



**Government  
of South Australia**

Technical Review of the Gene Technology Regulations 2001

**SA Officials' submission response:  
Options for regulating new technologies**

December 2016

This submission reflects a SA Government Officials position, developed through the SA Gene Technology Interdepartmental Committee (GT IDC). Public or targeted consultation has not been undertaken outside of the SA GT IDC, however independent expert technical advice has been sought in preparation of this response.

## **Generic comments re scope of technical review**

In assessing new technologies, it is important to ask if new forms of variation are being induced or if the changes are essentially the same as those resulting from accepted and / or unregulated technologies.

It is noted that; in contrast to the low risk of unintended genome changes that might occur through these new technologies (as outlined in the discussion document), unintended changes to the genome occur at high frequency in natural mutagenesis, induced mutagenesis, conventional breeding and by other unregulated (exempted) processes.

In many of these new technologies the outcome of the process *should* scientifically be considered based on the risk it presents to human health and the environment, and in comparison with already regulated / exempted processes. It is noted by the SA GT IDC that consideration of an outcomes based approach is outside of the remit of this review. However, we would like to stress the need for a wider review of the gene technology scheme that moves towards an outcome based assessment, as opposed to the current process based approach. It is noted that this could only be addressed in a review of the Act.

### **1. Which option/s do you support, and why?**

The SA GT IDC unanimously agrees that the *intent* of Option 4 should be proposed for the variation regulations. However, they understand that the current wording of this option, as presented in the discussion paper, is out of the scope of the review.

Option 4 is most reflective of the intention of the gene technology scheme, as it proposes to exclude organisms from regulation as GMOs if the genetic changes they carry are similar to or indistinguishable from the products of conventional breeding (e.g. chemical and radiation mutagenesis methods and natural mutations).

Regulating SDN-3 (whilst not regulating SDN-2) is the best option which balances the intent of the legislation, necessary burden on industry, whilst managing human and environmental risks. To incorporate this intent into the regulations a robust scientific definition of SDN-2 and SDN-3 would be required, to allow the exclusion of SDN-2.

Definitions of these processes could incorporate the intent of the changes and refer to the outcomes of the process. This would require a scientific evidence based line to be drawn between SDN- 2 and 3 such as; SDN -2 generate site-specific point mutations with changes to one or a few base pairs through homologous recombination and the copying of the repair template, whilst with SDN-3 the intention is to deliver a long stretch of DNA which can be several kilo base pairs long. The regulations would then be able to specifically exclude one process over the other. It is acknowledged that this would not be an easy process, but ultimately having a generally agreed definition would enable clarity for organisations using these techniques and the Regulator.

It is acknowledged that successive rounds of modification using SDN-2 or oligo-directed mutagenesis could result in substantial changes which would not be subject to regulatory oversight. The Gene Technology Technical Advisory Committee has advised the Regulator that successive rounds of modifications using SDN-2 and oligo-directed mutagenesis may result in similar outcomes (and therefore may pose risks similar) to inserting new genes or SDN-3.

However, this situation also occurs with repeated events of other unregulated processes, and the addition of record keeping (produced on request), could be considered to monitor this and if malicious circumventing of the legislation is detected, this exemption could be revoked.

Option 3 reflects the 2<sup>nd</sup> preference of the Gene Technology IDC.

Option 3 maintains the policy settings by reflecting the 'process trigger' concepts guiding the scope of the regulatory scheme at its inception.

Changes achieved using a template to direct repair *can* be substantially different from naturally occurring mutations. For example, homology-directed repair using a template can be used to introduce gene sequences based on sequences from other organisms. However, Option 3 may also subject some genetically identical but differently derived organisms to different regulatory requirements because they were made by different processes. For example, a single nucleotide change from chemical mutagenesis would not result in a regulated GMO whereas the same sequence change from oligo-directed mutagenesis would result in a GMO.

This therefore conflicts with the intent of the scheme which indicates that techniques should only be regulated if they produce products that could not occur naturally. This situation would present a challenge for the Regulator who could not monitor and enforce the scheme using laboratory detection methods.

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

There is rapid progress towards commercial applications of new technologies in Australia, with some applications commercialised overseas. The regulation (as GMOs) of products of oligonucleotide-directed mutagenesis and SDN-1 and SDN-2 (Option 1 and 2), may impede commercialisation of some products, and stifle innovation in early-stage research. The level and type of regulation may also influence public perception indicating that certain products are less safe (as they need regulating) than they actually are.

To ensure credibility of a regulatory scheme, regulated techniques must be eligible for monitoring and therefore enforceable, and this generally implies being analytically detectable. Many of the techniques under discussion will result in organisms that are indistinguishable from naturally occurring mutants or the products of techniques that are unregulated and not gene technology.

However, it should be noted that regulatory oversight does not need to rely solely on analytical testing; controlled documentation could also be requested to demonstrate processes employed although this would impose a high regulatory burden and cost on both the Regulator agencies and technology developers.

**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?**

Organisms which are indistinguishable should be regulated in the same way, regardless of how they were derived, because they present the same risks.

There is quite extensive scientific literature emerging around the use of CRISPR/Cas9 and related technologies. The evidence strongly indicates a low risk of off-target modification which makes this technology far more reliable and predictable than many unregulated technologies, such as induced mutagenesis.

The gene technology techniques (as outlined in the discussion document) are highly targeted but there is always a risk of off-target changes that might unintentionally interfere with the functioning of an organism's genome, for example through unforeseen interactions between altered genes and native genes, or through the altered genes having unexpected effects on biochemical pathways. Several studies have shown that oligonucleotide-directed mutagenesis and site-directed nucleases is highly precise. For example, a recent study in the model plant *Arabidopsis* using 14 different targets and deep sequencing of the genome found no off-target modifications (Peterson et al 2016. Genome-Wide Assessment of Efficiency and Specificity in CRISPR/Cas9 Mediated Multiple Site Targeting in *Arabidopsis*. PLOS One <http://dx.doi.org/10.1371/journal.pone.0162169>). While we cannot completely eliminate the risk of off-target modifications, we do know that they will be extremely rare – and therefore as a low risk technique they should not be regulated.

It should be further noted that there is a complete absence of credible data demonstrating any serious detrimental effects of this technology.

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

A process based regulatory regime, which can result in products that are indistinguishable from products produced via unregulated technology, will require the collection of documentation to authenticate the processes employed to ensure regulatory scrutiny.

While this is possible, it would represent a significant burden for research, particularly those in the public sector where such documentation is uncommon. This would act as a major impediment to research and innovation.

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

No submission for this 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.**

No submission for this 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.**

No submission for this question.

**8. Do you have proposals for amendments to any other technical or scientific aspects of the GT Regulations? All proposals should be supported by a rationale and a science-based argument.**

No