Australian Government
Department of Health
Office of the Gene Technology Regulator

Updating Gene Technology Regulation in Australia

Regulation Impact Statement for consultation

Contacts

Office of the Gene Technology Regulator
MDP 54
GPO Box 9848
Canberra ACT 2601 Australia

Telephone: 1800 181 030
Fax: (02) 6271 4202
Email: ogtr@health.gov.au
Website: www.ogtr.gov.au

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Executive summary

Significant scientific advances have occurred in the field of gene technology since completion of the last technical review of the Gene Technology Regulations 2001 (the GT Regulations). As a result, some areas of Australia's gene technology legislation are not providing clear and unambiguous requirements for those working with genetically modified organisms (GMOs).

On the whole, the GT Regulations are working well with no major changes to their overall operation proposed at this time. However feedback received from stakeholders as part of the *2016-17 Technical Review of the Gene Technology Regulations 2001* (the Technical Review), as well as operational experience from within the Office of the Gene Technology Regulator (OGTR), have demonstrated a need to address specific technical issues within the legislation.

The objective of the Technical Review is to keep the GT Regulations up to date with advances in technology and increased scientific understanding. The Technical Review is limited to the existing policy settings of the regulatory scheme, and cannot extend to topics outside of the current scope of the GT regulations, for example, the safety assessment and labelling of genetically modified food.

Following consultation on a discussion paper in late 2016, draft amendments to the GT Regulations have been developed and these are the focus of this consultation. Issues raised in submissions have contributed to the development of draft amendment proposals. The Regulator has also taken into account OGTR's experience, current scientific understanding, potential risks, regulatory burden implications for stakeholders, whether regulatory burden would be commensurate with risks, and the policy intent of the GT Act.

This Consultation Regulation Impact Statement (RIS) details the problems the amendments aim to address (section 1), the objectives of the Technical Review (section 2) and options to address the problems (section 3):

- Option 1 – retain the current GT Regulations
- Option 2 – amend the GT Regulations by introducing all elements of the draft amendments at Appendix C
- Option 3 – amend the GT Regulations by introducing some, but not all, of the amendment elements from Option 2.

Comments and submissions that address any or all of the options and the consultation questions in section 5 will assist the OGTR to develop a Decision RIS, including further analysis of the impact of these options.

How to provide feedback

Submissions can be made by email to ogtr@health.gov.au or by mail to the Regulations Review, Office of the Gene Technology Regulator (MDP 54), GPO Box 9848, Canberra ACT 2601. **Submissions must be made by Wednesday 21 February 2018.**

Introduction

This Consultation RIS forms part of a consultation package on draft amendments to the GT Regulations. This consultation is the final stage of an extensive consultation process undertaken by the Regulator as part of the *2016-17 Technical Review of the Gene Technology Regulations 2001*.

All dealings with GMOs must be conducted in accordance with the Commonwealth's *Gene Technology Act 2000* (the GT Act), the GT Regulations and, where applicable, corresponding State/Territory legislation. As such it is necessary to ensure that each piece of legislation remains up to date and fit for purpose.

The 2016-17 Technical Review of the GT Regulations (initiated by the Regulator) aims to provide clarity about whether organisms developed using a range of new technologies are subject to regulation as GMOs and ensure that new technologies are regulated in a manner commensurate with the risks they pose.

Previous Consultations

From 17 October to 16 December 2016, the Regulator sought submissions from all interested and affected parties on a discussion paper detailing four options for how new technologies could be regulated. The Discussion Paper also sought input on a range of other topics related to the effectiveness of the legislative framework for the regulation of GMOs.

Targeted consultations were conducted (face-to-face or by teleconference) with a number of stakeholders to further discuss issues raised in their submissions.

Submissions were considered by the Regulator and have contributed to the development of the draft amendments contained in this Consultation RIS. The Regulator's considerations have also taken into account OGTR's experience, current scientific understanding, potential risks, regulatory burden implications for stakeholders, whether regulatory burden would be commensurate with risks, and the policy intent of the GT Act. Regulatory burden implications will be further considered as part of the current consultation process.

What is a Consultation Regulation Impact Statement

If regulatory change is being considered, the regulatory impact of options for change must be assessed. The Council of Australian Governments (COAG) process for preparing and submitting a RIS comprises two stages. The first stage involves consultation on the costs and benefits of the proposed changes; this is known as the Consultation RIS. The second stage involves preparation of a recommendation report, or Decision RIS, that includes an analysis of comments on the Consultation RIS, as well as evidence on the costs and benefits of the proposed changes. The Decision RIS, along with the finalised amendments to the GT Regulations (if an amendment option is progressed) will be submitted to the Legislative and Governance Forum on Gene Technology (LGFGT) to support their consideration of whether or not to agree to the amendment proposals.

This Consultation RIS has been prepared to provide a preliminary examination of the cost and benefits of various options for amending the GT Regulations to provide clarity about whether organisms developed using a range of new technologies are

subject to regulation as GMOs. This RIS has been prepared in accordance with COAG best practice regulation requirements, and includes the following sections:

- a statement of the problem (section 1)
- a statement of the objectives and intended outcomes (section 2)
- a statement of the possible options to address the problem (section 3)
- a preliminary impact analysis of the options (section 4) and
- details of the consultation undertaken (section 5).

The OGTR is seeking information from stakeholders on a range of issues in relation to options set out in this RIS which will be used to prepare a Decision RIS that will be presented to decision makers (the LGFGT) and also made publicly available.

Current Gene Technology Regulations 2001

Australia's national regulatory scheme for gene technology is comprised of the Commonwealth GT Act and GT Regulations, and corresponding State and Territory laws. The Commonwealth GT legislation took effect on 21 June 2001.

Amendments to the GT Regulations have occurred through two technical reviews (amendments commencing 31 March 2007 and 1 September 2011), the 2005-6 statutory review of the GT Act (commencing 1 July 2007) and several other consequential amendments.

Many of the previous amendments have related to technical and operational matters that have enhanced the effectiveness of the GT scheme and assisted user compliance by making the Regulations clearer and easier to understand.

Proposed amendments

The draft amendments to the GT Regulations have been prepared on the basis of submissions received from stakeholders and learnings from within the OGTR.

The draft amendments at **Appendix C** are discussed in detail within sections 3 (options) and 4 (impact analysis) of this document. The key draft amendments under consideration cover the following topic areas:

- amendments in response to technological developments (implementing Option 3 from the October 2016 Discussion Paper and clarifying the regulatory status of some RNA interference techniques) – refer sections 1.1, 3 and 4
- amendments to keep the classification of contained dealings with GMOs up to date – refer sections 1.2, 3 and 4, and
- amendments that clarify, but do not change, the regulatory status of certain organisms – refer sections 1.3, 3 and 4.

A future law compilation of the draft amendments is available on the OGTR website, to aid understanding of the effect of the proposed amendments.

1. Statement of the problem

Since the last technical review of the GT Regulations, a number of issues have been identified which show that Australia's current gene technology legislation is not as effective as it could be in terms of providing clear and unambiguous regulatory requirements for those working with GMOs.

The issues identified include the following:

- **ambiguity in the GT Regulations due to technological developments** – new technologies for modifying genetic sequence and gene expression have developed rapidly and so in some cases it is not clear whether organisms modified by certain techniques are 'GMOs' or not.
- **the need to keep the categorisation of contained dealings with GMOs up to date** – the techniques and organisms used in gene technology research have changed since the GT Regulations were last reviewed, as has understanding of risk.
- **the need for improved clarity** regarding the regulatory status of organisms that are not themselves categorised as GMOs but have been derived from GMOs. There is no problem with the current regulatory status of these organisms; rather, improved clarity would assist user understanding and compliance.

Should the option to amend the GT Regulations be pursued, minor administrative amendments will also be introduced in addition to the issues indicated above. These administrative matters are summarised at **Appendix A** and included in the draft amendments at **Appendix C**.

In identifying these issues, OGTR recognises that the GT Regulations are fit for purpose, and appropriately support the object of the regulatory scheme (see section 2). The Technical Review is focusing on technical aspects of the regulatory scheme, within the current policy framework. Any other issues may be raised through other processes, such as the ongoing 2017 Review of the National Gene Technology Scheme.

1.1 Ambiguities in the GT Regulations due to technological developments – what is a GMO

Currently **ambiguities exist in the GT Regulations** because new technologies for altering genetic sequence and gene expression are not specifically addressed in the legislation. Under existing provisions, it is not clear whether (or not) organisms that have undergone several specific techniques are within, or excluded from, the scope of regulation under the GT Act:

- site-directed nuclease (SDN) techniques with or without a template to guide small changes (SDN-2 and SDN-1, respectively)
- oligo-directed mutagenesis (ODM) and
- some RNA interference (RNAi) techniques.

Additional information on SDN techniques, ODM and RNAi is provided at **Appendix E**.

Why is it a problem?

Australia's gene technology legislation does not in explicit terms address site-directed nuclease techniques, ODM or RNAi techniques. It has become apparent through interactions with regulated stakeholders that it is not clear whether organisms produced using some of these new techniques meet the definition of 'GMO' in the GT Act.

Item 1 of Schedule 1 (exclusions from the definition of 'GMO') has been a primary source of ambiguity in this area. The Schedule was established before many of the new technologies existed, and contains many undefined terms. In the absence of a clear meaning for this item, stakeholders may have interpreted it in a variety of ways, including in relation to the new technologies described above.

If organisms are GMOs, activities with them (defined as "dealings") require authorisation under the GT Act. Dealing with a GMO without appropriate authorisation is prohibited under the GT Act.

Ambiguity in the GT Regulations in these areas is therefore a problem because organisations or individuals undertaking work in this area are not able to confidently determine the regulatory requirements to which they must comply when using these new technologies.

What are the risks?

If regulatory requirements continue to be set against a baseline of legislative provisions that do not account for these technologies, there is a risk that the level of regulation may not be commensurate with risk. This could result in under-regulation, which could result in inappropriate management of risks to human health and safety and the environment, or over-regulation, which could inhibit research using these technologies.

Ambiguity in this area raises the risk that organisations or individuals will not seek the necessary approvals, mistakenly believing that such approvals are not required. If organisations or individuals undertake work with new technologies without appropriate approvals, they may be liable for breaching the GT Act and associated penalties may apply. In this scenario, necessary risk management measures may not be in place compromising the health and safety of people and the environment.

There is also a risk that ambiguity will inhibit use of the technologies, as organisations may delay their work because they are unsure about the regulatory requirements, or may not proceed with work because they mistakenly believe that there are prohibitive regulatory burdens. Possible consequences of this are that the progress of basic research may be held back, and that products (such as food crops or human or animal therapeutics) may not be commercialised. Alternatively there may be delays in bringing new products to market, meaning that the benefits from these products may not be made available in Australia. In the longer term, if uptake of these technologies continues to be inhibited this could hamper industry development and affect the international competitiveness of Australian businesses. It is also possible that the Regulator would be unable to successfully prosecute an intentional breach of the GT Act due to lack of legal clarity. The required legal arguments may be difficult to make given the absence of explicit references to the above described new technologies in the GT Regulations.

1.2 Keeping the categorisation of contained dealings with GMOs up to date

Dealings with GMOs that do not involve intentional release to the environment are categorised in the GT Regulations on the basis of risk:

- Exempt dealings, which have been assessed as posing negligible risks, and do not require approval from or notification to the Regulator
- Notifiable low risk dealings (NLRDs), which have been assessed as posing low risk provided that conditions are met, and must be assessed by an Institutional Biosafety Committee (IBC) and notified to the Regulator annually
- Dealings Not involving Intentional Release (DNIRs) to the environment, which must undergo case-by-case assessment by the Regulator and be carried out in accordance with tailored licence conditions.

Updating categorisations to ensure they are commensurate with risk has been a major focus of previous technical reviews of the GT Regulations, and there is again a need to update several aspects of categorisation of contained dealings.

Why is it a problem?

The need to update contained dealings classifications has come about because of ongoing scientific developments and improved understanding of risk, specifically:

- newly available technologies, for example use of CRISPR/Cas9 to make gene drive GMOs, have not been considered before
- new parent species are being used in gene technology research, and their categorisation has not been considered before
- with some categorisations becoming well established, GMO dealings posing equivalent risk should be considered for equivalent classification and
- over time, aspects of current classifications that initially were not clear enough have become apparent, e.g. dealings with viral vectors with no host.

What are the risks?

As use of technology changes or the organisms used in research change over time, the classification of contained dealings with these GMOs continues to be set by existing provisions, which were not written with the new applications in mind. As a result, classifications may set a greater level of oversight than is warranted on a risk basis, or may set an insufficient level of oversight than is required.

If contained dealings with GMOs are subject to excessive regulatory requirements, there is a risk that this part of the gene technology regulatory scheme could be seen by researchers as unnecessarily burdensome and may result in potentially valuable work with these organisms not being undertaken because of the regulatory requirements associated with them.

If contained dealings with GMOs are classified at a lower level than is appropriate for the risks they may pose, inadequate risk management measures may be applied.

This could possibly lead to harms to human health and safety and the environment, and being realised.

1.3 Clarifying the regulatory status of organisms derived from GMOs

OGTR stakeholders have sought clarity about the regulatory status of organisms derived from GMOs, but which have not inherited traits that occurred because of gene technology (also known as 'null segregants'), and organisms that previously were temporarily modified by gene technology but the modification (and any resulting traits) are no longer present in the organism. This demonstrates that the legislation does not provide enough clarity about these organisms.

Why is it a problem?

The current regulatory status of these organisms is commensurate with risk, and there is no proposal to make any changes to that status. However, it has become apparent from interactions with stakeholders that there are different understandings of the language used in the GT legislation to describe the regulatory status of these organisms.

What are the risks?

Some organisations or individuals are not able to determine the regulatory requirements to which they must comply when working with these organisms. Risks associated with this perceived lack of clarity are similar to those described in section 1.1, in particular, work in this area may be inhibited by uncertainty around regulatory requirements.

Can the GT Regulations address these problems?

The problems described in sections 1.1-1.3 may be addressed through amendments to the GT Regulations. For the problems described in section 1.2, the GT Regulations set the current regulatory requirements and changes to these requirements are the only effective means to address the problems.

For the problems described in sections 1.1 and 1.3, regulatory status could be clarified through amendments to the Regulations or through changes to the GT Act. However, only changes to the GT Regulations that are within current policy settings are possible through the Regulator's Technical Review.

There is no other existing regulation that addresses the regulatory status of and regulatory requirements for the above described organisms and dealings.

2. Objectives - the need for government action

The object of the GT Act is to

> "protect the health and safety of people, and to protect the environment, by identifying risks posed by or as a result of gene technology, and by managing those risks through regulating certain dealings with GMOs."

Australia's gene technology regulatory scheme was set up in 2000 in response to a growing community view that GMOs posed risks which should be managed through regulation of particular activities with GMOs. While the object of the scheme is to protect human health and safety and the environment, the framework to achieve this also provides a clear regulatory pathway from research to market for GMOs[1].

The gene technology scheme was designed to fill the gaps between regulatory schemes for human food, human therapeutics, veterinary medicines, agricultural chemicals and industrial chemicals. The scheme focuses on live and viable GMOs and managing any risks they pose as a result of gene technology.

Advances in technology

The objective of this consultation process is to keep the GT Regulations up to date with advances in technology and increased scientific understanding. This includes providing clarity about whether organisms developed using a range of new technologies are subject to regulation as GMOs and ensuring that gene technology is regulated in a manner commensurate with the risks posed.

The outcomes of this consultation process cannot alter the policy settings of Australia's gene technology regulatory scheme, meaning that no changes to the GT Regulations will be recommended if organisms or techniques already receive clear treatment in the legislation, and if the scientific understanding of the risks they pose has not changed.

Likewise, no changes will be recommended that relate to topics outside of the current scope of the GT regulations. For example, any issues raised through the consultation process which relate to the regulation of genetically modified food, marketing and trade issues, or the application of new technologies to humans or embryos cannot be considered further through this process.

[1] Paragraph 4(a) of the GT Act provides that the regulatory framework will provide "an efficient and effective system for the application of gene technologies".

3. Policy options under consideration

In order to address the described problems (section 1) and achieve the stated objective (section 2), this Consultation RIS considers three options:

- Option 1 – retain the current GT Regulations
- Option 2 – amend the GT Regulations by introducing all elements of the draft amendments at **Appendix C** and
- Option 3 - amend the GT Regulations by introducing some, but not all, of the amendment elements from Option 2.

Option one: retain the current GT Regulations

This option proposes there be no changes made to the GT Regulations.

Option two: amend the GT Regulations as proposed

This option proposes to amend the GT Regulations as per the draft amendments at **Appendix C**.

The draft amendments would address each of the 'problems' outlined in section 1. The key elements of the draft amendments are:

- Implementing option 3 from the Discussion Paper under which organisms modified using site-directed nucleases without templates to guide genome repair (i.e. SDN-1) would not be regulated as GMOs. Organisms modified using SDN-2 and ODM would continue to be regulated as GMOs.
- Listing the application of RNA molecules to induce RNAi as a technique that is not gene technology provided several requirements are met. RNAi techniques which involve inserting sequences into the genome or use of viral vectors would continue to result in GMOs which are subject to regulation.
- Requiring a licence for all contained dealings with gene drive GMOs.

These and additional amendments are detailed below, with further minor administrative amendments listed at **Appendix A**. **Appendix B** cross-references all proposals to items in the draft amendments at **Appendix C**.

New Technologies - SDN-1, SDN-2, ODM

Organisms modified using SDN-1 would be excluded from regulation, as organisms that are not GMOs, on the basis of risk, compliance enforceability and consideration of the policy settings of the regulatory scheme, as discussed below. If a template is used to guide genome repair (i.e. SDN-2) the resulting organisms are currently considered GMOs, as are organisms modified using ODM, and these would continue to be regulated.

In nature, DNA breaks in the genome of an organism can be caused by a range of natural factors, and cells have evolved mechanisms to scan DNA for breaks and to repair them. The same repair mechanisms are employed, regardless of the cause of the DNA break. In most cases, cells repair the DNA without any sequence changes or with small deletions only; occasionally, other sequence changes are the result.

These DNA changes give rise to the genetic variability which is the foundation for biological evolution, for example preventing expression of a protein, and altering or deleting a small part of a protein. Most commonly, these types of sequence changes reduce the fitness of the organism. Natural mutations are not regulated as gene technology.

SDN-1 involves using a site-directed nuclease to cause a DNA break at a chosen DNA sequence which is then repaired using the cell's natural mechanisms. The DNA repair is no more directed than the repair of DNA breaks occurring through other causes, resulting in the same range of possible DNA changes and the same range of possible changes to the characteristics of the organism.

Site-directed nucleases are known to cause DNA breaks at sequences that do not perfectly match their intended target sequences, known as off-target effects. While there is a much current research into improving the specificity of site-directed nucleases, and many published examples of highly specific applications, there are also publications demonstrating the prevalence of off-target effects in various experimental scenarios. Importantly, the repair of off-target DNA breaks leads to the same range of DNA changes as are possible through repair of naturally occurring DNA breaks.

Because the changes brought about through SDN-1, including off-target effects, are no different to natural mutations, they do not give rise to any different risks to natural mutations. At the commencement of the gene technology regulatory scheme, the list of 'organisms that are not GMOs' in Schedule 1 of the GT Regulations was intended to exclude techniques on the basis that they "give rise to organisms that can occur in nature and as such do not pose a particular biosafety risk to the environment or human health and safety."[2] Excluding organisms modified using SDN-1 from regulation is consistent with this intention, and appropriate on the basis that these organisms do not pose different risks to natural mutants.

Sequence changes brought about by SDN-1 are detectable with prior knowledge. However, sequencing to detect those changes cannot empirically determine the method by which they were produced, and cannot distinguish SDN-1 outcomes from natural mutations. The problem of detectability undermining compliance enforcement was considered when the scheme was originally put in place, when it was concluded that "… it would be impossible for government to effectively regulate some of the organisms [listed in Schedule 1], as these changes to their genetic make-up can occur in nature (i.e. without human intervention)."[3] All GMOs currently licenced for commercial release in Australia can be unambiguously identified by their introduced DNA sequence. This would not be possible for organisms modified using SDN-1.

Excluding organisms modified by SDN-1 from regulation would be consistent with GMOs being defined on the basis of having been modified by the process of gene technology (also known as a process regulatory trigger). The use of a template to direct sequence changes is a hallmark of the techniques generally considered to be gene technology since inception of the regulatory scheme. Organisms modified

[2] GT Regulations Regulation Impact Statement Section 4 part (a), discussion of listing a limited class of organisms as not being GMOs, published as part of the 2001 Explanatory Statement.

[3] GT Regulations Regulation Impact Statement Section 4 part (a), discussion of having no list of organisms that are not GMOs, published as part of the 2001 Explanatory Statement.

using SDN-2 and SDN-3, which use templates to guide sequence changes, would continue to be regulated as GMOs.

The draft amendments propose to list organisms modified using SDN-1 as organisms that are not GMOs. While listing SDN-1 as a technique that is not gene technology was considered, this approach was discarded because it would also exclude from regulation any intermediate GMOs produced in the course of SDN-1, for example organisms stably expressing a site-directed nuclease.

Item 1 Schedule 1

Repealing item 1 of Schedule 1 would improve clarity in the GT Regulations, particularly in relation to organisms modified using SDN-1, SDN-2 and ODM. The vast majority of organisms excluded from regulation under this item at the commencement of the regulatory scheme were organisms modified using mutagenesis techniques. The status of mutagenised organisms as not being GMOs was confirmed by amendments in 2006 listing chemical and radiation-induced mutagenesis as techniques that are not gene technology in Schedule 1A. As a result, the status of these organisms as not being GMOs would not change if item 1 of Schedule 1 was repealed.

OGTR is aware of two additional organisms currently excluded from regulation through item 1, NoGall and VaxSafe PM. To maintain their status, they would be specifically listed in replacement items on Schedule 1. The repeal of item 1 would commence operation 12 months later than all other amendments, to allow time for those working with any remaining organisms covered solely by item 1 to apply for the necessary GMO dealing authorisations before item 1 is repealed.

RNAi

RNAi techniques involving directly applying RNAs to temporarily induce RNAi, (referred to below as RNA-delivered RNAi), would be listed as techniques that are not gene technology. This would result in organisms modified using these techniques not being GMOs.

RNA-delivered RNAi involves gene-specific RNAs being introduced to an organism to reduce protein expression from the targeted gene until the introduced RNAs are degraded. This occurs through mechanisms that degrade the targeted RNA transcript, inhibit translation of the targeted RNA transcript into protein, and/or repress transcription by methylating the targeted genomic DNA. No new proteins are made through such processes.

The effects of genomic DNA methylation can persist for variable periods after the introduced RNAs are degraded, prolonging the effect on the target gene. The introduced RNAs may also reduce expression of genes with similar sequences to the target gene. However, both of these effects are within the range of effects possible through natural mutations, which can also reduce gene expression or inactivate genes. Excluding RNA-delivered RNAi techniques from regulation is consistent with the original intent of exclusions to regulation from 2001, some of which were listed on the basis that they “give rise to organisms that can occur in nature and as such

do not pose a particular biosafety risk to the environment or human health and safety."[4]

To ensure that only short-lived RNAi techniques are excluded, this measure would require that the organism's genomic DNA sequence cannot be changed by the technique. This relates only to nucleotide sequence changes, and not to genomic DNA methylation. RNAi techniques resulting in heritable changes in the organism's DNA sequence, such as vector-mediated RNA delivery or stable integration of hairpin transgenes, would continue to be regulated as gene technology.

To ensure that the range of excluded techniques cannot confer novel protein functions, which warrant regulatory oversight, the measure would also require that the introduced RNA cannot be translated into a protein. Finally, the measure would not apply if production of infectious agents is possible. Only RNAi techniques are the intended scope of this exclusion, not techniques involving infectious non-coding RNAs such as viroids.

This measure is intended to apply across any method to introduce RNA, including soaking or spraying plant parts with RNA solutions, exposing cultured cells to RNA solutions, or injecting RNA into animal tissues. RNA would be considered introduced into the organism it is directly applied to, and any organisms subsequently receiving it, for example insects feeding on plant parts to which RNA has been applied. Provided the other requirements are met, the forms of RNA within the scope of this measure include short interfering RNAs, short hairpin RNAs, double stranded RNAs, and artificial microRNAs, whether or not they match an endogenous sequence.

This amendment would not impact upon or change the requirements of product regulators such as the Australian Pesticides and Veterinary Medicines Authority or the Therapeutic Goods Administration in relation to these techniques.

Gene drives

Given the early stage of gene drive research in Australia and internationally, the Regulator will keep a watching brief on work with organisms containing GM gene drives. Increasing the level of oversight for contained dealings with GM gene drive organisms would enable the Regulator to ensure appropriate risk management requirements are in place, and would permit information gathering as well as monitoring the progress of research in this rapidly developing field.

Further information about gene drives is at **Appendix E**. There are three components to a functioning gene drive using CRISPR technology: the drive, the payload and the target sequence. All three need to be present in the GMO in order for the gene drive to function. Non-functional gene drives do not continue to be preferentially inherited, therefore the proposed amendment is focused only on functional gene drive GMOs.

Dealings with GMOs containing functional gene drives would require a DNIR licence, which would ensure case-by-case evaluation of risks and tailored risk management of activities with these organisms.

[4] GT Regulations Regulation Impact Statement Section 4 part (a), discussion of listing a limited class of organisms as not being GMOs, published as part of the 2001 Explanatory Statement.

This interim measure would allow the Regulator to collect more information on the development of this technology and the risks involved in dealings with gene drive GMOs. It would be appropriate to re-assess this position at the next Regulations review on the basis of any accumulated experience and scientific developments at that time.

Organisms derived from GMOs that are not themselves GMOs

The definition of 'GMO' in the GT Act does not include organisms derived from GMOs that have not inherited traits that occurred because of gene technology, also known as null segregants. Queries to OGTR suggest this status is not readily apparent to all, so null segregants would be listed as organisms that are not GMOs, for the avoidance of doubt. For the same reasons, organisms temporarily modified using gene technology that no longer have traits that occurred because of gene technology would also be listed as organisms that are not GMOs.

These listings would provide additional clarity that neither of these groups of organisms are within the intended scope of regulation. Neither group poses risks as a result of gene technology because they do not possess traits as a result of gene technology. In this context a trait includes a modified sequence or an outcome that occurred because of genetic modification (for example, expression of a novel protein), and includes both intended modifications and unintended modifications (for example, secondary insertions).

Cloned viral genomes

Dealings with cloned viral sequences, when at least one gene essential for viral multiplication is missing, are classified as exempt because they are unable to result in the production of virions or infectious agents. However, some cloned full length viral genomes are also unable to produce virions or infectious agents unless additional non-host genes or gene products are provided. Dealings with these full length clones pose directly equivalent risks and so the amendments would classify these as exempt, provided the required non-host genes or gene products are not available during the dealing. In both cases, risks associated with any potential for production of replication competent virus are avoided.

No change is proposed for cloned viral genomes which are able to give rise to infectious agents when introduced into a host cell. These cloned viral genomes, commonly referred to as infectious clones, will continue to be regulated as if they were the virus itself.

Viral Vectors with no host

The current lack of clarity about the classification of dealings with virions with no host would be resolved by amendments to classify these dealings at the same level as dealings involving the introduction of these vectors into listed exempt hosts. Where viral vectors are themselves GMOs, dealings with these vectors without a host would be listed as exempt dealings, provided other existing requirements for exempt classification are met. This would be limited to virions of replication defective viral vectors unable to transduce human cells, specified GM baculovirus genomes or virions, and specified GM bacteriophage genomes or virions.

These amendments are not intended to change the classification of any dealings, instead they are intended to aid IBCs in their decision-making by improving clarity.

New exempt hosts

OGTR has received requests to list several hosts as suitable for exempt dealings, which have not previously been considered for listing. Risk assessments support two host species being added to the list of host/vector systems for exempt dealings as both species have no history of causing harm to people, animals, plants, fungi, or the environment: *Zymomonas mobilis* and *Corynebacterium glutamicum.*

Clarifying wording around characteristics of modifications

The categorisation of some dealings in Schedule 3 depends upon the characteristics of products encoded by inserted genes. However, the same phenotypic outcome can be produced by other modifications which don't involve the introduction of full gene sequences. Therefore, some of the wording around pathogenic determinants and introduced DNA would be changed to shift the focus of the assessment towards the outcome of the modification (e.g. immunomodulatory effects, ability to cause harm) rather than the characteristics of the introduced sequences. This would ensure the appropriate classification of dealings involving modifications other than the introduction of DNA, such as deletions, small changes in nucleotide sequence and the introduction of sequences that induce RNAi. This would avoid dealings being classified at a lower level than is appropriate for the risks they may pose.

Option three: amend the GT Regulations with some but not all draft amendment proposals

This option proposes to amend the GT Regulations by introducing some but not all of the draft amendments, in line with stakeholder feedback (at **Appendix C**). Feedback is sought on which elements of the draft amendments stakeholders would support being introduced, and which elements stakeholders consider should not proceed.

As a broader consultation process has already been undertaken, feedback should be limited to the matters covered by the proposed amendments. Any feedback received on broader matters will need to be fully justified on a risk basis, with potential impacts fully explored, or would need to be based on new evidence.

Other options considered but not further developed

Discussion Paper options 2 and 4

Two further options were considered as part of the Discussion Paper and subsequent public consultation process. These options have not been further developed as viable options for this Consultation RIS for the reasons described below.

Option 2 from the Discussion Paper was to regulate dealings with all organisms developed using ODM, SDN-1 and SDN-2. However, as discussed above, organisms modified using SDN-1 do not warrant regulation for several reasons:

- they pose directly equivalent risks to organisms with natural mutations, and so regulating these organisms would not be commensurate with the risks they pose and
- reliably detecting organisms that might be indistinguishable from naturally occurring mutants or the products of techniques that are not gene technology presents a great challenge for enforcing compliance with the scheme.

Option 4 from the Discussion Paper was to amend the GT Regulations to exclude organisms produced by ODM, SDN-1 and SDN-2 from regulation. OGTR considers it appropriate to continue regulating organisms modified using SDN-2 and ODM for several reasons:

- Under the current policy framework, regulatory exclusions apply equally to all plants, animals and microbes modified by particular techniques. However, excluding all organisms modified using SDN-2 and ODM from regulation may not be commensurate with risk, particularly with pests or disease-causing organisms.
- Successive rounds of modification using SDN-2 or ODM could result in substantial changes which may pose risks warranting regulatory oversight.
- Many submitters supporting option 4, proposed it be implemented as an exclusion for outcomes equivalent to the sequence modifications possible through unregulated techniques. However, this would require broader consideration in the context of the policy settings of the scheme, and the regulatory status of established gene technology techniques. This broader consideration is not possible through a technical review of the GT Regulations.

On the basis of the reasons above, options 2 and 4 were not further developed.

Other proposals not progressed

A number of additional proposals to amend the GT Regulations were received in response to the Discussion Paper. Upon consideration by the OGTR, some were not supported for further development. These proposals are summarised at **Appendix D**.

4. Preliminary impact analysis

Australia's gene technology regulatory scheme has been operating for over 16 years with the requirements of the scheme well established, and a very high level of compliance demonstrated by individuals and organisations working with GMOs. The scale of the gene technology regulatory scheme is modest in comparison to other Australian regulatory regimes. There are a limited number of regulated stakeholders, with 171 accredited organisations and 26 other organisations as at November 2017. Additionally, over 97% of authorisations for dealings with GMOs over the last five years have been for NLRDs, a category imposing minimal regulatory burden.

The options outlined in this document do not propose to change the policy settings of the regulatory scheme or change the requirements for authorisation categories. Rather, the primary aim of the options to amend the GT Regulations is to improve clarity and bring the GT Regulations up to date with scientific developments.

A preliminary analysis of the costs and benefits for stakeholders of each of the options is provided below. Feedback received through this consultation process will be used to support further analysis of impacts as part of the Decision RIS.

Impact analysis of Option 1 – retain the current GT Regulations

Under Option 1, the GT Regulations will be retained in their current form, with ambiguities in the legislation and out-of-date provisions remaining.

The likely impact of retaining the GT Regulations in their current form is that risks related to these ambiguities (as described in the 'What are the risks' subheadings in section 1) will continue. This includes:

- Continuing uncertainty regarding the regulatory requirements for activities with certain organisms, which may impact on research progress and investment, as well as impact the ability of organisations or individuals to comply with legal requirements. This could slow industry development and reduce international competitiveness.
- Regulatory classifications that are not up to date can impose over-regulation (impacting stakeholders by imposing unnecessary regulatory burdens, which can lead to reduced investment and research and development outcomes), or under-regulation (potentially leading to unmanaged risks to human health and safety and the environment).

Impact analysis of Option 2 – amend the GT Regulations as proposed

Under Option 2, the GT Regulations would be amended as per the draft amendments at **Appendix C** (subject to alterations made to take into account feedback received through this consultation process). Minor administrative amendments (outlined at **Appendix A**) are not discussed below as these are not anticipated to result in operational changes.

The impacts described below are primarily on organisations and individuals working directly with the described technologies, and by association (but to a lesser extent)

the industry bodies that represent them. It is not expected that the proposed amendments will have any direct impact on members of the public or community groups, beyond an increased level of confidence that work with these organisms is being conducted in a manner that protects human health and safety and the environment. Specifically, the proposed changes will not have any impact on the pre-market safety assessment and labelling of foods derived from GMOs (this being the purview of Food Standards Australia New Zealand).

Potential impacts of the draft amendments are discussed below in relation to the three key issues identified in section 1.

Amendments to address ambiguities in the GT Regulations due to technological developments

As outlined in section 3, the draft amendments include provisions to:

- clarify that organisms modified using SDN-2 and ODM are GMOs
- list organisms modified using SDN-1 as organisms that are not GMOs
- list RNA-delivered RNAi techniques as not being gene technology and
- replace item 1 of Schedule 1.

These amendments potentially impact several stakeholder groups.

Researchers

Potential impacts from these changes include that the GT Regulations will become more efficient in that they will enable organisations and individuals undertaking research using these technologies to confidently determine the regulatory requirements that they must comply with, saving them time (and therefore money).

Submissions from research organisations to the Discussion Paper strongly supported clarifying the legislation, and anticipated they would benefit from improved clarity because they would spend less time determining regulatory requirements. With greater clarity, research may proceed more freely because researchers are no longer unsure about regulatory requirements. Additionally, the amendments would remove the risk that some activities would mistakenly be undertaken without required approvals, protecting organisations or individuals from being liable for breaching the GT Act.

These amendments would remove regulatory oversight of some research work involving new technologies. OGTR considers that the proposed amendments would provide a minor decrease in regulatory burden for the research sector, through a small decrease in the number of activities requiring authorisation as NLRDs, noting that few NLRDs would solely involve organisms to be excluded from regulation. OGTR has received no licence applications (DNIR or DIR) for relevant work, and OGTR anticipates there would be no substantial change to the number of organisations retaining accreditation or maintaining facility certifications.

Industry/product developers

Broader impacts of the proposed changes may include increased innovation and increased commercialisation of products (such as food crops or human or animal

therapeutics), because of reduced regulatory costs and anticipated increased consumer acceptance of product that are not GMOs. Submissions to the Discussion Paper indicated that companies are currently delaying investment in this area because of uncertainty about the regulatory status of potential products. By removing this barrier through removing ambiguities in the GT Regulations, the benefits from innovative new products may reach the Australian market. However, submissions indicated that regulating organisms modified using SDN-2 would dampen uptake of this technique (noting this is not a change from the status quo), on the basis of regulatory costs and anticipated market acceptance of the resulting GMOs.

There are no current general release approvals for organisms developed using these techniques, so no immediate changes in direct regulatory burden are anticipated for industry stakeholders. Submissions to OGTR suggested a variety of trade implications could arise, but many of these are dependent on the position Australia's trading partners take on these technologies, which is yet to become clear for most jurisdictions. Should non-alignment of regulatory treatment arise, industry would have access to market and other mechanisms to resolve such issues, as occurs for other commodities.

Members of the public

It is not expected that there will be any direct impact from the proposed amendments relating to new technologies on members of the Australian public. Through submissions on the Discussion Paper, individuals and community groups have expressed concern about the implications of this review for food labelling (i.e. their ability to choose to avoid GM foods) and the safety of GM foods, however the proposed changes will not alter the regulation of GM food in Australia, including how such foods are labelled. These matters are outside of the scope of the GT Regulations.

Amendments to update the categorisation of contained dealings with GMOs

As outlined in section 3, the proposed amendments include provisions to adjust the level of regulation of some contained dealings with GMOs to be more commensurate with risk:

- increase the categorisation of contained dealings with gene drive GMOs from NLRDs to DNIRs
- increase the categorisation of contained dealings with GMOs that have pathogenic or oncogenic effects (other than through expression of a protein with these properties), some from exempt to NLRD and others from NLRD to DNIR
- decrease the categorisation of some contained dealings with *Zymomonas mobilis* and *Corynebacterium glutamicum* from NLRD to exempt
- decrease the categorisation of some contained dealings involving cloned viral genomes from NLRD to exempt and
- clarify the categorisation of dealings involving viral vectors with no host.

The impact of these proposals is anticipated to be minor, as only some research organisations undertake contained dealings with the relevant GMOs. These organisations would experience variable increases and decreases in regulatory burden, depending upon the work they undertake. OGTR anticipates the amendments may improve research organisation's confidence that regulatory burden from the gene technology regulatory scheme is commensurate with risk.

Requiring case-by-case evaluation of risks and tailored risk management for activities with GM gene drive organisms may increase confidence for the Australian population that risks posed by these organisms are being appropriately managed. For organisations and individuals working with GM gene drives, the additional requirement to submit a DNIR application would increase regulatory burden for a very small number of organisations. While there are no application fees to submit a DNIR application, additional information is required by the Regulator, compared to what is required for NLRDs. The OGTR is aware of one NLRD project involving functional gene drive GMOs that would require a DNIR licence as a result of the proposed amendments.

Amendments to clarify the regulatory status of organisms derived from GMOs

The proposed amendments would not alter the regulatory status of the relevant organisms, as described in section 3, and as a result it is not anticipated that there will be any change to the regulatory burden on individuals and organisations working with these organisms.

Potential impacts from these changes include that the GT Regulations will become more efficient in that they will enable organisations and individuals working with these organisms to confidently determine the regulatory requirements that they must comply with.

Feedback sought to support impact analysis

Feedback is sought as part of this consultation process to support further analysis of the potential impacts of the proposed amendments. OGTR is seeking confirmation of whether the impacts described above are appropriately characterised, and whether further impacts should be considered. OGTR is also seeking to quantify how regulatory burden would change as a result of these proposals, specifically:

- the number of NLRD, DNIR and DIR authorisations that would change (and in what way)
- how the need to maintain facility certifications would change and
- how the amount of time needed to administer authorisations would change.

The impacts described above assume that the amendments will have their intended effect of removing ambiguities from the GT Regulations. If this effect is not realised, these positive impacts will not be seen. Feedback is therefore sought on whether the language of the proposed amendments (at **Appendix C**) will achieve their intended purpose (as described in section 3).

Impact analysis of Option 3 – amend the GT Regulations with some but not all draft amendment proposals

This option would see some, but not all, of the draft amendments at **Appendix C** being introduced. It is expected that stakeholders will identify elements of the proposed amendments that they support, elements that may need to be varied to achieve the required outcome of providing legal clarity, and elements they do not support. As a result, potential impacts of this option would be intermediate between Option 1 and Option 2, with no additional impacts expected.

5. Consultation

This Consultation RIS forms part of a consultation package on draft amendments to the GT Regulations. This consultation is the final stage of an extensive consultation process undertaken by the Regulator as part of the *2016-17 Technical Review of the Gene Technology Regulations 2001*.

5.1 Previous Consultation

From 17 October to 16 December 2016, the Regulator sought submissions from all interested and affected parties on a discussion paper detailing four options for how new technologies could be regulated. The Discussion Paper also sought input on a range of other topics related to the effectiveness of the legislative framework for the regulation of GMOs.

A summary of the 741 submissions received from the Discussion Paper consultation process is available on the OGTR website.

The OGTR also undertook targeted consultations (face-to-face or by teleconference) with a number of stakeholders to further discuss issues raised in their submissions.

Issues raised in submissions were considered and have contributed to the development of the draft amendments contained in this Consultation RIS. The Regulator's considerations have taken into account OGTR's experience, current scientific understanding, potential risks, regulatory burden implications for stakeholders, whether regulatory burden would be commensurate with risks, and the policy intent of the GT Act. Regulatory burden implications will be considered further as part of the current consultation process.

5.2 Consultation on this Regulation Impact Statement

The OGTR is seeking information from stakeholders in relation to the options set out in this RIS which will be used to prepare a Decision RIS that will be presented to decision makers (the LGFGT) and also made publicly available.

The key stakeholder groups who are expected to participate in this consultation process include:

- organisations and individuals working with GMOs (including licence holders, accredited organisations and IBCs)
- States and Territories, and relevant Australian Government agencies
- environmental and industry groups with an interest in gene technology regulation and
- Members of the public.

Consultation questions

By asking questions on the cost of current business practices and the expected impacts of these three options, the LGFGT will be able to consider the extent of the regulatory and financial impacts of the measures for industry, researchers and the community sector.

The Regulator is also consulting on the proposals to amend the categorisation of NLRDs and exempt dealings under Section 142 of the Act. These proposals were developed since consultation on the Discussion Paper, and information is now sought about whether these proposals are appropriate on a risk basis.

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1. What is your preferred option? Please explain why.
2. Do the draft amendments clearly implement the measures described in section 3? If not, which areas of the draft amendments do you think require additional clarification, and what clarification is needed?
3. If your preferred option is Option 3, please indicate which amendments (or parts thereof) you support being progressed and why.
4. What are the costs and benefits to you or your organisation from the proposed amendments? Please describe these compared to current arrangements, for each area of amendment:
    - 4.1 Clarifying the GT Regulations to take technological developments into account (i.e. in relation to SDN-1, SDN-2, ODM and RNAi)
    - 4.2 Repeal of Schedule 1 item 1, specifically whether you currently work with organisms that are not GMOs solely because of this item
    - 4.3 Updating the categorisation of contained dealings with GMOs
    - 4.4 Clarifying the regulatory status of organisms derived from GMOs that are not themselves GMOs
    - 4.5 minor administrative changes.
5. Are the proposals to change the classification of certain NLRDs and exempt dealings (identified in **Appendix B**) commensurate with any risks to the health and safety of people and the environment posed by the dealings? [5]
6. Are there any features in the options presented that you have concerns with? Or, are there any particular features that you believe should be included? Please explain why and give substantiating evidence where possible.

The Australian Government requires OGTR to work with the Office of Best Practice Regulation to examine potential impacts of these proposals. For this purpose, calculation of regulatory burden focuses on administrative costs (e.g. making applications, record keeping and reporting), substantive compliance costs (e.g. purchase and maintenance costs solely due to regulatory requirements) and delay costs (e.g. loss of income due to business, community organisations and/or individuals, as a result of government regulation).[6] OGTR encourages submitters to provide information on these matters to support further analysis of impacts. Opportunity costs and business-as-usual costs are outside the Office of Best Practice Regulation's considerations on regulatory burden.

[5] The Regulator is consulting on these proposals to amend NLRDs and exempt dealings under Section 142 of the Act.

[6] For further information about regulatory impacts please see this Office of Best Practice Regulation guidance note.

How to provide feedback

Comments and submissions that address any or all of the options and consultation questions described in this Consultation RIS are welcome. You are not required to address all options in the Consultation RIS; however, you should address the questions for your preferred option.

Submissions can be made by email to ogtr@health.gov.au or by mail to the Regulations Review, Office of the Gene Technology Regulator (MDP 54), GPO Box 9848, Canberra ACT 2601. **Submissions must be made by 21 February 2018.**

Submissions will be published on the OGTR website after the consultation period closes, however, OGTR can treat information of a confidential nature as such. Please ensure that material supplied in confidence is clearly marked 'IN CONFIDENCE' and is in a separate attachment to non-confidential material.

For privacy reasons, all **personal** details (e.g. signatures, phone, mobile and fax numbers) will be removed from your submission before they are published on the website. Please do not include these details in your submission unless necessary.

Next steps

Submissions received through this consultation process will be taken into account by the Regulator in finalising the proposed amendments and preparing a decision RIS which will be provided to the LGFGT.

The Regulator will seek agreement from the LGFGT in 2018 to any finalised amendments, as required by clause 40 of the Intergovernmental Gene Technology Agreement. If the LGFGT agrees to the amendments, the OGTR will commence the Commonwealth regulation-making process which requires approval from the Governor-General and tabling in Parliament.

Any progressed amendments will not commence until the above described steps have been completed. Organisations or individuals working with GMOs are cautioned to continue complying with all current requirements contained in the GT Regulations (as well as any guidance provided by the Regulator) until any amendments come into force.

Glossary

Term	Definition
COAG	Council of Australian Governments – the peak intergovernmental forum in Australia.
Consultation RIS	Consultation Regulation Impact Statement – a document prepared to facilitate consultation on the costs and benefits of proposed changes to regulation.
DNIR	Dealings Not involving an Intentional Release of GMOs into the environment – work with higher risk GMOs that is undertaken in contained facilities such as laboratories and requires case by case assessment and licencing from the Regulator.
FSANZ	Food Standards Australia New Zealand – a statutory authority in the Australian Government Health portfolio. FSANZ develops food standards for Australia and New Zealand.
GMO	Genetically modified organism which has the meaning as provided in section 10(1) of the GT Act.
GM	Genetically modified – an organism, or product of an organism, that has been changed by gene technology.
GT Act	*Gene Technology Act 2000*
GT Regulations	Gene Technology Regulations 2001
IBC	Institutional Biosafety Committee – IBCs provide on-site scrutiny of NLRD proposals through independent of NLRD proposals.
LGFGT	Legislative and Governance Forum on Gene Technology – the ministerial committee with responsibility for oversight of Australia's gene technology regulatory scheme.
NLRD	Notifiable Low Risk Dealing – activities with GMOs undertaken in containment (i.e. not released into the environment) that have been assessed as posing low risk.
ODM	Oligo-directed mutagenesis – a process for making small, precise changes to a genomic DNA sequence using a short single stranded synthetic nucleic acid (DNA or RNA) called an oligonucleotide (oligo) as a template.
OGTR	Office of the Gene Technology Regulator – staff supporting the Gene Technology Regulator.
Regulator	Gene Technology Regulator – an independent statutory office holder responsible for administering the GT Act and corresponding State and Territory laws.
RNAi	Ribonucleic acid (RNA) interference – a cellular mechanism that modulates gene expression and protects against viruses, which can be harnessed to reduce expression of proteins from targeted genes.
SDN, SDN-1, SDN-2 and SDN-3	Site-directed nuclease – specially designed proteins, or protein/nucleic acid combinations, that are capable of cutting DNA at a specific nucleotide sequence. Techniques to modify sequences following SDN action include: • SDN-1 –non-homologous end-joining repair of DNA breaks resulting in small random sequence changes. • SDN-2 – homology directed repair of DNA breaks using an oligo to guide a specific small modification of one or several nucleotides. • SDN-3 – homology directed repair of DNA breaks using a large template to guide insertion of new sequences.

Appendix A: Administrative changes to the Gene Technology Regulations 2001

In addition to the amendment proposals described in Section 3 (Option 2) the following administrative proposals are contained in the draft amendments at **Appendix C**. Refer to **Appendix B** to cross-reference these topics to provisions in the GT Regulations and amendment items.

Cross-references within Schedule 3

Parts 1 and 2 of Schedule 3 describe GMO dealings classified as NLRDs. Importantly, Part 3 (dealings which are not notifiable low risk dealings) qualifies the lists in Parts 1 and 2, so that a dealing of a kind described in Part 3 is not an NLRD even if it meets a description in Part 1 or Part 2. Dealings which do not meet the requirements for classification as exempt dealings or NLRDs must only be conducted if authorised by a licence issued by the Regulator. Proposed amendments to make the role of Part 3 more prominent are intended to ensure dealings are correctly categorised, and would not alter the categorisation of any dealings.

GMO risk group requirements

The previous review of the GT Regulations in 2011 introduced a new category of NLRD for dealings with risk group 3 micro-organisms (Schedule 3, Part 2.2) and required a licence for all dealings with risk group 4 micro-organisms (Schedule, 3.1(p)). This has led to some stakeholder confusion as to how these provisions should be applied, and whether the effect of the modification should also be taken into account when assessing the risk group of the GMO. The intent of the 2011 amendments, as described in the explanatory statement, was that the relevant risk group is that of the unmodified parent organism. The proposed amendments include new clauses to clarify this.

Suitability of facilities for NLRDs

Regulation 13(2) specifies the kinds of facilities suitable for undertaking different categories of NLRD. These considerations are relevant both during the IBC's initial assessment of the dealing (regulation 13B(a)(vii)) and also while the dealing is being conducted. The amendment proposals would clarify that IBCs must consider which facilities meet the suitability requirements at the time the NLRD is being assessed, and persons conducting NLRDs may only undertake NLRDs in suitable facilities, within the limits provided in the IBC record of assessment.

NLRD record of assessment and reporting requirements

The GT Regulations require that dealings IBCs assess to be NLRDs are notified to the Regulator. In recognition that instruments of accreditation provide a reporting requirement, including its timeframe, the timeframe for reporting for accredited organisations will be removed from the GT Regulations.

The GT Act allows for a 'person or persons' to undertake an NLRD, and the GT Regulations refer variously to organisations and accredited organisations in roles related to NLRDs. These references will be updated for consistency with the GT Act.

Importantly, the *Acts Interpretation Act 1901* provides that the term 'person' in legislation includes "a body politic or corporate as well as an individual". It is not intended that individuals would be named for NLRD reporting purposes; the name of a company or the description "members of X organisation" would meet the requirement.

NLRD time limits

Regulation 13A provides time limits for stopping NLRDs, with a phase-in of time limits for dealings assessed by an IBC before 31 August 2016. As this date has passed paragraphs (b) and (c) longer serve a purpose and this Regulation can be removed, allowing the five year time limit to be placed through Regulation 13.

Use of the symbol µ for micrograms

The Greek letter 'mu' (µ) is used throughout the GT Regulations as part of a recognised international symbol indicating 'micrograms'. This symbol is usually displayed correctly, however some devices may display it incorrectly (in Word and possibly HTML and PDF), making units read as 'mg' (milligrams), which significantly changes the meaning of the legislation. The symbol would be replaced by the word 'micrograms'.

References to GM products

The *Gene Technology Amendment Act 2015* removed the requirement for the Regulator to maintain a record of GM product approvals made by other agencies. Remaining references to 'GM products' no longer serve a purpose or have any legal effect, and will be removed.

Out of date material, typographical errors and drafting style updates

The GT Regulations contain cross-references to provisions in the GT Act that have since been amended, a broken web-link, an out-dated agency name and several typographical errors. These would be corrected, and as necessary the drafting style would be updated to match current practices of the Office of Parliamentary Counsel (most notably the table in Schedule 2 Part 2).

Appendix B: Summary of proposed changes to the GT Regulations

A future law compilation, showing the effect of the proposed amendments on the Gene Technology Regulations 2001, is available on the OGTR website.

Consultation question 5 refers to proposals to change the classification of certain NLRDs and exempt dealings, contained in the table below under the heading "Categorisation of Contained Dealings".

Topic area	**Amended provisions in the Gene Technology Regulations 2001**	**Amendment item in Gene Technology Amendment (2017 Measures No.1) Regulations 2017** (item in Schedule 1 unless noted otherwise)
Clarifying scope of Regulation - What is a GMO		
Organisms modified using SDN-1 are not GMOs	Schedule 1 – new item	Item 32
Organisms modified using SDN-2 and ODM are GMOs	4A - new Schedule 1B - new	Items 7 and 31
Replacing Item 1 of Schedule 1	Schedule 1, item 1 and two new items	Item 33 and Schedule 2
Some RNAi techniques are not gene technology	Schedule 1A – new item	Item 30
Organisms derived from GMOs	Schedule 1 – two new items	Item 33
Categorisation of Contained Dealings – refer also to consultation question 5[7]		
Gene drives	Schedule 3, 3.1 (r) & (s) - new	Item 69
New exempt hosts	Schedule 2, Part 2 – within new Item 6	Item 39
Cloned viral genomes	Schedule 2, Part 1, item 4(2)	Item 37
Viral Vectors with no host	3 – definition of host/vector system, Schedule 2 Part 2, Schedule 3, 1.1(c) and 2.1 (c), (d), (i)-(m), 3.1 (d)	Items 2, 3, 39, 41, 43, 48-52, 54-57, 59, 65

[7] The Regulator is consulting on proposals to change the classification of certain NLRDs and exempt dealings is being undertaken in accordance with Section 142 of the GT Act. Consultation question 5 refers to these proposals.

Topic area	**Amended provisions in the Gene Technology Regulations 2001**	**Amendment item in Gene Technology Amendment (2017 Measures No.1) Regulations 2017** (item in Schedule 1 unless noted otherwise)
Clarifying requirements for characterisation of modifications	3 – revised definition of "characterised" Schedule 3, 1.1(c), 2.1(d), (e), (k) & (m) and 3.1(d)-(f)	Items 1, 41, 44-46, 53, 58 and 65-68
Clarification of risk group considerations	13B(3) - new Schedule 3, 2.2(2) - new Schedule 3, 3.1(q) – new Schedule 3, 3.1 (2) & (3) - new	18, 40, 42, 60-63 and 69
NLRD Administration		
NLRD facilities	13, 13B	Items 14-16, 18, 21 and 22
NLRD record of assessment	13(1)(e), 13B	Items 13, 17, 20, 23
NLRD notification	13C, 39	Items 24, 25, 29
Role of Schedule 3, Part 3 in categorising dealings	12(1)(a), 13(1)(b), and 13B	Items 10, 11 and 21
NLRD time limit	13(1)(d), 13A	Items 12 and 19
Administrative changes		
Updating cross-references	21(2) note, 26(1)(b) and 32(c)	Items 26-28
Micrograms symbol	3 – definition of toxin-producing organism Schedule 2, Part 1, Item (4) Schedule 3, 3.1(a) & (b)	Items 4, 36 and 64
Remove reference to GM products	note to 3, 39	Items 5 and 29
Update to current styles	4, 5, Schedule 2, Parts 1 and 2 Schedule 3, 2.1(h)	Items 6, 8, 38, 39 and 47
Update agency name	9(f)	Item 9
Correcting typographical errors	Schedule 2, Part 2, item 4	34, 35

Appendix C: Draft Gene Technology Amendment (2017 Measures No. 1) Regulations 2017

EXPOSURE DRAFT

Gene Technology Amendment (2017 Measures No. 1) Regulations 2017

I, General the Honourable Sir Peter Cosgrove AK MC (Ret'd), Governor-General of the Commonwealth of Australia, acting with the advice of the Federal Executive Council, make the following regulations.

Dated 2017

Peter Cosgrove
Governor-General

By His Excellency's Command

Dr David Gillespie **[DRAFT ONLY—NOT FOR SIGNATURE]**
Assistant Minister for Health
Parliamentary Secretary to the Minister for Health

Contents

1 Name

This instrument is the *Gene Technology Amendment (2017 Measures No. 1) Regulations 2017*.

2 Commencement

(1) Each provision of this instrument specified in column 1 of the table commences, or is taken to have commenced, in accordance with column 2 of the table. Any other statement in column 2 has effect according to its terms.

Commencement information

Column 1	Column 2	Column 3
Provisions	**Commencement**	**Date/Details**
1. Sections 1 to 4 and anything in this instrument not elsewhere covered by this table	The day after the end of the period of 6 months beginning on the day this instrument is registered.	
2. Schedule 1	The day after the end of the period of 6 months beginning on the day this instrument is registered.	
3. Schedule 2	The day after the end of the period of 18 months beginning on the day this instrument is registered.	

Note: This table relates only to the provisions of this instrument as originally made. It will not be amended to deal with any later amendments of this instrument.

(2) Any information in column 3 of the table is not part of this instrument. Information may be inserted in this column, or information in it may be edited, in any published version of this instrument.

3 Authority

This instrument is made under the *Gene Technology Act 2000*.

4 Schedules

Each instrument that is specified in a Schedule to this instrument is amended or repealed as set out in the applicable items in the Schedule concerned, and any other item in a Schedule to this instrument has effect according to its terms.

Schedule 1—Amendments commencing 6 months after registration

Gene Technology Regulations 2001

1 Regulation 3 (definition of *characterised*)

Repeal the definition, substitute:

characterised means:

(a) in relation to a nucleic acid—the nucleic acid has been sequenced and there is an understanding of potential gene products or potential functions of the nucleic acid; or

(b) in relation to a genetic modification—the gene or genomic region which is modified has been sequenced and there is an understanding of:

(i) potential gene products or potential functions of the gene or genomic region; and

(ii) the likely effect of the genetic modification on the gene products or functions.

2 Regulation 3

Insert:

host/vector system has a meaning affected by subclause 2.1(3) of Schedule 2.

3 Regulation 3 (definition of *non-vector system*)

Repeal the definition, substitute:

non-vector system has the meaning given in Part 3 of Schedule 2.

4 Regulation 3 (definition of *toxin-producing organism*)

Omit "100 μg/kg", substitute "100 micrograms per kilogram".

5 Regulation 3 (note)

Omit "• GM product".

6 Regulation 4

Omit "section 10", substitute "subsection 10(1)".

7 After regulation 4

Insert:

4A Organisms that are genetically modified organisms

For the purposes of paragraph (c) of the definition of ***genetically modified organism*** in subsection 10(1) of the Act, an organism mentioned in Schedule 1B is a genetically modified organism.

8 Regulation 5

Omit "section 10", substitute "subsection 10(1)".

9 Paragraph 9(f)

Repeal the paragraph, substitute:

(f) that part of the Department known as the Therapeutic Goods Administration.

10 Paragraph 12(1)(a)

Repeal the paragraph, substitute:

(a) it is a dealing of a kind mentioned in Part 1 or 2 of Schedule 3; and

(aa) it is not a dealing of a kind mentioned in Part 3 of Schedule 3; and

11 Paragraph 13(1)(b)

Repeal the paragraph, substitute:

(b) the Institutional Biosafety Committee has assessed the dealing to be a kind of dealing mentioned in Part 1 or 2 of Schedule 3, and not mentioned in Part 3 of Schedule 3; and

12 Paragraph 13(1)(d)

Repeal the paragraph, substitute:

(d) the dealing is only undertaken no later than the day 5 years after the date of the assessment; and

13 Paragraph 13(1)(e)

After "is mentioned in", insert ", or is in a class of persons mentioned in,".

14 Paragraph 13(1)(f)

Repeal the paragraph, substitute:

(f) subject to subregulation (3), the dealing is undertaken in facilities that:

(i) are mentioned in, or are in a class of facilities mentioned in, the Institutional Biosafety Committee's record of assessment as being appropriate for the dealing; and

(ii) are facilities in which subregulation (2) permits the dealing to be undertaken; and

15 Paragraph 13(1)(h)

Omit "dealing; and", substitute "dealing.".

16 Paragraph 13(1)(i)

Repeal the paragraph.

17 Subregulation 13(1) (note)

Repeal the note.

18 Subregulation 13(3)

Repeal the subregulation, substitute:

(3) If a notifiable low risk dealing involves the transportation, storage or disposal of a GMO, the transportation, storage or disposal may happen outside a facility that complies with paragraph (1)(f) and subregulation (2), if it is conducted in accordance with:

(a) the *Guidelines for the Transport, Storage and Disposal of GMOs*, as in force from time to time, that have been issued by the Regulator under paragraph 27(d) of the Act; or

(b) transportation, storage or disposal requirements that the Regulator has agreed in writing are appropriate for the containment of the GMO.

(3A) For the purposes of subparagraph (2)(b)(ii), 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.

19 Regulation 13A

Repeal the regulation.

20 Subparagraph 13B(a)(i)

Omit "proposing to undertake the dealing", substitute "that submitted the proposal".

21 Subparagraphs 13B(a)(iii) and (iv)

Repeal the subparagraphs, substitute:

(iii) its assessment whether the dealing is a kind of dealing mentioned in Part 1 or 2 of Schedule 3, and not mentioned in Part 3 of Schedule 3;

(iv) if the Committee has assessed the dealing as being a kind of dealing mentioned in Part 1 or 2 of Schedule 3 (and not mentioned in Part 3 of Schedule 3)—which kind of dealing in those Parts that the dealing is;

22 Subparagraph 13B(a)(vii)

After "dealing", insert ", having regard to the requirements of subregulation 13(2)".

23 Subparagraph 13B(a)(x)

Omit "the name of the person or accredited organisation", substitute "the person or persons".

24 Subregulations 13C(1) and (2)

Repeal the subregulations, substitute:

(1) A person or accredited organisation that has been given a copy of a record of assessment by an Institutional Biosafety Committee under paragraph 13B(b) must, if the dealing has been assessed by the Committee as a notifiable low risk dealing:

(a) for an accredited organisation that is required, as a condition of accreditation, to give an annual report to the Regulator—include a record

of the dealing in the organisation's annual report for the year in which the Institutional Biosafety Committee made the assessment; and

(b) in any other case—give to the Regulator collated records of all such dealings assessed in a single financial year.

(2) A record of a dealing for the purposes of subregulation (1) must include:

(a) the particulars, prescribed under regulation 39 in relation to the dealing, to be included in the Record of GMO Dealings; and

(b) the name of the Committee that assessed the dealing; and

(c) the name of the person or accredited organisation that submitted the dealing to the Committee for assessment.

(2A) For the purposes of paragraph (1)(b), the collated records must be given to the Regulator:

(a) in a form approved by the Regulator; and

(b) as soon as practicable after the end of the financial year and no later than 30 September in the following financial year.

25 Subregulation 13C(3)

After "Institutional Biosafety Committee", insert "under paragraph 13B(b)".

26 Subregulation 21(2) (note)

Omit all the words after "section 27B of that Act".

27 Paragraph 26(1)(b)

Omit "to whom paragraph 100(7A)(a) or (b) of the Act applies", substitute "who is also a member of the Ethics and Community Committee".

28 Paragraph 32(c)

Repeal the paragraph, substitute:

(c) the reference in paragraph 26(1)(b) to the Ethics and Community Committee were a reference to the Gene Technology Technical Advisory Committee or the Australian Health Ethics Committee; and

29 Regulation 39

Repeal the regulation, substitute:

39 Record of GMO Dealings

For the purposes of subsection 138(4) of the Act, the following particulars are prescribed in relation to a notifiable low risk dealing that is notified to the Regulator:

(a) the person or persons that proposed to undertake the dealing, as recorded by the Institutional Biosafety Committee that assessed the dealing as a notifiable low risk dealing;

(b) the kind of notifiable low risk dealing, in terms of Part 1 or 2 of Schedule 3;

(c) the identifying name given to the dealing by the person or accredited organisation that submitted the dealing to the Institutional Biosafety Committee for assessment;

(d) the date of assessment by the Institutional Biosafety Committee that the dealing is a notifiable low risk dealing.

30 Schedule 1A (at the end of the table)

Add:

11	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.

31 After Schedule 1A

Insert:

Schedule 1B—Organisms that are genetically modified organisms

Note: See regulation 4A.

1.1 Genetically modified organisms

For the purposes of regulation 4A, organisms mentioned in the following table are genetically modified organisms.

Organisms that are genetically modified organisms	
Item	**Description of organism**
1	An organism that has had its genome modified by oligonucleotide-directed mutagenesis
2	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

32 Schedule 1 (after table item 3)

Insert:

4	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.

33 Schedule 1 (at the end of the table)

Add:

8	An organism that is descended from a genetically modified organism (the ***initial organism***), but which has not inherited any traits that occurred in the initial organism because of gene technology.
9	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.
10	*Agrobacterium radiobacter* strain K1026 (known as NoGall).
11	*Pasteurella multocida* strain PMP1 (known as Vaxsafe PM).

34 Part 1 of Schedule 2 (table item 4, column headed "Description of dealing", subparagraph (2)(a)(ii))

Omit "harm;", substitute "harm; and".

35 Part 1 of Schedule 2 (table item 4, column headed "Description of dealing", example)

Omit "transmissibility; and", substitute "transmissibility.".

36 Part 1 of Schedule 2 (table item 4, column headed "Description of dealing", paragraphs (2)(b) and (c))

Omit "100 μg/kg", substitute "100 micrograms per kilogram".

37 Part 1 of Schedule 2 (table item 4, column headed "Description of dealing", subparagraph (2)(e)(i))

Repeal the subparagraph, substitute:

(i) cannot give rise to virions or infections agents when introduced into a host as part of the dealing, without additional genes or gene products that are not available in the host cell and that will not become available during the dealing; and

38 Part 1 of Schedule 2 (table item 5, column headed "Description of dealing")

Omit "item 1 of", substitute "items 1 to 6 of the table in".

39 Part 2 of Schedule 2

Repeal the Part, substitute:

Part 2—Host/vector systems for exempt dealings

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

	Column 1	Column 2	Column 3
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*; (e) *B. thuringiensis*	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*
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)	Ri plasmids or non-tumorigenic disarmed 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*;	Non-conjugative plasmids

Hosts and vectors			
	Column 1	**Column 2**	**Column 3**
Item	**Host class**	**Hosts**	**Vectors**
		(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*	
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) Ri plasmids, or non-tumorigenic disarmed Ti plasmids, in *Agrobacterium radiobacter*, *Agrobacterium rhizogenes* (disarmed strains only) or *Agrobacterium tumefaciens* (disarmed strains only);

Hosts and vectors			
	Column 1	Column 2	Column 3
Item	Host class	Hosts	Vectors
			(b) non-pathogenic viral vectors

40 Clause 1.1 of Schedule 3

Omit "13(3)(b)", substitute "subregulation 13(3)".

41 Paragraph 1.1(c) of Schedule 3

Repeal the paragraph, substitute:

(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.

42 Clause 2.1 of Schedule 3

Omit "13(3)(b)", substitute "subregulation 13(3)".

43 Paragraph 2.1(d) of Schedule 3

Omit "host and vector not mentioned as a host/vector system", substitute "host/vector system not mentioned".

44 Subparagraphs 2.1(d)(ii) and (iii) of Schedule 3

Omit "donor nucleic acid", substitute "genetic modification".

45 Paragraph 2.1(d) of Schedule 3 (example)

Omit "Donor nucleic acid", substitute "A genetic modification".

46 Subparagraph 2.1(e)(i) of Schedule 3

Repeal the subparagraph, substitute:

(i) is characterised, and the characterisation shows that it may increase the capacity of the host or vector to cause harm; or

47 Paragraph 2.1(h) of Schedule 3

Omit "item 1 of", substitute "items 1 to 6 of the table in".

48 Paragraph 2.1(i) of Schedule 3

Omit "the introduction", substitute "virions".

49 Paragraph 2.1(i) of Schedule 3

Omit "into", substitute "and".

50 Paragraph 2.1(j) of Schedule 3

Repeal the paragraph, substitute:

(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);

51 Paragraph 2.1(k) of Schedule 3

Omit "the introduction", substitute "virions".

52 Paragraph 2.1(k) of Schedule 3

Omit "into", substitute "and".

53 Subparagraph 2.1(k)(ii) of Schedule 3

Repeal the subparagraph, substitute:

(ii) the donor nucleic acid does not confer an oncogenic modification or immunomodulatory effect in humans;

54 Paragraph 2.1(l) of Schedule 3

Omit all the words before subparagraph (i), substitute:

(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:

55 Subparagraph 2.1(l)(i) of Schedule 3

Omit "into a virion", substitute "new virions".

56 Paragraph 2.1(m) of Schedule 3

Omit "the introduction", substitute "virions".

57 Paragraph 2.1(m) of Schedule 3

Omit "into a host", substitute "and a host".

58 Subparagraph 2.1(m)(i) of Schedule 3

Repeal the subparagraph, substitute:

(i) the donor nucleic acids does not confer an oncogenic modification or immunomodulatory effect in humans; and

59 Subparagraph 2.1(m)(ii) of Schedule 3

Omit "into a virion", substitute "new virions".

60 Clause 2.2 of Schedule 3

Before "Any", insert "(1)".

61 Clause 2.2 of Schedule 3

Omit "(3)(b)", substitute "subregulation 13(3)".

62 At the end of clause 2.2 of Schedule 3

Add:

(2) For the purposes of subclause (1), 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.

63 Clause 3.1 of Schedule 3

Before "A dealing", insert "(1)".

64 Paragraphs 3.1(a) and (b) of Schedule 3

Omit "100 μg/kg", substitute "100 micrograms per kilogram".

65 Paragraph 3.1(d) of Schedule 3

Repeal the paragraph, substitute:

(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);

66 Paragraph 3.1(e) of Schedule 3

Omit all the words after "if the", substitute "genetic modification confers an oncogenic modification or immunomodulatory effect in humans;".

67 Sub-subparagraph 3.1(f)(ii)(B) of Schedule 3

Omit "donor nucleic acid", substitute "genetic modification".

68 Subparagraph 3.1(f)(ii) of Schedule 3 (example)

Omit "Donor nucleic acid", substitute "A genetic modification".

69 At the end of clause 3.1 of Schedule 3

Add:

; (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.

Schedule 2—Amendments commencing 18 months after registration

Gene Technology Regulations 2001

1 Schedule 1 (table item 1)

Repeal the item.

Appendix D: Summary of amendment proposals received in Discussion Paper submissions

OGTR's Discussion Paper[8] consultation from October-December 2016 sought submitter proposals for additional amendments to the GT Regulations, and required a supporting rationale and science-based argument be provided. The proposals received in response ranged from purely administrative items that do not require amendments through to broad policy issues that could only be addressed through amendments to the GT Act, and from proposals with no supporting argument or justification to considered, well-referenced proposals. Amendment proposals received by OGTR since the previous technical review were also considered.

The proposals not warranted due to risk, or because insufficient supporting information was provided, included:

7. adding *Bacillus megaterium*, *Vibrio natriegens* and all organisms on the US-FDA generally recognised as safe (GRAS) list to Schedule 2, Part 2 (exempt host/vector list);
8. adding some dealings with GM *Arabidopsis*, mice (*Mus musculus*), rice (*Oryza sativa*), and plants with GM plant parts to Schedule 2 (dealings exempt from licencing);
9. including the use of synthetic nucleic acids to Schedule 1A (techniques which are not gene technology); and
10. increasing the 25 litre culture volume limit on exempt and other dealings.

Several submitters proposed that dealings with GM *Drosophila melanogaster* and GM Zebrafish (*Danio rerio*) should be reclassified from PC2 NLRDs to PC1 NLRDs, providing detailed arguments to support their proposals. OGTR does not support these proposals on the basis that generic PC1 requirements do not adequately contain these organisms, making the potential for unintentional release unacceptable.

A submitter also requested adding all dealings with cloned viral genomes in a bacterial host to Schedule 2. This was not supported; however, as discussed in section 3, it is proposed that some dealings with cloned viral genomes which cannot give rise to infectious agents when introduced into a host cell will be included in Schedule 2.

A submitter requested a definition for the term "naked", when used in reference to naked nucleic acid in Schedule 1 item 2; this request was not further considered as the word is taken to have its common meaning. The accompanying request to reconsider the GMO status of, and regulatory requirements for, dealings involving a human modified by the introduction of non-naked plasmid DNA into their somatic cells was not progressed as it is considered appropriate for the Regulator to undertake a case by case assessment of the capacity of the non-naked DNA to enter germline cells during the conduct of such dealings.

[8] For further information about the Discussion Paper consultation see the OGTR website.

Submitters also proposed changes to the management of certification that could only be achieved through changes to the GT Act. This request was more suitable to be considered as part of the Legislative Governance Forum on Gene Technology's (LGFGT) Review of the National Gene Technology Scheme and was passed to the review secretariat for their consideration.

The Regulator also received requests that related to licensing, including application forms, the processing of applications and the imposition of licence conditions. These administrative processes are not prescribed by the Regulations and so cannot be addressed through this review. The requests were passed on to the relevant areas of the OGTR for their consideration.

Appendix E: Introduction to new technologies

Oligo-directed mutagenesis

Oligo-directed mutagenesis (ODM) is a process for making small, precise changes to a genomic DNA sequence using a short piece of single stranded synthetic nucleic acid (DNA or RNA) called an oligonucleotide (oligo) as a template. The oligo is designed so that the majority of the sequence is identical to the target gene sequence. However, the middle of the oligo contains the desired sequence change. Oligos typically range from around 20 nucleotides to 100 nucleotides in length, and the longer the oligo, the more changes it can contain.

For organisms with large genomes, e.g. plants, the oligo is introduced into a cell and binds to the matching sequence in the target gene. The cell's proof-reading enzymes then recognise that the two sequences are not a perfect match and changes one of them so that they match. If the oligo is changed to match the original strand then the cell's DNA is not changed. However, if the cell's DNA is changed to match the oligo then the cell's DNA will contain the new sequence.

For plants, ODM is carried out on cells in tissue culture, and whole plants are grown from these cells. For organisms with small genomes, such as viruses and bacteriophages, the reaction can take place in a tube with a mixture of oligos, nucleotides and enzymes rather than in a cell.

The small change(s) made via ODM can switch off a gene, change how much of the gene product is made, or change the function of a protein by changing the amino acid sequence produced from a gene.

Site-directed nuclease techniques

Site-directed nucleases (SDNs) such as zinc finger nucleases, TALENs (transcriptional activator-like effector nucleases), CRISPR/Cas9 (clustered regularly-interspaced short palindromic repeats/CRISPR-associated protein 9) and meganucleases are becoming widely used in biological research. These are specially designed proteins, or protein/nucleic acid combinations that are capable of cutting DNA at a specific nucleotide sequence.

Once the DNA has been cut, there are two main pathways by which the cut can be repaired, both of which involve natural repair mechanisms:

Non-homologous end-joining, which joins the two ends back together. This can be an error prone process with the potential for nucleotides to be added, lost or changed at the cut site. If the cut is repaired correctly, then there is no sequence change and the sequence may be cut again by the SDN. However, if a mistake is made during non-homologous end-joining, a small random sequence change may alter how the gene functions. Additionally, repair of two nearby cuts can delete the sequence between them, creating substantial deletions. This technique is known as SDN-1.

Homology-directed repair can be used to deliver predetermined sequence changes. The cellular process for homology-directed repair is very similar to ODM, where an oligo acts as a template to direct modifications. Without human intervention, homology-directed repair can occur using

sequences available naturally within the cell. The process can be directed by providing a piece of DNA with ends matching the sequence surrounding the DNA cut site to achieve a predetermined sequence change. This piece of DNA can be an oligo to guide a specific small modification of one or several nucleotides (SDN-2) or a large DNA cassette which includes new sequences such as additional genes, regulatory sequences or selectable markers (SDN-3).

One of the earliest uses of the SDN-1/2/3 terminology was by Lusser *et al.* in their 2011 report for the European Commission's Joint Research Centre, New Plant Breeding Techniques; state-of-the-art and prospects for commercial development. Lusser *et al.* described the outcomes of modification using zinc finger nucleases as ZFN-1, ZFN-2 and ZFN-3.

SDN techniques can be used on animal embryos so that germline tissues carry the resulting sequence changes and offspring of that animal will uniformly carry the sequence change. SDN techniques can be used on plant cells in tissue culture, from which whole plants can be grown.

Successive rounds of modification using SDNs can be used to accumulate sequence changes to a genome. Alternatively, multiple sequences can be targeted at once by using a variety of SDNs (with or without different repair templates) at the same time.

Gene drives

Gene drives are genetic elements that are able to be inherited at a greater than expected rate. Most sexually reproducing organisms have two sets of genes, one from each parent. They then pass on half of their genes (a random mix from each parent) to their offspring. Gene drives are mechanisms that ensure that certain genetic elements are passed on to more than half of the offspring. In some cases gene drives may even be passed to all the offspring. This means that the genetic elements associated with the gene drives are able to increase in prevalence in a population at a faster rate than other genes.

Scientists have known about various naturally occurring gene drive mechanisms for decades, but it is only recently, with the development of CRISPR/cas9 and other site directed nucleases, that scientists have been able to build and test their own gene drives.

Initial experiments suggest that these GM gene drives work well in highly inbred laboratory populations of insects or mice. However, it has been suggested that these drives may be less effective in wild populations with greater genetic variability.

Internationally, there is rapidly growing research interest in using gene drives for a variety of purposes. Potential applications include:

- Reducing or eliminating populations of invasive animals, for example exotic rodents, to protect natural environments
- Reducing transmission of diseases from insects to humans, for example malaria from mosquitoes, by modifying the ability of insects to carry the disease or by reducing insect populations
- Controlling weeds of natural or agricultural environments.

It should be noted that there are other types of genes and genetic mechanisms that may be able to become rapidly dominant within a population. For example, bacterial

genes for antibiotic resistance rapidly become widespread when that antibiotic is present. Genes which are inherited in a sex specific manner, or which influence the sex ratio or reproductive capacity of offspring may also cause changes in the genepool at the population level. However, these are not gene drives.

RNA interference

RNAi, also known as gene silencing, is a group of natural cellular mechanisms in most higher organisms that reduce the production of specific proteins. RNAi relies on gene-specific small RNAs, processed from longer RNAs, which guide mechanisms to reduce the amount of protein produced from that gene. RNAi can take effect via degradation of the target gene's RNA transcript; repression of translation of the transcript into protein; methylation of the target gene; or a combination of these mechanisms.

RNAi is an important natural mechanism to regulate the level of each protein present in the cell, and RNAi also plays an important role in defence against viral infections. RNAi can also be utilised to silence the expression of a chosen target gene, permanently or temporarily.

Silencing a chosen target gene can be achieved by expression of target-specific RNAs that form a double-stranded structure (e.g. short or long hairpin RNAs). The double-stranded RNAs are processed by native enzymes into short interfering RNAs, which guide further RNAi enzymes to cause the silencing effect. To achieve stable silencing these RNAs are expressed from genomic insertions, delivered by standard gene technology techniques for introducing transgenes, or from vectors that propagate outside an organism's genome. The RNAi effect is inherited by offspring inheriting the genomic insertions or vectors.

Short-lived RNAi can be achieved through short-term expression of double-stranded RNAs, e.g. from introduced GM *Agrobacterium tumefaciens* that does not integrate sequences into the genome in plant cells, or using viral vectors. Other short-lived RNAi techniques, referred to in this document as RNA-delivered RNAi techniques, involve directly introducing double-stranded RNAs, short interfering RNAs or microRNAs into an organism. The silencing effect of short-lived RNAi techniques occurs while the triggering RNA is present, and may persist for variable periods afterwards due to genomic DNA methylation.