



**AusBiotech submission on the Technical Review of the Gene
Technology Regulations 2001 in response to the Discussion Paper:
Options for Regulating New Technologies**

To: Regulations Review
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1. Introduction

AusBiotech is pleased to submit to the Technical Review of the Gene Technology Regulations 2001, Discussion paper: Options for regulating new technologies. The submission represents a collation of comments and submissions from AusBiotech members engaged in delivering economic benefits to Australia through the commercialisation of biotechnology.

AusBiotech is a well-connected network of over 3,000 members in the life sciences industry, which includes bio-therapeutics, medical technology, food technology, industrial and agricultural biotechnology sectors. The industry consists of an estimated 900 biotechnology companies and employs in excess of 45,000 Australians.

Within AusBiotech the agriculture, food and industrial biotechnology sectors are represented by the AusAg & Foodtech Committee, a special interest industry group dedicated to support AusBiotech with its mission to:

“...foster a growing, strong and profitable biotechnology and life science industry in Australia through representation, advocacy and the provision of services and benefits to its members to help the industry realise its nationally important economic potential.”

Australia has a proud history of agricultural innovation. It is critical for the competitiveness of our industry that Australia maintains the capacity to support innovation and deliver its outcomes (i.e. commercialisation) to ensure that Australia maintains its global leadership in developing technologies that will benefit all Australians.

Inconsistencies within, and uncertainty of regulation, is the single most influential factor impacting the decision of major research providers to invest in Australia. This uncertainty is being exacerbated with the development and introduction of new technologies at a time when policy and regulation has not kept pace with these developments.

New technologies have demonstrated that when adopted by plant and animal breeders they have the potential to facilitate greater efficiency, effectiveness and economies of scale associated with producing high performance plant varieties and animals that will be required to address the increasing demand to feed the world, environmental sustainability and animal welfare.

In the Australian agriculture sector, where there is a continued focus on exporting agricultural and horticultural produce, Australia needs to be cultivating plant varieties and animals with the best genetics (from a productivity and efficiency perspective). Given that countries that directly compete in the agricultural sector, such as the United States of America (USA) and Canada, have ostensibly product based regulatory frameworks¹, some products derived using some new techniques may be preferentially commercialised in these jurisdictions affording these farmers a competitive advantage over Australian producers. It also means that plant breeders, in particular, in those countries are able to use innovative techniques that are restricted via regulation to Australian plant and animal breeders. From a plant breeding perspective alone, if Australia does not embrace new breeding techniques, there is the real chance that the long term competitiveness of the Australian agricultural and horticultural industries will be affected as our genetics fail to keep pace with the rest of the world.

1 Wolt, JD, Wang, K, Yang, B (2016) The Regulatory Status of Genome-edited Crops, Plant Biotechnology Journal 14: 510-518

2. Robust regulatory framework

AusBiotech's members recognise that a robust gene technology regulatory framework, based on global best practice, is critical to build confidence and certainty; it underpins public investment and ensures Australia's global competitiveness. AusBiotech is strongly aligned with other science-based organisations such as the Australian Academy of Science (AAS) and the Australian Academy of Technological Sciences (ATSE). AusBiotech contends that a robust regulatory framework should be developed with the understanding that:

- Extensive variations in breeding techniques have existed prior to now, and have historically been accepted without a need for regulation.
- Plants and animals developed through 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 health and safety of people and the environment posed by the products developed using most new technologies are comparable to those of earlier breeding methods.
- 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 be inhibited by regulation that is not commensurate with risk.
- Generally applicable environmental, health and food safety regulations 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 ; and
- Regulatory oversight should be science- and evidence-based, transparent, predictable, proportional to risk, time- and cost-effective, non- redundant, enforceable, globally harmonised and politically independent.

AusBiotech supports a gene technology regulatory regime based on outcomes or products rather than process, but we recognise that under Australia's current gene technology regulatory scheme the central policy setting is the process trigger. We also acknowledge the Government's intention for legislative review and look forward to the review of the Gene Technology Act 2000 (the GT Act). However, it is disappointing that the effort employed by all involved in this consultation process to clarify the GT Regulations may be in vain given the review of the *Gene Technology Act 2000* (the GT Act) is scheduled to be initiated next year, which may require this, or a similar, consultation process to be repeated.

3. Recommendations

AusBiotech makes the following recommendations, which are consistent with the principles of a robust regulatory framework described above:

1. Adopt Option 4: Exclude certain new technologies from regulation on the basis of the outcomes they produce.
2. Redefine Schedule 1, Item 1 to '*A mutant organism in which the mutational event did not involve the introduction of any non-homologous DNA sequences from a non-sexually compatible species.*'
3. Exclude ODM, SDN-1 and SDN-2 from regulation under the GT Act 2000 by including these new technologies in Schedule 1A.
4. Exclude cisgenesis from regulation under the GT Act 2000, by including cisgenesis in Schedule 1A.

4. Consultation questions

4.1. Which option/s do you support, and why?

AusBiotech strongly supports the adoption of Option 4 because it offers the most consistent alignment with AusBiotech's position for a robust regulatory framework. Option 4 can be implemented within the current policy setting by excluding techniques that do not pose a new or unique risk to the health and safety of people. Options 1-3 are not consistent with AusBiotech's Principles and pose risk to Australia's ability to innovate and compete globally.

Recommendation 1: Adopt Option 4: exclude certain new technologies from regulation on the basis of the outcomes they produce.

To clarify which of the new techniques should not be regulated, via inclusion in Schedule 1A, AusBiotech recommends that item 1 of Schedule 1 be redefined to provide more clarity to the definition of GMOs that are not regulated under the GT Act.

Recommendation 2: Redefine Schedule 1, Item 1 to 'A mutant organism in which the mutational event did not involve the introduction of any non-homologous DNA sequences from a non-sexually compatible species.'

4.1.1. ODM, SDN-1 and SDN-2

The new technologies ODM, SDN-1, SDN-2 have not been given clear treatment in the GT Act and do not pose new risks compared to products derived from techniques that are not regulated by the OGTR.

These new techniques introduce targeted mutations or changes to endogenous DNA. In fact, we suggest that these techniques should be defined as a chemical mutagenesis technique under Schedule 1A as no definition for chemical mutagenesis is given in either the GT Act or GT Regulations. The term 'chemical' is not defined in the regulation, however, it is a widely used and relatively well-defined term. We contend that any molecule could be described as a chemical and the definition should not restrict the definition of 'chemicals' to molecules that are artificially synthesised but rather accept a broader definition that includes the product of a biological process. Further, these techniques do not involve the introduction of non-homologous DNA sequences from a non-sexually compatible species, nor do they involve the introduction of whole gene sequences. Products developed using these techniques could be derived by conventional breeding techniques, such as particle radiation-induced mutagenesis and chemical-induced mutagenesis², which are excluded from regulation by inclusion in Schedule 1A.

² Pauwels, K., Podevin, N., Breyer, D., Carroll, D., Herman, P. (2014) Engineering nucleases for gene targeting: safety and regulatory considerations, *New Biotechnology* 31(1): 18-27

4.1.1.1. Off-target effects

While off-target effects have been reported with the use of SDN techniques in plants, the GTTAC³ did resolve that off-target effects do pose risks different to the intended effects. Due to the inherent precision of site directed techniques the frequency of off-target effects is considered to be well below that which occurs with conventional mutagenesis techniques and comparable to that which occurs with conventional cross-breeding. Off-target effects can also be greatly limited by designing highly binding-specific SDNs or oligonucleotides, followed by downstream selection to remove undesired phenotypes. It should be recognised that off-target effects do not always result in an organism that poses an enhanced biosafety risk via expression of a toxin or allergen, or greater fitness. Further, the rigour of selection processes for commercially viable plants and animals involves exclusion of organisms that possess commercially undesirable traits.

4.1.1.2. Risk

The novelty of a technique does not, by default, confer inherent risk. The GTTAC, in their Communiqué³ of 2016 resolved that the risks posed by organisms altered by SDN-1 are unlikely to be different to naturally mutated organisms; and SDN-2 and oligo-directed mutagenesis are unlikely to pose risks that are different to natural mutations, conventional breeding or mutagenesis. Multiple scientific reviews have drawn this same conclusion^{4,5,6,7,8}. The Discussion Paper acknowledges that organisms that are indistinguishable should be regulated in the same way, regardless of how they were derived, because they present the same risks.

There are substantial benefits to employing new technologies such as ODM, SDN-1 and SDN-2, which are predominately associated with the precision afforded by these directed technologies. Instead of introducing multiple random mutagenic changes, as induced by chemical- or particle-

3 The Gene Technology Technical Advisory Committee (GTTAC), Communiqué of 6 June 2016

4 European Academies of Science Advisory Council (EASAC) (2015) Statement: New Breeding Techniques, http://www.easac.eu/biosciences/reports-and-statements/detail-view/article/easac-statement-2.html?cHash=1391bc5bc5e0ca47ffe1d7301f3dd51b&no_cache=1&sword_list%5B0%5D=new&sword_list%5B1%5D=breeding&sword_list%5B2%5D=techniques

5 European Food Safety Authority Panel on Genetically Modified Organisms (2012) Scientific opinion addressing the safety assessment of plants developed using Zinc Finger Nuclease 3 and other Site-Directed Nucleases with similar function, EFSA Journal 10: 2943

6 Gaj, T, Gersbach, CA, Barbas, CF (2013) ZFN, TALEN, and CRISPR/Cas-based methods for genome engineering, Trends in Biotechnology 31: 397-405; Pauwels, K, Podevin, N, Breyer, D, Carroll, D, Herman, P (2014) Engineering nucleases for gene targeting: safety and regulatory considerations, New Biotechnology 31: 18-27; Wolt, JD, Wang, K, Yang, B (2015) The regulatory status of genome-edited crops, Plant Biotechnology Journal doi: 10.1111/pbi.12444

7 Hartung, F, Schiemann, J (2014) Precise plant breeding using new genome editing techniques: opportunities, safety and regulation in the EU, The Plant Journal 78: 742-752; Podevin, N, Davies, HV, Hartung, F, Nogue F, Casacuberta, JM (2013) Site-directed nucleases: A paradigm shift in predictable, knowledge-based plant breeding, Trends in Biotechnology 31: 375-383

8 Wageningen, UR (2015) Opportunities of New Plant Breeding Techniques. Netherland Ministry for Economic Affairs.

radiation-induced mutagenesis, these new technologies are directed to the site/s of mutation or where change is known. The predictability of these techniques reduces the potential for unpredictable off-target effects.

The inclusion of Schedule 1A in the Regulation confirms that the risks associated with conventional breeding (including chemical-induced mutagenesis and particle radiation-induced mutagenesis both excluded from regulation under Schedule 1A) are accepted. The new techniques ODM, SDN-1 and SDN-2 introduce changes to the organism's own DNA and are essentially chemical mutagenesis techniques and therefore should be regulated in the same way as chemical mutagenesis and included in Schedule 1A.

4.1.1.3. Detection and enforcement

As organisms developed using ODM, SDN-1 and SDN-2 can hardly, if at all, be distinguished from conventionally bred organism, detection and enforcement would be difficult, if not impossible, while imposing unreasonable costs on the sector. The Discussion Paper acknowledges that because it may not be possible to detect these organisms without prior knowledge of the modification, it may not be possible to enforce compliance if these technologies were subject to regulation. An unnecessary or expensive compliance regime with no scientific-based benefit will have the effect of stifling research and innovation in these sectors and disadvantage Australia's international competitiveness.

Therefore based on the relative risks posed by ODM, SDN-1 and SDN-2 compared to conventional breeding and the fact that it may not be possible to detect organisms produced with these techniques without prior knowledge of the modification or distinguish them from conventionally bred organisms, AusBiotech makes the following recommendation:

Recommendation 3: Exclude ODM, SDN-1 and SDN-2 from regulation under the GT Act 2000 by including these new technologies in Schedule 1A.

4.1.2. Cisgenesis

The technique cisgenesis involves the transfer of an entire gene, including the gene's own regulatory sequences, from the same or sexually compatible species⁹. The genetic material introduced using cisgenesis is derived only from the sexually compatible pool of genetic material for that species. This technique has not been given clear treatment in the GT Act. Products produced using cisgenesis could be derived using conventional breeding methods and therefore organisms produced using this technique do not pose new or unique risks and therefore should not be regulated differentially to conventionally bred organisms^{10,11}. The arguments above with regard to off-target effects, risks and

9 Cardi, T (2016) Cisgenesis and genome editing: Combining concepts and efforts for a smarter use of genetic resources in crop breeding, *Plant Breeding* 135: 139-147.

10 Wageningen, UR (2015) Opportunities of New Plant Breeding Techniques. Netherland Ministry for Economic Affairs

11 European Food Safety Authority Panel on Genetically Modified Organisms (2012) Scientific opinion addressing the safety assessment of plants developed through cisgenesis and intragenesis, *EFSA Journal* 10: 2561

detection and enforcement are in the most part applicable to cisgenesis, acknowledging that unlike ODM, SDN-1 and SDN-2 the process of cisgenesis introduces a gene, potentially including regulatory sequences. The EFSA Panel concluded that similar hazards can be associated with cisgenic and conventionally bred plants.

Recommendation 4: Exclude cisgenesis from regulation under the GT Act 2000, by including cisgenesis in Schedule 1A.

New techniques that produce equivalent outcomes to the unregulated techniques of conventional breeding including techniques such as chemical- or particle radiation-induced mutagenesis should also be unregulated. AusBiotech believes that it is difficult to establish a credible scientific based argument to the contrary.

4.2. Are there other risks and benefits of each option that are not identified in this document?

AusBiotech has noted risks and benefits already. There are significant risks to the prosperity of Australia's research and industry sectors, with direct consequences on international competitiveness.

The benefits of the technologies such as ODM, SDN-1 and SDN-2 are their precision and the enhanced predictability of off-target effects compared to conventional breeding techniques. Exclusion of cisgenesis from regulation is supported by AusBiotech on the basis that products of cisgenesis and their associated hazards are similar to products derived from conventional breeding techniques and therefore do not pose novel or unique risks.

4.3. Is there any scientific evidence that any of options 2-4 would result in a level of regulation not commensurate with risks posed by gene technology?

This question has been addressed above in this submission.

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

Clarifying the GT Regulations as recommended by AusBiotech would reduce the unnecessary and unjustified regulatory and compliance burden imposed on research and industry. In addition removing uncertainty will encourage investment in in this innovative sector in Australia.

4.5. How do you use item 1 of Schedule 1, and would it impact you if this item was changed?

AusBiotech strongly recommends amending item 1 of Schedule 1 as given in Recommendation 2.

4.6. 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.

This is not a matter that is relevant to our membership, however AusBiotech acknowledges the draft discussion paper produced by AAS: <https://www.science.org.au/support/analysis/sector-consultation/gene-drives-australia>

4.7. 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.

Gene expression can be silenced or modulated using RNA interference (RNAi) techniques, an endogenous biological process identified in many eukaryotic organisms and initiated by the presence of double stranded (ds)RNA. Organisms generated by RNAi techniques that do not involve the introduction of non-homologous DNA sequences from a non-sexually compatible species should be excluded from regulation under Schedule 1 (refer to Recommendation 2). Further, RNAi techniques should be exempt from regulation where the double-stranded RNA (dsRNA) is applied topically with the purpose of silencing or modulating the expression of specific endogenous genes in a target organism. Products based on this technology should be regulated in accordance with existing schemes for biological plant protection products.

4.8. Do you have proposals for amendments to any other technical or scientific aspects of the GT Regulations?

AusBiotech supports the OGTR's position, as stated in the Discussion Paper, that the the GT Act can be clearly interpreted for a range of the techniques sometimes described as new technologies, listed below; and agrees the OGTR should seek to make the regulatory status of the techniques listed below clearer to stakeholders in any amendments that result from this review:

- plants comprised of genetically modified parts grafted to non-GM parts are GMOs
- null segregants (offspring of GMOs that have not inherited the genetic modification or a trait from genetic modification) are not GMOs
- organisms that are genetically modified in a transient manner (e.g. using agro-infiltration) are GMOs while the genetic modification or trait is present, and are no longer GMOs once both the trait and genetic modification are no longer present.

4.8.1. Types of Dealings with GMOs classified as Notifiable Low Risk Dealings (NLRDs) – 25L trigger for PC2 containment

As stated previously the Regulations should be evidence-based and commensurate with the risks posed. A case in point is Schedule 2 Part 1 Item 4, AusBiotech questions the scientific evidence and commensurate risk assessment that supports the volume determination that "...no more than 25 litres of GMO culture in each vessel containing the resultant culture". Volumes of 25L or more of

cultures of exempt host/vector organisms require PC2 containment that imposes a significant cost burden on business in the absence of an objectively determined risk. AusBiotech encourages the OGTR review to consider the scientific basis of this determination towards increasing the permissible volume and AusBiotech suggests review of this Regulation could be undertaken by the GTTAC.

4.8.2. Domestic and international regulatory harmonisation

Synchronicity and mutual recognition between regulatory agencies when approving food, feed and environmental approvals could make an important difference to Australia. The lack of global alignment of regulatory schemes (i.e. asynchronous and asymmetric approvals) is of growing concern for its potential impact on international trade and Australia's competitiveness. In particular where products, such as Cibus Canola Event 5715, (canola that is tolerant to Imidazolinone and sulfonylurea herbicide) developed using ODM, are either unregulated or deregulated in jurisdictions that compete directly with Australia for trade such as Canada and the US but regulated by the OGTR in Australia. Harmonisation between international regulators that govern existing and new techniques will serve to stimulate innovation in Australia and internationally.

Examples of international regulatory determinations regarding new techniques, include:

- **Germany:** Federal Office of Consumer Protection and Food Safety determined that gene-edited canola (Cibus) was not within the scope of national GMO regulation, as the modification could also be produced using conventional methods.
- **Finland and Sweden:** CRISPR/Cas9-modified *Arabidopsis* plants that did not contain foreign DNA were not GMOs within the scope of national GMO regulation.
- **United Kingdom:** Government Advisory Committee on Releases to the Environment (ACRE) considered zinc finger nuclease (ZFN) a form of mutagenesis that should be excluded from national GMO regulation.
- **United States Department of Agriculture:** has determined about 30 types of modified plants do not fall under its regulatory remit, including:
 - Dupont's CRISPR Waxy corn that produces high amylopectin starch content
 - Dow's ZFN-modified corn designed to have lower phytate content
 - Pennsylvania State University's CRISPR/Cas9 non-browning white button mushrooms
 - Calyxt's TALENs powdery mildew-resistant wheat developed with genetic elements from disease-causing bacteria but not contained in the final crop.

AusBiotech recommends that the Australian Government remove the redundancy within the gene technology regulatory scheme to reduce the burden on research and industry, and that definitions of gene technology are applied with consistency and clarity in a timely fashion across Australian regulatory agencies.

5. Conclusion

In summary, agricultural biotechnology offers a set of innovative tools for Australia industries that will create new and improved food and fibre products and more efficient and resilient farming systems and supply chains. The benefits and value from the adoption of agricultural biotechnology will underpin future food security by delivering far-reaching agronomic, environmental, nutritional, human health and economic benefits to Australian agriculture and consumers. Such benefits will strengthen Australia's competitive position in global food and fibre markets and provide increased surety of supply for domestic consumers. Whilst not all farmers will want access to these

technologies, those that see a commercial benefit should be afforded the choice to use these technologies and be able to compete with on a level playing field with their global competitors.

We cannot emphasise strongly enough the imperative that regulation must keep pace with innovation, to enable the benefits from new technologies to be realised. AusBiotech strongly encourages clarification of regulation for new innovative techniques within the current regulatory framework. However, we implore the Australia Government to initiate a review of the GT Act expeditiously to ensure broader and more meaningful discussion of the policy setting of the gene technology regulatory scheme.