

**Technical Review of the Gene Technology Regulations 2001  
Consultation Draft October 2016**

**Response by UNSW Australia**

UNSW Australia offers the following feedback on the draft document titled 'Technical Review of the Gene Technology Regulations 2001', based on discussion at the UNSW Gene Technology Research Committee:

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

The UNSW Gene Technology Research Committee supports Option 3, whereby the use or absence of nucleic acid template to guide DNA repair would determine whether techniques are regulated under the Gene Technology Act. Of the other options, Option 2 is preferable to Option 4, but would lead to a degree of unnecessary over-regulation. Option 3 achieves the best balance between administrative burden and necessary precaution.

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

Based on the experience of researchers at UNSW, there are no other significant risks or benefits associated with any of the options.

**3. Is there any scientific evidence that any of options 2-4 would result in a level of regulation of commensurate with risks posed by gene technology?**

As written, Option 3 still poses some risk of over-regulation as it encompasses all SDN-2 (short oligonucleotide directed) techniques. This may be unavoidable given the continuum of oligonucleotide sizes from short to long template, and the extent of sequence change envisaged. Since SDN-2 involves few changes that are more precise than those generated by "natural" mutagens (which are not regulated), such changes might be regulated, but be deemed Exempt.

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

Currently most researchers using SDN technologies have applied through the University regulatory system so there is unlikely to be significant extra burden on the system.

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

If Option 3 is adopted, this item does need to be modified and would be best if it included a definition of SDN1-3 (we suggest using Figure 1 or an appropriate part of Figure 2 from the Discussion Paper).

**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?**

With regard to Gene drives (Q6), which are genes favoured for inheritance, these should be considered as being higher risk under conditions where it is intended that the organism be released into the environment. Under conditions within a contained laboratory setting however, research on gene drives should not be considered at higher risk than other similar dealings.

**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.**

UNSW's dealings using RNA interference can be summarised below:

1. Non-vector based and not currently regulated are siRNA transfections with purified short double stranded synthetic RNA molecules delivered by electroporation or chemical based deliveries.
2. Vector based systems are covered by existing Exempt dealings through the transfection of shRNA or miRNA molecules encoded within plasmid vectors.
3. Viral delivery systems covered generally by PC2.1(I) dealings that package shRNA or miRNA and deliver to the genome of transduced cells using typically third generation lentiviral vectors pseudotyped with the

Vesicular Stomatitis Envelope Glycoprotein.

Our Committee agreed that in the context of its permanence siRNA is nothing without the vector. As such any technique in which RNA is directly transfected/ transferred into cells should not be covered under OGTR regulations (Q7).

**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.**

There has recently been confusion within largely virology researchers regarding the classification of transformed bacteria that are used to propagate various plasmids that may contain full length viral genomes. In the context of many mammalian viruses (e.g. HIV, CMV), the viral products within the plasmids are never expressed in transformed bacteria and are not "available" during these dealings. Antibiotic resistance is often encoded on the same plasmid and is available as a gene product during transformed bacteria dealing. In the context of biological risk, propagation of the above plasmids does not expose the researcher to viral products. Needle stick injuries and/or exposure to these transformed bacteria have never been documented to lead to a viral infection. Typically transformed bacteria contain approximately 10 nanograms of plasmid DNA per microlitre of culture and for establishment of a viral infection (e.g. SIV for instance) requires microgram quantities of purified plasmid DNA (Virology. 1997 Nov 10; 238(1):57-60.; AIDS Res Hum Retroviruses. 1999 Mar 20;15(5):445-50.). One could argue based on risk that purified plasmid DNA encoding full viral genomes represents an order(s) of magnitude higher risk in acquiring a viral infection through needlestick or equivalent exposure, as the plasmid DNA is readily available for uptake, and to obtain a similar level of DNA exposure in transformed bacteria, one would need to be exposed to several ml of bacterial culture through needlestick (e.g. Injection of greater than 5 to 10ml bacteria). Given the above detail, we request clarification in the document that:

1. Transformed bacteria with full-length viral genomes (where the viral products are never expressed/available) be classed as exempt type 4 dealings
2. In this specific case, purified plasmid DNA be covered under the regulations based on the abovementioned risk (NLRD PC2)