JOINT SUBMISSION TO THE OFFICE OF THE GENE TECHNOLOGY REGULATOR DISCUSSION PAPER: OPTIONS FOR REGULATING NEW TECHNOLOGIES

The Australian Academy of Science (AAS) and the Australian Academy of Technology and Engineering (ATSE) welcome the opportunity to respond to the Office of the Gene Technology Regulator (OGTR) *Discussion Paper: Options for regulating new technologies* (the Discussion Paper).

AAS and ATSE hold a shared view on the future options for regulating new 'gene editing' technologies, and submit a joint response to the Discussion Paper in support of this. Key points from the submission are as follows:

- AAS and ATSE support ***Option 4****: exclude certain new technologies from regulation on the basis of the outcomes they produce.*
- Regulations must be proportional to risk.
- In Schedule 1, 'foreign' nucleic acid should be further defined as 'non-homologous DNA sequences from non-sexually compatible species'.
- There is a need for a nuanced approach to regulations in relation to gene drives and RNA interference.

In addition to responding to the specific options and questions listed in the Discussion Paper, the Academies consider the regulatory framework should be developed with the understanding that:

- Extensive genetic variations have been introduced by a range of previously available breeding techniques that have historically been accepted without a need for regulation.
- Plants and animals modified using new technologies should not be differentially regulated if they are similar to, or indistinguishable from, those that could have been produced through earlier breeding methods (i.e. those exempted from regulation under Schedule 1A).
- The risks to the environment or human health posed by the products developed using the majority of new technologies are comparable to those of earlier breeding methods. Where risks are significantly greater for some new technologies, these should be identified and appropriately managed.
- New technologies are more targeted and precise than earlier, non-regulated breeding methods.
- Products developed using new technologies have significant socio-economic, environmental, health benefits that may potentially not be realised if their development is inhibited by regulation that is not commensurate with risk.
- All other relevant regulation should continue to apply.
- Beyond the generally applicable regulations, any additional regulatory oversight should be based on the risks inherent in the end-product, not the process used to develop that product as far as possible[1]; and
- Regulatory oversight should be science based, transparent, proportional to risk and politically independent.

1 AAS and ATSE note that the policy settings of the regulatory scheme cannot be considered in the technical review. The Academies believe there is a compelling case for the exemptions in the Gene Technology Regulations to focus upon the outcome/product rather than the process and that there should be careful consideration of changing the basis of the regulatory scheme in the same way in the upcoming review of the *Gene Technology Act*.

New breeding technologies (NBTs) provide a medium-sized country like Australia a renewed opportunity to participate in global biotechnology. At least partly in response to pressure from interest groups opposed to genetic modification, regulation has developed that has become a significant barrier to entry. Small firms, and most publicly-funded research institutions, have found it difficult to bring new genetically modified organisms to market. The high cost of taking new products through the Australian and global regulatory system which has developed over the last 20 years has meant that only the biggest and wealthiest international firms can currently do so.

The emergence and accessibility of NBTs now has the potential to provide a second chance at the scientific and economic rewards for small- and medium-sized businesses and medium-sized economies such as Australia, provided future regulatory arrangements do not suffocate innovation. In other words, it is economically and scientifically vital for Australia that future regulatory arrangements for new breeding technologies are strictly in proportion to real levels of risk.

Specific responses to the consultation questions are provided below.

Question 1: Which option/s do you support, and why?

The Academies share the objective of the Discussion Paper to reach a consistent approach to regulating new technologies. Both Academies consider that ***Option 4:*** *exclude certain new technologies from regulation on the basis of the outcomes they produce*, to be the most effective means of accommodating new, precision technology, without limiting innovation and further developments in this area, and that this option provides an appropriate level of regulation. It is critically important that the Regulations continue to be based on scientific evidence and best-practice regulatory principles. Best-practice regulation is proportionate to the risk being managed and consistent with measures already in place, ensures that the benefits of regulation outweigh the costs and risks it imposes, and is practically enforceable.

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The scientific community agrees that 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[2]. Mutation breeding has a long history of safe use and is not currently captured by gene technology regulation. By capturing only techniques that integrate foreign DNA, and excluding techniques that produce changes not considered to pose greater risks than conventional breeding, Option 4 provides regulation that is commensurate to risk.

Options 2 and 3 are not recommended since their implementation would impose regulation on techniques that are functionally equivalent to mutation breeding and make it possible that two genetically identical products could be regulated differently depending on how they were developed. This is an undesirable outcome for the industry, the public, and government.

Best practice regulatory frameworks also ensure that the benefits of regulation outweigh the costs and risks regulation imposes.
Because the risks of ODM, SDN-1 and SDN-2 to human health and the environment are no greater than existing mutagenic techniques, regulation is unnecessary. It is important also to note that compliance with gene technology regulation is costly. The costs associated with commercialising a genetically modified (GM) crop, are significant, representing as much as 25% of the total cost of bringing the crop to market[3]. Imposing this high cost unnecessarily is likely to impose a significant burden on users of NBTs and to disadvantage the broader community by preventing access to the beneficial traits of the crop. Likely negative impacts would include:

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2 European Academies Science Advisory Council. Statement. New breeding techniques. July 2015.

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

- Further consolidation of the seed industry as high regulatory costs discourage small companies from engaging in the development and commercialisation of GM crops[4 5]
- Under-investment in minor crops with loss of productivity benefits derived from NBT for growers as GM technology has mainly been used in major field crops such as maize and soybean[6]
- Exclusion of Australia as a target market by 'seed and traits' life sciences companies in preference for other larger markets.
- Hindrance of innovation and opportunity cost of technologies not brought to market, since only those products that are likely to repay the high cost of bringing them to market are expected to succeed.
- Disadvantage to Australian agricultural supply chains due to failed delivery of technologies that would have provided significant productivity gains.

Best practice regulatory frameworks must also be practically enforceable.
Option 4 poses fewer enforceability challenges than Options 2 and 3. Organisms produced by ODM, SDN-1 and SDN-2 may be indistinguishable from organisms arising from spontaneous or induced mutations. While these organisms can be detected with prior knowledge of the expected sequence changes, there is no way to demonstrate conclusively that they did not arise through a natural process, making enforcement unfeasible. In contrast, the stable integration of foreign DNA by SDN-3 techniques enables the attribution of sequence changes in the organism to an NBT.

Question 2: Are there other risks and benefits of each option that are not identified in this document?

The recommendation for Option 4 supported by the Academies is contingent on a workable definition of the integration of 'foreign' nucleic acid, with a suggested definition to be 'non-homologous DNA sequences from non-sexually compatible species'.

In addition, although Option 4 provides a practical approach for dealing with new breeding techniques, special consideration should be given to the modification of genes that do or may affect the virulence or fitness of pathogenic or pest organisms, or may be subject to Dual Use Research of Concern considerations. These considerations need not be effected through the Gene Technology Regulations and may be better handled via biosecurity and defence trade controls.

Question 3: Is there any scientific evidence that any of option 2-4 would result in a level of regulation not commensurate with risk posed by gene technology?

Random mutagenesis achieved via radiation or chemical exposure, where no foreign nucleic acid has been introduced, is already excluded from the Regulations through Schedule 1A. Organisms produced via ODM, SDN-1 or SDN-2 similarly involve modifications to endogenous gene sequences, albeit in a more targeted fashion. Given that these modifications can be achieved through the use of non-regulated techniques, the Academies support ODM, SDN-1 and SDN-2 being treated in a similar way. Advice from the GTTAC supports this position. In addition, as outlined in the Discussion Paper, it is not possible to distinguish between organisms produced by currently non-regulated techniques versus the new breeding technologies (where no foreign DNA has been introduced), making it impossible to enforce a system where these new techniques are regulated differently to existing techniques.

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4 Schenkelaars P, H de Vriend and N Kalaitzandonakes (2011) *Drivers for consolidation in the seed industry and its consequences for innovation.* Schenkelaars Biotechnology Consultancy for COGEM (report CGM 2011-11). Page 64

5 Dons H and N Louwaars (2012), Breeding business: *Plant breeder's rights and patent rights in the plant breeding business, in Improving Agricultural Knowledge and Innovation Systems: OECD Conference Proceedings*, OECD Publishing, Paris. Page. 268 DOI: http://dx.doi.org/10.1787/9789264167445-22-en

6 Schenkelaars P, H de Vriend and N Kalaitzandonakes (2011) *Drivers for consolidation in the seed industry and its consequences for innovation.* Schenkelaars Biotechnology Consultancy for COGEM (report CGM 2011-11). Page 66.

Question 4: How might options 2-4 change the regulatory burden on you from the gene technology regulatory scheme?

No response.

Question 5: How do you use item 1 of Schedule 1, and would it impact you if this item was change?

No response.

Question 6: Might contained laboratory research on GM gene drive organisms pose different risks to other contained research with GMOs, and how could these risks be managed? Supporting information and science-based arguments should be provided where possible.

AAS and ATSE emphasise the importance of examining gene drives separately, as it is difficult at this early stage of development to predict the outcomes of deployment, given their potential to spread genetic change rapidly throughout a population. The self-perpetuating nature of gene drives means that careful consideration needs to be given to appropriate containment measures for laboratory-based research and development projects. The level of containment will depend on the organism involved and the nature of the gene drive system being developed (e.g. high threshold or rapidly propagating drives have different containment implications to low threshold drives). However all gene drives have the potential to impact on natural populations and should be considered with caution, with a level of regulatory oversight that is commensurate with risk.

In the context of Option 4, gene drives would require particular caution. For instance, there could be a high incidence of unforeseen mutation produced in the genome (at rates well above natural levels), which could lead to unplanned deleterious or harmful phenotypes. Because of the potential for these phenotypes to be rapidly propagated, caution will need to be exercised in considering work using these techniques. Further to this, gene drives targeting pest species or disease vectors would need to be treated differently than organisms where the focus is on agricultural products.

AAS is currently preparing a discussion paper on the use of gene drives in Australia. This has been made available for public consultation in draft form with a view to finalisation in early 2017 (https://www.science.org.au/support/analysis/sector-consultation/gene-drives-australia). The paper's initial findings include that synthetic gene drives have the potential to solve intractable problems in public health, environmental conservation and agriculture; but that they may also have the potential to cause negative environmental and human health effects.

The paper's draft recommendations to guide the approach to gene drives in Australia include the need for clear and transparent regulation of synthetic gene drives generated using gene technology, and suggest that stringent, multiple containment measures be applied during their development.

Question 7: What RNA interference techniques are you using, and are there RNA interference techniques that you believe have unclear regulatory status? Please provide details of the techniques and science-based arguments for whether these techniques pose risks to human health or the environment.

The proposed Option 4 approach is also suitable for the regulation of RNA interference, however the qualifications raised regarding pathogenic or pest organisms in response to Question 2 also apply here. This treatment would be similar in effect to the exemption provided under Item 2 of Schedule 1.

Harmonisation and consistency

AAS and ATSE support the OGTR's desire for harmonisation across international markets. To achieve this, developments in key partner countries should be taken into account (such as recent decisions by

the US Department of Agriculture to exempt some gene edited organisms from regulation[7], which is consistent with the approach being proposed in Option 4) and should consider the outcomes of the review of the US Coordinated Framework for the Regulation of Biotechnology[8] .

Nevertheless, Australia must continue to make decisions in relation to its own regulatory frameworks and to reflect the needs of its own constituents. Therefore, AAS and ATSE urge that action be taken to ensure national harmonisation by reflecting any amendments to the definition of gene technology in response to new technologies in the Gene Technology Regulations 2001 in all other legislation.

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 OGTR process. The relevant Academy contacts are Dr Chris Hatherly, AAS Director, Science Policy & Projects (02 6201 9458 or chris.hatherly@science.org.au) and Dr Matt Wenham, ATSE Executive Manager, Policy and Projects (03 9864 0926 or matt.wenham@atse.org.au).

7 http://www.nature.com/news/gene-edited-crispr-mushroom-escapes-us-regulation-1.19754

8 https://www.whitehouse.gov/blog/2016/09/16/building-30-years-experience-prepare-future-biotechnology