



Regulations Review  
Office of the Gene Technology Regulator  
(MDP 54) GPO Box 9848, Canberra, ACT 2601

07 December 2016

Dear Dr Raj Bhula,

Re: UWA IBC Submission to OGTR on technical review 'options for regulating new technologies'

1. Which Options Do you support, and why?

This Committee supports Option 4.

The main advantage of this option is that it will result in the GMO-classification and regulation of SDN-3, ie the insertion of long stretches of foreign DNA into the genome. At the same time, this option rules out short oligo-directed repair (SDN-2), as well as non-homologous end joining (SDN-1) from GMO classification and regulation.

From a scientific perspective, it is possible for any of the SDN approaches to significantly alter the phenotype of the organism, with potentially harmful effects should the organism be released. However, from a practical perspective SDN-1 and SDN-2 will induce changes that could occur naturally and will in each case produce very small-scale localised mutations. It would be illogical to exempt 'mutagenesis' from the GMO definition, yet include SDN-1 and SDN-2. If, at a future date, 'mutagenesis' was to be re-classified as creating GMO, then SDN-1 and SDN-2 could also be included in the mutagenesis category.

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

A potential risk of both option 3 and option 4 is that SDN-1 could potentially result in very large-scale deletions and/or chromosomal translocations, if two SDN-directed cuts are made at the same time, at distal sites in the genome. When the cell repairs the breaks it may join these distal sites together. Evidence for this application has been published. For example, Zhang et al (2015) deleted 65kb of the mouse genome in blastocysts, resulting in viable offspring ("Large Genomic Fragment Deletions and Insertions in Mouse Using CRISPR/Cas9", PLOS One 2015 DOI:10.1371/journal.pone.0120396). Jiang et al (2016) achieved Chromosomal translocations in murine embryonic stem cells with two cut sites ("Induction of site-specific chromosomal translocations in embryonic stem cells by CRISPR/Cas9", Scientific Reports 2016, doi:10.1038/srep21918).

As with other applications of SDN-1, it could be argued that large deletions and translocations are still a natural process, albeit occurring with low frequency in nature. One way to circumvent this issue may be to set maximal distances between cut sites as a limitation of the SDN-1 definition.

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

At present, the regulatory burden for standard GMO experiments is not onerous. Thus, adding SDN technology to the existing framework should not be problematic. This committee would caution against future new regulatory burdens, for example the requirement of whole genome sequencing for every GMO

organism created in a laboratory setting (eg. Mammalian Cell lines, plants, mice). There should be a progression of regulation as an organism moves closer to potential application or use as a product. Once a milestone is passed along this pipeline, then perhaps at that point a full genome sequence for the organism could be performed.

Thank you,

The University of Western Australia Institutional Biosafety Committee

Prof. Lawrie Abraham, chair

Dr. Carina Marshall, executive officer