AGRICULTURE VICTORIA

Submission to the technical review of the *Gene Technology Regulations 2001*

December 2016

Executive summary

Agriculture Victoria welcomes the opportunity to provide a submission in response to the Office of the Gene Technology Regulator's (OGTR) technical review of the *Gene Technology Regulations 2001* (Cwth) (the Regulations). Agriculture Victoria is a Government department that seeks to improve livability and drive sustainable economic growth in the food and fibre sectors, which contributes to a productive, competitive and sustainable Victorian economy.

As part of the review, the OGTR seeks submissions in response to options and questions contained in its discussion paper, *Options for Regulating New Technologies,* October 2016. Agriculture Victoria's submission identifies its preferred option, and provides technical information and proposes amendments to the Regulations in support of its preferred option. Agriculture Victoria's submission focuses on the application of new technologies to plant breeding.

Agriculture Victoria supports **Option 4** in the OGTR's discussion paper, 'exclude certain new technologies from regulations on the basis of the outcomes they produce.' Agriculture Victoria proposes that option 4 could be characterised as excluding techniques that do not integrate foreign nucleic acid as part of the process of creating genetic change. With this alternative characterisation, option 4 could be considered to be process rather than outcome driven. Agriculture Victoria supports this option because it:

- best captures techniques that result in the stable integration of foreign DNA into the genome and excludes techniques that do not integrate foreign DNA into the genome;
- reduces the risk of two genetically identical products being subject to different regulation depending on how they were developed; and
- is consistent with the intent of the regulatory framework and fulfils the OGTR's central consideration of the review that organisms should be regulated commensurate with the risks they pose as a result of gene technology: scientific consensus is that NBTs that do not incorporate foreign nucleic acid do not pose any greater risk than conventional mutation breeding techniques.

The original intent of the regulatory scheme under the *Gene Technology Act 2000* (the Act) was to capture techniques that result in genetically modified organisms (GMOs). Techniques that mimic natural processes and work using natural mechanisms, for example mutation-based breeding, do not result in GMOs and are not currently captured by regulation. The development of a suite of new breeding technologies (NBT), in particular site-directed nuclease techniques and oligonucleotide-directed mutagenesis (see Appendix I), has made the distinction between GMOs and non-GMOs less clear.

This situation results in regulatory uncertainty for companies and organisations that are developing organisms using NBTs. This in turn, could lead to inefficiencies in product value chains. NBTs are on a spectrum that may not be easily categorised as either genetic modification or non-genetic modification. Agriculture Victoria considers that a distinction may be drawn between techniques that incorporate foreign DNA, and those that create deletions or point

mutations, analogous to the existing mutation-based techniques that are currently excluded from the Regulations. It is on this basis that Agriculture Victoria supports Option 4.

Agriculture Victoria's submission provides technical information that may assist the OGTR in identifying an approach to regulating NBTs that provides clarity and certainty for these technologies. Agriculture Victoria notes that the OGTR has concerns that Option 4 may go beyond the existing policy settings of the Act, making it beyond the scope of this Review. If this is the OGTR's position, Agriculture Victoria strongly supports this option being addressed in the forthcoming review of the Act.

Background

The objective of the 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.* Section 4(a) of the Act states that this objective is achieved through a regulatory framework that provides an efficient and effective system for the application of gene technologies.

The OGTR's technical review of the Regulations aims to ensure the Regulations reflect current technology and scientific knowledge by clarifying whether organisms developed using a range of new technologies are subject to regulation as GMOs. The original intent of the regulatory scheme was to capture techniques that move genes between species as gene technology resulting in GMOs (transgenics). Techniques that mimic natural processes and work using natural mechanisms, for example mutation-based breeding, do not result in GMOs and are not captured by regulation. The development of a suite of NBTs, in particular site-directed nuclease techniques and oligonucleotide-directed mutagenesis (see Appendix I), has made the distinction between GMOs and non-GMOs less clear.

Agriculture Victoria emphasises the importance of providing clarity for research organisations and companies investing in NBTs. Currently there is regulatory uncertainty for organisations developing organisms using NBTs, with the risk of creating inefficiencies in product value chains.

NBTs are on a spectrum that may not be easily categorised as either genetically modified or non-genetically modified. However, Agriculture Victoria considers that a distinction may be drawn between techniques that incorporate foreign DNA and those that create deletions, point mutations or minor nucleotide additions, analogous to existing mutation-based techniques that are currently excluded from the Regulations. Option 4 captures techniques that result in stable integration of foreign DNA into the genome, consistent with the original intent of the regulatory framework. It excludes techniques that do not integrate foreign DNA into the genome. One of the OGTR's stated central considerations in the review of the Regulations is the principle that organisms should be regulated commensurate with the risks they pose as a result of gene technology. Agriculture Victoria considers that option 4 provides regulation commensurate with the low level of risk posed by NBTs that do not incorporate foreign nucleic acid into the genome.

Scope of the technical review of the Regulations

Agriculture Victoria understands that the OGTR has concerns that option 4 may lie beyond the scope of the review. The intent of the Act is to create a flexible framework that accommodates new technologies. Through the Regulations, a gene technology technique can be excluded from regulation, a thing can be declared to be a GMO and a thing can be declared not to be a GMO.

In its discussion paper, the OGTR characterises option 4 as excluding certain new technologies from regulation on the basis of the outcome it produces. The OGTR questions whether this option is appropriate within the current policy settings, which focus on the process of genetic modification.

Agriculture Victoria proposes that option 4 could equally be characterised as excluding techniques that do not integrate foreign nucleic acid as part of the process of creating genetic change. This approach focuses on whether or not the process integrates foreign DNA, in the same way as option 3 focuses on whether or not the process includes

provision of a template to guide DNA repair. Agriculture Victoria considers that with this alternative characterisation, option 4 could be considered to be process rather than outcome driven.

Implementing either option 3 or option 4 will require amendments to the Regulations to exclude specific techniques or organisms from regulation. In support of option 4, Agriculture Victoria proposes the following amendments to the Regulation:

- NBTs that cause mutations (SDN-1 and SDN-2) are listed under Part 7, Schedule 1A (regulation 4), alongside the existing mutagenic techniques that are excluded from regulation, and
- to further to clarify that organisms created without integration of foreign DNA are not genetically modified organisms, Agriculture Victoria proposes the following amendment under Part 7, Schedule 1 (regulation 5), item 1: a mutant organism in which the mutational event did not involve the *integration* of any foreign nucleic acid (that is, DNA from a *non-sexually compatible species*).

If the OGTR cannot pursue option 4 due to its view of the review's policy scope, Agriculture Victoria strongly supports this issue being addressed at the upcoming review of the Act. In that scenario, Agriculture Victoria has concerns that delaying clarification of the regulatory status of NBTs until the review of the Act sends mixed signals to industry and the public and will not provide the certainty that the industry seeks.

Option 4 provides an appropriate level of regulation

It is important that the Regulations continue to be based on scientific evidence and best-practice regulatory principles. Best-practice regulation has the following characteristics:

- it 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.

Regulation needs to be commensurate with risk

Best-practice regulation is proportionate to the risk being managed and consistent with measures already in place. The scientific community agrees that organisms produced by techniques that mimic natural mutagenesis, that is, oligo-directed mutagenesis (ODM), SDN-1 and SDN-2, present the same risks as those developed using conventional breeding methods[i,ii]. 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 with risk.

Implementing options 2 and 3 would impose regulation on techniques that are functionally equivalent to mutation breeding. Under either of those options, there is the possibility that two genetically identical products could be regulated differently depending on how they were developed. This is an undesirable outcome for the regulatory framework.

Unnecessary regulation is costly

Best practice regulatory frameworks ensure that the benefits of regulation outweigh the costs and risks it imposes. Because the risks of ODM, SDN-1 and SDN-2 to human health and the environment are no greater than existing mutagenic techniques, the level of regulation proposed in options 2 and 3 is inappropriate. Furthermore, compliance with gene technology regulation is costly. The costs associated with commercialising a genetically modified (GM) crop are as much as 25 per cent of the total cost of bringing the crop to market[iii]. Imposing this high cost unnecessarily is likely to impose a significant burden on users of NBTs and to disadvantage the broader community. Likely negative impacts include:

- Further consolidation of the seed industry as high regulatory costs discourage small companies from engaging in the development and commercialising of GM crops[iv,v].
- 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 like maize, soybean, canola and cotton[vi].
- Exclusion of Australia from the marketing territories of seed and chemical companies in preference for other larger markets. For example, a survey study by the Australian Farm Institute (2010) showed that cost, timing and uncertainty of registration are the major factors discouraging investment in agricultural R&D by private firms in Australia[vii].
- Hindrance of innovation and opportunity cost of technologies not brought to market: very few products make it through the research continuum as only those products that are likely to repay the high cost of bringing them to market succeed. Any additional regulation adds to these costs and lessens the chance of success.
- Disadvantage to Australian agricultural supply chains due to failed delivery of technologies that would have provided productivity gains.

Compliance and enforcement must be feasible

Best practice regulatory frameworks must 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 mutation. 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.

Alignment with the Food Standards Code

In the bi-national Australia–New Zealand food regulatory system, consumer choice is an important consideration, as outlined in the *Food Standards Australia New Zealand Act 1991*. The *Australia New Zealand Food Standards Code* mandates that food produced using gene technology must be labelled to inform consumer choice. If foods produced using certain NBTs are not classified as produced using gene technology, no mandatory labelling will apply. This approach is supported by Agriculture Victoria as these techniques are not new technologies that significantly change the final properties of food or present new food risks to consumers.

It is imperative that the approach adopted by the OGTR for the regulation of new breeding techniques is consistent with the approach adopted by Food Standards Australia New Zealand (FSANZ) for the regulation of food produced using gene technology. This is because the same food-producing organism or product may, at different stages, be regulated by both. In addition, having clear regulation across the domestic supply chain will enable businesses to better manage any risks associated with differing approaches to regulations of NBTs internationally. Agriculture Victoria encourages the OGTR to work closely with FSANZ to ensure harmonisation of gene technology regulation within the Australian food value chain.

Further considerations

Agriculture Victoria notes that the OGTR is conducting a technical review of the Regulations and accordingly, has provided a largely technical response. Agriculture Victoria encourages the OGTR to also consider the additional issues set out below in arriving at a decision on the regulation of NBTs.

Community expectations

Community attitudes towards GMOs have influenced their regulation in Australia. The scientific community broadly accept that GMOs are safe but public acceptance presents a more complex challenge. Any change to the Regulations will need to ensure public confidence and trust in the regulation of the gene technology scheme is maintained. While education is important for informing the community, communicating scientific information may not alleviate perceived concerns regarding risks posed to human health and the environment.

Option 4 of the OGTR's discussion paper concludes that organisms generated by certain new breeding techniques are indistinguishable from the products of organisms generated by conventional breeding techniques. For organisms and their resulting products produced by these technologies, there is no scientific argument for an increased safety risk, making regulation inappropriate. Communicating this message to the public, however, will require a considered strategy that explains that certain NBTs produce outcomes more analogous to conventional breeding than transgenics. However, there is a risk that consumers will not accept certain technologies being unregulated. Agriculture Victoria encourages the OGTR to develop a detailed communications strategy as part of implementing any changes to the Regulations. This communication strategy will need to draw on expertise in risk communication. Non-regulatory measures are also available to address consumer choice concerns such as industry response to consumer demand.

International and domestic harmonisation of NBT regulation

Agriculture Victoria notes that many countries are considering the regulation of NBTs[viii]. Agriculture Victoria encourages the OGTR to continue to monitor the outcomes of these reviews and, where possible, work towards international harmonisation of NBT regulation, although it is noted that global consensus on the regulation of NBTs is unlikely.

Agriculture Victoria considers it of greater importance that Australia's regulatory frameworks governing organisms developed using NBTs are aligned throughout the domestic supply chain. Agriculture Victoria encourages the OGTR and FSANZ to ensure harmonisation of their regulatory frameworks, to ensure consistency of regulation throughout the supply chain for foods derived from organisms developed by NBTs.

Appendix I: Definitions of new breeding techniques

The NBTs in question all take advantage of cells' inherent ability to repair DNA breaks and sequence mismatches, which occur naturally in response to exposure to mutagens such as ionising radiation. Mutations are introduced in instances when repair mechanisms are inaccurate.

Oligo-directed mutagenesis

Makes small, precise changes to genomic DNA using a short piece of single stranded synthetic nucleic acid called an oligonucleotide as a template. The oligonucleotides are designed so that they are identical to the target gene sequence, however, the middle of the oligonucleotide contains the desired sequence change. For plants the oligonucleotide is introduced into a cell and binds to the matching sequence in the target gene. The cell's proof-reading machinery then recognises that the two sequences are not a match and changes one of the sequences so that they are. In cells where the native DNA is changed to match the oligonucleotide, the desired genetic change will be incorporated into the genome and propagated into plant material generated from that cell.

Agriculture Victoria proposes that instances where oligo-directed mutagenesis is used to introduce foreign DNA would be captured by regulation. When oligo-directed mutagenesis is used to make small genetic changes that do not integrate foreign DNA, the preferred option 4 proposes that this would not be regulated.

Site-directed nucleases

Site directed nucleases (SDNs) are specifically designed proteins or protein/nucleic acid combinations that cut DNA at specific nucleotide sequences. These techniques are classified as SDN-1, SDN-2 or SDN-3 depending on the nature of the repair to the cut and the genetic change introduced.

SDN-1

The repair is made using the non-homologous end-joining mechanism to join the two ends back together. This is an error prone process with the potential for a small number of nucleotides to be deleted, substituted or added at the cut site. Alternatively, repair of two nearby cuts can delete the sequence between them, creating larger deletions.

SDN-2

Homology-directed repair is used to edit gene sequences. The process is directed by providing a synthetic DNA sequence (an oligonucleotide) with ends matching the native sequence surrounding the nuclease targe site. This oligonucleotide guides the editing of an existing gene by replacing one to several nucleotides.

SDN-3

This process also makes use of homology-directed repair but results in the stable integration of a DNA cassette which includes foreign DNA, such as additional genes, regulatory sequences or selectable markers. SDN-3 includes instances where a sequence expressing the nuclease itself is stably incorporated in the genome of the target organism.

References

[i] European Academies Science Advisory Council. Statement. New breeding techniques. July 2015. http://www.interacademies.net/File.aspx?id=28130

[ii] Gene Technology Technical Advisory Committee (2016) 49th Meeting 6 June 2016, Canberra. Communiqué.

[iii] Phillips McDougall (2011) The cost and time involved in the discovery, development and authorisation of a new plant biotechnology derive trait. Crop Life International. https://croplife.org/wp-content/uploads/2014/04/Getting-a-Biotech-Crop-to-Market-Phillips-McDougall-Study.pdf

[iv] 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. http://webcache.googleusercontent.com/search?q=cache:A_Dxbqd_LZoJ:www.cogem.net/showdownload.cfm%3Fobjectid%3Dfd19882d-1517-64d9-cce48761143669bd%26objecttype%3Dmark.hive.contentobjects.download.pdf+&cd=1&hl=en&ct=clnk&gl=au

[v] 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

[vi] 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. http://webcache.googleusercontent.com/search?q=cache:A_Dxbqd_LZoJ:www.cogem.net/showdownload.cfm%3Fobjectid%3Dfd19882d-1517-64d9-cce48761143669bd%26objecttype%3Dmark.hive.contentobjects.download.pdf+&cd=1&hl=en&ct=clnk&gl=au

[vii] Keogh M (2011) Private Sector Investment in Agricultural Research and Development in Australia. Australian Farm Business Management Journal, Vol. 8, no. 2, 13–18.

[viii] Schuttelaar & Partners (2015) The regulatory status of New Breeding Techniques in countries outside the European Union. http://www.nbtplatform.org/background-documents/rep-regulatory-status-of-nbts-oustide-the-eu-june-2015.pdf