AUSTRALIAN ACADEMY OF TECHNOLOGY AND ENGINEERING
AUSTRALIAN ACADEMY OF SCIENCE
JOINT SUBMISSION TO THE
REVIEW OF THE NATIONAL GENE TECHNOLOGY SCHEME 2017

The Australian Academy of Technology and Engineering (ATSE) and the Australian Academy of Science (AAS) welcome the opportunity to participate in the Review of the National Gene Technology Scheme (the Review).

The Academies consider that accrued experience with gene technology, combined with experience with a diverse range of genetically modified organisms, and the increasing sophistication of the technology, may justify moving to legislation that provides regulation based on the products and outcomes of technology applications rather than on the technical process used to achieve them. However, in view of the complexity and extended time frame that would be involved in changing the 'trigger' for the regulatory scheme, the Academies recommend that the focus of the current review should be 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 system to continuously respond to emerging technical developments.

Key points to facilitate this are as follows:

1. Improve efficiencies in the legislative framework to provide clear and transparent processes for exempt dealings, including the introduction of notifications for small scale releases of technologies with a history of safe use.
2. Introduce a continuous assessment approach to the evolution of gene technologies that would enable the legislative framework to adapt appropriately to new types of genetic modification without requiring frequent legislative amendments.
3. Ensure that definitions, and risk and containment categories for gene technology research are clear and consistent with the known level of risk based on accumulated experience both nationally and globally.
4. Give synthetic gene drives special consideration, based on their potential to rapidly spread genetic change throughout a population.
5. Provide funding models that do not hinder innovation in the public sector or prevent Australian SMEs from gaining access to competitive technologies available in other countries.

1. Opportunities for Australia

Genetic modification technologies provide Australia with considerable opportunity to participate in global biotechnology. While our legislative framework is well respected internationally it can, nevertheless, present challenges to full engagement in these emerging markets, in some cases presenting a significant barrier to entry. Small firms, and most publicly funded research institutions, have found it difficult to bring genetically modified organisms to market. The high cost of taking such products through the Australian and global regulatory systems that have developed over the last 20 years means that only the largest and wealthiest multinational firms have been able to do so. Improvements to, and

simplifications of, the regulatory framework will assist government researchers and industry to enhance their competitiveness in this important area of innovation.

For example, the costs associated with commercialising a genetically modified (GM) crop, are significant (representing as much as 25% of the total cost of bringing it to market[1]). High regulatory costs on products of new, improved technologies, such as gene editing, would impose a significant financial burden on developers and disadvantage the broader community by limiting access to the beneficial traits of the crop and does not reflect the risk. Likely negative impacts of such over-regulation could include:

- Disadvantage to Australian agricultural supply chains due to failed delivery of technologies that would have provided significant productivity gains or enhanced global competitiveness.
- Under investment in minor species of national interest (e.g. ryegrass, tall fescue, white clover) with loss of productivity benefits from new technologies for growers as GM technology has mainly been used in major field crops.
- Exclusion of Australia as a target market by 'seed and traits' life sciences companies in preference for larger markets and regions where these products are not regulated as GM.
- Hindrance of innovation and opportunity cost of technologies, since only those products that are likely to repay the high cost of bringing them to market are expected to succeed.
- Further consolidation of the overseas seed industry as high regulatory costs discourage small companies and public sector organisations from engaging in the development and commercialisation of GM crops.

Furthermore, products developed using new technologies that have significant socio-economic, environmental, and/or health benefits may not be realised if their development is inhibited by regulation that is not commensurate with risk.

It is critically important that the regulatory system continues to be based on scientific evidence and best-practice regulatory principles, is transparent and consistent, proportionate to risk, ensures that the benefits of regulation outweigh the costs and risks it imposes, and is practically enforceable.

2. Increased efficiencies in implementing the legislative framework

As gene technology continues to develop improved techniques are emerging that provide reduced timeframes and greater precision for genetic modifications. Efficiencies in the legislative framework could be increased with an exemption model for work with modifications are indistinguishable from those that can be made using conventional breeding, natural mutations or mutagenic techniques. Where risks are significantly greater for new technologies, these should be identified and appropriately managed. However, the risks

1 Phillips McDougall (2011) The cost and time involved in the discovery, development and authorisation of a new plant biotechnology derived trait. Crop Life International.

to the environment or human health posed by many of the products developed (or being developed) using the majority of new gene technologies are comparable to those of earlier breeding methods that have historically been accepted without a need for regulation. As articulated in the Academies' submission to the review of the Gene Technology Regulations 2001[2], organisms produced by techniques that are analogous to natural mutagenesis, i.e. oligo-directed mutagenesis (ODM), SDN-1 and SDN-2 present the same risks as those developed using conventional breeding methods.

Further, the introduction of a simplified regulatory process that enables the release of trait/organism combinations with a history of safe use to be fast tracked through a streamlined risk assessment process would improve efficiencies and outcomes for researchers.

The case study below illustrates that regulatory efficiencies may be achieved by reducing the level of regulatory oversight during the research and development phases. This would in turn allow technologies to be evaluated under Australian conditions so that they can attract further investment or provide data for subsequent commercialisation:

Case Study: Simplifying the approval process for Field Trials with a well-proven GM crop - Cotton

Cotton (*Gossypium hirsutum* L.) is an important economic crop for Australia and the fibre earns up to $2 billion in exports annually (the area grown varies between 300,000 and 550,000 hectares depending on water availability). Cotton is a progressive industry - because of its high production costs it was the first major agricultural industry in Australia to adopt gene technology for enhanced pest and weed control. The first commercial release of a GM cotton occurred in 1996. Currently, most of the crop is GM. The added traits include resistance to caterpillar pests utilising genes for insecticidal proteins from *Bacillus* species and herbicide tolerance genes that confer altered herbicide binding properties. The GM traits were deployed under license from Monsanto and Bayer CropScience and bred into highly adapted and high yielding varieties produced by CSIRO. The new cotton varieties were commercialised through an Australian owned cotton seed company, Cotton Seed Distributors.

Background

Commercial release was achieved only after many small and medium scale field trials over 25 years under Dealings involving Intentional Release (DIR) Licenses from the OGTR and authorisations from its predecessor, the Genetic Manipulation Advisory Committee.

2 Joint submission to the Office of the Gene Technology Regulator Discussion Paper: Options for regulating new technologies, December 2016 (https://www.atse.org.au/Documents/submissions/options-regulating-new-gene-editing-technologies.pdf)

These provided the research needed to establish measures for the effective containment of the traits during early development (size and nature of pollen buffers, separation distances from other trials etc.) and to test resistance management strategies (refuge crops, pupae busting etc.) required by the Agricultural Pesticides and Veterinary Medicines Authority to ensure the longevity of the traits once commercially released.

Of the 157 DIR Licences issued since the Gene Technology Act was passed into legislation, approximately 50 have been for cotton and 11 of those have been for commercial production of insect and herbicide tolerant GM cotton (with several more carried out under GMAC).

As a government agency, CSIRO has had 15 approved DIR Licences and several Planned Releases prior to the introduction of the current regulatory system so have been a large user of the regulatory system. More recently CSIRO has acted under Licences issued to the technology providers, such as Monsanto, Bayer and Syngenta, to simplify the number of Licences needing to be assessed and issued, but has been responsible for the conduct of all of its own breeding and evaluation trials under those licences. Many of the releases (often at several different geographical sites each year under each Licence) were for the testing of the insect and herbicide traits now being used commercially, but also numerous experimental traits for enhanced product quality (longer fibres, higher yields or altered seed oil composition) for tolerance to diseases or environmental extremes stemming from Australian research efforts.

Regulatory inefficiencies

25 years of field testing, however, has not changed the level of assessment and timeframes required to conduct small scale field testing of a new GM cotton. A small scale field test still needs the preparation of a 50 page descriptive document and a lengthy prescribed assessment period for the preparation of a Risk Assessment and Risk Management Plan (RARMP), public consultation and advice sought from the Gene Technology Technical Advisory Committee (GTTAC) and other committees and agencies that overall still takes several months from application to approval. With the accumulated experiences of many hundreds of individual trials over the last 25 years the RARMP and detailed Licence Conditions specified for any GMO cotton trial involving simple GM traits now varies little, if at all. This process represents inefficient use of the resources within the OGTR.

Recommended improvements to regulatory processes

Regulatory processes could be considerably simplified and sped up if Australia were to adopt a system of notification for small scale field testing of specific classes of GM traits and crop species, similar to that used in the United States

Such a system could be administered by relevant Institutional Biosafety Committees (IBCs) who have the local knowledge and expertise to assess applications for such trials, with the OGTR still be able to trigger a full or more streamlined risk assessment after notification of the intentions of an institution to conduct such releases.

New traits being evaluated may also arise from overseas research, but there is now sufficient experience with the biology of major crops that field testing them in Australia is unlikely to generate any different risk scenarios than they would have encountered overseas. Crops with such traits should not require a detailed assessment, provided they meet specified guidelines for small scale release. Once any GM trait has proven itself in small scale testing, any large scale testing or commercialisation would need to trigger a full-scale assessment by the OGTR and other agencies.

Crop plant DIRs represent the bulk of the administrative activities of the OGTR in terms of assessment and compliance monitoring. The situation with cotton is beginning to arise with other crops, such as canola, and will eventually affect work with GM wheat, barley and sorghum.

3. Ensure a responsive and efficient legislative framework

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 system 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 system (one of the most open and 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.

A more efficient regulatory system could be achieved by 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 should free up resources within the OGTR to focus on medium and high risk gene technology activities.

The Gene Technology Technical Advisory Committee (GTTAC) could also have a more defined role, 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.

4. Clear and workable definitions and risk and containment categories

An agreed and workable definition of the integration of 'foreign' nucleic acid is necessary. The Academies suggest an acceptable definition to be 'non-homologous DNA sequences from non-sexually compatible species'. Special consideration should continue to be given to the modification of genes that affect the virulence, spread or impact of pathogenic or pest organisms, and/or may be subject to Dual Use Research of Concern considerations.

Further, risk and containment categories specified in the Act need to be reviewed and adjusted in the light of experience. While the Regulations must continue to be based on scientific evidence and best-practice regulatory principles, we now have over thirty years of experience both in Australia and overseas on the conduct of "conventional" gene technology research in many species of plants, animals and microbes. It is now appropriate to re-evaluate the level of risk that those technologies pose to human health and the environment, in both contained and uncontained situations, and hence the level of regulatory oversight required.

All plant GMO research, for example, is designated as requiring PC2 containment. However, prior to flowering, and in many cases even post flowering, there is little risk of "escape". In most situations, these plants represent no greater risk to human health or the environment than many exempt dealings such as working with standard laboratory microbes like *E. coli.* While standard laboratory/ glasshouse practices would still be applied, the removal of a legislated requirement for PC2 level standards could significantly reduce overheads for research organisations who currently invest heavily in maintaining and building new infrastructure to be PC2 compliant.

Similar situations are likely to apply to other areas and research classified as DNIRs because of the volumes of organisms being cultured may, in the light of experience, be downgraded to Notifiable Low Risk Dealings without increasing risks to health or the environment.

4.1 Synthetic Gene Drives

A recent AAS discussion paper on the implications of synthetic gene drives for Australia found that while they have the potential to solve intractable problems in public health, environmental conservation and agriculture; they may also have the potential to cause negative environmental and human health effects[3].

Accordingly ATSE and AAS are of the view that regulation of gene drives requires special consideration as it is difficult at this early stage of research and development to predict the outcomes of deployment, given their potential to spread genetic constructs rapidly throughout a population and produce genetic and ecological changes in target and non-target species.

3 Synthetic gene drives in Australia: Implications of emerging technologies, Australian Academy of Science, June 2017 (https://www.science.org.au/support/analysis/reports/synthetic-gene-drives-australia-implications-emerging-technologies)

Initial gene drive development will mostly involve laboratory-contained research and development projects. The appropriate level of containment will depend on the organism involved and the potential for the gene drive system being developed to spread and persist in the environment (e.g. drives with a high threshold for invasion and/or slow rate of propagation have different containment implications to drives that can rapidly spread from a low initial frequency).

5. Funding arrangements

The OGTR must be funded at a sustainable level to support the level of innovation currently underway in Australia. This funding should continue to be provided by government to ensure co-ordination between different regulatory agencies, for the following reasons:

- It is important that the OGTR is seen to be independent and unbiased, given public concerns regarding the use of gene technology.
- A user pays model would increase inefficiencies as the bulk of gene technology research and development is carried out within government funded agencies and teaching institutions so would only result in a cost shifting exercise.
- The small size of the biotechnology industry in Australia would not generate sufficient revenue at a reasonable level of fees and charges to recover costs. Any imposition of fees would only inhibit the commercialisation of GM products and would not be in the public interest.

6. Recommendations

The Academies consider that a valuable outcome of this review will be improvements to the regulatory model that streamline regulatory oversight to enable more agile responses to accumulated experience with existing gene technologies and to new technologies. These could include the following:

1. Increasing efficiencies in the legislative framework 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.

2. Introducing a continuous assessment approach to the evolution of gene technologies:
    - Require GTTAC to maintain a ‘watching brief’ on emerging technologies and empower it to trigger a review of the regulations in specific areas when necessary, with a maximum review period of three years.

3. Effective definitions, and risk and containment categories:
    - Introduce a definition of ‘foreign’ nucleic acid as ‘non-homologous DNA sequences from non-sexually compatible species’.
    - Examine the level of risk actually posed to human health and the environment in both contained and uncontained situations by the technologies that have been in use over the last 30 years and re-assess the level of regulatory oversight that should be required.

4. Giving synthetic gene drives special consideration:
    - Ensure that the risks gene drive technologies may impose on human health and the environment in both contained and uncontained situations are appropriately assessed and managed.

5. Funding models that do not hinder innovation in the public sector; prevent Australian SMEs from developing or gaining access to competitive technologies available in other countries; or discourage international commercial investment.

The Academies would be pleased to provide further information to expand on these views if required, and Fellows of the Academies are available to further assist the Review process. The relevant Academy contacts are Dr Matt Wenham, ATSE Executive Manager, Policy and Projects (03 9864 0926 or matt.wenham@atse.org.au and Dr Chris Hatherly, AAS Director, Science Policy & Projects (02 6201 9458 or chris.hatherly@science.org.au).