AUSTRALIAN ACADEMY OF TECHNOLOGY AND ENGINEERING

AUSTRALIAN ACADEMY OF SCIENCE

JOINT SUBMISSION TO THE REVIEW OF THE NATIONAL GENE TECHNOLOGY SCHEME 2017 (SECOND PHASE CONSULTATION)

The Australian Academy of Technology and Engineering and the Australian Academy of Science (collectively, the Academies) welcome the opportunity to further participate in the Review of the National Gene Technology Scheme (the Review) in the second phase of consultation.

As stated in our joint submission to the first phase of consultation, accrued experience with gene technology and with a diverse range of genetically modified organisms, together with increasing sophistication of the technology, may in some cases justify moving to legislation that provides regulation based on the products and outcomes of technology applications rather than on the technical processes used to achieve them. In all cases, the emphasis of regulation should be placed on the potential of modified organisms to harm human health or the Australian environment.

Accordingly, the Academies maintain the position from their submission to the first phase of consultation, that the current review process should focus on improving the existing process-based legislative framework by reducing the level of regulatory oversight of proven modifications with a history of safe use, supported by an approach that enables the Scheme to continuously respond to emerging technical developments.

Summary of key points

- **The Gene Technology Scheme should retain its legislated purpose, its regulatory powers and its basis in scientifically informed risk assessment.**
- **There is a long history of safe use of genetic modification of plants in the agricultural sector.** The regulatory scheme should recognise this safe use, in order to simplify regulation of well-studied traits and well-characterised crops. Genetically modified crops, particularly cotton and canola, are now a staple of the Australian agricultural industry and are continuing to expand.
- **The present regulatory scheme is sufficient for laboratory level research.** The existing Scheme involving exempt, notifiable low-risk and licenced dealings has proven adequate for the regulation of laboratory level research.
- **The Gene Technology Regulator should have the capacity to respond to technological developments.** This should include a horizon-scanning capacity and the capacity to amend definitions and processes (under advice) to streamline the regulatory scheme. A continuous assessment approach to the evolution of gene technologies would enable the legislative framework to adapt appropriately to new types of genetic modification without requiring continuous legislative amendments.
- **The Academies support a risk-tiering approach to facilitate movement of safe technologies to market.** A notification system for low risk releases overseen by accredited Institutional Biosafety Committees would provide efficiencies for the Regulator and for practitioners. Such a system should still be subject to regular audits.

Response to consultation questions.

Theme 1 - Technical Issues

1. What technological advances can be foreseen that might pose regulatory challenges for the Scheme?

The Academies have identified two techniques which will need to be accommodated within any new regulatory scheme or exempted from regulation, depending on their perceived level of risk. Note that neither of these techniques would trigger a product-based regulatory scheme based on the introduction of 'foreign' DNA.

- **Disabled Cas9 enzymes (dCas9)**

Disabled Cas9 enzymes (dCas9) bind to DNA using their specific guide RNAs but do not cut the DNA. This generates potential new uses for the gene editing machinery in both plants and animals beyond the initial application of making double stranded breaks and repairing them with or without a DNA repair template.[1]

One such application is to fuse the dCas9 with chromatin modification or methyltransferase enzymes to make epigenetic changes to specific parts of a genome. This will lead to generational consequences on gene expression without actually changing DNA sequence *per se*.

Another application is the fusion of dCas9 to deaminase enzymes to specifically deaminate cytosines close to the guide RNA binding site, thus converting them to thymines. This effects a C → T base change without cutting the DNA or using a DNA repair template.[2] Other systems allow different edits, such that it is now possible to achieve all four transitions–C → T, A → G, T → C, and G → A–in the genomic DNA of any species.[3]

- **Cas9 ribonucleoproteins**

There are a number of systems for the delivery of Cas9 ribonucleoproteins (RNPs) into cells, including transient (viral) delivery systems or systems involving *in vitro* assembly of RNPs and injection into cells.[4] These gene editing systems do not require the initial production of a transgenic cell or organism and do not integrate any novel DNA into the final host. Genome outcomes are similar to existing methods involving transgenics, with a higher specificity due to the rapid turnover of the RNP complex relative to that produced in a transgenic organism. The risks posed are therefore similar or less, and may not need any different regulation.

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[1] See Thakore PI, Black JB, Hilton IB, Gersbach CA. Editing the Epigenome: Technologies for Programmable Transcriptional Modulation and Epigenetic Regulation. Nature methods. 2016;13(2):127-137. doi:10.1038/nmeth.3733.

[2] For example, see Zong, Y et al., Precise base editing in rice, wheat and maize with a Cas9-cytidine deaminase fusion. Nat. Biotechnol. 2017, 35:438–440. doi:10.1038/nbt.3811.

[3] See Gaudelli et al., Programmable base editing of A•T to G•C in genomic DNA without DNA cleavage. Nature 2017, 551:464–471. doi:10.1038/nature24644.

[4] See Kim, Sojung, et al. Highly efficient RNA-guided genome editing in human cells via delivery of purified Cas9 ribonucleoproteins. Genome research 2014, 24(6):1012-1019. doi:10.1101/gr.171322.113

2 What are the potential impacts of the capability to make small edits in the DNA of an organism using no foreign DNA?

The technology currently exists to perform gene “knockouts” and “knockdowns” in crop and horticultural plants, animals or microorganisms. The ability to make deletions in specific genes is enabling advances in the diagnosis and treatment of genetic diseases and has led to biotechnology products that are currently appearing in global markets, such as waxy corn and non-browning mushrooms. Such agricultural products are being approved for commercial use in their countries of origin on the basis that they are considered to pose no greater risk to human health or the environment than identical products generated through conventional selection of natural variants (base changes, insertions or deletions) or mutagenic processes (chemical or radiation).

The technological capacity to make these changes with greater ease, efficiency and specificity does not necessarily impose a greater risk over that presented by the earlier technologies, as the types of changes remain the same. Unregulated technologies, such as chemical- or radiation-induced mutation, generate changes randomly throughout the genome; modern genetic modification methods are more precise and have fewer off-target effects.

There are many potential benefits that could be achieved through simple gene editing techniques such as enhancements in food quality, removal of allergens, increases in resistance to pathogens and even enhanced yield.[5] The recent decision by the Gene Technology Regulator to exempt these simple gene edits from being considered as genetically modified organisms is a welcome initial step under the current legislative scheme and will allow better harmonisation with our global trading partners as these products move into general commerce.

A logical extension of gene editing technology is to direct small changes to the genome sequence to achieve a specific desired alteration in sequence that may be associated with some agronomic or agricultural production advantage, such as herbicide tolerance or altered enzymatic function, or to more rapidly and precisely generate specific allelic variants or combination of alleles. These functions may already occur in germplasm, but are less accessible through cross breeding because of, for example, the positioning of the genes on the chromosomes. Targeted changes may be achieved by either allowing a random misrepair, or may be directed using a guide DNA molecule. If the changes are relatively minor and occur naturally in that or a related species, such modifications would not pose any greater risk than the natural allelic variation generated during conventional or mutation breeding. In practice, it will be difficult to identify whether such changes were generated by conventional breeding practices or by template-directed gene editing. This will create difficulties for the regulatory scheme.

[5] For example, see van de Wiel CCW et al., New Traits in Crops Produced by Genome Editing Techniques Based on Deletions. Plant Biotech Reports 2017, 11:1-8. doi:10.1007/s11816-017-0425-z.

3. Under what circumstances might it be practical, efficient or appropriate to regulate gene editing under the GT Act when, from an enforcement perspective, it may not be possible to distinguish the products of gene editing from the products of conventional methods?

In cases where organisms modified by gene editing cannot be distinguished from those modified by conventional methods or indeed from unmodified organisms, it would not be efficient to regulate such organisms under a scheme designed to regulate traditional genetically modified organisms containing substantial 'foreign DNA'. Regulation of all organisms containing directed base changes (unless they were in genes with known elevated risks, such as toxins or virulence genes) would place an undue burden of proof on practitioners to demonstrate that an organism was not generated through gene editing, especially if such a modification happened many generations ago, possibly in another country. Moreover, there would be a clear incentive in this regard for practitioners to disavow, or maintain ignorance of, any gene modification in an organism's lineage, representing a risk to the integrity of the Scheme.

The global trade in foods and the international nature of germplasm exchange, particularly but not exclusively in plant breeding, would make it almost impossible to know what material has been derived from gene editing and what has not.

The unintentional global propagation of the orange petunia, a conventional gene modification product that unexpectedly found its way into many conventional breeding programs at some time in the 1990s and was discovered only this year, provides an example of the difficulties that such a requirement for disclosure might present. In this case, there was an easily identifiable genetic trait–provided the practitioner knew what they were looking for–but the petunia was unwittingly propagated using traditional breeding, with the GM trait identified by US regulators in ten varieties of petunias so far, with a further 21 varieties implicated as potentially genetically modified and the seeds and plants being sold unwittingly throughout the world.

The phenotypes of modified organisms carrying simple genome modifications through genome editing are unlikely to be sufficiently novel or risky to require regulation from a gene technology perspective. They are similar to mutants or natural allelic variants although, depending on their phenotype, they may still need to trigger regulation through one of the other, product-oriented, federal agencies such as FSANZ, APVMA or TGA if they are to be used as foods, require an altered use of herbicides or pesticides or are to be used therapeutically.

Regulation of products that are likely to pose little or no risk compared to conventionally produced products is counterproductive and not in the public interest, as well as being inefficient and uneconomical. It ultimately disadvantages Australian consumers and producers through loss of access to new products or traits. Companies that can commercialise those products in other countries will withhold those products from any Australian markets if the regulatory overhead was seen as too high. The emphasis of regulation should be placed on the potential of modified organisms to harm human health or the Australian environment rather than the process by which they were achieved.

The Academies recommend either a change in the triggers for regulation or specific exemptions for classes of gene edited organisms that pose minimal risk to health or the environment compared to wild-type organisms or existing genetically modified organisms.

4. Do these applications of gene technologies present unique issues for consideration? If so, how might these issues be best addressed by the Scheme?

The new gene technologies discussed in the Consultation Paper are synthetic biology, gene drives and human germline gene therapy.

The existing process-based regulatory scheme of Contained and Licenced Dealings has proven to be sufficient to manage the sort of gene technology research now taking place in Australia. There is public confidence in the current process. At a laboratory level, all applications of gene technology involving the use of recombinant DNA, regardless of their intended outcomes and including gene editing, should remain as Contained Dealings under the oversight of the Gene Technology Regulator and Institutional Biosafety Committees (IBCs) of accredited institutions, so that they are transparently documented. Novel organisms generated through synthetic biology and gene drives should be captured within the existing framework through notifiable low-risk dealings and dealings not involving intentional release (NLRDs and DNIRs) as proposed in the recent Technical Review of the Regulations. Where there is some risk identified that containment may be more difficult, or where there is uncertainty around the risk to human health or the environment of the organisms being generated then IBCs would seek advice of the Regulator as is the case at present, and a higher level of scrutiny and containment could be required. Where there are any gaps in coverage these should be addressed through appropriate modifications to the definitions in the Act so that they can be dealt with under the existing regulatory scheme of DNIRs, and appropriate guidance provided to the IBCs.

Issues with the current process-based Scheme and new technologies only arise when there is an intention to release modified organisms into the environment, either as a limited and controlled release for trialling purposes or a commercial release. At this point, a product based approach may be more relevant than the present process-based approach, and better able to capture and manage the risks posed by both old and new technologies. The risks presented by a gene edited plant capable of surviving only within a domesticated setting and unable to exchange genes with other plants are clearly distinct from those involving a radically altered or completely new organism, or from organisms containing gene drives intended to control pests. Continued case-by-case assessment of novel technologies and organisms should occur until there is sufficient scientific certainty before they are released into the environment.

It should be noted that “synthetic biology” is a broad term, and there are a number of applications that would be appropriately considered as exempt dealings, or are outside of the Gene Technology Scheme as a whole. Rather than attempt to encompass the synthetic biology field as a whole, the Regulator should include genetic modification applications of synthetic biology within a watching brief, as part of a continuous assessment approach to the evolution of genetic technologies.

5. What are the potential implications of the release of a GMO targeting an invasive species in Australia?

6. What are the technical issues to consider in the scenario of a GMO used to target an introduced plant, vertebrate or invertebrate pest?

Australia has many invasive species—plant, insect and animal—that currently require control measures, with varying degrees of effectiveness and expense. New gene technologies (particularly gene drives) are being developed that may have an advantage over existing chemical and biological control measures, and these warrant investigation by Australian researchers. However, as in all ecosystem level control measures a careful approach should be taken, given the known and measured impacts of failed or poorly considered approaches. The introduction of the cane toad is often held up as a salutary example, but this is but one example of a deliberate or accidental release of an organism into the Australian environment with disastrous consequences.

It is expected that there would be both community support and community concern around gene technology approaches, particularly in relation to gene drives, and these need to be accommodated within the Regulatory Scheme. On a technical level, driving organisms to extinction will be difficult and take time, as well as proving ultimately to be unsuccessful: there are already concerns populations can respond to gene drives and evolve to overcome them. Multilevel approaches have the highest chance of controlling feral animal or weed populations, meaning that gene drives should be regarded as one of several tools available to environmental managers. Across-government co-ordination will be critical in ensuring the benefits of gene drives are realised.

The predicted expansion in the use of gene drives for the control of feral pests and disease vectors may challenge the existing expertise of the OGTR and its advisory bodies, the Gene Technology Technical Advisory Committee (GTTAC) and the Gene Technology Ethics and Community Consultative Committee (GTECCC). An increase in representation of specialists grounded in population biology and ecosystems sciences would be appropriate. GTTAC's watching brief on emerging technologies should be accompanied by the power to trigger a review of the Gene Technology Regulations in specific areas when necessary, with a maximum review period of three years.

Theme 2 - Regulatory Issues

1. What do you think is the most appropriate regulatory trigger for Australia in light of extensions and advancements in gene technologies?

The most meaningful trigger for the regulation of organisms modified by gene technology would be the presence in the organism of novel DNA from outside the natural genetic variation of that species. This might be extended to the genus or even family level, for simple gene editing applications of accelerated breeding or domestication, exempting them from regulatory requirements. The trigger might then also be tempered by other factors including the history of use of the species in human activities (is it domesticated and well-characterised, for example, and is it therefore predictable in its behaviour?), the difference in functional attributes (intended or unintended outcomes of modification) of the modified organism relative to its unmodified parent, and the environments or ecosystems into which it will be released. All of these factors may alter the level of risk and potential impacts of the organism and hence the need for control measures to mitigate those risks.

This would allow, for example, new species to be brought into agricultural production more rapidly by editing their genomes to manipulate many of the key 'domestication' traits or genes such as non-shattering seed pods, larger fruits or seeds, or day length insensitivity. These traits have historically been modified by selection of our key crop and animal species. Gene editing could potentially be used to make those changes in a single generation, and hence circumvent decades of breeding. This could provide substantial benefits without imposing any undue risks to health or the environment.

2. What factors need to be taken into account in the design of a product-based or a hybrid process/product regulatory scheme?

The design of a product-based or a hybrid process/product regulatory scheme should be efficient and agile both in progressing existing types of GMOs and organisms produced through the new genetic technologies to move into agriculture and food production or human and animal diagnostics and therapeutics. Such products potentially offer considerable economic and social benefits and will keep Australia competitive with other global producers.

Within Australia, this could be achieved through:

- Maintaining the primary focus on assessing and managing the risks and hence potential impacts on human health or the environment of any research in the laboratory, from small scale releases into the environment, to large-scale contained production and commercial release involving products of gene technology, as contained in the *Gene Technology Act 2000*.
- Being practical and not imposing an unreasonable administrative or financial burden on practitioners that would otherwise inhibit new technological developments and hence loss of potential benefits that genetic modification might bring to Australian consumers and the Australian environment.
- Continuing to empower the Regulator with sufficient legal powers of enforcement to ensure that gene technology research is carried out safely according to best practice. A history of the safe, large scale global use of many of the early products of gene technology—now over twenty years for many genetically modified crops, vaccines, medical products and food additives—means that it is appropriate for the Scheme to evolve. This history provides a sound basis from which the Scheme can be simplified and/or devolve some of its oversight functions to organisational IBCs in

cases where the risks are likely to be low. The Regulator can focus on activities with higher risk and that have a greater need for scrutiny.

- Further devolving responsibilities from the OGTR to existing advisory bodies. Institutional Biosafety Committees (IBCs), for example, are an underutilised resource of expertise that could take over some of the roles of the OGTR in assessing and authorising low risk Dealings Not involving Intentional Release (DNIR) and Dealings involving Intentional Release (DIR) activities, such as small-scale field releases of well-studied GM crop plants. This would free up resources within the OGTR to focus on medium and high risk gene technology activities.
- Assigning a more defined role to the Gene Technology Technical Advisory Committee (GTTAC), particularly in advising on advances in gene technology and their need for regulation. GTTAC could be tasked to be proactive in examining new technology developments and empowered to initiate a review of the regulations in specific areas when necessary, with a maximum review period of three years.
- Referring to international experience. Experience from the Canadian regulatory system highlights two key issues that would need to be addressed to successfully transition to a product-based trigger:
    - Such a change would mean that researchers, product developers and manufacturers who do not currently need to comply with the gene technology regulatory scheme would be regulated under the new system. Hence a comprehensive education strategy would be required to ensure that they were made aware of any new obligations.
    - The process-based trigger for the Gene Technology Act was predicated on the assumption that rDNA technologies were inherently more dangerous than conventional technologies. This was based in large part on experience with the latter's safe use accumulated over time, and some applications of gene technology have now acquired a similar level of confidence. Hence, it would be important to carefully design exemptions that ensure that modifications and modified organisms with this safe history of use are not subjected to unnecessary oversight.

3. Are there any 'fixes' the scheme needs right now to remain effective?

4. How would you streamline the existing scheme?

5. What efficiencies could be gained through adjusting the interface between the Scheme and other regulators?

There is a need to implement a responsive and efficient regulatory framework that can address changes in gene technology as they occur, minimising market inefficiencies and recognising the pace of change in the sector.

The Australian regulatory framework for gene technology was established at a time when the technology was new, the risks were poorly defined, and there were few commercial products. Consequently, the focus was on ensuring the safety of new work in research facilities and tightly controlled small scale field trails and provided only limited scope for revision of risk assessment and risk management processes as knowledge and experience grew.

Hence, a significant limitation of the current regulatory scheme is the structure of the Act, which proscribes detailed procedures and time frames for all aspects of the regulatory process that are not always commensurate with risks to public health or the environment. This level of proscription was an important intention of the original legislation, largely to give the public confidence in the regulatory scheme (one of the most transparent in the world) and to provide industry with a clear,

nationally consistent pathway to obtaining regulatory approvals. However, history has shown that the bulk of the research undertaken by Australian government agencies, universities and SMEs does not warrant such a level of oversight. Institutions find that the conduct of their research, certification of facilities and reporting are inhibited by regulation, which in turn inhibits innovation and the commercialisation of products that would benefit the Australian economy.

As an example, the Act very precisely defines timelines and triggers for assessment and management of risks, but is unable to take into account the track record of existing genetic modification products. This means that a new application for a small scale field trial of, for example, a modified cotton with only modest changes to its genetic structure would require the same documentation and approval process as a wholly novel organism, including public consultations, licencing and field trials. This in turn creates an erroneous impression for the public that a safe, predictable modified crop carries a large potential danger.

Increasing efficiencies in the legislative framework can be achieved by:

- Developing an exemption (or notification) model for organisms containing genetic modifications that are indistinguishable from those that can be made using conventional breeding, natural mutations or mutagenic techniques with a history of safe use.
- Introducing a streamlined risk assessment process for low risk DNIRs and field trials with well-studied GMOs that devolves responsibility for assessments and authorisations to IBCs.

6. What support exists for a regulatory framework providing for tiered risk?

7. What examples exist of licence applications to the Regulator that could be 'fast-tracked', under a risk tiering system, with evidence of scientific and technical integrity that the aims of the Scheme (protection of human health and the environment) will be delivered?

8. Under a regulatory framework to tier risk for environmental release, what efficiencies might be delivered to regulated stakeholders?

Most practitioners of genetic modification, particularly in the agricultural sector, would support a simpler scheme of approvals especially for small scale testing of genetically modified organisms. Such tests are critical components of the proof-of-concept research that generates data necessary to take a product further and attract investment for further development and commercialisation. The current regulatory scheme, while appropriately rigorous, is also relatively inflexible, presenting an impediment to both government and university sector researchers, and certainly prohibitive for any small Australian start-up company.

As proposed earlier, a notification system or separate tier for low risk releases, particularly in well characterised crop plants, would be desirable. This would still need to be administered by IBCs, with a requirement to report to the Regulator. The IBCs and researchers would be subject to random audits of trials to provide public confidence in the veracity of the system. Efficiencies would be gained both by the research organisations (who would no longer require dedicated regulatory compliance officers) and the Regulator, who would no longer need to directly assess proposals for release of organisms with little or no risk to human health or the environment.

Commercialisation of genetically modified organisms would still need to be assessed separately, preferably with a product-based trigger when appropriate. This would enable the commercial approval process to be streamlined based on past experiences with particular organisms, while maintaining public confidence in the process.

10. What justification is there to regulate animals, plants or microbes differently?

11. In what way might different applications be treated differently (e.g. medical, agricultural, industrial, environmental, etc)?

Many genetic modification applications in crops rely on precise genetic changes to enhance or turn off specific genes or functions in plants. There is sufficient experience with these types of organisms to support a more relaxed regulatory scheme, certainly at the trial or data gathering stages of research and potentially even with commercialisation. This easing of the regulatory burden would encourage Australian innovation in a key industry, enhance the use of gene technology in basic research and allow GM products from overseas to be properly evaluated under Australian conditions prior to Australian business or government investment in those products. Oversight by a relevant and accredited IBC and a requirement for reporting should be maintained, particularly of any unintended effects. The Regulator should continue to randomly audit records and compliance with trial guidelines developed for those releases. This should be sufficient to provide public confidence in a streamlined system for small scale field evaluation for some types of domesticated organisms.

Regulatory oversight of commercial releases of gene technology products could likewise be simplified in some cases, such as products similar to those already on the market, or products with a history of safe use elsewhere in the world. These will still need to be approved by other relevant agencies depending on their intended use. An example of an opportunity for efficiency for the Regulator can be demonstrated in the recent commercial approval for the VIPCot 102 transgenic cotton event produced by Syngenta (DIR157). This product went through an independent approval process despite having already been approved for commercial use as part of Bollgard III cotton (a three insecticidal gene GM that included the COT102 event) currently used on hundreds of thousands of hectares throughout Australia. This was a technical issue to allow the sale of Bollgard III cotton products into some overseas jurisdictions, and consumed a considerable amount of resources within the applicant organisation and the OGTR. A more flexible regulatory scheme would have allowed that approval to be fast-tracked.

Genetically modified animals are still a relatively new phenomenon. Until some products are widely and safely used in agriculture or food production then it may be too early to reduce regulation on those organisms. As experience accumulates with modified animals, however, our regulatory scheme should be structured to enable the level of oversight to be modified over time.

Genetically modified microbes should be regulated on a case by case basis, depending on the nature of the modifications and the intended exposure to the environment. For example, broadcast treatments with GM microbes for environmental remediation or enhancements of agricultural production would need to be evaluated differently to well-characterised micro-organisms intended for use in foods or food manufacture, noting that such applications would also trigger regulatory oversight from other regulators such as the FSANZ, APVMA and TGA.

12. How might the Scheme accommodate the DIY-biology movement?

The DIY biology movement, and other non-institutionally based synthetic biology practitioners, represent a significant challenge to regulators in that they are outside the communication channels normally used to convey information about regulatory obligations and processes. In this, they are somewhat similar to the currently unregulated community that would need to be informed if product-based triggers were introduced. Again, a specific communication strategy and clarity regarding what activities are subject to regulation would be essential.

14. What opportunities are there for principles-based regulation in the Gene Technology Scheme? What advantages could be gained from doing this? What drawbacks are there from such an approach to regulation?

In essence the objective of Gene Technology Act itself provides an appropriate principle for the regulatory scheme, as the required outcome is to protect the health and safety of people and the environment by identifying and managing risks posed by or as a result of gene technology. A major advantage of adopting principles-based regulation would be to provide the Regulator with greater flexibility to, for example, streamline regulatory processes in the light of operational experience and enhance 'future proofing' by being able to respond to new issues and developments without needing to create new rules. The potential drawbacks include a lack of clarity and increased uncertainty on what is required to ensure compliance for those who are subject to regulation.

16. What are the potential impacts on market access for exporters of animal or plant derived food products?

While some impacts are likely on, for example, exports to Europe or other jurisdictions that are opposed to GMOs, such impacts should be assessed at an industry or government level. The Regulator should focus on health and environmental impacts. Generally, the market will decide such issues: Australian growers have found it more economic to grow GM cotton, for example.[6]

Regulatory harmonisation with external jurisdictions is essential to prevent inconsistences and to encourage access to new technologies from overseas for Australian farmers and consumers.

[6] Cotton Seed Distributors, the sole supplier of cotton seed in Australia, sold 16 x 20 kg bags of non-GM cotton seed in 2016. Gross seed sales were 6,700 tonnes (CSD Annual Report, 2017).

Theme 3 - Governance Issues

1. What will reassure the Australian public and regulated communities of the integrity of the Scheme?

Australia is acknowledged internationally as having one of the most rigorous and transparent regulatory schemes. Any changes will need to maintain and grow public confidence, with information related to the regulatory oversight remaining accessible, such as on the internet.

The Regulator should continue to have a monitoring and compliance role, and the strong legislative powers of enforcement to complement any reforms to assessment processes. IBCs currently perform an important role in the management and record keeping around low risk contained laboratory activities; their functions could be extended to low risk small scale releases of genetically modified organisms without compromising confidence in the Scheme.

2 What mechanisms could address the challenges that making changes in the Scheme might entail:

- **Domestically–across a federated government system experiencing different political agendas and community sentiments?**
- **Internationally–relating to other agreements, trade agreements, and harmonised regulatory approaches?**

The Academies support the nationally consistent approach to regulation provided by the intergovernmental Gene Technology Agreement, and support continued efforts to ensure that there is clarity in the regulation environment. Effective communication between State and Federal agencies and with stakeholder groups will help reduce politicisation of the regulatory process.

As noted above, regulatory harmonisation with external jurisdictions is essential to prevent inconsistences and to encourage access to new technologies from overseas for industry and consumers.

3. What principles should guide the level at which a decision is made within the Scheme?

4. Does reviewing the Scheme every five years best address the needs of the Scheme? Is there a preferable option?

The pace of technological change is now faster than it is reasonable to expect any rules-based legislative system to respond to. The embedding of prescriptive definitions, timelines and processes for the Regulator in the Gene Technology Act precludes frequent review and prevents agile change. This would be supported by introducing a continuous assessment approach to the evolution of gene technologies, such as requiring GTTAC to maintain a continuous assessment of emerging technologies and empowering it to trigger a review of the regulations in specific areas when necessary.

This would also allow creation of processes for amending definitions, providing exemptions from regulation, or adapting to new technologies, which are under the aegis of the Regulator (with suitable advice from its advisory bodies.

A number of regulatory agencies are currently undertaking reviews of their governing legislation and their processes. This makes it an ideal time to ensure that there are consistent definitions and complementary regulatory processes, and to ensure that all potential new applications are

appropriately captured by the relevant agency. It is also an appropriate time to ensure that there are harmonised data standards across those agencies so that common data sets such as those on efficacy, toxicity, allergenicity can be shared between agencies and reduce the burden upon applicants caused by different data standards.

5. Is the existing role of the Forum the most suitable way of providing oversight and guidance for the Scheme?

6. What criteria should be used to determine what legislative amendments are minor and could be progressed without going to the Forum?

As the Scheme is underpinned by complementary Commonwealth, State and Territory Legislation, and the Legislative and Governance Forum comprises ministers appointed by their respective jurisdictions, this appears to be the most appropriate way of providing oversight and guidance for the Scheme, despite being somewhat resource-intensive. The group of officials that supports the Forum could potentially act collectively on behalf of their respective governments to determine, and potentially authorise minor legislative amendments.

10. Are existing mechanisms, when used effectively, sufficient to ensure the emerging health, environmental and manufacturing benefits of gene technology that were not anticipated at the establishment of the Scheme, can be harnessed for Australians?

11. Should other policy principles be developed that are tailored to horizon technology management? What other factors could be considered in the regulatory decision?

As stated in the response to other questions, the key deficiencies of the current Scheme are in its lack of capacity to modify its processes in the light of additional knowledge, and in its lack of ability to respond to technological developments outside of its legislated definitions. The first issue leads to over-regulation of technological applications that are known to be safe, which raises the costs of developing and commercialising these applications and slows their entry into the market. The second issue creates uncertainty around whether these new technological developments are included in the scheme, which also presents an impediment to developing and exploiting the technology.

The Academies strongly support a flexible policy arrangement which allows the Regulator, with appropriate advice, to respond flexibly to unanticipated developments in technology.

The Academies consider that regulatory decisions should continue to be science based. The consideration of benefits would risk compromising the integrity of the Scheme and undermine confidence in the achievement of the objective to protect the safety of people and the environment. Consideration of benefits is more appropriately considered in the context of efficacy which is rightly within the purview of the product approval agencies.

14. What aspects of gene technology would benefit from greater policy position clarity?

15. What other mechanisms would provide suitable policy clarity that would enhance the Scheme and support compliance?

The Academies support efforts to provide policy clarity for the Gene Technology Scheme. The Regulator might consider targeted materials to provide specific guidance to different audiences: academic, agricultural, or medical. This may take the form of decision trees that would guide applicants on the right paths and regulatory data required to obtain the approvals required for research and to commercialise their products.

16. What are the pressure points at the boundaries between regulatory schemes that are caused by regulatory gaps or overlaps?

17. How can existing coordination functions be utilised more effectively to support the Scheme to be agile and facilitate transitions across regulatory framework boundaries? What other activities would enhance this?

Proactive information exchange on relevant applications, as well as opportunities for regular interaction to provide updates on the progress of assessment and discuss issues of common interest, would be of value in enhancing coordinated decision making.

Care should be taken to avoid duplication of regulatory effort in respect to clinical trials. There are significant regulatory requirements for the development of human therapies; there are opportunities for streamlining the process in places where these requirements overlap with those of the Gene Technology Scheme.

19. How could some aspects of the Scheme be funded through other mechanisms that will support innovation and competition in gene technology, whilst retaining public confidence in the Scheme?

Streamlining regulation with respect to applications known to be safe will provide efficiencies for the Regulator. Devolving some Regulator functions to accredited IBCs will mean host institutions have a greater support role for the Scheme. The Australian biotechnology sector is largely driven by government, medical research institute and university researchers. The private sector is too small to support a user pays system for gene technology regulation. In addition, such systems are often viewed with some cynicism by the community, as they can fuel negative perceptions of corporate involvement with gene technology. Accordingly, to maintain the integrity of the Scheme, the Australian Government should continue to fund the OGTR.

Theme 4 - Social and Ethical Issues

1. **How do we help the community to best understand the benefits and risks of a complex, science-based technology?**
2. **Where does the community have confidence in the gene technology regulatory scheme? How can this be maintained?**
3. **Where is there a lack of community confidence in the gene technology regulatory scheme? Why might this be, and how can confidence be built?**
4. **What does the public need to know?**
5. **Who is best placed to provide that information?**

The Regulator operates in a transparent manner, with thorough and accurate communication around its complex subject matter. This is essential for public trust in the Regulator, and helps build public trust in the sector as a whole. This would be supplemented by raising general awareness of the Regulator, the OGTR, and the Gene Technology Scheme.

The Regulator could usefully consider expanding its series of fact sheets with a suite of technology explainers looking at the details of genetic modification, as well as its applications and uses. This would supplement the OGTR's communications about its own functions. However, the OGTR may wish to have this information provided at arm's length from its official functions, as it could create a perception of advocacy for the technology that may call into question its objectivity. In that case, the information should come from trusted organisations such as the CSIRO or the Learned Academies, or from government agencies such as the Departments of Health, Agriculture, or the Environment.

Confidence in the Scheme is increased by transparency and visible fairness. It is essential for the obligations and responsibilities of producers of genetic modification technology to be made clear. This includes clear information about the consequences of acting outside of the regulatory scheme, violating licencing determinations, or otherwise acting illegally with respect to gene technology.

It is important to work with the community in relation to the status of gene technology and the role of the regulator in ensuring processes and outcomes are safe both for the public and for the environment. This is important in the context of the potential international consequences of having such a rigorous regulatory scheme in Australia. The health and safety as well the environments of developing countries may be disadvantaged by these countries adopting a highly prescriptive system modelled on Australia's. Recognition that certain genes that have been used safely in crops for several years would mean that they could readily be granted the equivalent of an exemption status, making them easier to regulate and use in other jurisdictions, particularly in humanitarian situations.

6. What does the public need in order to accept the increasing availability and range of use of gene technologies?

7. What does the public need in order to determine whether to provide social licence for the adoption and embedding of gene technology into the culture, lifestyle, economy and health sector?

8. What are the ethical considerations for enabling access to medical treatments?

It is important that the public understands and accepts the safety and utility of gene technologies. Transparency, clarity and consultation are key drivers of public understanding and acceptance. In calling for the rationalisation of regulation of "safe" technologies, the Academies understand the ultimate arbiters of the acceptable level of public and environmental safety are not the practitioners of the technology but rather the public.

It is also important the public understands that the risks of genetic technology are appropriately managed, that regulation of the technology holds human health and environmental concerns to be paramount, and that there are clear penalties for breaches of the regulations.

The question of adoption and embedding of gene technology into the culture, lifestyle, economy and health sector, including ethical considerations for enabling access to medical treatments, is the responsibility of all stakeholders. However, in general the acceptability of new technologies is strongly influenced by perceived relevance, which can vary widely between individuals, and confidence in the provider. Surveys consistently show that the public is generally more accepting of gene technology with respect to medical treatments and human health. This extends to genetic therapies, assisted by the ease with which their effectiveness can be demonstrated in a readily comprehensible manner; the consequences of not applying the technology are similarly clear.

9. How do we ensure that information is available to the community on the value of GM and what it can do? Who is responsible for providing this, and why?

10. Is the Scheme putting up barriers to research and development and commercialisation of agricultural applications?

Under its legislation the Regulator is responsible for protecting human health and the environment. However, in assessing the risks of the technology, the Regulator should also be mindful of the benefits; it may be useful for the Regulator to include fact sheets about general applications of the technology for context in its communication.

At present, the Scheme represents some impediments to agricultural applications, chiefly those involving well known and well characterised domesticated organisms. Some laboratory based research would also benefit from some requirements being streamlined. These impediments have been discussed at length in this submission. However, the Academies strongly support the National Gene Technology Scheme and look forward to further constructive engagements with the Department and the Regulator.

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