Review of the Gene Technology Regulations 2001: Responses from Deakin University

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

The responses received supported two options. A slightly higher number of respondents supported option 1 (no amendment to the GT Regulations) while the rest supported option 4 (exclude certain new technologies from regulation on the basis of the outcomes they produce).

Those who support option 1 stated that as the efficacy of these technologies is largely dictated by the vector in which they are delivered and the host system that they are delivered to, the existing GT regulations provides adequate coverage to deal with these new technologies without explicitly mentioning them. They feel that trying to distinguish between mutagenesis and transgenes will only make the process more complicated and that it is not clear as to whether site-directed mutagenesis should be viewed any differently to transgenes when much of the time the phenotypic outcomes from mutagenesis are unknown.

Those who support option 4 mentioned that they do not support Options 2 and 3 because SDN-1 and SDN-2/ODM technologies do not introduce foreign DNA. For SDN-2/ODM to work, a DNA template based on the host genome's DNA, but with a few altered nucleotides is utilised. This is consistent with Schedule 1 (regulation 5) of a non-GMO and they should be considered similar to radiation or chemically-induced mutagenesis. The only consideration would be the delivery system in the sense that if a DNA template is introduced using a viral vector then alternate considerations will have to be made. In regard to SDN-3, this involves the introduction of foreign material (possibly) to the host's genome, however it is not a full transgene. Perhaps this could come under the consideration of whether the introduction of the material is known to be oncogenic or not (i.e. is there a DNA element in there that may block apoptosis or drive cell division for example). Again, the delivery system needs to be a consideration.

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

Those who supported option 1 felt that if option 2 – 4 are adopted it would lead to additional, unnecessary bureaucracy, where the IBCs would have to spend more time ruling on the exemption status of the applications. This therefore is an additional risk that has not been identified for options 2 – 4, according to those who support option 1.

From an administrate point of view we would like to urge caution on the part of the regulator before deciding on any of the options where certain techniques would be completely excluded. As was mentioned in the discussion paper and noted from our own research it seems that, although oligo-directed mutagenesis and site-directed nucleases may be safer than chemical or radiation methods of mutagenesis, their precision haven't been completed established. Risks posed by off-target genetic changes should also be a consideration at all times. Generalizing that these techniques that make small genetic changes like a change in a single base pair will give rise to organisms that can occur in nature, and as such do not pose a particular biosafety risk to the environment or human health and safety can be misleading as this very much depends on the organism that would be modified. For example there are a number of published papers that describe how a change in a single base pair or similar small changes can increase the virulence or expand the host range of different influenza viral strains:

A single mutation in the PB1-F2 of H5N1 (HK/97) and 1918 influenza A viruses contributes to increased virulence
By: Conenello, Gina M.; Zamarin, Dmitriy; Perrone, Lucy A.; et al.
PLOS PATHOGENS Volume: 3 Issue: 10 Pages: 1414-1421 Article Number: e141 Published: OCT 2007

Changes in the haemagglutinin and the neuraminidase genes prior to the emergence of highly pathogenic H7N1 avian influenza viruses in Italy
By: Banks, J; Speidel, ES; Moore, E; et al.
ARCHIVES OF VIROLOGY Volume: 146 Issue: 5 Pages: 963-973 Published: 2001

A Single Base-Pair Change in 2009 H1N1 Hemagglutinin Increases Human Receptor Affinity and Leads to Efficient Airborne Viral Transmission in Ferrets
By: Jayaraman, Akila; Pappas, Claudia; Raman, Rahul; et al.
PLOS ONE Volume: 6 Issue: 3 Article Number: e17616 Published: MAR 2 2011

Most of the material presented in the discussion paper as well as most published literature talks about using these techniques for modifying plants. Since any decision taken by the regulator will also affect the use of these techniques in microorganisms and animals we would like to urge caution, unless the regulator would like to consider adopting these exclusions only for plant work, at least for the moment, because most of the information is available for using these techniques in plants.

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?

Those who support option 4 mentioned that these technologies arguably bring greater specificity, less off-target effects and therefore may be even safer than random radiation and chemical mutagenesis. Therefore they did not feel that there would be any increased risk posed by these technologies. They also commented that these technologies are getting smarter and using the host's own natural system to alter DNA content.

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

Those who support option 1 felt that if option 2 – 4 are adopted IBCs would have to spend more time deciding on whether the applications really fall within the regulations or not and that this will put an unnecessary burden on the committees.

Those who support option 4 mentioned that these technologies (SDN-3 specifically) are not significantly different from any other current ones that generate GMOs and would require similar regulation.

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

No specific response were received from researchers for this question.

If this question is answered from an administrative point of view, we would like to declare that it would be timely if this item can be changed. If this definition is strictly adhered to then products

created by knocking-out and / or overexpressing genes of the same species will not be considered as GMO. But almost all the time, because of the delivery systems used, or the process used for the creation, these products do fall under the category of GMOs under the current regulatory framework. So it would be extremely appropriate if this item can be revised or removed to get rid of its mismatch to the rest of the regulatory framework.

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 specific responses were received 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.

One of the responses received mentioned that, RNA interference including miRNAs (which are naturally occurring systems from plants, lower organisms to worms) in general terms reduces the expression of specific endogenous genes. They do not target the host's DNA, per se, but the mRNA transcripts or subsequent translation of the transcripts. The technological system doesn't pose risk in terms of generating a GMO; however, if the expression of a tumour suppressor protein is inhibited then that may have dire physiological consequences.

If this question is answered from an administrative point of view, we've had applications that proposed to use siRNA and miRNA techniques and we were able to successfully use the current regulatory framework in determining the classification of those applications.