. As the risk analysis for GMO dealings proposed in the new application would be significantly informed by the risk assessment and risk management plan prepared for the surrendered licence, the new application could be streamlined under the new model.
- the dealings with the GMO have been assessed and authorised by reputable regulatory agencies overseas. The application process could be streamlined where the overseas risk analysis is available and could be considered by the Regulator. An assessment would however still be required to ensure that the findings of the international risk analyses are relevant to the New Zealand context.
    - For example, commercial release of GM soybean authorised for commercial release in Canada or the commercial release of a GM vaccine authorised in Europe.

Regulatory process for expedited assessments

Applicants could apply to the new Regulator for a licence using the expedited assessment form.

In addition to the administrative, financial and compliance checks undertaken for a permit, the new Regulator would perform a risk analysis to determine if all risks can be managed and to identify risk management measures (this would involve preparing a risk assessment and risk management plan). An expedited assessment would involve consultation if the new Regulator identified issues warranting consultation, or otherwise may involve limited or no consultation on the basis of one or more of the following:

- the new Regulator has consulted on similar GMO dealings in the past,
- the new Regulator has previously assessed and approved a similar GMO dealing and the proposed dealing would not involve intentional release to the environment or
- a comparable overseas regulator has approved the GMO for commercial use in another country. Following an expedited assessment, the new Regulator would either issue a licence (with conditions imposed based on the risk analysis) or refuse to issue a licence.

It is considered that having first categorised the type of dealing, an expedited assessment (for medium-high indicative risk dealings) would be a relevant to all three categories of dealing types (i.e. contained dealings, dealings involving the intentional release of a GMO into the environment, and clinical trials and medical applications).

Full assessment

It is considered that a full assessment could be required for dealings with a high indicative risk or where there may be substantial uncertainty as to risk. This assessment would involve a case-by-case risk analysis and full consultation.

In essence, this licence type would be available for GMO dealings for which the new Regulator has no or limited regulatory experience.

It is considered that a full assessment could only be necessary for two of the three categories of dealings, that is 'dealings involving intentional release' and 'clinical trials and medical applications'. Where dealings are contained, a full assessment would not be required given that any risks associated with these dealings are sufficiently managed by the containment conditions applied.

Regulatory process for full assessments

Applicants would apply to the new Regulator for a licence using the full assessment form.

Consistent with the other licence types, the new Regulator would perform applicant suitability checks and a risk analysis to determine if all risks can be managed and to identify risk management measures. The assessment of these applications would involve consultations with other relevant central government agencies, relevant advisory committees (if these are established) and the public.

Processing full assessment licences would therefore involve three components: applicant suitability, writing a risk assessment and risk management plan and consultation with stakeholders and relevant groups. The timeframe for the assessment of these applications would depend on the breadth of consultations needed. For instance, it is anticipated that the assessment timeframe of a broad release of a novel GM animal may require more consultation than the commercial release of a GM field crop. Likewise, a commercial release of a GM plant and a field trial of a GM plant may require the same consultation and therefore have the same assessment timeframe.

Following a full assessment, the new Regulator would either issue a licence (with conditions imposed based on the risk analysis) or refuse to issue a licence.

Annex 6: Additional definitions provided

Word requiring a technical definition	NZ	Australia	Suggested improvements
Organism	***organism***— **(a)** does not include a human being: **(ab)** includes a human cell: **(b)** includes a micro-organism: **(c)**includes a genetic structure, other than a human cell, that is capable of replicating itself, whether that structure comprises all or only part of an entity, and whether it comprises all or only part of the total genetic structure of an entity: **(d)** includes an entity (other than a human being) declared to be an organism for the purposes of the Biosecurity Act 1993: **(e)** includes a reproductive cell or developmental stage of an organism ***host organism*** means an organism that is the subject of a genetic modification procedure ***inseparable organism*** means any organism which is unable to be separated from any other organism ***qualifying organism*** means a new organism that is or is contained in a qualifying medicine or qualifying veterinary medicine	***organism*** means any biological entity that is: (a) viable; or (b) capable of reproduction; or (c) capable of transferring genetic material.	

Word requiring a technical definition	NZ	Australia	Suggested improvements
	human cells— **(a)** means human cells, human cell lines, or human tissues that are being grown or maintained outside the human body; and **(b)** includes human reproductive cells or human embryonic cells that are being grown or maintained outside the human body		
Product related	***qualifying medicine*** means a medicine or new medicine (as defined in section 3 of the Medicines Act 1981) that— **(a)** is or contains a new organism; and **(b)** meets the criteria set out in section 38I(3) ***qualifying veterinary medicine*** means a veterinary medicine (as defined in section 2(1) of the Agricultural Compounds and Veterinary Medicines Act 1997) that— **(a)**is or contains a new organism; and **(b)**meets the criteria set out in section 38I(3)	***GM product*** means a thing (other than a GMO) derived or produced from a GMO.	
Environment	***environment*** includes— **(a)**ecosystems and their constituent parts, including people and communities; and **(b)**all natural and physical resources; and **(c)** amenity values; and **(d)** the social, economic, aesthetic, and cultural conditions which affect the matters stated in paragraphs (a) to (c) or which are affected by those matters ***intrinsic values***, in relation to ecosystems, means those aspects of	***environment*** includes: (a) ecosystems and their constituent parts; and (b) natural and physical resources; and (c) the qualities and characteristics of locations, places and areas.	

Word requiring a technical definition	NZ	Australia	Suggested improvements
	ecosystems and their constituent parts which have value in their own right, including— **(a)** their biological and genetic diversity; and **(b)** the essential characteristics that determine an ecosystem's integrity, form, functioning, and resilience		
	containment means restricting an organism or substance to a secure location or facility to prevent escape; and includes, in respect of genetically modified organisms, field testing and large-scale fermentation ***containment facility*** means,— **(a)**in relation to new organisms (other than genetically modified organisms), a facility registered as a containment facility under the Biosecurity Act 1993; **(b)**in relation to genetically modified organisms, a facility which complies with the controls imposed by an approval granted under any of sections 42, 42A, 42B, or 45 ***containment structure*** means a containment facility that is a vehicle, room, building, or other structure, set aside and equipped for the development of genetically modified organisms	***facility*** includes, but is not limited to, the following: (a) a building or part of a building; (b) a laboratory; (c) an aviary; (d) a glasshouse; (e) an insectary; (f) an animal house; (g) an aquarium or tank.	

THE SECOND MEETING OF THE GENE TECHNOLOGY TECHNICAL ADVISORY GROUP - MINUTES [excerpts – topics 3 and 5]

Date and time:	9am – 11am Thursday 4 April
Location:	Microsoft Teams
Chair:	Emily Parker (Ferrier Institute, Department Science Advisor MBIE)
Invitees:	Tim Hore (Otago), Billy Sheppard (Auckland), Alec Foster (Scion), Andy Allan (Plant and Food Research), Nikki Freed (Daisy Lab), Rachel Perret (Malaghan), Ariana Estoras (AgResearch) Richard Scott (AgResearch), Jasna Rakonjac (Massey), Neil Gemmell (Otago), David Ackerley from 10.00am (VUW)
MBIE attendees:	s 9(2)(a) Simon Rae (MBIE, Policy Director Emerging Technologies)
Apologies	Maui Hudson (Waikato)

Item	Discussion
Topic 3: Regulation of Specific Technologies	The TAG was asked to consider exemptions for Site Directed Nuclease Modifications. Points raised by members of the TAG: • SDN3 definition of donor organism is problematic as the sequence for insertion could be synthetic with no clear source. • The term 'sexually compatible' is problematic. • Additional DNA in an organism is often a trigger point. SDN1 exemptions could be seen as lower risk as no additional DNA. • In EU plants, animals and microbes considered differently with respect to exemptions. In plant breeding there are off target effects but they are not considered significant issues, same for gene technology in plant breeding. However, this is a significant issue for animals (animal welfare and ethics considerations required). • Noted that more modern systems have the hybrid approach to regulation. • Group generally agreed that exemption of SDN1 would be low risk and enabling. More consideration needed for SDN2. • Could be useful to document off targets effects of SDN3 for commercial IP protection and public assurance, could include a requirement to document the changes. Noted that this could be difficult if there is no reference genome. • Provide clarity when an application goes down a different pathway (e.g. ACVM). For example for animal genetic modification sent down an animal ethics rather than gene technologies pathway

	• More clarity on economic impacts may assist with considering exemptions. Group discussed options to put requirements in tertiary legislation not in the primary legislation (the Act), this would flexibly accommodate future technological developments. Points raised by members of the TAG regarding which organisms exemptions do and do not apply to: • Group agreed to exclude high risk modification of pathogens. Group asked if highly pathogenic organisms are covered in any other legislation, but potentially allow 'trusted' researchers with PC3 facilities more leeway. • Need to be appropriate consultation when thinking about editing in Taonga species. • A values-based approach to genetic modification of native species may be required, especially in light of climate change and other emergent risks. • Consider the mechanisms that the EPA have already put in place for Taonga species, such as Ngā Kaihautū Tikanga Taiao • Balancing enabling mechanisms for science community to undertake this work but consideration Māori interests and rights is required. • SDN3 – consider reframing, 'The DNA repair template is sourced" to the "sequence is sourced". Comments s 9(2)(ba)(i) A hybrid approach makes sense but the primary problem with regulating new technologies is the speed at which they evolve and how to shift more established technologies from the process based track to an exempt track over time. The legislation would need to have a process for this with the appropriate community consultation to support the shift out of the process based space. If something like this is in place then the process of identifying exemptions will be easier because it isn't just a one time process. This could be important given the tight timeframes for having legislation in place. *Annex 1: Technologies not regulated by the HSNO Act, as listed under the Not-GM regulations and confirmed via statutory determination and Annex 2: Technologies not regulated under the Australian Gene Technology Act* Points raised by members of the TAG: • the need for more time to consider these annexes. • that the AU Act determines that "Eukaryotic cells treated with double-stranded RNA" does not result in a GMO, area we need to fix in our Act going forward given vaccine technologies, and other RNA technologies that may develop in the future.

	• Replication defective viral vectors are not GMO's this is missing from the AU list. **The TAG members noted the following key points to be considered by MBIE's policy team:** • **Exemption of SDN1. Some species may need to be considered more carefully, for example taonga species and high-risk pathogenic organisms.** • **Potential to require information/verification of off-target modifications with SDN3.** • **Plants and animals could be treated differently with potential alternative pathways for animal modifications (e.g. consideration of animal ethics via other legislation pathways).** • **Mechanisms and processes are already in place for consideration of Māori rights and interests in the EPA** • **New Act may need to consider appropriate consultation mechanisms for taonga species.**
Topic 5: Streamlining field trials, releases and medical use	The Group discussed a risk-matrix for contained, non-contained and medical dealings.  Points raised by members of the TAG: • Risk matrix proposal would work for clinical and medical applications. • Specific examples of what is in each box in the visual representation (above) would be useful.

	• Unclear what goes in what box in the visual representation above. • Will be important to grandfather current approvals across to any new system, a large amount of work is currently being undertaken on notifiable organisms in containment, don't want to create more work or bottle necks. • Definition of non-notifiable and notifiable will be critical. • In AU Institutional biosafety committees determine if the dealing is notifiable or not. Unlike under previous HSNO IBSC delegations where these committees assessed applications and put controls in place. Could be unintended consequences of this pathway. • Could be advantages to treating clinical and medical applications in a different lane as community groups have different perceptions of GE in the health context. This could help with education and understanding. • Notifiable dealings: Not all institutions have a Biological Safety Committee, could consider delegation to facility operator but don't want to create another roadblock. • Not clear if dividing up different purposes in the risk matrix means there are different risks for different use of technologies, potential for this to cause hold ups in other areas (e.g agricultural use). • Checks and balances still need to be in place, an example scenario, create a plant in containment, progeny are SDN1 so become non notifiable, can then be released into the environment – what are the checks in place? **The TAG members noted the following key points to be considered by MBIE's policy team:** • **The need to test various scenarios in the different 'lanes' to better evaluate the implications of this approach** • **How current approvals will be transferred to a risk matrix** **Action:** TAG was reminded to provide MBIE with examples and scenarios to test within the proposed risk matrix.

MINISTRY OF BUSINESS, INNOVATION & EMPLOYMENT
HĪKINA WHAKATUTUKI

Industry Focus Group

23rd April 2024

Foreword…

- Collecting insight to help inform the system design.

- Objectives:
    1. Risk proportionate,
    2. Enabling,
    3. Accessible,
    4. Future focussed, and
    5. Protects rights and interests

- Advantages and potential consequences.

To Discuss Today:

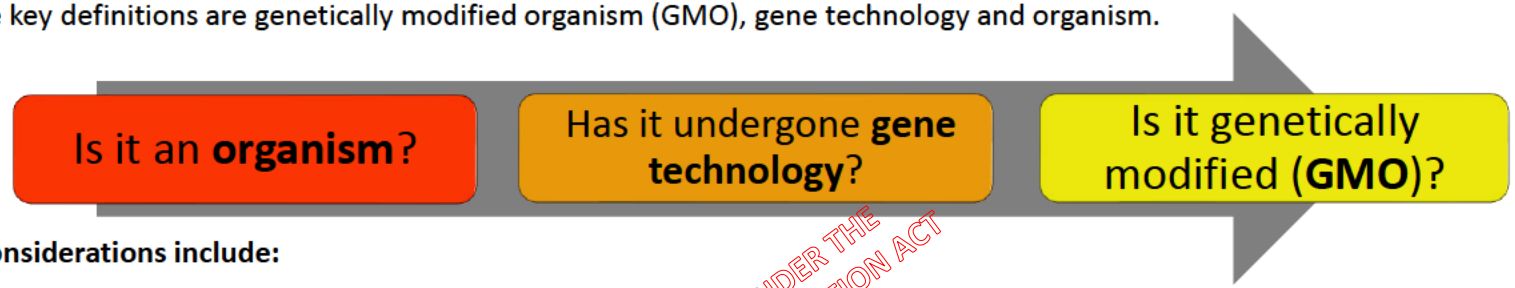
1. Regulated Definitions
2. Technologies and Organisms
3. Authorisations
4. Examples

Regulated definitions

GMO, Gene technology and Organism

We are modifying how we regulate gene tech (future-proofing)

- We are reviewing the key statutory definitions from the HSNO Act and the Australian Gene Technology Act.
- The key definitions are genetically modified organism (GMO), gene technology and organism.



Key considerations include:

- Consistent definitions across statutes.
- Human beings will not be deemed a GMO.
- Include all techniques of ***modification***. Consider excluding techniques where genetic material has been altered in a way that does not occur naturally by reproduction and/or natural recombination.
- **Organisms** will extend beyond biological entities to manufactured entities and will include microorganisms.
- It may also be necessary to define some or all native flora, fauna and taonga species as organisms requiring separate consideration.

Questions - what are the potential implications for industry groups and different sectors if:

1. Definitions were extended beyond modification techniques and include alteration and construction of genetic material?
2. Human beings are regulated as organisms subject to gene technologies?

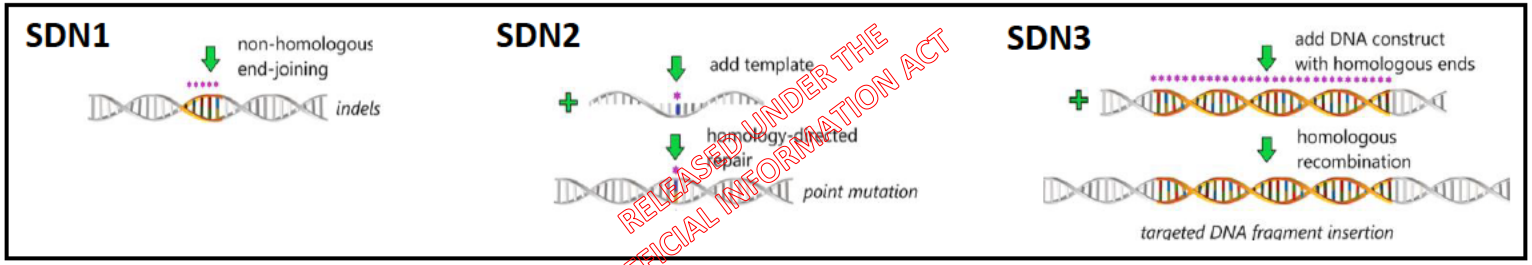
Technologies and organisms

Gene editing techniques and non-regulated technologies

There will be techniques that are exempt (gene editing)

There are a range of gene editing techniques and their application to different types of organisms (eg plants, animals, microorganisms) can create different risks.

This regulatory reform programme presents the opportunity to consider **whether and what gene editing techniques may be specifically exempted from regulatory oversight**.



Questions - **what are the potential implications for industry groups and different sectors if:**

1. For all organisms – we consider exempting gene editing techniques that produce modifications that are a result of natural cell repair mechanisms, from regulation?

2. For plants only – we consider exempting gene editing techniques that produce modifications that produce results equivalent to those that could arise from conventional breeding, on the basis that there are no unique risks posed when compared to conventional breeding practices?

3. What would this mean for supply chains? And in particular GM-free supply chains?

There will be technologies that are not regulated

Currently the HSNO Act regulations can be used to define technologies as not producing a genetically modified organism but these have not been used to exempt gene editing techniques as they have in Australia.

Statutory determinations are utilised to clarify whether specific techniques fall within non-regulated categories set out in legislation. Some of these are still regulated under the current Australian system as GMOs (replication deficient viral vectors).

Australian legislation codifies a greater number of specific techniques that are not or do not produce GMOs. This is provided as a **list of non-regulated technologies in secondary legislation**.

Examples of non-regulated technologies / non-GMOs (non-exhaustive)

- Organisms that result from controlled pollination
- Somatic cell nuclear transfer
- Embryo rescue
- In vitro fertilisation
- Null segregants
- Eukaryotes treated with dsRNA
- Epigenetics
- Replication-defective viral vectors

Questions **- what are the potential implications for industry groups and different sectors if:**

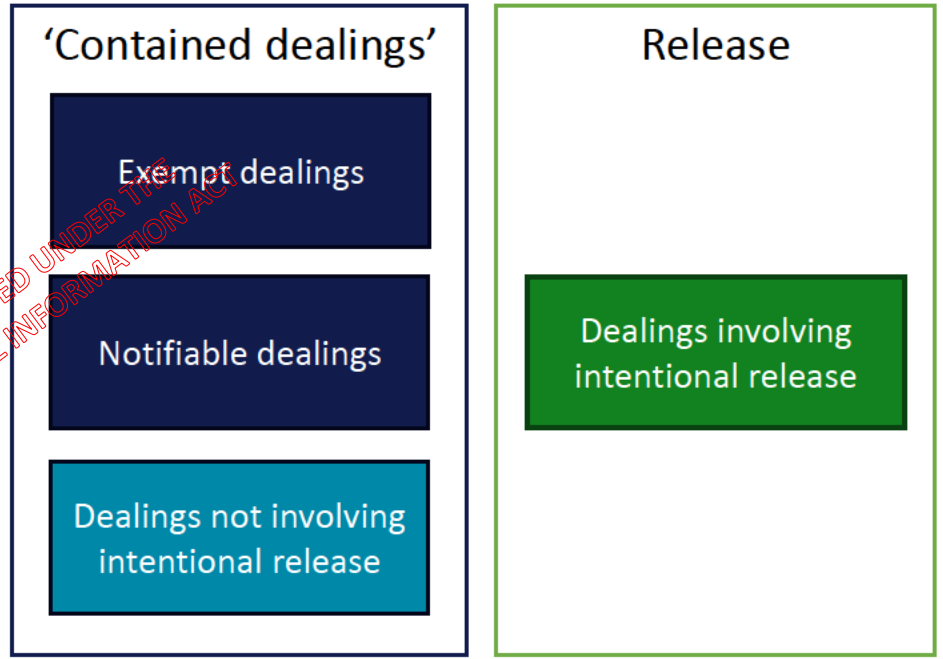
1. NZ adopts the Australian system and current list of non-regulated technologies, while also considers codifying previous New Zealand EPA statutory determinations that are currently regulated under the Australian system (i.e., replication deficient viral vectors)?
2. Do you see any advantages or disadvantages in this approach?

Authorised activities

Laboratory research, medical use and environmental release

Current Australian system

- Comprehensive risk-tiering framework, for laboratory research.
- Other ‘dealings’ for field trials, medical use and full release are licensed and require case-by-case assessment.
- Under the current system the OGTR has struggled with where medical use should fit.



A risk matrix will guide the regulatory intervention

Regulated

Not Regulated

Contained activities	Intentional release	Medical use	Not Regulated
Non-notifiable	Non-notifiable	Non-notifiable	Exempt techniques
Notifiable	Notifiable	Notifiable	Non-regulated technologies
Full assessment	Permit Expedited assessment Full assessment	Permit Expedited assessment Full assessment	

Description of risk tiers

Non-Notifiable Activities

Characteristics:

- Very low risk.

Requirements:

- Must not be released into the environment.
- Must be conducted in containment (does not have to be an approved Physical Containment facility).

Notifiable Activities

Characteristics:

- Low risk.

Requirements:

- Must not be released into the environment.
- Must be conducted in an approved Physical Containment facility (usually PC1 or PC2).
- Users must send details of the activities to regulator each year.

Licenced Activities

Characteristics:

- Doesn't meet the non-notifiable or notifiable criteria.
- Or are activities which the regulator specifies *cannot* be notifiable activities.
- Example: Pathogenic organisms or GMOs containing genes from pathogens or that encode toxins.

Requirements:

- Requirements would be set by the regulator on a case-by-case basis.

Overseas information and expertise will be used

Recognised Regulators

Provision would allow the new regulator to assess certain licensed assessments through the expedited pathway where an application has previously been assessed by a 'recognised' regulator.

Overseas regulators that are 'recognised' in advance by the New Zealand regulator would need to have sufficiently similar regimes and have data that was readily available.

Joint Reviews

Provision would allow the new regulator to undertake joint assessments of applications with other overseas regulators.

Applicants would apply to all regulators at the same time and parts of the application would allocate between regulators.

Regulators would retain the ability to make their own sovereign decisions.

Recognised Approvals

Medical treatments that are approved by 'recognised' regulators would be automatically approved under the New Zealand system.

The criteria by which overseas regulators are 'recognised' by the New Zealand regulator for this automatic approval provision *may* be different from the expedited pathway recognition.

Thank you.

Questions?

Ministry of Business, Innovation & Employment
www.mbie.govt.nz

Additional slides if needed

Regulated definition	NZ's HSNO Act	Australian Gene Technology Act
GMO	***Genetically modified organism*** means, unless expressly provided otherwise by regulations, any organism in which any of the genes or other genetic material: (a) have been modified by in vitro techniques; or (b) 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. *Refers to the Regulations for when organisms are not genetically modified.*	***Genetically modified organism*** means: (a) an organism that has been modified by gene technology; or (b) an organism that has inherited particular traits from an organism (the initial organism), being traits that occurred in the initial organism because of gene technology; or (c) anything declared by the regulations to be a genetically modified organism, or that belongs to a class of things declared by the regulations to be genetically modified organisms; **but does not include:** (d) a human being, if the human being is covered by paragraph (a) only because the human being has undergone somatic cell gene therapy; or (e) an organism declared by the regulations not to be a genetically modified organism, or that belongs to a class of organisms declared by the regulations not to be genetically modified organisms
Gene Technology		***Gene technology*** means any technique for the modification of genes or other genetic material, but does not include: (a) sexual reproduction; or (b) homologous recombination; or (c) any other technique specified in the regulations for the purposes of this paragraph.

Regulated definition	NZ's HSNO Act	Australian Gene Technology Act
Organism	***Organism*** does not include: (a) human being: (ab) includes a human cell: (b) includes a micro-organism: (c) includes a genetic structure, other than a human cell, that is capable of replicating itself, whether that structure comprises all or only part of an entity, and whether it comprises all or only part of the total genetic structure of an entity: (d) includes an entity (other than a human being) declared to be an organism for the purposes of the Biosecurity Act 1993: **(e)** includes a reproductive cell or developmental stage of an organism	***organism*** means any biological entity that is: (a) viable, or (b) capable of reproduction, or (c) capable of transferring genetic material.

Gene Technology Industry Focus Group – meeting minutes

Excerpts

First meeting of the Gene Technology Industry Focus Group 23 April 2024

Key Points from the discussion were:

- Supportive of adapting and improving the legislative framework of Australia, to fit New Zealand's specific context and circumstances. However, it was noted that there are aspects of the Australian legislation that we should improve on by looking to other countries.
- Important to align with our major trading partners.
- Gene technology is moving rapidly and there is a need to ensure any new regulatory framework is future proofed.
- Need to streamline regulatory approvals to avoid some of the complex interactions with other regulators and legislation, this could include co-approvals between different regulators and different countries.
- Support for continued function of institutional biosafety committees for low risk applications but compliance and auditing needs to be streamlined.
- Widespread support for exempting low risk gene editing technologies.
- Industry can play a role in stewardship by developing their own quality management systems.
- Concerns from organics about gene-edited organisms entering their supply chains, and potential increased costs to certify their products as non-GM (this also applies to non-organic products for some markets or customers).

The new Gene Regulator:	**Regulated Definitions** The IFG discussed that: Important to get the "definitions" updated and in a manner that reflects the nuances of the various techniques and risks (noting that these also need to be future proofed). Critical to get definitions right. Trigger for whether things are regulated. FSANZ is amending their definitions to trigger whether pre-market safety assessment requested for foods produced by genetic technologies and the definition of gene technology. Alignment important. Align definitions of GE with those under Cartagena. Important to distinguish between modified microbes and mammalian cell lines that aren't viable outside of the lab or human body. Avoid unnecessary restrictions.

	Definition of GE needs to take a clear position on 'mutagenesis' and not only align with Australia. Important to align with major trading partners and to not fall behind, nor do we want to get too far ahead of the curve. Important to ensure there is continuity of definitions across countries and jurisdictions to enable collaboration to continue. Potential opportunity merging for regulators to work together on approvals. E.g. FSANZ and Health Canada – agree to co-approve an application. Health Canada accepting FSANZ's findings. However, can become complex if multiple regulators/agencies are involved. Some members of the IFG felt that regulation for GE in medical and health sector should be treated differently to agriculture. Others had the converse view and felt that biomed should not be treated differently. Need to consider if the modification is traceable, detectable and therefore if the legislation is enforceable. Concerns raised about applying future definitions retrospectively so as not to restrict ability to use things we have been doing for a long time. New definitions need to factor in nuances around techniques, how they are applied and the risks they pose. **Authorised activities** IFG discussed: Risk tiers: under the gene tech framework clinical trials will be licensed activities – will need to consider interaction with the proposed Therapeutics Products Act or whatever replaces it to ensure the process is cost effective and efficient. If information from overseas regulators could be used to assess risks? For example, for medical treatments. Mutual recognitions used in some overseas jurisdictions, for example if a medical application has been approved in other OECD countries then could automatically be approved. The role of institutional biosafety committees in the proposed compliance framework. Play a big role in exempt and non-notifiable in the AU system. Compliance of containment and transitional facilities are managed by MPI, hurdles are significantly higher than in AU.

	[MBIE noted that IBSC function would be retained and incorporated into notifiable risk tier.] Limitations of large volumes of batch culture in microbial systems. For example, in the AU system if you grow more than 25L of an organism you move up a risk tier. Increasing the volumes for precision fermentation would be advantageous. [MBIE noted the increased risks with larger volumes such as containing spills. Exploring an outcome-based criteria]. Some members noted an outcome based approach would be useful. Timelines critical in medical applications (e.g. xeno transplantation and CarT therapy) and could be legislated to improve the outcome for patients. Trials vs use – as soon as move into therapy, need a license specific to treatment in new system will treating a patient with single dose of CarT cells an environmental release? [MBIE noted this type of application is the why MBIE is considering splitting out medical use in the risk matrix]. Dealings not involving an intentional release (DNIR) applications require a lot of information in AU system and take a long time (90 working days). It will be critical to get the timeframes right for commercialisation. Useful to have a system that has emergency powers, for example in the AU system used emergency powers to fast-track approvals (e.g. Melbourne Cup – horse flu outbreak, approved GMO vaccine). Consider physical containment (PC) different for microorganisms and mammalian cells and animals (e.g. PC1 and PC2), based on risk.

Meeting of the Gene Technology Industry Focus Group 5 June 2024

The key points from the discussion were:

- Consumer research into GM is being undertaken by several industries – willingness to share.
- Variety of views on consideration of costs and benefits; regulator should focus on a technical evaluation of the risks, benefits assessment will need to considered somewhere (by applicant or regulator).
- Industry would consider risks to market assess and trade agreement irrespective of the regulator. Would need to be considered somewhere in the system.

Specific policy options to test with you	**Costs and benefits** Challenging to look at economic impact as returns are multifactorial. Regulator and applicant should consider risks and benefits, if not looking at benefit as well then always behind, note that there are always higher risks with new technologies. Depends on the purpose of the proposed legislative change, if purpose is to enable the use of the technology, then difficult to imagine how you can only look at one side of the equation (i.e. the risks). Benefits consideration raises questions of tolerating higher environmental risk for a higher benefit. Should have a consistent risk tolerance (or baseline) over which not prepared to go. Would expect there to be a good commercial reason (strong beneficial aspect) to applications. Concerns with regulator balancing risks and benefits, regulator should focus on pure risk evaluation. Issues with current system is regulator assessing wide range of considerations, takes a very long time and is stifling innovation – the more complicated we make regulators job the more stifling it is.

Meeting of the Gene Technology Industry Focus Group: 13 June 2024

The key points from the discussion were:

- Alignment with trading partners and other regulatory frameworks (e.g. FSANZ) important.
- Need to streamline regulatory approvals to avoid some of the complex interactions with other regulators and legislation (e.g Medsafe), this could include co-approvals between different regulators and different countries.
- Industry can play a role in stewardship by developing their own quality management systems.
- Coexistence of GMO and non-GMO supply chains is not a new issue and is possible with industry assurance programmes and a rigorous standard.
- Concerns about unintentional release and how this will be managed.
- Variety of views on consideration of costs and benefits; regulator should focus on a technical evaluation of the risks, benefits assessment may be useful an environmental release.

Recap of proposed changes	The IFG discussed: How risk matrix dealt with unintentional release. [MBIE noted this would be dealt with by MPI, under Biosecurity Act would be considered an unwanted organism and could respond as a biosecurity incursion] The trigger for regulation being like the AU regime, adopt same definitions as proposed for OGTR for gene technology and genetically modified organisms. Alignment important, align definitions of genetically modified organism with those under Cartagena and FSANZ. [MBIE is talking with FSANZ]. OGTR and FSANZ not aligned. Will need to work with MOH as the Medicines Act is looked at to ensure regulation of gene tech-based therapies and vaccines is not overly burdensome, slow, or a costly parallel regulatory process. [MBIE looking at ways to streamline joint approvals process e.g. joint reviews with Medsafe, use of overseas data from recognised regulators to allow for expedited license.] Careful to avoid gene tech regulator being inundated with applications for therapeutics as is the case in AU. [MBIE noted that the proposed medical use stratification would allow low risk to be put in non-notifiable category to reduce burden on the regulator.] Where field trials will sit in the risk matrix [MBIE noted that field trials would not be a specific category in the proposed

	risk tier system and would likely be environmental conditional releases]. Fermentation volume restrictions in AU is 25 litres, in containment, this has been challenging for startups. For micro-algae this volume is based on ability to form a population in the environment, needs to be risk proportionate. Gene edited endophyte research – potentially low risk but large proportion of NZ economic output relies on rye grass – critical to get things right. Clarified the risk being discussed is biological risk. [MBIE noted that market access and consumer risks still live policy discussion]. In AU grains industry developed a document called 'Delivering market choice with GM crops'. Endorsed by State and Federal Government. Engagement involved organics industry. Put market and consumer choice back to the industry, not the role of Government to regulate consumer choice. David Hudson happy to talk to any interested parties about this approach. Important for farmers to have optionality.

Papers for Technical Advisory Group meeting 2 May 2024

2. Paper title	Key issues: Scope and definitions, authorised activity, gene editing techniques and non-regulated techniques
Meeting date	9am – 11am Thursday 2 May 2024
Approved by	Simon Rae

Item purpose and summary

This paper focuses on the legislative questions, namely definitions, regulatory approach and authorisations that will be discussed by the Gene Technology Ministerial Group. MBIE has provided advice on key aspects of the legislation including:

- Scope and definitions
- Authorised activity
- Gene editing techniques and non-regulated techniques

Recommendations have considered advice from the TAG, workshops with other key government agencies, Industry Focus Group, Māori Focus Group and targeted stakeholder engagements.

Key perspectives that have inputted into our advice are:

- Current definitions are outdated, and new definitions need to be future focussed. Modification of genes and genetic material need to include 'alteration' and 'construction' (in addition to modification) and better represent the technologies that are used for modifying genes.
- It is critical to future proof new legislation allow for review and response to technological advancement.
- The organism definition includes microorganisms, virus vectors and bacteriophages.
- Widespread support for exempting low risk gene editing technologies, and more specifically, there is strong support for a level of permissiveness provided through adoption of approaches taken by justifications such as the UK, with industry supportive of implementing exemptions of gene editing that are closer aligned to our major trading partners' exemptions.
- The research community have expressed some dislike of statutory determinations, specifically that they must be applied for and cannot be initiated by the EPA; and existing statutory determinations are publicly available but may not be easily discoverable by researchers or companies. We note, however, that it is not necessary to seek a statutory determination.
- There has been support for adopting the Australian system while making additions to reflect previous New Zealand's statutory determinations, including organisms that are still regulated as GMOs under the Australian system.
- Rights and interests of Māori specific to NZ and should be carried forward from the HSNO Act.
- Attendees of the MBIE-hosted roundtable at the Life Sciences Summit observed that joint reviews (where regulators jointly review an application with an overseas regulator) were viewed favourably by industry and worked well for veterinary medicines under the ACVM Act.
- Our colleagues from the Australian Office of the Gene Technology Regulator in particular noted that they have found their current settings challenging and ill-suited

for medical applications, as the settings do not currently differentiate between uses in a medical setting and in the environment.

- The organics industry and other parts of the primary sector have expressed concerns about gene-edited organisms entering their supply chains, and also increasing the cost to certify their products as non-GM (this also applies to non-organic products for some markets or customers).
- Regarding the risk matrix option proposed but not yet implemented in Australia, members of the TAG considered that the matrix structure would likely work well for medical and clinical trial applications.
- Early conversations with Māori indicate an emerging of changed attitudes toward genetic tools being used to save the environment and a change of attitude in general. Māori are generally enthusiastic about opening a dialogue and being part of the policy and decision-making process but have also expressed concerns that the ambitious timeframe does not provide adequate time for consultation.

Discussing how the new regime should protect Māori rights and interests is ongoing.

Discussion questions

- **Are there any remaining fishhooks or perspectives that have not been considered?**

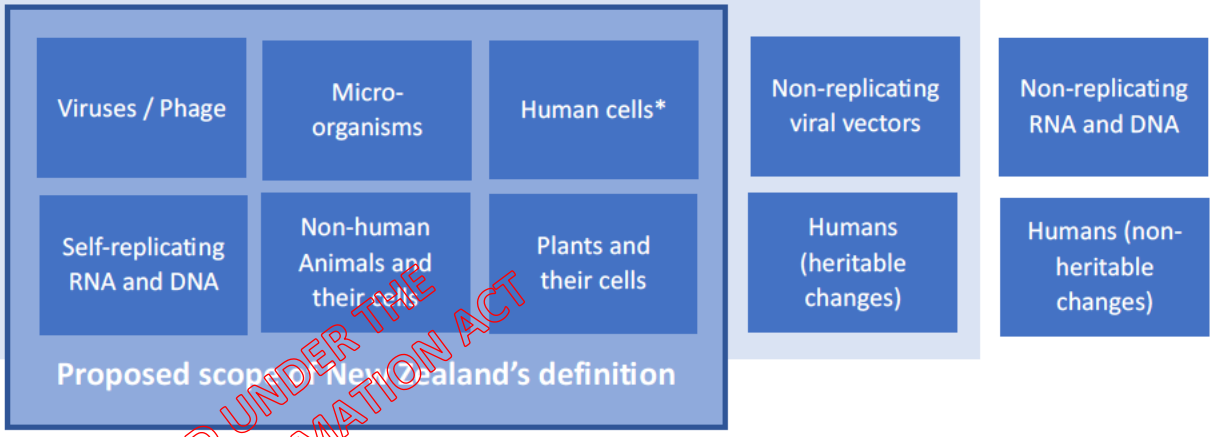
Scope of the Genetically Modified Organism definition

Definition with proposed modifications

Genetically modified organism means:

- an organism that has been modified or ***constructed*** by gene technology; or…

Scope of Australia's GMO definition

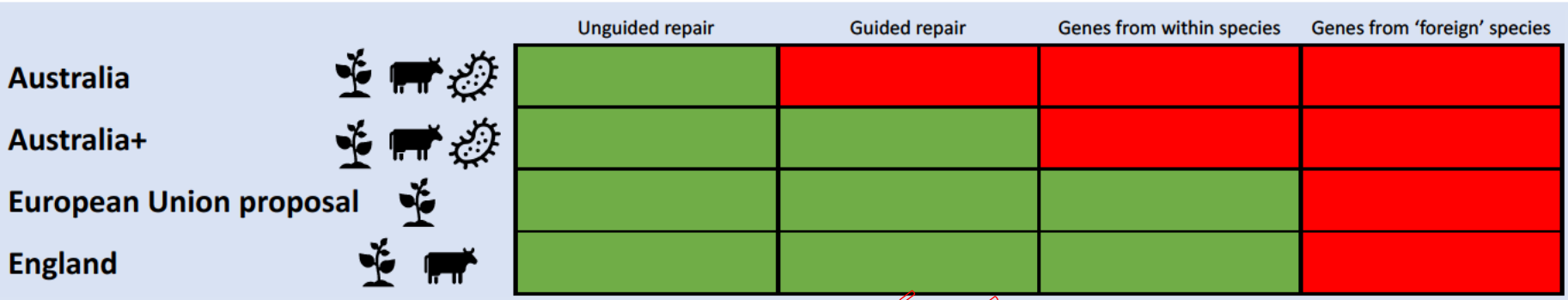


Key features

- GMOs will include organisms modified or constructed by gene technology. Inclusion of *construction* is intended to future proof the definition given advances in synthetic biology.
- Human beings will be specifically excluded from the GMO definition to remove the possibility of humans being unnecessarily subject to regulatory oversight.
- Regulatory oversight of heritable changes to human beings is already sufficiently achieved through the HART Act, making additional oversight through new legislation unnecessary.
- The scope will include replicating RNA but will exclude non-replicating RNA and viral vectors (which are currently used in vaccines, gene therapies and cell therapies).
- Management of very low risk organisms, such as human cells, through the proposed risk matrix is considered more future proof than explicit exclusion under the GMO definition.

*As under the HSNO Act, human cells would include reproductive cells, like gametes, and embryonic cells.

Gene-editing techniques



Non-regulated technologies

Null segregants	Protoplast fusion	Epigenetics
In vitro fertilisation	Zygote implantation	Replication-defective viral vectors
Embryo rescue	Introduction of RNA	dsRNA treatment
Radiation-induced mutagenesis	Chemical mutagenesis	Gene-editing exemptions (as above)

Blue = Australia non-regulated technologies (non-exhaustive) Green = Additions from New Zealand statutory determinations and new exemptions (non-exhaustive)

Key considerations

- There are a range of gene editing techniques and their application to different types of organisms can create different risks.
- International jurisdictions are exempting or proposing to exempt gene editing techniques based on their equivalency to unregulated techniques or the equivalency of their effect to those that could arise from conventional breeding.
- These techniques are exempt from regulatory oversight due to the inability to detect if the change occurred naturally or as a result of gene editing, and because they do not introduce new risk compared to conventional breeding practices.

The New Regime Would be Built Around Graduated Risk Management Processes

Non-Regulated Technology

These regulations would specify those techniques and technologies that are not regulated, including certain gene editing techniques, null segregants, mutagenesis.

GMO Register

The register would specify those very low risk GMOs that aren't tied to a license and can be used by anybody.

Regulated activities under the risk matrix framework

The regulator is able to assign activities to risk tiers, with requirements graduated based on risks. Pathways would be tailored for laboratory and industrial use, environmental release, and medical use.

Laboratory and Industrial	Environmental Release	Medical Use
Non-notifiable	Non-notifiable	Non-notifiable
Notifiable	Notifiable	Notifiable
Licensed: Full assessment	Licensed: Permit, Expedited Assessment, Full assessment	Licensed: Permit, Expedited Assessment, Full assessment

Key features

- Regulated activities would be assigned by the regulator to a risk tier within three categories: laboratory research and industrial use, environmental release, and medical use. Recognises that medical use is not the same as environmental release.
- Allows low-risk activities to be managed through self-regulation, while still allowing higher-risk licensed activities to be regulated on a (graduated) case-by-case basis where necessary.
- Medical treatments approved by 'recognised' regulators would be automatically approved under the new system.
- The new regulator would be given the ability to undertake joint assessments of applications with other overseas regulators, while still retaining the ability to make decisions based on the joint review – this is essential for environmental release to account for New Zealand's unique environment.
- The new regulator would be given the ability to assess certain applications through an expedited pathway where an application has previously been assessed by a 'recognised' regulator.

3. Paper title	Scenarios
Meeting date	9am – 11am Thursday 2 May 2024
Approved by	Simon Rae

Item purpose and summary
To discuss the examples and scenarios to test.
Discussion questions
• What scenarios are required to test the proposed regulatory system?

Gene Technologies Examples and Applications.

Organism modified	What genetic change	Purpose/application/outcome	Other notes	Present regulation	Proposed regulation
Filamentous fungus – ie Penicillium	Insert genes encoding biosynthetic pathway from another fungus	Biomanufacturing of valuable therapeutics or agrichemicals	GMO needs to be grown at scale	Development through EPA – restricts to host. Restrictions on fermentation scale	s 9(2)(f)(iv)
Banana	Inserting genes from other banana species or from other organisms such as nematodes	Disease resistance to Fusarium	Triploid – therefore no seed		
Ryegrass fungal endophyte	Disrupt gene so it doesn't make a toxin – no introduced genetic material	Retain protective effects but remove compounds toxic to grazing animals		Field trials release require full application process	

High metabolizable energy ryegrass	Inclusion of specific trans genes	Increased lipid content and higher energy for greater productivity	Field trials in US?		s 9(2)(f)(iv)
CAR T-cell therapy	Insertion of genes encoding antigen receptors into patient's T-cells	Insertion of chimeric antigen receptors into the patients T-cells enables these T-cells to target cancer cells expressing specific marker proteins	Regulated under Australian legislation	Currently requires approval from both the EPA and Medsafe	
Trichoderma reesei	Insertion of genes encoding the proteins required to produce casein and whey	Production of animal-free proteins for high-end niche products	Not regulated under Australian legislation	Currently requires containment approval from both the EPA and MPI	
Wilding Pines	Sterile lines produced by disrupting genes responsible for reproductive function.	Produce sterile pines for industry use, preventing unwanted spread in the environment.	No nucleic acid template to guide repair, not a GMO, so not regulated under Australian legislation.	Subject to GMO regulations. Field trials release require full application process.	

4. Paper title	Risk matrix
Meeting date	9am – 11am Thursday 2 May 2024
Approved by	Simon Rae

Item purpose and summary
Below are the Exempt Dealings and Notifiable Low Risk Dealings under the current Australian legislation. Note: These risk tiers are also outlined under Schedule 2 and Schedule 3 of the Australian regulations.
Discussion questions
• Are these activities categorised appropriately? • Are there changes that could be made to these categories that would make them more risk proportionate? • What would you add? What would you remove? What would you shift around?

Risk tier 1: Exempt dealings

Part 1

Item	Description of dealing
2	A dealing with a genetically modified *Caenorhabditis elegans*, unless: (a) an *advantage* is conferred on the animal by the genetic modification; or (b) as a result of the genetic modification, the animal is capable of secreting or producing an infectious agent.
3	A dealing with an animal into which genetically modified somatic cells have been introduced, if: (a) the somatic cells are not capable of giving rise to infectious agents as a result of the genetic modification; and (b) the animal is not infected with a virus that is capable of recombining with the genetically modified nucleic acid in the somatic cells.
3A	A dealing with an animal whose somatic cells have been genetically modified *in vivo* by a replication defective viral vector, if: (a) the *in vivo* modification occurred as part of a previous dealing; and (b) the replication defective viral vector is no longer in the animal; and (c) no germ line cells have been genetically modified; and (d) the somatic cells cannot give rise to infectious agents as a result of the genetic modification; and (e) the animal is not infected with a virus that can recombine with the genetically modified nucleic acid in the somatic cells of the animal.

4	(1) Subject to subitem (2), a dealing involving a host/vector system mentioned in Part 2 of this Schedule and producing no more than 25 litres of GMO culture in each vessel containing the resultant culture. (2) The donor nucleic acid: (a) must meet either of the following requirements: (i) it must not be derived from organisms implicated in, or with a history of causing, disease in otherwise healthy: (A) human beings; or (B) animals; or (C) plants; or (D) fungi; (ii) it must be characterised and the information derived from its characterisation show that it is unlikely to increase the capacity of the host or vector to cause harm; and Example: Donor nucleic acid would not comply with subparagraph (ii) if its characterisation shows that, in relation to the capacity of the host or vector to cause harm, it: (a) provides an advantage; or (b) adds a potential host species or mode of transmission; or (c) increases its virulence, pathogenicity or transmissibility. (b) must not code for a toxin with an LD_{50} of less than 100 micrograms per kilogram; and (c) must not code for a toxin with an LD_{50} of 100 micrograms per kilogram or more, if the intention is to express the toxin at high levels; and (d) must not be uncharacterised nucleic acid from a toxin-producing organism; and (e) if the donor nucleic acid includes a viral sequence—cannot give rise to infectious agents when introduced into any potential host species, without additional non-host genes or gene products that: (i) are not available in the host cell into which the nucleic acid is introduced as part of the dealing; and (ii) will not become available during the dealing; and (f) if the donor nucleic acid includes a viral sequence—cannot restore replication competence to the vector.
5	A dealing involving shot-gun cloning, or the preparation of a cDNA library, in a host/vector system mentioned in items 1 to 6 of the table in Part 2 of this Schedule, if the donor nucleic acid is not derived from either: (a) a pathogen; or

	(b) a toxin-producing organism.

Part 2

2.1 - Hosts and vectors

(1) A reference to a host mentioned in this Part is a reference to a host mentioned in column 2 of an item of the table in this clause.

(2) A reference to a vector mentioned in this Part is a reference to a vector mentioned in column 3 of an item of the table in this clause.

(3) A reference to a ***host/vector system*** mentioned in this Part is a reference to any of the following:

(a) a system involving a host mentioned in column 2 of an item of the table in this clause and a vector mentioned in column 3 of the same item;

(b) a non-vector system involving a host mentioned in column 2 of an item of the table;

(c) a system involving a GMO mentioned as a vector in column 3 of an item of the table (except item 7), without a host.

Note: Column 1 of the table is included for information only.

Hosts and vectors table

Item	Host class	Hosts	Vectors
1	Bacteria	*Escherichia coli* K12, *E. coli* B, *E. coli* C or *E. coli* Nissle 1917—any derivative that does not contain: (a) generalised transducing phages; or (b) genes able to complement the conjugation defect in a non-conjugative plasmid	Any of the following: (a) non-conjugative plasmids; (b) lambda bacteriophage; (c) lambdoid bacteriophage; (d) Fd, F1 or M13 bacteriophage
2	Bacteria	*Bacillus*—asporogenic strains of the following species with a reversion frequency of less than 10^{-7}: (a) *B. amyloliquefaciens*; (b) *B. licheniformis*; (c) *B. pumilus*; (d) *B. subtilis*;	Any of the following: (a) non-conjugative plasmids; (b) other plasmids and phages whose host range does not include *B. cereus*, *B. anthracis* or any other pathogenic strain of *Bacillus*

		(e) *B. thuringiensis*	
3	Bacteria	*Pseudomonas putida* strain KT2440	Non-conjugative plasmids
4	Bacteria	The following *Streptomyces* species: (a) *S. aureofaciens*; (b) *S. coelicolor*; (c) *S. cyaneus*; (d) *S. griseus*; (e) *S. lividans*; (f) *S. parvulus*; (g) *S. rimosus*; (h) *S. venezuelae*	Any of the following: (a) non-conjugative plasmids; (b) plasmids SCP2, SLP1, SLP2, pIJ101 and derivatives; (c) actinophage phi C31 and derivatives
5	Bacteria	Any of the following: (a) *Agrobacterium radiobacter*; (b) *Agrobacterium rhizogenes* (disarmed strains only); (c) *Agrobacterium tumefaciens* (disarmed strains only)	Disarmed Ri or Ti plasmids
6	Bacteria	Any of the following: (a) *Allorhizobium* species; (b) *Corynebacterium glutamicum*; (c) *Lactobacillus* species; (d) *Lactococcus lactis*; (e) *Oenococcus oeni* syn. *Leuconostoc oeni*; (f) *Pediococcus* species; (g) *Photobacterium angustum*; (h) *Pseudoalteromonas tunicata*; (i) *Rhizobium* species; (j) *Sphingopyxis alaskensis* syn. *Sphingomonas alaskensis*; (k) *Streptococcus thermophilus*; (l) *Synechococcus* species strains PCC 7002, PCC 7942 and WH 8102; (m) *Synechocystis* species strain PCC 6803; (n) *Vibrio cholerae* CVD103-HgR; (o) *Zymomonas mobilis*	Non-conjugative plasmids

7	Fungi	Any of the following: (a) *Kluyveromyces lactis*; (b) *Neurospora crassa* (laboratory strains); (c) *Pichia pastoris*; (d) *Saccharomyces cerevisiae*; (e) *Schizosaccharomyces pombe*; (f) *Trichoderma reesei*; (g) *Yarrowia lipolytica*	All vectors
8	Slime moulds	*Dictyostelium* species	*Dictyostelium* shuttle vectors, including those based on the endogenous plasmids Ddp1 and Ddp2
9	Tissue culture	Any of the following if they cannot spontaneously generate a whole animal: (a) animal or human cell cultures (including packaging cell lines); (b) isolated cells, isolated tissues or isolated organs, whether animal or human; (c) early non-human mammalian embryos cultured *in vitro*	Any of the following: (a) plasmids; (b) replication defective viral vectors unable to transduce human cells; (c) polyhedrin minus forms of the baculovirus *Autographa californica* nuclear polyhedrosis virus (ACNPV)
10	Tissue culture	Either of the following if they are not intended, and are not likely without human intervention, to vegetatively propagate, flower or regenerate into a whole plant: (a) plant cell cultures; (b) isolated plant tissues or organs	Any of the following: (a) Disarmed Ri or Ti plasmids in *Agrobacterium radiobacter*, *Agrobacterium rhizogenes* (disarmed strains only) or *Agrobacterium tumefaciens* (disarmed strains only); (b) non-pathogenic viral vectors

Risk tiers 2 and 3: Notifiable low-risk dealings suitable for at least Physical Containment level 1 and Physical Containment level 2

Part 1—Notifiable low risk dealings suitable for at least physical containment level 1
Note: Because of subregulation 12(1), a dealing mentioned in this Part is not a notifiable low risk dealing if it is also a dealing of a kind mentioned in Part 3

1.1 Kinds of dealings suitable for at least physical containment level 1
The following kinds of notifiable low risk dealings must be undertaken, unless paragraph 13(2)(c) or subregulation 13(3) applies, in facilities certified to at least physical containment level 1 and that are appropriate for the dealings:

(a) a dealing involving a genetically modified laboratory guinea pig, a genetically modified laboratory mouse, a genetically modified laboratory rabbit or a genetically modified laboratory rat, unless:

(i) an advantage is conferred on the animal by the genetic modification; or

(ii) the animal is capable of secreting or producing an infectious agent as a result of the genetic modification;

(c) a dealing involving virions of a replication defective vector derived from *Human adenovirus* or from *Adeno-associated virus*, either without a host or with a host mentioned in item 9 of Part 2 of Schedule 2, if the donor nucleic acid:

(i) cannot restore replication competence to the vector; and

(ii) does not confer an oncogenic modification or immunomodulatory effect in humans.

Part 2—Notifiable low risk dealings suitable for at least physical containment level 2 or 3
Note: Because of subregulation 12(1), a dealing mentioned in this Part is not a notifiable low risk dealing if it is also a dealing of a kind mentioned in Part 3.

2.1 Kinds of dealings suitable for at least physical containment level 2
The following kinds of notifiable low risk dealings must be undertaken, unless paragraph 13(2)(c) or subregulation 13(3) applies, in facilities certified to at least physical containment level 2 and that are appropriate for the dealings:

(a) a dealing involving whole animals (including non-vertebrates) that:
(i) involves genetic modification of the genome of the oocyte or zygote or early embryo by any means to produce a novel whole organism; and
(ii) does not involve any of the following:
(A) a genetically modified laboratory guinea pig;
(B) a genetically modified laboratory mouse;
(C) a genetically modified laboratory rabbit;
(D) a genetically modified laboratory rat;
(E) a genetically modified *Caenorhabditis elegans*;

(aa) a dealing involving a genetically modified laboratory guinea pig, a genetically modified laboratory mouse, a genetically modified laboratory rabbit, a genetically modified laboratory rat or a genetically modified *Caenorhabditis elegans*, if:
(i) the genetic modification confers an advantage on the animal; and

(ii) the animal is not capable of secreting or producing an infectious agent as a result of the genetic modification;

(b) a dealing involving a genetically modified plant;

(c) a dealing involving a host/vector system not mentioned in paragraph 1.1(c) or Part 2 of Schedule 2, if neither host nor vector has been implicated in, or has a history of causing, disease in otherwise healthy:
  (i) human beings; or
  (ii) animals; or
  (iii) plants; or
  (iv) fungi;

(d) a dealing involving a host/vector system not mentioned in Part 2 of Schedule 2, if:
  (i) the host or vector has been implicated in, or has a history of causing, disease in otherwise healthy:
    (A) human beings; or
    (B) animals; or
    (C) plants; or
    (D) fungi; and
  (ii) the genetic modification is characterised; and
  (iii) the characterisation of the genetic modification shows that it is unlikely to increase the capacity of the host or vector to cause harm;
  Example: A genetic modification would not comply with subparagraph (iii) if, in relation to the capacity of the host or vector to cause harm, it:
    (a) provides an advantage; or
    (b) adds a potential host species or mode of transmission; or
    (c) increases its virulence, pathogenicity or transmissibility.

(e) a dealing involving a host/vector system mentioned in Part 2 of Schedule 2, if the donor nucleic acid:
  (i) is characterised, and the characterisation shows that it may increase the capacity of the host or vector to cause harm; or
  (ii) is uncharacterised nucleic acid from an organism that has been implicated in, or has a history of causing, disease in otherwise healthy:
    (A) human beings; or
    (B) animals; or
    (C) plants; or
    (D) fungi;

(f) a dealing involving a host/vector system mentioned in Part 2 of Schedule 2 and producing more than 25 litres of GMO culture in each vessel containing the resultant culture, if:
  (i) the dealing is undertaken in a facility that is certified by the Regulator as a large scale facility; and
  (ii) the donor nucleic acid satisfies the conditions set out in subitem 4(2) of Part 1 of Schedule 2;

(g) a dealing involving complementation of knocked-out genes, if the complementation is unlikely to increase the capacity of the GMO to cause harm compared to the capacity of the parent organism before the genes were knocked out;
  Example: A dealing would not comply with paragraph (g) if it involved complementation that, in relation to the parent organism:
    (a) provides an advantage; or
    (b) adds a potential host species or mode of transmission; or
    (c) increases its virulence, pathogenicity or transmissibility.

(h) a dealing involving shot-gun cloning, or the preparation of a cDNA library, in a host/vector system mentioned in items 1 to 6 of the table in Part 2 of Schedule 2, if the donor nucleic acid is derived from either:
  (i) a pathogen; or
  (ii) a toxin-producing organism;
(i) a dealing involving virions of a replication defective viral vector unable to transduce human cells and a host not mentioned in Part 2 of Schedule 2, if the donor nucleic acid cannot restore replication competence to the vector;
(j) a dealing involving virions of a replication defective non-retroviral vector able to transduce human cells, either without a host or with a host mentioned in Part 2 of Schedule 2, if:
  (i) the donor nucleic acid cannot restore replication competence to the vector; and
  (ii) the dealing is not a dealing mentioned in paragraph 1.1(c);
(k) a dealing involving virions of a replication defective non-retroviral vector able to transduce human cells and a host not mentioned in Part 2 of Schedule 2, if:
  (i) the donor nucleic acid cannot restore replication competence to the vector; and
  (ii) the donor nucleic acid does not confer an oncogenic modification or immunomodulatory effect in humans;
(l) a dealing involving virions of a replication defective retroviral vector able to transduce human cells, either without a host or with a host mentioned in Part 2 of Schedule 2, if:
  (i) all viral genes have been removed from the retroviral vector so that it cannot replicate or assemble new virions without these functions being supplied *in trans*; and
  (ii) viral genes needed for virion production in the packaging cell line are expressed from independent, unlinked loci with minimal sequence overlap with the vector to limit or prevent recombination; and
  (iii) either:
    (A) the retroviral vector includes a deletion in the Long Terminal Repeat sequence of DNA that prevents transcription of genomic RNA following integration into the host cell DNA; or
    (B) the packaging cell line and packaging plasmids express only viral genes *gagpol*, *rev* and an envelope protein gene, or a subset of these;
(m) a dealing involving virions of a replication defective retroviral vector able to transduce human cells and a host not mentioned in Part 2 of Schedule 2, if:
  (i) the donor nucleic acids does not confer an oncogenic modification or immunomodulatory effect in humans; and
  (ii) all viral genes have been removed from the retroviral vector so that it cannot replicate or assemble new virions without these functions being supplied *in trans*; and
  (iii) viral genes needed for virion production in the packaging cell line are expressed from independent, unlinked loci with minimal sequence overlap with the vector to limit or prevent recombination; and
  (iv) either:
    (A) the retroviral vector includes a deletion in the Long Terminal Repeat sequence of DNA that prevents transcription of genomic RNA following integration into the host cell DNA; or
    (B) the packaging cell line and packaging plasmids express only viral genes *gagpol*, *rev* and an envelope protein gene, or a subset of these.***

Part 3—Dealings that are not notifiable low risk dealings

Note 1: The following list qualifies the list in Parts 1 and 2, and is not an exhaustive list of dealings that are not notifiable low risk dealings.

Note 2: If a dealing is not a notifiable low risk dealing, or an exempt dealing, as provided by these Regulations, a person undertaking the dealing must be authorised by a GMO licence unless the dealing is within one of the other exceptions to licensing provided by the Act: see section 32 of the Act.

3.1 Kinds of dealings

(1) A dealing of any of the following kinds, or involving a dealing of the following kinds, is not a notifiable low risk dealing:

(a) a dealing (other than a dealing mentioned in paragraph 2.1(h)) involving cloning of nucleic acid encoding a toxin having an LD_{50} of less than 100 micrograms per kilogram;

(b) a dealing involving high level expression of toxin genes, even if the LD_{50} is 100 micrograms per kilogram or more;

(c) a dealing (other than a dealing mentioned in paragraph 2.1(h)) involving cloning of uncharacterised nucleic acid from a toxin-producing organism;

(d) a dealing involving virions of a replication defective viral vector and a host not mentioned in Part 2 of Schedule 2, if:

(i) the donor nucleic acid confers an oncogenic modification or immunomodulatory effect in humans; and

(ii) the dealing is not a dealing mentioned in paragraph 2.1(i);

(e) a dealing involving a replication competent virus or viral vector, other than a vector mentioned in Part 2 of Schedule 2, if the genetic modification confers an oncogenic modification or immunomodulatory effect in humans;

(f) a dealing involving, as host or vector, a micro-organism, if:

(i) the micro-organism has been implicated in, or has a history of causing, disease in otherwise healthy:

(A) human beings; or

(B) animals; or

(C) plants; or

(D) fungi; and

(ii) none of the following sub-subparagraphs apply:

(A) the host/vector system is a system mentioned in Part 2 of Schedule 2;

(B) the genetic modification is characterised and its characterisation shows that it is unlikely to increase the capacity of the host or vector to cause harm;

(C) the dealing is a dealing mentioned in paragraph 2.1(g);

Example: A genetic modification would not comply with sub-subparagraph (B) if, in relation to the capacity of the host or vector to cause harm, it:

(a) provides an advantage; or

(b) adds a potential host species or mode of transmission; or

(c) increases its virulence, pathogenicity or transmissibility.

(g) a dealing involving the introduction, into a micro-organism, of nucleic acid encoding a pathogenic determinant, unless:

(i) the dealing is a dealing mentioned in paragraph 2.1(g); or

(ii) the micro-organism is a host mentioned in Part 2 of Schedule 2;

(h) a dealing involving the introduction into a micro-organism, other than a host mentioned in Part 2 of Schedule 2, of genes whose expressed products are likely to increase the capacity of the micro-organisms to induce an autoimmune response;

(i) a dealing involving use of a viral or viroid genome, or fragments of a viral or viroid genome, to produce a novel replication competent virus with an increased capacity to cause harm compared to the capacity of the parent or donor organism;

Example: A dealing would comply with paragraph (i) if it produces a novel replication competent virus that has a higher capacity to cause harm to any potential host species than the parent organism because the new virus has:

(a) an advantage; or

(b) a new potential host species or mode of transmissibility; or

(c) increased virulence, pathogenicity or transmissibility.

(j) a dealing, other than a dealing mentioned in paragraph 2.1(l) or (m), with a replication defective retroviral vector (including a lentiviral vector) able to transduce human cells;

(k) a dealing involving a genetically modified animal, plant or fungus that is capable of secreting or producing infectious agents as a result of the genetic modification;

(l) a dealing producing, in each vessel containing the resultant GMO culture, more than 25 litres of that culture, other than a dealing mentioned in paragraph 2.1(f);

(m) a dealing that is inconsistent with a policy principle issued by the Ministerial Council;

(n) a dealing involving the intentional introduction of a GMO into a human being, unless the GMO:

(i) is a human somatic cell; and

(ii) cannot secrete or produce infectious agents as a result of the genetic modification; and

(iii) if it was generated using viral vectors:

(A) has been tested for the presence of viruses likely to recombine with the genetically modified nucleic acid in the somatic cells; and

(B) the testing did not detect a virus mentioned in sub-subparagraph (A); and

(C) the viral vector used to generate the GMO as part of a previous dealing is no longer present in the somatic cells;

(o) a dealing involving a genetically modified pathogenic organism, if the practical treatment of any disease or abnormality caused by the organism would be impaired by the genetic modification;

(p) a dealing involving a micro-organism that satisfies the criteria in AS/NZS 2243.3:2010 for classification as Risk Group 4;

(q) a dealing involving a micro-organism that satisfies the criteria in AS/NZS 2243.3:2010 for classification as Risk Group 3 and that is not undertaken:

(i) in a facility that is certified by the Regulator to at least physical containment level 3 and that is appropriate for the dealing; or

(ii) in a facility that the Regulator has agreed in writing is a facility in which the dealing may be undertaken;

(r) a dealing involving a GMO capable of sexual reproduction, the sexual progeny of which are, as a result of the genetic modification, more likely to inherit a particular nucleotide sequence or set of nucleotide sequences (when compared to inheritance from the unmodified parent organism);

(s) a dealing involving a viral vector that can modify an organism capable of sexual reproduction, so that the sexual progeny of the organism are more likely to inherit a particular nucleotide sequence or set of nucleotide sequences (when compared to inheritance from the unmodified parent organism).

Note: A modification that increases the likelihood of inheritance of a nucleotide sequence or sequences, as described in paragraphs (r) and (s), is generally known as an engineered gene drive.

(2) For the purposes of paragraph (1)(p), a genetically modified micro-organism is taken to satisfy the criteria in AS/NZS 2243.3:2010 for classification as Risk Group 4 if the unmodified parent micro-organism satisfies those criteria.

(3) For the purposes of paragraph (1)(q), a genetically modified micro-organism is taken to satisfy the criteria in AS/NZS 2243.3:2010 for classification as Risk Group 3 if the unmodified parent micro-organism satisfies those criteria.

(4) However, subclause (3) does not apply in relation to a replication defective retroviral vector that meets the criteria in paragraph 2.1(l) or (m).

THE SECOND MEETING OF THE GENE TECHNOLOGY TECHNICAL ADVISORY GROUP - MINUTES (excerpts on topics 2-4)

Date and time:	9am – 11am Thursday 2 May
Location:	Microsoft Teams
Chair:	Emily Parker (Ferrier Institute, Departmental Science Advisor MBIE)
Invitees:	Tim Hore (Otago), Billy Sheppard (Auckland), Alec Foster (Scion), Andy Allan (Plant and Food Research), Nikki Freed (Daisy Lab), Rachel Perret (Malaghan), Richard Scott (AgResearch, joined at 9.30am), Neil Gemmell (Otago), David Ackerley (VUW), William Rolleston (South Pacific Sera Limited)
MBIE attendees:	s 9(2)(a) Simon Rae (MBIE, Policy Director Emerging Technologies), s 9(2)(a)
Apologies	Maui Hudson (Waikato), Jasna Rakonjac (Massey), Ariana Estoras (AgResearch)

At the end of each section, in bold are the key points that the TAG members noted should be considered by MBIE's policy team, these are summaries of the discussion and do not reflect group consensus. As per the Technical Advisory Group Terms of Reference members are not expected to reach consensus.

Item	Discussion
Key issues	**Paper 2. Key issues: Scope and definitions, authorised activity, gene editing techniques, and non-regulated techniques** This paper summarised early advice from the TAG, workshops with other key government agencies, Industry Focus Group, Māori Focus Group and targeted stakeholder engagements. • A member of the TAG noted that the potential increased costs for the organics industry to certify their products should not be a cost for the whole industry. Points raised by members of the TAG at the meeting: *Scope of the Genetically Modified Organism definition* • Inclusion of self-replicating RNA and DNA, replication is self-limiting, likely to be used in vaccines. Carefully consider not including that in the scope of a GMO. *Graduated risk management process:* • Separating laboratory/industrial, environmental release and medical use may move away from the risk-based assessment we're striving towards. Putting different regime on a class of outcomes / usages gives the public the impression that the risks are increased. *Gene editing techniques and non-regulated techniques:* • More consideration needs to be given to SDN2 guided repair, particularly around the productivity gained by guided repair when compared to random repair (SDN1).

	• Need to ensure updates to non-regulated techniques and technologies are easily enabled. • TAG asked for more information on how EU regulates genetically modified microorganisms (GMMs) (not included in the table as not part of the proposed NZ system). **Action** - Provide more information on the modification of GMMs in the EU and UK. *Management of dealings not subject to regulatory oversight:* • Need to ensure that if institutional biological safety committees (IBSC) are responsible there is clarity on conditions that need to be met and this doesn't create more barriers, including for MPI audits of facilities. • What burden of proof is required and will IBSC be willing to take the responsibility of determining something is not subject to regulatory oversight (e.g. exempt gene editing techniques?) • How would this work for organisations with no IBSC? • May be useful to have the ability of the regulator to provide advice on low-risk organisms/non-regulated technologies. [MBIE noted that this may create delays and/or need to be a paid service]. • Clarification sought around risk tiering and the corresponding physical containment levels required. Example given of application of technology in contained lab for development e.g. lentivirus to alter human cell line, once change made would no longer need to be in containment, this would be the ideal scenario. Once the lentivirus is gone, it's a 'normal' human cell line. *Scenario tables* • Plant examples in the scenarios table are reasonable. **Action** – Chair to circulate the scenario table word document for TAG member input. The TAG had a general discussion on classifying exempt organisms as non-GMOs (example given in UK where term precision breeding is used) TAG noted that labelling will be important and that some sectors would continue to call exempt organisms GMOs which could lead to confusion. **The TAG members noted the following key points to be considered by MBIE's policy team:** • **Self-replicating RNA and DNA should not be included in the definition of a GMO because their replication is self-limiting and they are not considered an organism.** • **General agreement that dealings not subject to regulatory oversight should be managed at the IBSC level with proper guidance to avoid creating more barriers. Will need to**

	consider how things will work for organisations with no IBSC and for smaller organisations..
Risk Tiers	The TAG was asked to provide advice on 'Exempt Dealings and Notifiable Low Risk Dealings' under the current Australian legislation. Points raised by members of the TAG at the meeting: • Opportunity for improvements in part 2, can become quickly out of date so try to retain flexibility. Example given of key biotech organisms not included in the table and the reference to "producing no more than 25 litres of GMO culture in each vessel containing the resultant culture' unclear why 25 L was chosen. This limit has implications for biomanufacturing applications that should be carefully considered. • [MBIE noted the risk tier tables could sit under secondary legislation to enable change more readily]. • Potential for risk tier tables to sit under secondary or tertiary, who will make this decision? Example given of previous sustainability council case[1], we need to be very clear about who will make those decisions. Decision making authority for types of secondary legislation needs to be in the primary legislation. • Part 1, 3b "the replication defective viral vector is no longer in the animal" what is the mechanism require to assure this is the case? How do we manage endogenous retroviruses? • Suggested that a wider group of researchers could discuss the lists of organisms in the risk tier tables. • Need to manage risk of researchers interpreting the lists in a liberal way, and/ or institutions pushing decisions into a higher risk tier. **The TAG members noted the following key points to be considered by MBIE's policy team:** • **Risk tier tables need to be flexible and easy to update, a way to do this could be for them to sit in secondary (or tertiary) legislation.**

[1] Sustainability Council of New Zealand Trust v. The Environmental Protection Authority: Gene editing technologies and the law.

MEETING PAPERS: 5 JUNE 2024 GENE TECHNOLOGY TECHNICAL ADVISORY GROUP (excerpt – paper 3)

3. Paper title	Scenarios
Meeting date	9am – 11am Thursday 5 June 2024
Approved by	Simon Rae

Item purpose and summary
The table below contains examples of the types of genetic modifications and a comparison of the current and proposed regulations.
Discussion questions
• Acknowledging that development of key criteria for the different risk tiering levels are subject to further decision, do you see any areas of ambiguity that may need further consideration illustrated through these scenarios?

Sector	Organism modified	Application	Other notes	Description of genetic change	Current Regulation		Proposed Regulation		Other agency approval still required
				Type of gene edit (SDN)	GMO?	Authorized activity	GMO?	Authorized activity	
Human	CAR T-cell therapy	Insertion of chimeric antigen receptors into the patients T-cells enables these T-cells to target cancer cell that express specific marker proteins	Regulated under Australian legislation	SDN3 cisgenics: Deletions and insertion of genes encoding antigen receptors into patient's T-cells	Yes (human cells)	Full EPA assessment resulting in full release without controls, MEDSAFE assessment.	s 9(2)(f)(iv)		Yes MEDSAFE

[1] Would not require approval from the gene technology regulator)

Sector	Organism modified	Application	Other notes	Description of genetic change	Current Regulation		Proposed Regulation		Other agency approval still required
				Type of gene edit (SDN)	GMO?	Authorized activity	GMO?	Authorized activity	
	Mouse (laboratory)	Targeted guided edit made to mouse gene to model human kidney gene variant. Used to study potential pathogenic mechanisms related to gout		SDN2: CRISPR knock in of human kidney gene	Yes	New organism – Containment	s 9(2)(f)(iv)		Yes Institutional Biosafety and Ethics Committees, Health Research Council, MPI Animal Welfare Act (Animals used in research)
	Human	In vivo gene therapy where a gene encoding a functional protein is delivered to repair a genetic defect, e.g. blood disorders.		SDN3 cisgenics: Functional replacement of defective gene	Yes (treated tissue)	EPA, MEDSAFE and ethical assessment required			Yes MEDSAFE Ethics Committee
	E. coli	*E.coli* transformed to produce a plasmid encoding CAR		SDN3 transgenics: Insertion of human origin gene into	Yes	New organism – Containment			

Sector	Organism modified	Application	Other notes	Description of genetic change	Current Regulation		Proposed Regulation		Other agency approval still required
				Type of gene edit (SDN)	GMO?	Authorized activity	GMO?	Authorized activity	
		transgene. Research tool to produce large quantities of plasmid to create CAR lentivirus.		plasmid transformed into E. coli.			s 9(2)(f)(iv)		
All (One Health)	Filamentous fungus – e.g. *Penicillium*	Biomanufacturing of valuable therapeutics or agrichemicals. Consideration: anti-microbial resistance (AMR).	GMO needs to be grown at scale	SDN3 cisgenics: Insert genes encoding biosynthetic pathway from another fungus	Yes	New organism – Containment			Yes MEDSAFE (Medicines Act) and/or MPI (ACVM Act)
	Bacteriophage	Enhancement of antibacterial properties as an alternative to antibiotics, decreasing antibiotic resistance spread. Removal of genes encoding	Single application chosen as example.	SDN2: template guided repair	Yes	New organism – Containment			Yes MEDSAFE (Medicines Act) and/or MPI (ACVM Act)

Sector	Organism modified	Application	Other notes	Description of genetic change	Current Regulation		Proposed Regulation		Other agency approval still required
				Type of gene edit (SDN)	GMO?	Authorized activity	GMO?	Authorized activity	
		virulence factors.					s 9(2)(f)(iv)		
Primary industries - plants	Ryegrass fungal endophyte	Retain protective effects but remove compounds toxic to grazing animals		SDN1: Disrupt gene so it doesn't make a toxin	Yes (potentially low risk)	Containment – field test			Yes MPI (ACVM Act – agricultural compound)
	Hi-CT White Clover	Increased production of condensed tannins (CT) in White Clover to reduce incidence of ruminant bloat and potential greenhouse gas emissions.	While both donor and recipient organisms are Trifolium species, they are very distant genetically and as such could not be cross bred through conventional methods.	SDN3 transgenic: insertion of a gene from a clover species of the same genus. Regulatory elements and selection markers from 'foreign' species.	Yes	New organism - containment			Yes MPI (ACVM Act – agricultural compound)
	Banana	Disease resistance to Fusarium	Triploid – therefore no seed	SDN3 transgenic: Insertion of genes from	Yes	New organism – Containment			Yes MPI (ACVM Act)

Sector	Organism modified	Application	Other notes	Description of genetic change	Current Regulation		Proposed Regulation		Other agency approval still required
				Type of gene edit (SDN)	GMO?	Authorized activity	GMO?	Authorized activity	
				other banana species or from other organisms such as nematodes			s 9(2)(f)(iv)		
	High metabolizable energy ryegrass	Increased lipid content and higher energy for greater productivity	Field trials in US?	SDN3 transgenic: Insertion of rice genes	Yes	Containment (development and field test)			Yes MPI (ACVM Act – agricultural compound)
	Apple	Fast flowering trait	Fast flowering trait	SDN3 transgenic: Insertion of viral origin promoter and birch transgene.	Yes	New organism - containment			Yes MPI FSANZ
	Apple	Fast flowering trait	SDN3 transgenic: Insertion of viral origin promoter and birch transgene produce fast flowering trait to accelerate	Null segregant	No	Not regulated			No

Sector	Organism modified	Application	Other notes	Description of genetic change	Current Regulation		Proposed Regulation		Other agency approval still required
				Type of gene edit (SDN)	GMO?	Authorized activity	GMO?	Authorized activity	
			selection of new trait from breeders genetic pool, but not present in final organism.				s 9(2)(f)(iv)		
	Apple	Fast flowering trait and guided repair CRISPR gene editing in parallel to introduce allele of interest.	SDN3 transgenic: Insertion of viral origin promoter and birch transgene used to accelerate selection of new trait from breeders genetic pool, but not present in final organism.	SDN2- guided repair of allele of interest	Yes	New organism - containment			FSANZ

Sector	Organism modified	Application	Other notes	Description of genetic change	Current Regulation		Proposed Regulation		Other agency approval still required
				Type of gene edit (SDN)	GMO?	Authorized activity	GMO?	Authorized activity	
	Trichoderma reesei	Production of animal-free proteins for high-end niche products -fungus converts large amounts of cellulose to glucose.	Exempt Dealing in Australia (note: not exempt from regulation)	SDN3 transgenic: Insertion of genes encoding the proteins required to produce casein and whey	Yes	Containment approval from both the EPA and MPI	s 9(2)(f)(iv)		Yes MPI (ACVM Act – biological compound)
Primary industries - animals	Sheep and Cattle	Increase sheep and cow tolerance to Facial Eczema (FE) – will lead to improved animal welfare and increased production through reduced subclinical and clinical cases.		SDN3 cisgenics: Insert immune complex genes encoding for FE tolerance, taking advantage of within species genetic variation.	Yes	New organism – Containment			Yes MPI (Animal Welfare Act)
	Cattle	Inhibit development of horns in cattle to produce polled cattle. Preventing		SDN3 cisgenics: Replication of naturally occurring phenotype using CRISPR guided	Yes	New organism – Containment			Yes MPI (Animal Welfare Act)

Sector	Organism modified	Application	Other notes	Description of genetic change	Current Regulation		Proposed Regulation		Other agency approval still required
				Type of gene edit (SDN)	GMO?	Authorized activity	GMO?	Authorized activity	
		manual horn removal (polling). Replicating a naturally occurring genotype and phenotype.		small deletion and insertion to replicate loci duplication.			s 9(2)(f)(iv)		
Pest control	Douglas fir	Produce sterile conifers for industry use, preventing unwanted spread of 'wilding pines' in the environment.	No nucleic acid template to guide repair, not a GMO, so not regulated under Australian legislation.	SDN1: Sterile lines produced by disrupting genes responsible for reproductive function	Yes (potentially low-risk)	Containment and Conditional Release possible			Yes MPI – (ACVM Act agricultural compound) Biosecurity and Department of Conservation
	Vespula vulgaris Wasp	Potential for a CRISPR Cas gene drive to eradicate or suppress globally invasive	Gene drive. Application is *in-vivo*, development *in-vitro*. Need to	SDN3 cisgenic or transgenic[2]: A gene drive using spermatogenesis genes and	Yes	Containment			Yes MPI - (ACVM Act agricultural compound) Biosecurity

[2] The potential for a CRISPR gene drive to eradicate or suppress globally invasive social wasps | Scientific Reports (nature.com) and Full article: The potential for the use of gene drives for pest control in New Zealand: a perspective (tandfonline.com)

Sector	Organism modified	Application	Other notes	Description of genetic change	Current Regulation		Proposed Regulation		Other agency approval still required
				Type of gene edit (SDN)	GMO?	Authorized activity	GMO?	Authorized activity	
		wasp species predominant in Beech forests to protect native fauna and honey bees.	carefully assess and exploit variation in target genes to limit the potential of GM wasps affecting populations in the native range.	affecting spermatogenesis in Vespula wasps.			s 9(2)(f)(iv)		and Department of Conservation

MINISTRY OF BUSINESS, INNOVATION & EMPLOYMENT
HĪKINA WHAKATUTUKI

MINUTES GENE TECHNOLOGY TECHNICAL ADVISORY GROUP: 5 JUNE 2024 (excerpt – paper 3)

Date and time:	9am – 11am Thursday 5 June 2024
Location:	Microsoft Teams
Chair:	Emily Parker (Ferrier Institute, Department Science Advisor MBIE)
Invitees:	Tim Hore (Otago), David Ackerley (Victoria), Billy Sheppard (Auckland), Alec Foster (from 9.23am) (Scion), Jasna Rakonjac (Massey), Andy Allan (Plant and Food Research, Auckland), Nikki Freed (Auckland, Daisy Lab), Rachel Perret (Malaghan), Neil Gemmell (Otago), Richard Scott (from 10 am) (AgResearch), William Rolleston (South Pacific Sera Limited), Maui Hudson (Waikato), Ariana Estoras (AgResearch)
Invited guests	Matt Glenn and Roger Hellens (Kiwi Fruit Breeding Centre)
MBIE attendees:	Simon Rae, s 9(2)(a)
Apologies	

At the end of each section, in bold are the key points that the TAG members noted should be considered by MBIE's policy team, these are summaries of the discussion and do not reflect group consensus. As per the Technical Advisory Group Terms of Reference members are not expected to reach consensus.

Item	Discussion
What does the whole system look like?	*Scenarios* Points raised by members of the TAG at the meeting: • Issue that genetically modified human somatic cells are a GMO but *in vivo* gene therapy does not create a GMO, this could be confusing. • [MBIE noted this was a good example of where using the term "GMO" would not be useful as it raises a scientific discrepancy. Could use regulated and non-regulated technologies, but might also be problematic]. • Further example of issue: testing of CAR T-cells in an external laboratory would require a transfer permit, however, transfer of patient blood containing modified CAR T-cells would not. Will need to consider transfer permits for non-notifiable activities. If an activity is in the non-notifiable category transfer should be without constraints. • Not clear where bacteriophages fit in the risk tier system. s 9(2)(f)(iv) **Action**: TAG to provide more examples of 'grey areas' in the risk tiering that need more consideration.

	The TAG members noted the following key points to be considered by MBIE's policy team: • **Scenarios illustrated where categorisation in the risk tier system was difficult.**

MINISTRY OF BUSINESS, INNOVATION & EMPLOYMENT
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Gene Technology Regulator: Industry Focus Group

June 2024

The information on these slides are draft policy options only and may change, they are not government policy

Purpose of today is to

- test specific parts of the reform proposals to understand the advantages and potential consequences from your perspective
- ask you how 'enabling' specific parts of the reforms will be to help drive research advancement and business innovation?
- answer your questions

Background

- The Government has tasked officials to advise on reforms to gene technology regulation.
- This work is led by the Ministry of Business, Innovation and Employment (MBIE), with support from the Ministry for the Environment, the Ministry of Primary Industries, and the Ministry of Health.
- The reform programme aims to address the problem of current regulatory settings for gene technology being overly restrictive and disproportionate to the risks, out of date, and inflexible to emerging science and technology.
- We are considering regulatory systems in other countries, particularly Australia, the UK and EU while making additions to reflect New Zealand's specific context and circumstances.
- The Bill to allow for greater use of gene technology is set to be introduced by the end of this year. The Government will welcome feedback on the proposed legislation through the select committee process.

Objectives

- **Risk-proportionate** – it proportionately manages the risks that gene technology poses, to protect New Zealand's environment and supporting ecosystems, and the health and safety of its people and communities.
- **Enabling** – it enables the safe use of gene technologies to deliver better health, environmental, societal, cultural and economic outcomes for New Zealanders.
- **Accessible** – its processes facilitate the efficient assessment and approval of safe and ethical technologies and are easy for applicants to navigate.
- **Future focused** – it anticipates and flexibly accommodates future technological developments to benefit New Zealanders.
- **Rights and Interests** – it appropriately reflects potential obligations to actively protect Māori rights and interests under Te Tiriti o Waitangi/The Treaty of Waitangi.
- **Internationally aligned** – settings are consistent with our international obligations and commitments and are in step with New Zealand's major trading partners and other comparable jurisdictions to facilitate trade and improve New Zealand's ability to access new technologies.

What we heard @ first IFG meeting on 23 April

- Supportive of adapting and improving the legislative framework from overseas, to fit New Zealand's specific context and circumstances.
- Important to align with our major trading partners.
- Gene technology is moving rapidly and there is a need to ensure any new regulatory framework is future proofed.
- Need to streamline regulatory approvals to avoid some of the complex interactions with other regulators and legislation, this could include co-approvals between different regulators and different countries.

What we heard …

- Support for continued function of institutional biosafety committees for low-risk applications but compliance and auditing needs to be streamlined.
- Widespread support for exempting low risk gene editing technologies.
- Industry can play a role in stewardship by developing their own quality management systems and assurance programmes.
- Concerns from organics about gene-edited organisms entering their supply chains, and potential increased costs to certify their products as non-GM (this also applies to non-organic products for some markets or customers)

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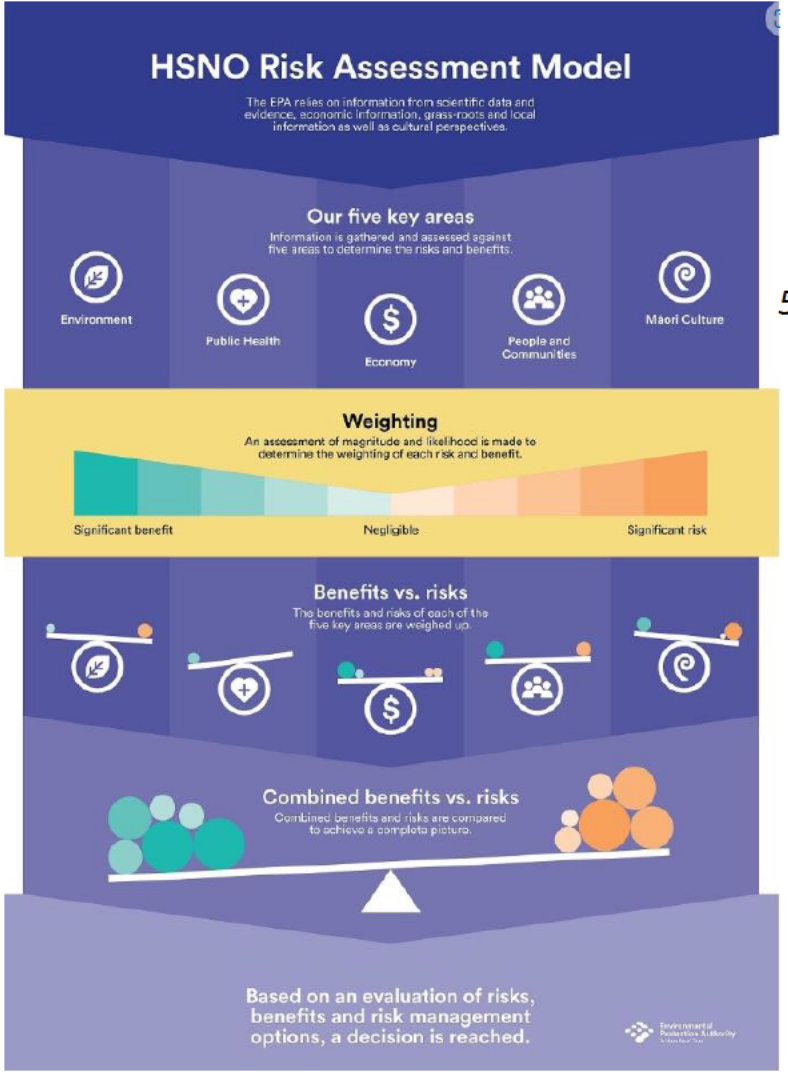
Recap of proposed changes

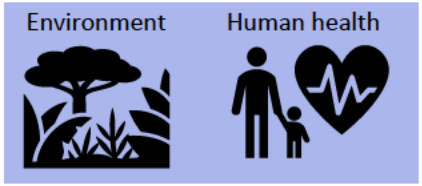


Purpose

Gene Tech Risk Assessment Model

The regulator relies on evidence from technical sources

5 areas to 2 areas



Benefits aren't assessed and not balanced with risks

Risks may be weighted (e.g. for taonga species)

Focus will be on risk management

Risk context – *risk tiers

↓

Risk assessment

↓

Risk management plan

The narrower focus on managing risks to human health and the environment will enable a consistent, evidential, and transparent approach to evaluating applications and making decisions.

Public consultation **only if** significant risk if/when released

Decision is made to authorise GMO activity if the regulator is satisfied the **risks can be managed**

Operationalisation of the Purpose

HSNO Act
All applications require pre-consultation.

All applications pass through the EPA committee and the Ngā Kaihautū.

Most applications require a pre-submission consultation.

Applications not been approved as low risk are publicly notified with hearings if required.

Most decisions are delegated to a committee. The HSNO Act also provides for the Minister to make decisions on an application if they consider it will have significant effects (call-in process).

Proposed new Act

- A range of very low risk gene editing techniques could be exempt from regulatory oversight (e.g. that could be achieved through conventional breeding practices)
- Risk tiers: Low risk laboratory work could be undertaken with limited regulatory oversight; whilst higher risk would require a risk assessment by the regulator.
- A risk matrix could guide the regulatory intervention (e.g. contained in a lab, intentional release, medical use)
- Applications do not require a pre-submission consultation.
- Public consultation on regulator risk management plan only for environmental release of medium to high risk

The proposed risk matrix

Laboratory and Industrial*	Environmental release	Medical use
Non-notifiable	Non-notifiable	Non-notifiable
Notifiable	Notifiable	Notifiable
Licensed Expedited assessment	Licensed Permit Expedited assessment Full assessment	Licensed Permit Expedited assessment Full assessment

Non-Notifiable Activities

Very low risk.

Notifiable Activities

Low risk.

Activities must be verified by an Institutional Biosafety Committee.

Regulator must be notified on an annual basis.

Under the Laboratory and Industrial category, activities must be conducted in an approved Physical Containment facility.

Licensed Activities

Risks: Medium-to-High or uncertain.

Assessed on a case-by-case basis.

*Under the **Laboratory and Industrial** category, release into the environment would be prohibited.

What does this mean for you

- Some low risk gene editing techniques will no longer be regulated
  - Eg s 9(2)(f)(iv)
- Very low risk activities will be able to proceed without restrictions under the gene technology regulations (non-notifiable)
  - Eg s 9(2)(f)(iv)
- Low risk activities will have institutional and MPI oversight (where containment facilities are required)
  - Standard research in containment
- Specific category for medical use and clinical trials
  - Eg s 9(2)(f)(iv)

Medicines under the new regulations

- Under the proposed risk matrix, its intended that medical use would have its own category. This category would only apply to GMO activities when they are being used as a medicines or therapeutic product, not during their development in containment.
- Non-notifiable and notifiable activities, which would cover medicines and therapeutic products that present a very low or low risk to the environment and public health wouldn't have direct oversight from the gene technology regulator. Assessment under other legislation would still be required.
- It's also proposed that the gene technology regulator would have ability to recognise specific overseas regulators so that GM medicines and therapeutic products approved under those jurisdictions would be automatically approved (under the gene technology regulations) here.
- It is also likely that a provision would be included under new legislation so that in specific circumstances the regulator would have the ability to delegate a risk assessment of an application under the new legislation to another regulator.
- Whether the provisions described here could apply to veterinary medicines in addition to human medicines is under discussion. We would welcome your thoughts on this question.

New Zealand's brand and consumer preference

Question from industry:

- What are the impacts of a more enabling system on market access (the effects of losing GM freedom in NZ, impacts on clean green brand)?

Background:

- We see that there are other consumer preferences which could outweigh GMO status
- We are investigating what factors are important to retain access in non-GMO markets
- We are not assessing specific market requirements or consumer preferences in detail

Key questions:

- Have you carried out market research on consumer attitudes towards GMO (or alternatively the benefits) of non-GMO in your industry? If so, what have you learned?

Coexistence of GMO and non-GMO supply chains

Question from industry:

- How does industry provide assurance that their product is not produced using gene technologies for customers and markets requesting non-GM products?

Background:

- Frameworks exist internationally which allow for non-GMO and GMO supply chains to coexist.
- With appropriate supply chain separation, it is possible to protect market access for non-GMO production.

Key questions:

- Is this a Government or Industry responsibility?
- Do you know how this is managed by your industry in other countries?
- What effort is required to gain non-GMO assurance in your key markets?
- How could this assurance be implemented? *E.g. seed certification schemes*

Any other key issues we have missed?

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Specific policy options to test with you

Should the regulator consider costs and benefits of GMO applications?

- The Australian Gene Regulator Act does not consider benefits when deciding whether an application should be approved. This was a deliberate choice to focus the regulator on a scientific evaluation of the risks, and to avoid making value-laden judgments about social, economic and cultural factors which are more difficult to assess and compare.
- Benefits assessments can require applicants to prove benefits outweigh the risks. This increases the evidential burden on applicants and is a particular problem when benefits are uncertain or unproven, which is typically the case for innovative products.
- Benefits assessment may be more appropriate for full environmental releases.
- What are your thoughts on the regulator considering costs and benefits?

Should the regulator consider risks to market access and trade of GMO applications?

- The Agricultural Compounds and Veterinary Medicines Act 1997 (the ACVM Act considers risks of the proposal to market access and trade.
- While this mechanism appears to work well in the ACVM Act, it may present challenges similar to those encountered in benefits assessments.
- What are your thoughts on the regulator considering trade agreements **and** market access risks?

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MEETING PAPERS: 5 JULY 2024 GENE TECHNOLOGY TECHNICAL ADVISORY GROUP

3. Paper title	Category Definitions
Meeting date	9am – 11am Thursday 4 July 2024
Approved by	Simon Rae

Item purpose and summary
Under the proposed risk matrix, authorisations to carry out an activity with a GMO will be grouped into three categories: *Laboratory and Industrial*, *Environmental Release*, and *Medical Use*. The definition of these categories needs careful consideration. We are interested in your thoughts on how we can successfully establish these categories.
Discussion questions
• How do we usefully define the specific categories? • Do you see any potential complications with our thinking on when a biomedical application should shift from the *Laboratory and Industrial* category to the *Medical Use* category, i.e., when it is proposed to be used on a human or animal? • It is intended that veterinary medicines would come under the Medical Use category. What might we need to consider when defining these categories so that veterinary medicines come under the *Medical Use* category rather than the *Environmental Release* category? What regulatory ambiguities might this create? • In your view, is "*Medical Use*" the right name for that category? Australia has proposed calling that category "*Clinical trials and medical applications*".

Under the proposed risk matrix, authorisations to carry out an activity with a GMO will be grouped into three categories: *Laboratory and Industrial*, *Environmental Release*, and *Medical Use*. The definition of these categories needs careful consideration.

It isn't our intention with the risk matrix for, say, laboratory research on a GMO that is intended to eventually be released into the environment or eventually be used medically, to be categorised into either of those two categories. For one, much research is fundamental in nature, and any eventual use might be unknown.

It is intended that activities will fall into a category based on their present stage of development or their next stage if they are applying for an approval, rather than their final future intended use.

For example, research on a medical therapy that is currently being conducted in a laboratory would fall into the *Laboratory and Industrial* category. Likewise, an application for a licence for a potential medical therapy that is still under development in a laboratory setting would also come under the *Laboratory and Industrial* category. It would only be when a medical therapy or medicine is proposed to be used in a human or animal medically (in a trial, clinical trial or for general commercial use, for instance), that an application under the *Medical Use* category would be relevant.

4. Paper title	Risk tier criteria
Meeting date	9am – 11am Thursday 4 July 2024
Approved by	Simon Rae

Item purpose and summary
Under each category of the risk matrix will be non-notifiable and notifiable risk tiers that will contain activities that are determined to be very low risk and low risk, respectively. The Australian legislation nor the HSNO Act defines "very low risk" or "low risk", and it is not currently our intention to define these terms under this legislation. However, there will be a set of criteria for these risk tiers. We are interested then in your views on what factors might be appropriate for each risk tier's set of criteria and the implications of the matrix approach in setting these criteria
Discussion questions
• What sort of factors would be appropriate, in your view, for the non-notifiable and notifiable risk tiers? (And for each of the Physical Containment levels under the notifiable risk tier?) • How do you think we or the regulator should approach developing these criteria? • What do you think would work well from the Australia legislation and/or from the New Zealand legislation?

You will find the criteria for the Australian risk tiers equivalent to non-notifiable and notifiable under *Schedule 2 and Schedule 3 of the Gene Technology Regulations 2001*. You might also wish to consider the criteria for low-risk genetic modifications under the *Hazardous Substances and New Organisms (Low-Risk Genetic Modification) Regulations 2003*.

5. Paper title	Non-notifiable and notifiable medicines
Meeting date	9am – 11am Thursday 4 July 2024
Approved by	Simon Rae

Item purpose and summary
Given the newness of the non-notifiable and notifiable risk tiers for the *Medical Use* category (we don't have the Australian legislation to look to), we'd like to get your views on what medicines and therapies you think should be considered 'very low risk' and 'low risk' *to the environment and the health and safety of people*.
Discussion questions
• What are some GM medicines and therapies that might be appropriate for the non-notifiable and notifiable risk tiers of the *Medical Use* category?   ○ Why would they be appropriate for those categories, in your view?

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MINUTES GENE TECHNOLOGY TECHNICAL ADVISORY GROUP: 4 JULY 2024

Date and time:	9am – 11am Thursday 4 July 2024
Location:	Microsoft Teams
Chair:	Emily Parker (Ferrier Institute, Department Science Advisor MBIE)
Invitees:	Tim Hore (Otago), David Ackerley (Victoria), Billy Sheppard (Auckland), Alec Foster (Scion), Jasna Rakonjac (Massey), Andy Allan (Plant and Food Research, Auckland), Nikki Freed (Auckland, Daisy Lab), Neil Gemmell (Otago), Richard Scott (AgResearch), William Rolleston (South Pacific Sera Limited), Maui Hudson (Waikato) from 10 am, Ariana Estoras (AgResearch)
MBIE attendees:	Simon Rae, s 9(2)(a)
Apologies	Rachel Perret (Malaghan), s 9(2)(a)

At the end of each section, in bold are the key points that the TAG members noted should be considered by MBIE's policy team, these are summaries of the discussion and do not reflect group consensus. As per the Technical Advisory Group Terms of Reference members are not expected to reach consensus.

Item	Discussion
Category Definitions	The TAG was asked to consider how to successfully establish the three categories (Laboratory and Industrial, Environmental Release, and Medical) under the proposed risk matrix. Points raised by members of the TAG: • Laboratory and industrial category supported, protects discovery phase – serendipitous discoveries can breach scope of approved research in current system, this limits innovation. • Straightforward that veterinary medicines would come under the 'Medical Use' category, a patient can be human or animal. • Prefer Australian proposed framework and description (*Clinical trials and medical applications*), more descriptive and allows for applications that potentially span a variety of categories. Example given, transgenic pigs as source of transplant organ, would span field, veterinary and medicines. • Production of a medicine would be under laboratory and industrial category until the point of approval for use where it transitions to medical use category and moves to MedSafe for approval. Point of difference for medicines will where medicines go from development to production. Suggest notifiable and non-notifiable

	categories under medical use not useful.
	
	The TAG members noted the following key points to be considered by MBIE's policy team:
	• **General support for:**
	  ○ **Three categories.**
	  ○ **Activities sitting in laboratory and industrial during development (e.g. medicines) i.e. the stage of development rather than the end use.**
	  ○ **Australian proposed framework and description (Clinical trials and medical applications).**
	  ○ **Follow up how applications that span different categories are managed (e.g. transgenic pigs).**

Risk tier criteria	The TAG was asked to consider the factors might be appropriate for each risk tier's (e.g. non-notifiable and notifiable risk tiers) set of criteria and the implications of the matrix approach in setting these criteria. Points raised by members of the TAG: • AU regulations are easier to navigate than current HSNO, could be useful to map what we commonly do in NZ and compare to AU system. Look at gaps and which regime is more versatile and sensible. • Risk criteria in secondary legislation in AU system. • Suggest use international standards to define physical contaminant rather than "PC". • s 9(2)(f)(iv) [redacted] • Useful to look back at the scenarios and see how they fit in the risk tiers. • Challenge in this area is balancing perceived risk vs actual. • Current legislation prevents risk rather than managing risk, example given, current legislation seeks to prevent all pollen movement rather than look at the impact of pollen moving. **The TAG members noted the following key points to be considered by MBIE's policy team:** • **Useful to map current gene technology work in NZ and compare to AU system.** • s 9(2)(f)(iv) [redacted] • **Useful to look back at the scenarios and see how they fit in the risk tiers.**

	Action: Map AU and NZ low risk activities. **Action:** TAG to familiarise themselves with the risk tiers AU regs and HSNO and consider some of the applications in your technical space. Preparation for next TAG meeting.
Non-notifiable and notifiable medicines	The TAG was asked to consider what medicines and therapies you think should be considered 'very low risk' and 'low risk' *to the environment and the health and safety of people*. Points raised by members of the TAG: • Noted again that risk tiers for medical use may not be useful. • Need to ensure risk assessments are balanced between GMO and non-GMO medicines. Example given of a non-GMO vaccine-derived poliovirus in the environmen,. [MBIE noted environmental risks are not in scope for MedSafe]. • Risk consideration should be focussed on things that are transmissible. [MBIE noted that common example used for non-notifiable medicines are CAR T-cells].

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HĪKINA WHAKATUTUKI

Summary of Māori stakeholder interviews – July 2024

Interviewees

s 9(2)(ba)(i)

Format

1. MBIE conducted five interviews with Māori stakeholders in July 2024 to seek their perspectives on the proposed gene technology reforms. The interviewees were chosen because of their knowledge of genetic modification or connections with their iwi or hapu.

2. The interviews involved a short presentation from MBIE summarising the design of the regime, before asking interviewees for their general impressions and feedback. MBIE did not raise specific topics and follow-up questions were based on interviewees' comments.

Opportunities from gene technologies

3. The interviewees were generally supportive of reforms to gene technology legislation. There was a consistent theme that new generations were expecting solutions to challenges in conservation (eg Myrtle Rust), healthcare and from climate change. It was difficult to oppose gene technologies if they could provide these solutions.

4. This support varied depending on the technique and application:

    a. Cisgenic applications (modifying organisms with genetic material from the same species) were preferred over transgenic applications (using material from different species).

    b. There was more support for modifying plants than animals, and strong opposition to modifying humans (excluding medical treatments like gene therapies)

    c. There was general comfort with exemptions for gene editing techniques if limited to those that deliver results indistinguishable to conventional practices.

5. Several attendees mentioned mātauranga to explain their support, such as stories of some Māori in the Bay of Plenty descending from intermarriages with tūrehu (other beings or peoples) as examples of acceptance of forms of genetic modification. Some discussed mauri and whakapapa, noting that while there were some concerns, successful responses to pathogens like myrtle rust would be beneficial overall.

6. Interviewees saw it as critical that, if reforms progressed, Māori could benefit from gene technologies. There was a theme of Māori using new technologies as ways to recover from the impacts of colonisation and there was strong interest in the economic opportunities for Māori.

7. Several noted that their iwi are conducting or considering research like genome mapping to identify possible applications of taonga species (eg UMF factor in Manuka honey), and that cisgenic gene editing could accelerate the breeding process once the desired traits were identified.

Concerns

Environmental impacts

8. Interviewees were unanimously concerned about unexpected consequences from releasing GMOs into the environment. Several noted that scientific assessments had failed in the past (eg introduction of invasive species like ferrets) and so the new regime could not guarantee successful risk management.

9. All agreed that strong post-release processes (such as monitoring and license revocation) would be needed to mitigate this risk. One interviewee preferred a precautionary approach to approvals, based on testing technologies overseas before approving release in New Zealand.

10. Interviewees agreed with MBIE's presentation that mentioned the need to protect taonga species but did not raise the topic for further discussion.

Operation

11. There was a strong preference for a partnership model in decision making to effectively consider Māori interests and to build social license for the regime with Māori. Interviewees noted that Māori advisory committees did not meet this aspiration and needed decision-making powers to have an impact.

12. Some recommended that the regulator work with Māori to develop a tikanga approach to decision-making and noted the need for face-to-face engagement. This meant that the regulator would need Māori staff with relationship management expertise ("the right people in the right places") in addition to its scientific capabilities.

13. These attendees noted the importance of education around gene technologies, to inform people of how to navigate the regulatory process, how they could potentially benefit from these technologies, and to build social license. They noted that, outside of Ngāi Tahu and Ngāpuhi's HSNO Committees, iwi have had limited engagement with the current HSNO regime to date.

14. Interviewees noted the need to consult with Māori on applications to ensure all risks were considered and managed. However, some noted that there were challenges in identifying the appropriate consultation requirements and contact points even for Māori (an example was given of an iwi breeding programme for a taonga species on their land). Some suggested that Māori staff within the regulator could help with this,

while one recommended supporting Māori to develop tools to map relevant relationships.

15. Attendees did not raise any concerns with the authorisations framework (e.g. risk tiers) but noted this was the first time they had seen the material.

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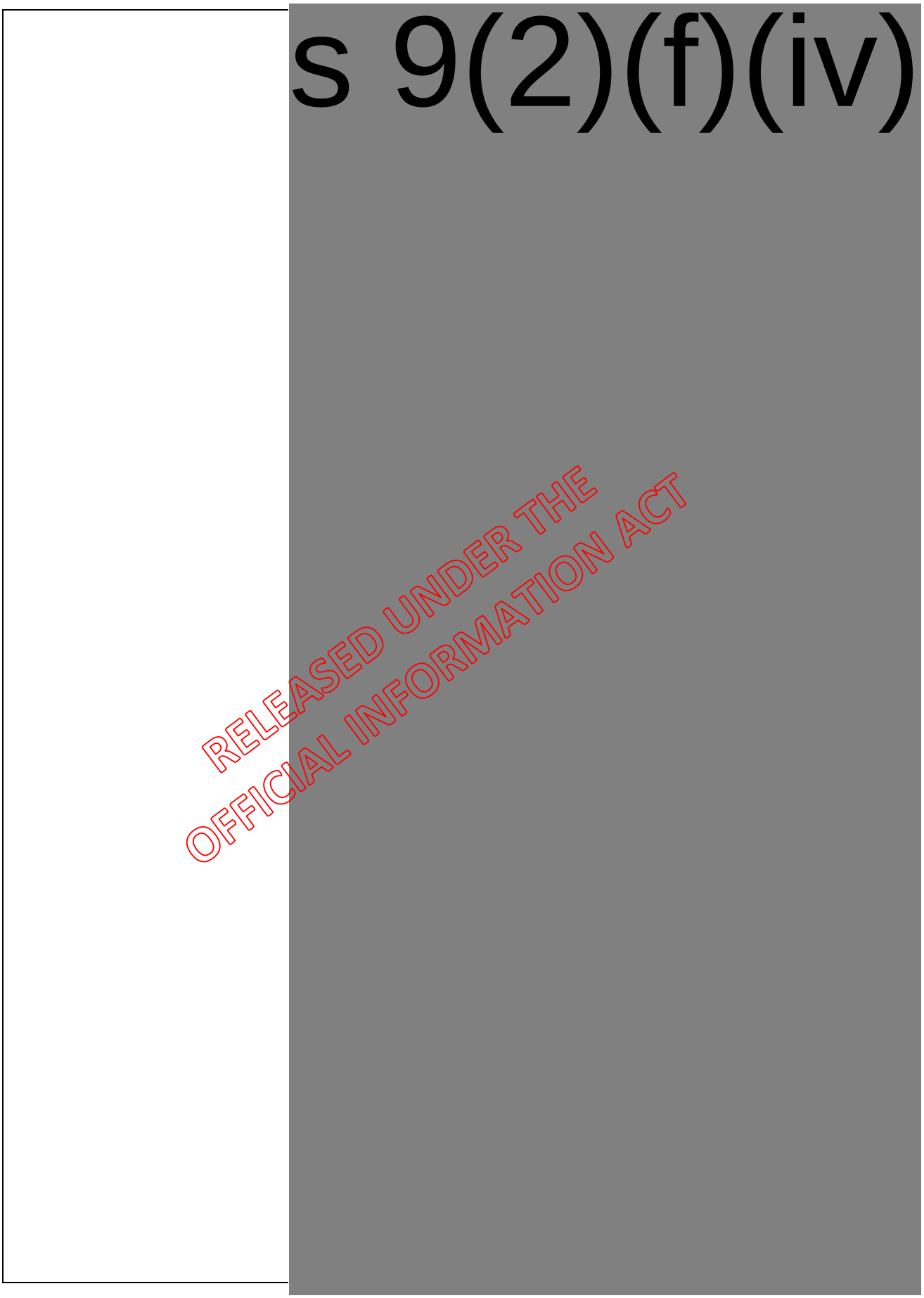
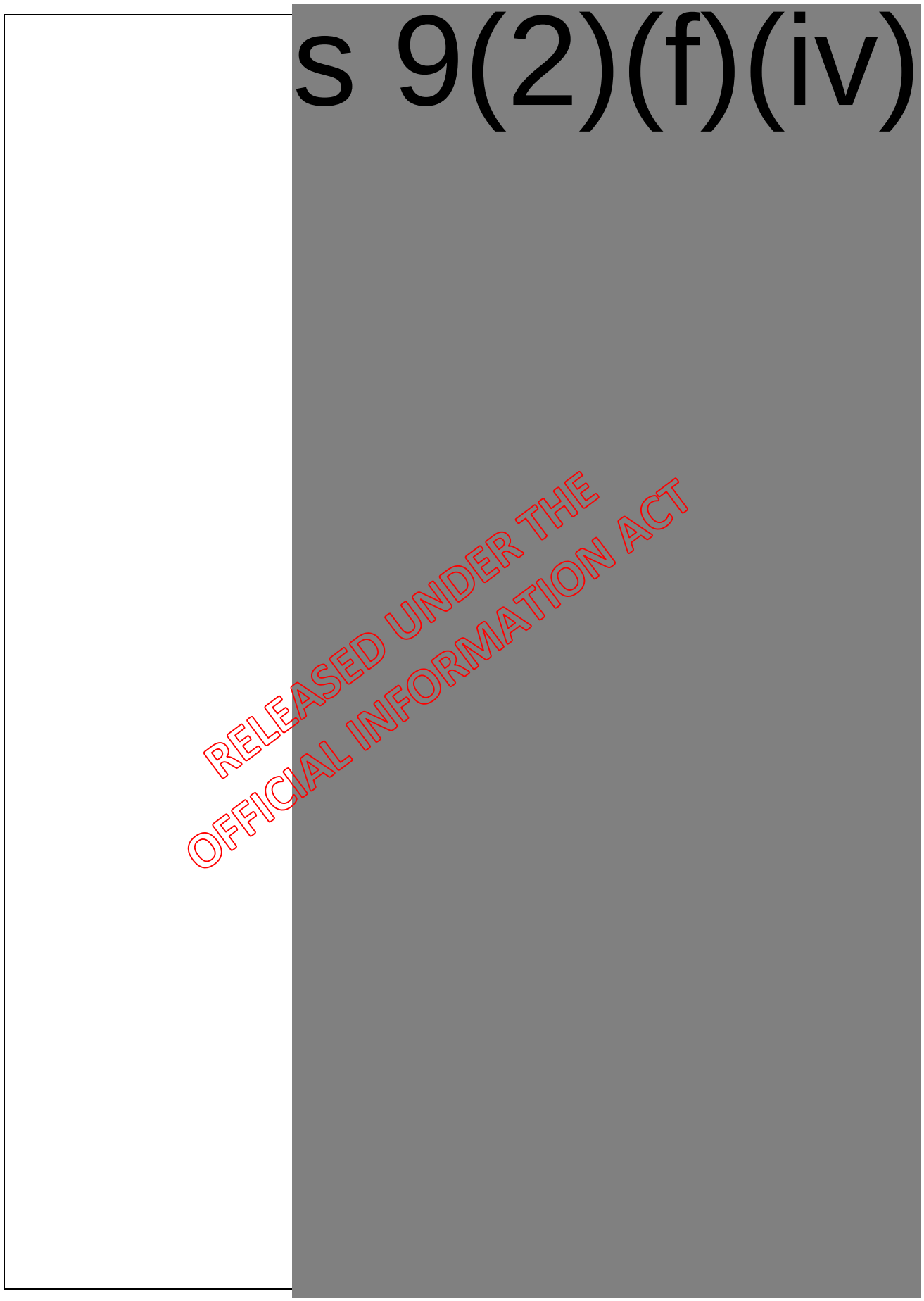
MINUTES: GENE TECHNOLOGY TECHNICAL ADVISORY GROUP MEETING 1 AUGUST (excerpt – breakout group discussions)

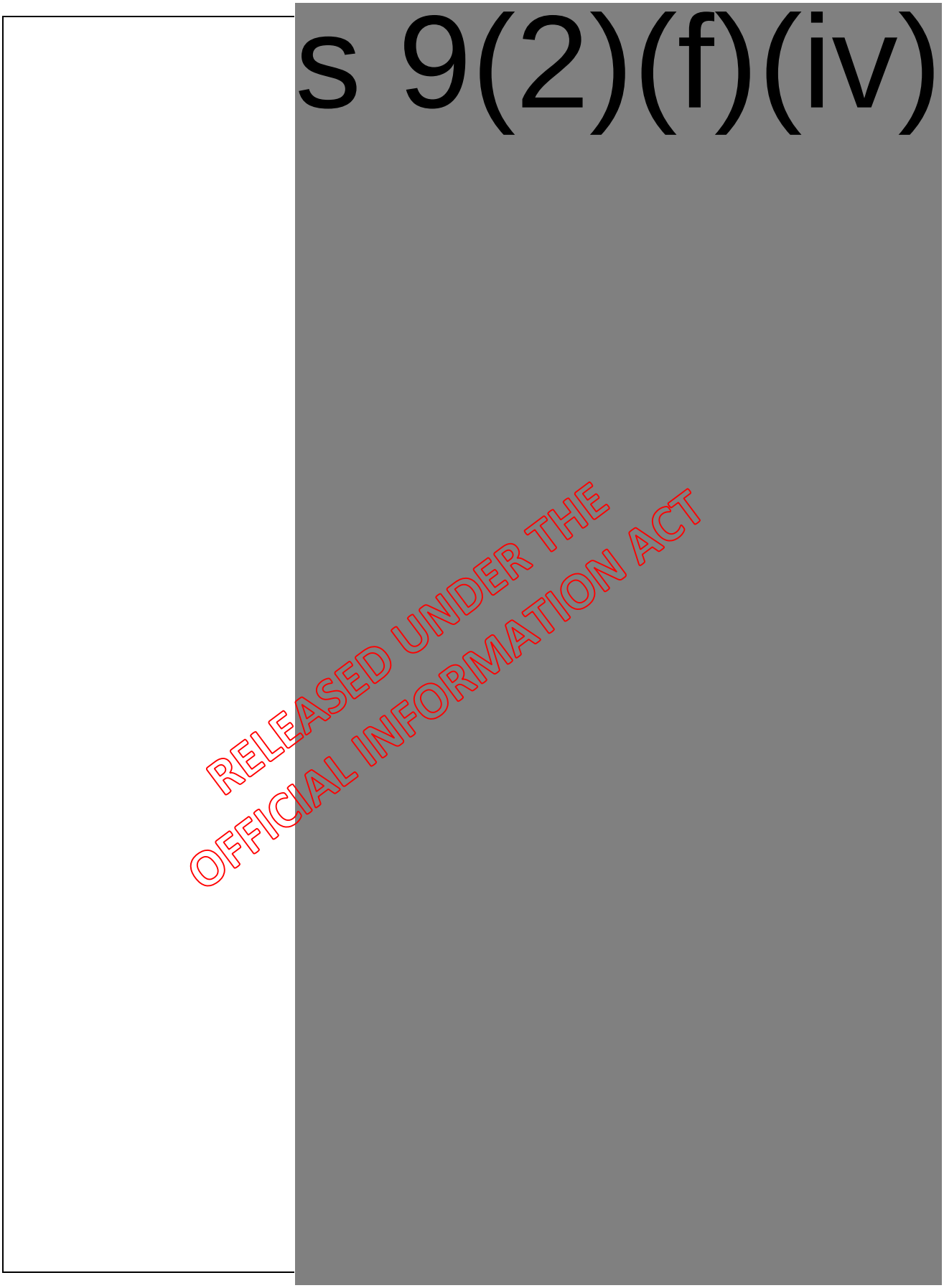
Date and time:	9am – 11am Thursday 01 August 2024
Location:	Microsoft Teams
Chair:	Emily Parker (Ferrier Institute, Department Science Advisor MBIE)
Invitees:	Tim Hore (Otago), David Ackerley (Victoria), Billy Sheppard (Auckland), Alec Foster (Scion), Jasna Rakonjac (Massey), Andy Allan (Plant and Food Research, Auckland), Nikki Freed (Auckland, Daisy Lab), Neil Gemmell (Otago), Richard Scott (AgResearch), William Rolleston (South Pacific Sera Limited), Maui Hudson (Waikato) from approx. 9.30 am, Rachel Perret (Malaghan)
MBIE attendees:	s 9(2)(a)
Apologies	Ariana Estoras (AgResearch), Simon Rae, Tony de Jong

At the end of each section, in bold are the key points that the TAG members noted should be considered by MBIE's policy team, these are summaries of the discussion and do not reflect group consensus. As per the Technical Advisory Group Terms of Reference members are not expected to reach consensus.

Item	Discussion
Context for break out groups	The Chair provided the TAG with the context for the meeting. • High-level policy objective is to exempt gene-editing techniques that produce results that could have been produced through traditional processes or natural changes, and do not introduce new genetic material. • Have proposed that these changes would be minor, need to define what constitutes a minor change. Policy proposal does not use terminology SDN1-3 Points raised by members of the TAG: • Support not using SDN1-3 terminology as already out of date.
Break out group 1 - Gene editing definitions.	s 9(2)(f)(iv)







s 9(2)(f)(iv)

Additional points:

- Need to carefully consider how 'exempt' category is referenced in the primary legislation. TAG would like to see this clause. Important if in primary leg that the clause does what the AU

	system does (allows for ”anything else that is considered exempt by regulations”). • [MBIE noted that primary leg will have a general provision to enable exemptions to be set, secondary legislation will have the exemption list and define “specific minor changes"]. **Action:** MBIE to share clause on exemptions in primary legislation

MEETING PAPERS: MINUTES GENE TECHNOLOGY TECHNICAL ADVISORY GROUP 12 SEPTEMBER 2024 (excerpt – paper 2 and slide)

Paper title	s 9(2)(f)(iv)
Meeting date	12 September 2.30pm – 4.30pm
Approved by	Tony de Jong

Item purpose and summary
The high-level policy objective approved by Cabinet is to exempt from regulation (i.e., deem non-regulated) technologies or organisms that involve either minimal risk or cannot be distinguished from those achievable by conventional techniques. More specifically, organisms that have been modified by gene editing techniques that produce specific minor changes, or were modified by template(s), and do not introduce new genetic material. At the TAG meeting on 1 August, we asked you to provide technical advice on the specific characteristics of modifications s 9(2)(f)(iv) or these policy settings. **The TAG discussed the following:**

s 9(2)(f)(iv)

s 9(2)(f)(iv)

Discussion questions

- Would these options provide for an organism agnostic approach while maintaining the same risk profile as products of conventional techniques?
- Are there any further key considerations that need to be accounted for from a scientific perspective?
- Are there any technical issues from a scientific perspective?
- Are there specific sectors where this option would be enabling or a barrier?

Break out discussions

These are initial options for gene edited products that will not have any regulatory oversight once released, any further modifications would be regulated in a risk proportionate manner through the risk matrix.

s 9(2)(f)(iv)

- Would these options provide for an organism agnostic approach while maintaining the same risk profile as products of conventional techniques?
- Are there further considerations that need to be accounted for from a scientific perspective?
- Are there any technical issues from a scientific perspective?
- Are there specific sectors where either of these options would be enabling or a barrier?

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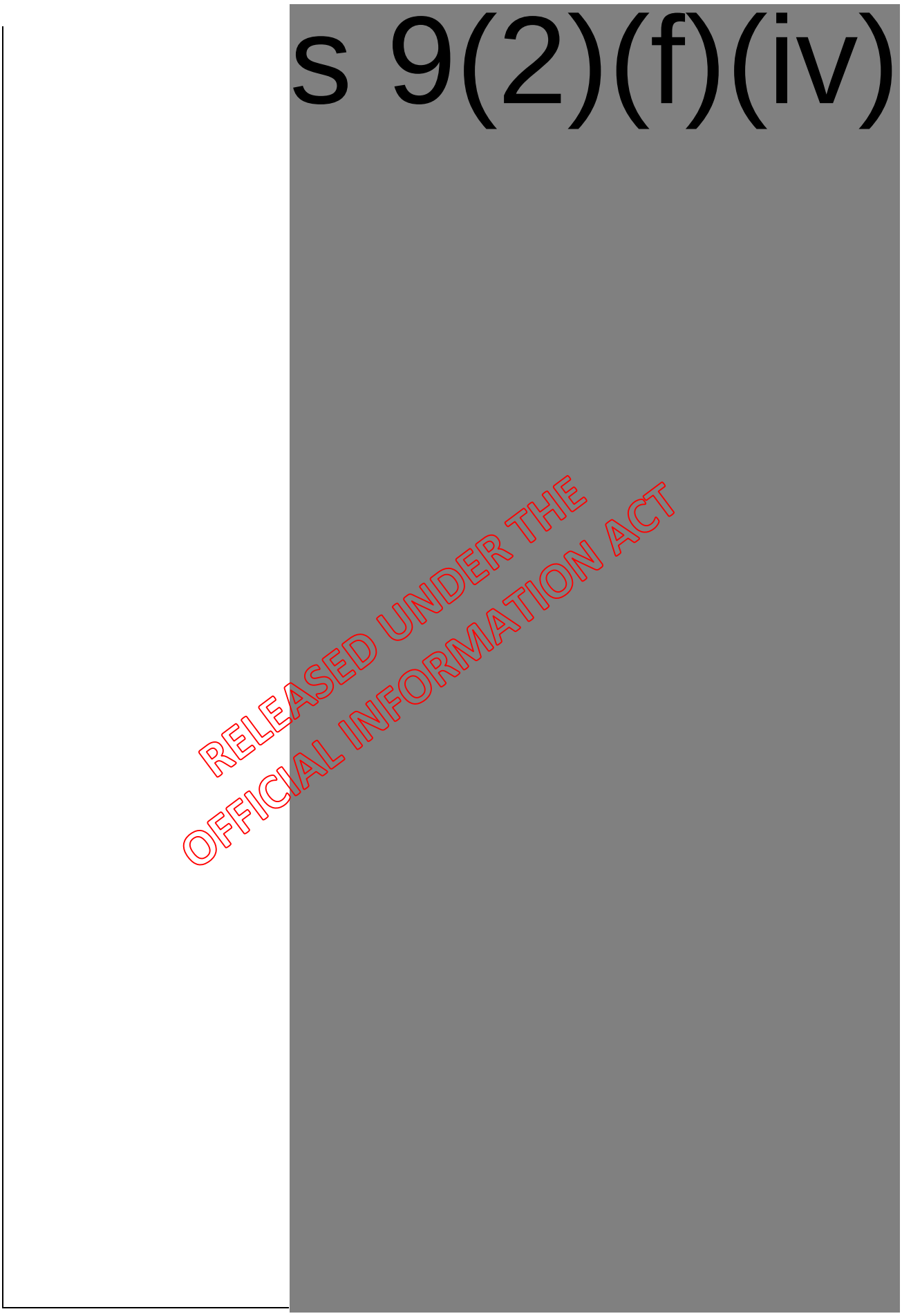
MINUTES: GENE TECHNOLOGY TECHNICAL ADVISORY GROUP MEETING 12 SEPTEMBER 2024 (excerpts re paper 2 and breakout discussion)

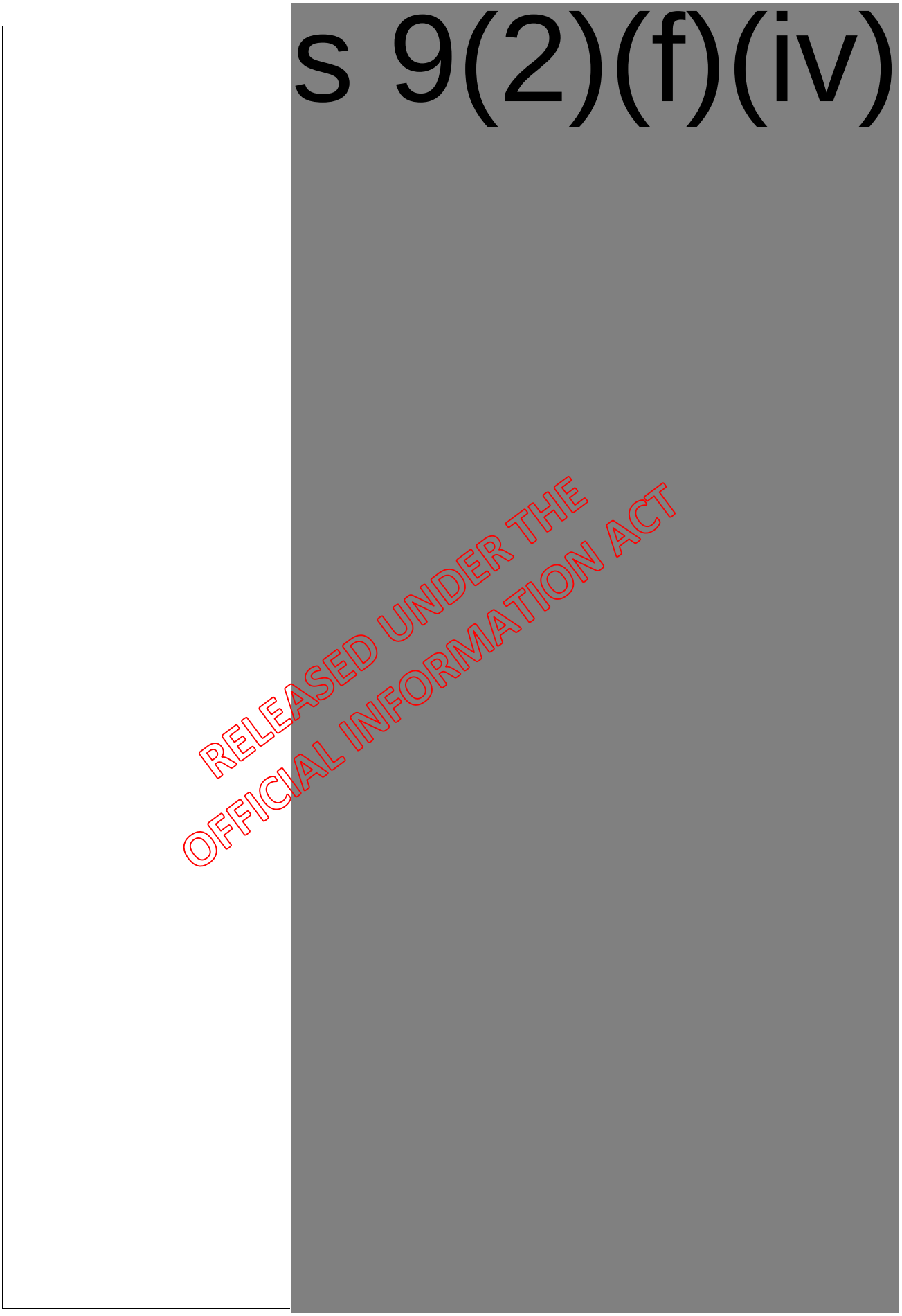
Date and time:	2.30pm – 4.30pm Thursday 12 September 2024
Location:	Microsoft Teams
Chair:	Emily Parker (Ferrier Institute, Department Science Advisor MBIE)
Invitees:	Tim Hore (Otago), David Ackerley (Victoria), Alec Foster (Scion), Jasna Rakonjac (Massey), Andy Allan (Plant and Food Research, Auckland), Nikki Freed (Auckland, Daisy Lab), Rachel Perret (Malaghan), Neil Gemmell (Otago), Richard Scott (AgResearch), William Rolleston (South Pacific Sera Limited), Maui Hudson (Waikato)
MBIE attendees:	Tony de Jong, s 9(2)(a)
Apologies	Billy Sheppard (Auckland), Ariana Estoras (AgResearch)

At the end of each section, in bold are the key points that the TAG members noted should be considered by MBIE's policy team, these are summaries of the discussion and do not reflect group consensus. As per the Technical Advisory Group Terms of Reference members are not expected to reach consensus.

Item	Discussion
Non-regulated technologies	MBIE gave an overview of the proposed options for non-regulated technologies. **Institutional legal perspective** An institutional legal perspective was provided to the TAG: • Clarity is vitally important for deciding on proceeding with a gene technology application, in the non-regulated space or regulated space. • Clarity also important to enable comfort with approach taken. • Institutes are conservative, haven't had to make any decisions about putting GE technology in the field for a long time because of the de facto ban. Will require mind set change to pursue these technologies more actively in the field. • Potentially an even bigger step to be making decision about non regulated technologies – haven't thought about the approach for this, will require careful reflection. • Certainty will be required that the dealing is very clearly non-regulated, having the line between non and regulated well delineated is going to be important. Provide comfort to institutional decision makers that they are working within the regime and not stepping outside it, concern about doing the right thing and not being in breach of the legislation. TAG discussed:

	• What clarity and certainty are being sought? Certainty around what is regulated and non-regulated or the liability if things go wrong? • Public and users will want to know where the liability sits (who plays to clean it up). • [MBIE noted that the proposal is that offences and penalties regime will largely mirror HSNO and the Australian regime]. • Proposal for non-regulated technologies does not go as far as the English system where genes from within species for plants are classed as non-regulated. These plant species would not be allowed to grow here without regulation and the change may not be detectable. • s 9(2)(f)(iv) [redacted] • More clarity will be required for the current broad approvals held by some institutes that include a variety of different activities (e.g. very low, low and high risk). Going to need to be very clearly explained. • [MBIE noted that there will be transitional provisions, activities already approved will be moved into new categories. If there are higher requirements in current applications these will be voided]. • Interruptions to activities while institutions understand their obligations under the new regime will put a barrier in place for researchers. **Action:** MBIE will prepare a paper to circulate on proposed approach to non-regulated technologies.
Break out session	s 9(2)(f)(iv) [redacted]





	s 9(2)(f)(iv)
	Point of clarification: unregulated can be out in the environment whereas non-notified similar but can't be released into the environment, except if it sits in the environmental release category. The AU regime does not have the environmental release category so we have limited guidance. Useful for MBIE to provide more clarification. **Action:** MBIE provide more clarification on definitions of categories at the TAG workshop on 2/3 October.

MINISTRY OF BUSINESS, INNOVATION & EMPLOYMENT
HĪKINA WHAKATUTUKI

MEETING PAPERS GENE TECHNOLOGY TECHNICAL ADVISORY GROUP 2 DAY WORKSHOP 2/3 OCTOBER 2024 – papers 2, 3

2. Paper title	Developing the criteria for risk tiers and lists
Meeting date	2/3 October 2024
Approved by	Tony de Jong

Item purpose and summary
This session discusses the criteria the regulator will use to assign activities to four of the authorisation categories; non-notifiable, notifiable, general use, and pre-assessed activities (via secondary legislation). We would like your feedback and suggestions to ensure that the criteria: would ensure activities are assigned to the right categories (risk-proportionate) are predictable and transparent – it should be easy to explain why an activity is in a certain tier are unambiguous, and so provide the regulator with confidence to assign things to tiers with lower oversight We would also like your views on how we should define the laboratory use, medical use, and environmental release sub-categories for the notifiable and non-notifiable authorisations.
Discussion questions
• Are we looking at the right criteria for these authorisations? • Do the same criteria work for each sub-category (contained, medical, environmental release) or are bespoke criteria needed for each one? • Do the criteria have the right level of detail? (ie not too restrictive or permissive) • Is it helpful to specify the 'risk level' for each authorisation in the criteria, or would this be too ambiguous and open to challenge? (e.g. non-notifiable activities must pose *very low* risks) • (eg "the regulator must be satisfied that non-notifiable activities pose very low risks to people and the environment")

MINISTRY OF BUSINESS, INNOVATION & EMPLOYMENT
HĪKINA WHAKATUTUKI

Authorisation criteria

September 2024

The information on these slides are draft policy options only and may change, they are not government policy

Te Kāwanatanga o Aotearoa
New Zealand Government

Non-regulated technologies and the authorisation framework

Technologies and organisms not regulated

Non-GM technologies and organisms

Chemical mutagenesis, Radiological mutagenesis, Null segregants, RNA interference, Epigenetics, etc.

Exemptions

Techniques involving minimal risks or producing results indistinguishable from conventional practices

- Unguided repair (SDN-1)
- Guided repair (SDN-2)

Risk matrix framework

Contained	Environmental Release	Medical Use
Non-notifiable	Non-notifiable	Non-notifiable
Notifiable	Notifiable	Notifiable
Licensed Expedited assessment	Licensed Pre-assessed Expedited assessment Full assessment	Licensed Pre-assessed Expedited assessment Full assessment

Activities Approved for General Use

This list would contain specific GMOs able to be used by anybody, due to the minimal risks they present to human health or the environment

Emergency Authorisations

The Minister will be able to temporarily approve the use of GMOs needed to respond to an actual or imminent threat to human health or the environment

Not Government policy

Recap of the tiers

Non-notifiable

- Very low risk (ie doesn't require a PC facility)
- For activities that are very safe if done a certain way (eg in containment) so don't require checking from the regulator.
- Few conditions (mostly containment) and no notification

s 9(2)(f)(iv)

Notifiable

- Low risk
- Slightly higher risk, so notification enables regulator to check on things if any concerns.
- May involve general conditions (but no case-by-case assessment). For contained use, this usually means PG1 or higher. Regulator or IBSCs may be needed to verify containment processes.
- Must be notified to the regulator (either in advance or reported once a year)

s 9(2)(f)(iv)

General use

- Very low risk
- Covers specific varieties/products that the regulator knows pose minimal risks from its knowledge or experience.
- Few conditions (if any)
- Similar to an exemption, except easier to establish and revoke

s 9(2)(f)(iv)

Pre-assessed activities (permit)

- Medium risk– requires an application unlike others listed here
- Covers higher risk activities where regulator knows risks can be managed if certain general conditions are followed.
- Assessment is about confidence in applicant's ability to successfull follow those conditions- doesn't reassess the general risks of the activity.

s 9(2)(f)(iv)

Not Government policy

Notifiable & non-notifiable – defining laboratory, medical and environmental release

We propose:

Contained use: The use of a regulated organism in a setting that is intended to prevent its entry into the environment

Containment will be further defined by the risk tier, eg non-notifiable doesn't require a PC lab whereas notifiable will usually require at least PC-1.

Medical use: The therapeutic use of a regulated organism in a patient or animal

I.e. the point Medsafe gets involved, prior development is under 'contained use'

Environmental release: Any activity not covered by the above.

Mostly for the intentional release of a regulated organism into the environment. We've worded this more broadly to avoid cases where something doesn't fit any category.

What does Australia do? (Gene Technology Act 2000)

Typically high level, focused on judgement of whether risks can be managed. Example from their notifiable authorisation:

74 Notifiable low risk dealings

(1) The regulations may declare a dealing with a GMO to be a notifiable low risk dealing for the purposes of this Act.

(2) Before the Governor-General makes regulations declaring a dealing with a GMO to be a notifiable low risk dealing, the Regulator must be satisfied that the dealing would not involve the intentional release of a GMO into the environment.

(3) Before the Governor-General makes regulations declaring a dealing with a GMO to be a notifiable low risk dealing, the Regulator must consider:

(a) whether the dealing with the GMO would involve any risk to the health and safety of people, or to the environment, taking into account:

(i) the properties of the GMO as a pathogen or pest; and

(ii) the toxicity of any proteins produced by the GMO; and

(b) if there is such a risk—whether one or more of the requirements prescribed in the regulations for the purposes of subsection 75(2) would be sufficient to manage that risk; and

(c) any other matter the Regulator considers appropriate.

Australia – proposed amendment

Australia recently proposed some changes to the authorisations in their legislation. These don't look to have a material impact on the criteria but are included below for reference.

Notifiable activities

- No change to criteria
- Two types – some must be notified in advance, while others can follow Institutional Biosafety Committee processes
- Mostly for contained activities (eg no 'environmental release' category) – but proposed to also include activities approved by other domestic regulators

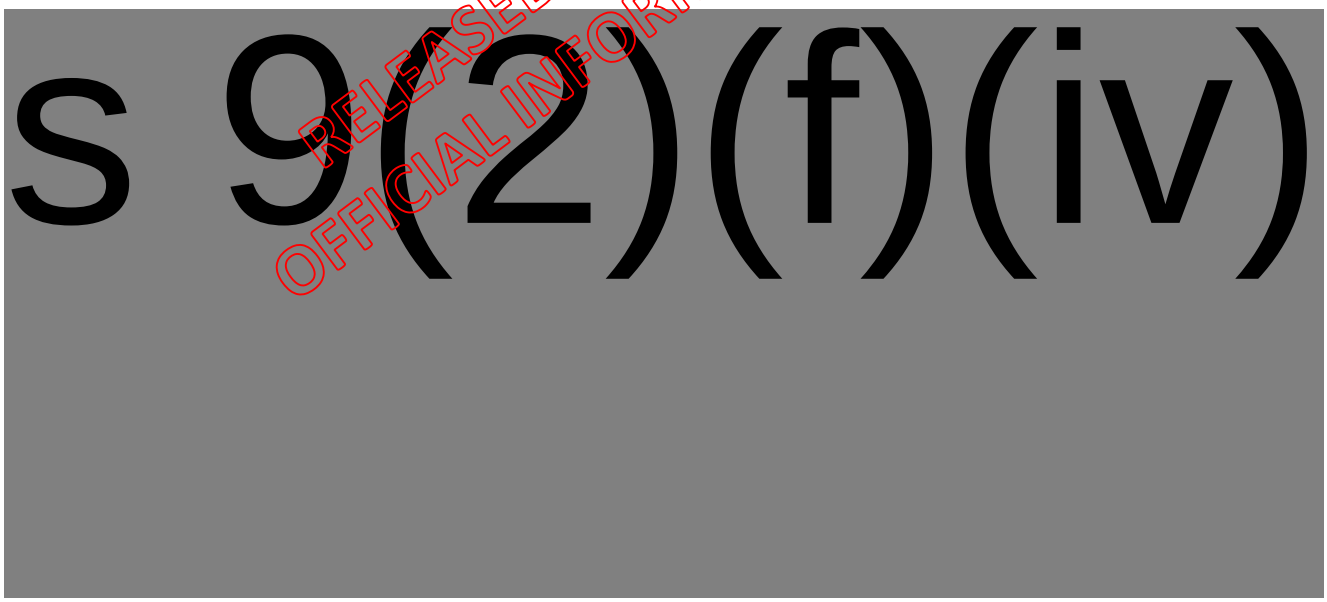
Non-notifiable activities

- New to Australia, effectively how they plan to do exemptions (includes their old 'exempt dealings' plus some low-risk gene editing techniques)
- Note determining them is a ministerial power, not their regulator's

GMO register (our 'general use')

- Currently restricted to activities previously approved through a license, and where the regulator is satisfied the risks are minimal. Australia has proposed removing the prior license requirement.

What the criteria could look like



3. Paper title	Populating non-notifiable and notifiable risk tiers
Meeting date	2/3 October 2024
Approved by	Tony de Jong

The purpose of this session of the workshop is to use your technical expertise to help populate the non-notifiable and notifiable risks tiers for the three categories of the new risk tiering framework:

- Contained activities,
- Clinical trials and medical use, and
- Activities involving intentional environmental release.

(The 'clinical trials and medical use' session will be led by Rachel at 3:30pm, while the 'activities involving intentional environmental release' will be led by Alec and Andy at 4:10pm.)

More than those organisms that would *clearly* fit into a particular risk tier, we are particularly interested in those organisms that are "marginal calls". We think it would be most beneficial for you to:

1. Firstly, allocate/confirm those organisms that clearly fit into particular risk tier, then
2. Discuss those organisms for which the risk tier they should fall into is unclear.

As a starting point, appendices 1 and 2 outline those organisms that are currently listed as non-notifiable and notifiable under Australia's Gene Technology Regulations 2001.

Because not all of those organisms listed under the Australian non-notifiable risk tier are not-new organisms or the listings are set at the genus level, appendix 3 shows those organisms that either have an unknown status (indicated by an orange font) and or those organisms for which only some species in a genus are confirmed as not-new organisms.

In case it is helpful, we have also included excerpts from the University of Auckland's institutional low risk approval, listing those organisms that are included in this approval (appendix 4). As well as those microorganisms, plants and animals that are confirmed to be not-new organisms by the EPA (appendices 5, 6 and 7).

Discussion questions

- Are there organisms that you think should be shifted from:
  - Notifiable to non-notifiable, or vice versa,
  - To a lower or higher Physical Containment level under the notifiable activities risk tier.
- Are there organisms that you think should be added to a particular risk tier from the list of organisms in the institutional low risk approval or the not-new organisms list?
- Are there organisms that you think should be removed from a particular risk tier completely?
- Are there conditions attached to particular organisms that you think should be amended?
- Are there aspects of the institutional low risk approval that are better than the Australian risk tier format (for example, the list of vectors approved for use or the conditions attached to certain activities)?
- Are there conditions or listings that you find confusing that you think could be better worded or that you think need to be clarified?

Non-notifiable activities – Contained activities – Australia's Exempt Dealings:

Item	Organism	Relevant conditions
2	*Caenorhabditis elegans*	(a) an *advantage* is conferred on the animal by the genetic modification; or (b) as a result of the genetic modification, the animal is capable of secreting or producing an infectious agent.
3	Animal into which genetically modified somatic cells have been introduced	(a) the somatic cells are not capable of giving rise to infectious agents as a result of the genetic modification; and (b) the animal is not infected with a virus that is capable of recombining with the genetically modified nucleic acid in the somatic cells.
3A	A dealing with an animal whose somatic cells have been genetically modified *in vivo* by a replication defective viral vector	(a) the in vivo modification occurred as part of a previous dealing; and (b) the replication defective viral vector is no longer in the animal; and (c) no germ line cells have been genetically modified; and (d) the somatic cells cannot give rise to infectious agents as a result of the genetic modification; and (e) the animal is not infected with a virus that can recombine with the genetically modified nucleic acid in the somatic cells of the animal.
4	Host/vector system mentioned in Part 2 of this Schedule and producing no more than 25 litres of GMO culture in each vessel containing the resultant culture	(2) The donor nucleic acid: (a) must meet either of the following requirements: (i) it must not be derived from organisms implicated in, or with a history of causing, disease in otherwise healthy: (A) human beings; or (B) animals; or (C) plants; or (D) fungi; (ii) it must be characterised and the information derived from its characterisation show that it is unlikely to increase the capacity of the host or vector to cause harm; and *Example: Donor nucleic acid would not comply with subparagraph (ii) if its characterisation shows that, in relation to the capacity of the host or vector to cause harm, it:* *(a) provides an advantage; or* *(b) adds a potential host species or mode of transmission; or* *(c) increases its virulence, pathogenicity or transmissibility.* (b) must not code for a toxin with an LD50 of less than 100 micrograms per kilogram; and (c) must not code for a toxin with an LD50 of 100 micrograms per kilogram or more, if the intention is to express the toxin at high levels; and

		(d) must not be uncharacterised nucleic acid from a toxin-producing organism; and (e) if the donor nucleic acid includes a viral sequence—cannot give rise to infectious agents when introduced into any potential host species, without additional non-host genes or gene products that: (i) are not available in the host cell into which the nucleic acid is introduced as part of the dealing; and (ii) will not become available during the dealing; and (f) if the donor nucleic acid includes a viral sequence—cannot restore replication competence to the vector.
5	A dealing involving shot-gun cloning, or the preparation of a cDNA library, in a host/vector system mentioned in items 1 to 6 of the table in Part 2 of this Schedule, if the donor nucleic acid is not derived from either:	(a) a pathogen; or (b) a toxin-producing organism.

Host/vector systems for exempt dealings:

Host/vector systems

(1) A reference to a *host/vector system* is a reference to any of the following:

(a) a system involving a host mentioned in a row of this table and a vector mentioned in the same row;

(b) a non-vector system involving a host in this table;

(c) a system involving a GMO mentioned as a vector in this table (except fungi), without a host.

(2) *code for*, in relation to a toxin, means to specify the amino acid sequence of the toxin.

(3) *non-conjugative plasmid* means a plasmid that is not self-transmissible, and includes, but is not limited to, non-conjugative forms of the following plasmids:

(a) bacterial artificial chromosomes (BACs);

(b) cosmids;

(c) P1 artificial chromosomes (PACs);

(d) yeast artificial chromosomes (YACs).

(4) non-vector system means a system in which donor nucleic acid is or was introduced into a host cell:

(a) in the absence of a nucleic acid-based vector; or

(b) using a nucleic acid-based vector in the course of a previous dealing and the vector is:

i. no longer present; or

ii. present but cannot be remobilised from a host cell.

Item	Host	Vector
1	*Escherichia coli* K12, *E. coli* B, *E. coli* C or *E. coli* Nissle 1917—any derivative that does not contain: • generalised transducing phages; or • genes able to complement the conjugation defect in a non-conjugative plasmid	• Non-conjugative plasmids • Lambda bacteriophage • Lambdoid bacteriophage

		• Fd, F1 or M13 bacteriophage
2	*Bacillus*—asporogenic strains of the following species with a reversion frequency of less than 10^{-7}: • *B. amyloliquefaciens;* • *B. licheniformis;* • *B. pumilus;* • *B. subtilis;* • *B. thuringiensis*	• Non-conjugative plasmids • Other plasmids and phages whose host range does not include *B. cereus*, *B. anthracis* or any other pathogenic strain of *Bacillus*
3	*Pseudomonas putida* strain KT2440	Non-conjugative plasmids
4	The following *Streptomyces* species: • *S. aureofaciens*; • *S. coelicolor*; • *S. cyaneus*; • *S. griseus*; • *S. lividans*; • *S. parvulus*; • *S. rimosus*; • *S. venezuelae*	• Non-conjugative plasmids • Plasmids SCP2, SLP1, SLP2, pIJ101 and derivatives; • Actinophage phi C31 and derivatives
5	Any of the following *Agrobacterium* species: • *Agrobacterium radiobacter* • *Agrobacterium rhizogenes* (disarmed strains only) • *Agrobacterium tumefaciens* (disarmed strains only)	Disarmed Ri or Ti plasmids
6	*Allorhizobium vitis*	Non-conjugative plasmids
6	• *Lactobacillus acidophilus* • *Lactobacillus brevis* • *Lactobacillus buchneri* • *Lactobacillus casei* • *Lactobacillus coryniformis* • *Lactobacillus crispatus*	Non-conjugative plasmids

	• *Lactobacillus crustorum* • *Lactobacillus curvatus* • *Lactobacillus delbrueckii* • *Lactobacillus diolivorans* • *Lactobacillus fermentum* • *Lactobacillus gasseri* • *Lactobacillus harbinensis* • *Lactobacillus helveticus* • *Lactobacillus hilgardii* • *Lactobacillus iners* • *Lactobacillus jensenii* • *Lactobacillus kefiri* • *Lactobacillus kimchi* • *Lactobacillus paracasei* • *Lactobacillus parafarraginis* • *Lactobacillus paralimentarius* • *Lactobacillus perolens* • *Lactobacillus plantarum* • *Lactobacillus pontis* • *Lactobacillus rapi* • *Lactobacillus reuteri* • *Lactobacillus rhamnosus* • *Lactobacillus rossiae* • *Lactobacillus ruminis* • *Lactobacillus sakei* • *Lactobacillus salivarius* • *Lactobacillus sanfranciscensis* • *Lactobacillus zeae*	
6	• *Pediococcus acidilactici* • *Pediococcus parvulus* • *Pediococcus pentosaceus*	Non-conjugative plasmids
6	• *Rhizobium etli* • *Rhizobium leguminosarium* • *Rhizobium meliloti*	Non-conjugative plasmids

	• *Rhizobium phaseoli* • *Rhizobium radiobacter* • *Rhizobium sullae*	
6	• *Synechococcus* species strain PCC 7002 • *Synechococcus* species strain PCC 7942 • *Synechococcus* species strain WH 8102	Non-conjugative plasmids
6	• *Synechocystis* species strain PCC 6803	Non-conjugative plasmids
6	• *Corynebacterium glutamicum*; • *Lactococcus lactis*; • *Oenococcus oeni* syn. *Leuconostoc oeni*; • *Photobacterium angustum*; • *Pseudoalteromonas tunicata*; • *Sphingopyxis alaskensis* syn. *Sphingomonas alaskensis*; • *Streptococcus thermophilus*; • *Vibrio cholerae* CVD103-HgR; • *Zymomonas mobilis*	Non-conjugative plasmids
7	• *Kluyveromyces lactis*; • *Neurospora crassa* (laboratory strains); • *Pichia pastoris*; • *Saccharomyces cerevisiae*; • *Schizosaccharomyces pombe*; • *Trichoderma reesei*; • *Yarrowia lipolytica*	All vectors
8	*Dictyostelium* species	*Dictyostelium* shuttle vectors, including those based on the endogenous plasmids Ddp1 and Ddp2
9	Any of the following if they cannot spontaneously generate a whole animal: • animal or human cell cultures (including packaging cell lines);	• Plasmids • Replication defective viral vectors unable to transduce human cells

	• isolated cells, isolated tissues or isolated organs, whether animal or human; • early non-human mammalian embryos cultured *in vitro* See EPA list of animals present in New Zealand (appendix 7)	• Polyhedrin minus forms of the baculovirus *Autographa californica* nuclear polyhedrosis virus (ACNPV)
10	Either of the following if they are not intended, and are not likely without human intervention, to vegetatively propagate, flower or regenerate into a whole plant: • plant cell cultures • isolated plant tissues or organs See EPA list of plants present in New Zealand (appendix 6)	• Disarmed Ri or Ti plasmids in *Agrobacterium radiobacter*, *Agrobacterium rhizogenes* (disarmed strains only) or *Agrobacterium tumefaciens* (disarmed strains only) • Non-pathogenic viral vectors

MINISTRY OF BUSINESS, INNOVATION & EMPLOYMENT
HĪKINA WHAKATUTUKI

MEETING PAPERS GENE TECHNOLOGY TECHNICAL ADVISORY GROUP 7 NOVEMBER 2024 (excerpt – item 2)

2.Paper title	Summary of TAG workshop
Meeting date	7 November 2024 1pm – 3pm
Approved by	Tony de Jong

Item purpose and summary
To enable the gene tech regime to be in place in late 2025 it is necessary to develop secondary legislation in parallel to the primary legislation (The Gene Technology Bill). Development of some areas of the secondary legislation will require significant technical advice from the Technical Advisory Group (TAG). The purpose of the two-day workshop was to focus on key areas where technical advice is required to support policy development, these areas were: setting out the criteria for non-notifiable, notifiable and pre-assessed activities; and populating the risk tiers. MBIE invited technical expertise in the following areas to supplement the TAG's expertise: animal genetics, human genetics and mātauranga. The list of workshop participants is given in Annex one
Discussion questions
• Are there any key points missing?

Summary: Gene Technology Technical Advisory Group workshop 2/3 October 2024

Out of Scope

Out of Scope

- The workshop participants agreed that criteria for assigning activities to risk tiers needed a risk-based approach combining the likelihood and impact of environmental and/or human health risks. In assessing the environmental and/or human health risk consideration would need to be given to relevant properties of the GMO such as a pathogen or pest, gene flow, impacts on non-target organisms and impacts on biodiversity. Some members of the workshop raised concerns regarding how Taonga species were considered in the risk tiers and that an equivalent to the MAC may be required to advise on this prior to the regulator being established.

- The workshop participants agreed that a good approach to populating the notices was to use lists of non-notifiable and notifiable organisms under Australia's Gene Technology Regulations 2001 AND criteria applied (under Australia's Gene Technology Regulations 2001), and NZ EPA approvals.

- The key requirements in the joint MAF/ERA standards s 9(2)(f)(iv)

Out of Scope

Out of Scope

Out of Scope

1. Non-notifiable and notifiable risk tiers in the contained category

Workshop participants were asked to test the criteria for assigning activities against risk tier (non-notifiable, notifiable general use and pre-assessed activities). The group were asked to consider criteria that:

- would ensure activities are assigned to the right categories (risk-proportionate)
- are predictable and transparent – it should be clear why an activity is in a certain tier
- are unambiguous, and so provide the regulator with confidence to assign things to tiers with lower oversight

The draft criteria are given in Annex two. The workshop participants were asked to consider two potential options:

s 9(2)(f)(iv)

There were differing views between participants on their preferred options. s 9(2)(f)(iv)

[redacted]

[redacted]

[redacted]

Some members of the workshop raised concerns regarding how Taonga species were considered in the risk tiers. The group noted that assigning an activity to a notice would go through the Māori Advisory Committee (MAC), except in the first iteration where MBIE is assigning activities to categories, some members of the group noted that there may need to be a proxy for the MAC to advise on this first iteration prior to the regulator being established.

There was general agreement on the following criteria across all the categories (Contained Activities, Environmental Activities and Medical Activities):

The regulator can/should assign activities to the notified tier if it is satisfied that risks to human health & safety and the environment would be low, considering the:

- impact of any adverse effects on human health & safety and the environment; and
- likelihood of these effects

Participants broadly agreed on the following factors for the regulator to consider when making an assessment, but noted there was some duplication:

In making this assessment, the regulator should consider:

[redacted]

2. Non-notifiable and notifiable activities for 'Contained Activities', 'Environmental Use' and 'Clinical trials and Medical use'

Workshop participants were asked to use their technical expertise to help populate the non-notifiable and notifiable risks tiers for the three categories of the new risk tiering framework:

- Contained activities,
- Clinical trials and medical use, and
- Activities involving intentional environmental release

The workshop participants were given the list of organisms that are currently listed as non-notifiable and notifiable under Australia's Gene Technology Regulations 2001, excerpts from the University of Auckland's institutional low risk approval, listing those organisms that are included in this approval, and those microorganisms, plants and animals that are confirmed to be not-new organisms by the EPA.

The workshop participants discussed that:

- the list of organisms in Australia's Gene Technology Regulations 2001 is limited and a lot of commercial microbial strains are absent.
- volume restrictions (currently 25 litres of GMO culture in each vessel containing the resultant culture) need to be reviewed to enable biomanufacturing s 9(2)(f)(iv) [redacted]
- microbe risk groups need to be incorporated in addition to Australian list to interpret where these things fit.

The workshop participants agreed that a good approach to populating the notices was s 9(2)(f)(iv) [redacted]

3. Updating current containment facility standards

The MAF Biosecurity New Zealand and ERMA New Zealand Standards (2007) need to be updated in order for these standards to be more enabling for the New Zealand research sector.

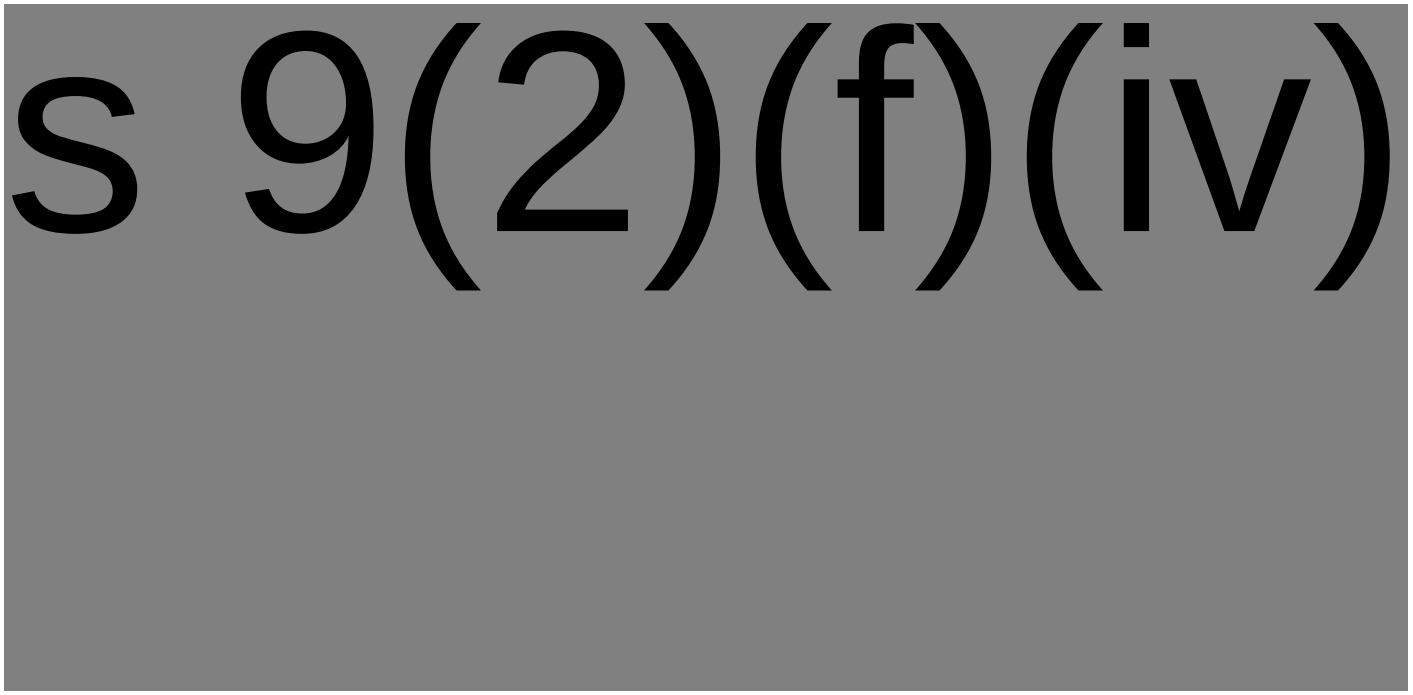
Updating standards commonly takes between 2-3 years (and sometimes longer), which will not align with the current timeline for the gene technology work programme. However, there could be the potential to make minor specific changes to standards through an expedited process.

Workshop participants were asked to identify aspects of the current containment facility standards that they found to be a barrier; they were asked to consider requirements that are:

- minor but are carried out frequently
- significant even though it is only carried out infrequently.
- particularly disproportionate to the risks involved.

The two key requirements that were identified by the TAG workshop participants were:

s 9(2)(f)(iv) [redacted]



Next steps

Following the advice from the TAG workshop participants MBIE undertook further policy work on the category definitions and the criteria for assigning activities against risk tier. These will be tested with the TAG at the next meeting in November, as well as with MBIE legal and the PCO.

The approach to populating the notices s 9(2)(f)(iv) will be discussed with the EPA and further tested with the TAG at the meeting on 5 December.

The next TAG meeting is 7 November, at this meeting MBIE will:

- Test the category definitions and criteria for assigning activities to risk tiers
- Further discuss how Taonga species are considered in the risk tiers and the possibility of establishing a MAC equivalent.
- Discuss planned approach to update containment standards.

Annex One: List of workshop attendees

Workshop Chair: Emily Parker (Ferrier Institute, Department Science Advisor MBIE)

Workshop Attendees:
Tim Hore (Otago)
David Ackerley (Victoria)
Billy Sheppard (Auckland)
Alec Foster (Scion)
Jasna Rakonjac (Massey)
Andy Allan (Plant and Food Research, Auckland)
Nikki Freed (Auckland, Daisy Lab)
Rachel Perret (Malaghan)
Neil Gemmell (Otago)
Richard Scott (AgResearch)
William Rolleston (South Pacific Sera Limited)
Maui Hudson (Waikato)
Alana Alexander (Otago)
Shannon Clarke (AgResearch)
Stephen Robertson (Otago)

Annex Two: Draft definitions and criteria

Out of Scope

Criteria

The workshop participants were asked to consider two potential options:

s 9(2)(f)(iv)

MINISTRY OF BUSINESS, INNOVATION & EMPLOYMENT
HĪKINA WHAKATUTUKI

AGENDA: GENE TECHNOLOGY TECHNICAL ADVISORY GROUP (minutes excerpts – items 2, 4 and 5)

Date and time:	1.00pm – 3.00pm 7 November 2024
Location:	Microsoft Teams
Chair:	Emily Parker (Ferrier Institute, Department Science Advisor MBIE)
Invitees:	Tim Hore (Otago), David Ackerley (Victoria), Billy Sheppard (Auckland), Alec Foster (Scion), Jasna Rakonjac (Massey), Nikki Freed (Auckland, Daisy Lab), Rachel Perret (Malaghan), Neil Gemmell (Otago), Richard Scott (AgResearch), William Rolleston (South Pacific Sera Limited), Maui Hudson (Waikato), Alana Alexander (Otago), Shannon Clarke (AgResearch)
MBIE attendees:	Tony de Jong, s 9(2)(a) [redacted]
Apologies	Andy Allan, Stephen Robertson

Item	Paper
Documents for review – minutes of previous meeting and summary of TAG workshop outcomes No comments or concerns were raised. Members were either happy with the documents or had not reviewed yet and would send comments via email.	Paper 2
Category definitions and criteria <u>Category definitions</u> No significant discussion or concerns. <u>Criteria</u> Members agreed with the overall approach but noted the list of organism properties that the regulator should consider was too plant centric (specifically weediness and plant pest potential) and the terms needed to be broadened to account for animals and microorganisms.	Paper 4
Exemptions – final policy decisions No significant discussion or concerns. One member commented the general exemption power needed to be flexible.	Oral