SA Pathology IBC response to Consultation Questions

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

We support option 3. There is clearly a gap between the gene technologies described in the regulations and the new technologies that have emerged and are being used. This has created difficulties in interpreting what dealings are within the scope of the GT Regulations. For this reason we strongly support moves to update the GT Regulations and to ensure that they appropriately regulate relevant genetic technologies without imposing unnecessary or irrelevant regulatory restrictions. The exclusion of organisms generated by SDN-1 is reasonable considering the random nature of the repair process. We also feel that the fact that SDN-1 is site-directed makes it a controlled process and as such organisms generated by SDN-1 are inherently superior or safer than organisms generated by the purely random mutagenesis approaches which are currently not regulated.

The inclusion of organisms generated by SDN-3 is also reasonable as this method is comparable to existing transgenic technologies. However, while we understand the limitations of what changes can be introduced as a result of a technical review of the GT Regulations, we don't feel that the inclusion of organisms generated by SDN-2 in Option 3 is warranted based on risk. As indicated in the discussion paper, SDN-1 and SDN-2 could generate identical genetic modifications with little if any difference in potential risk and yet organisms arising from these two processes would be subject to different regulatory requirements.

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

No obvious ones.

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?

As stated in Q1, Option 3 provides a reasonable regulation of the SDN-1 and SDN-3 technologies relative to their potential risks. While organisms generated by SDN-2 are regulated through Option 3, this does not accurately reflect the likely level of risk associated with this process.

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

This depends on the changes adopted, but apart from learning and understanding the changes, it would presumably clarify and expedite current “tricky” applications which are not clearly identified in the current regulations. Potentially, the current classification of some dealings might change (as in the past) and this would necessitate changes in the dealing classification adding a level of work to IBCs initially.

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

Item 1 of Schedule 1 clearly infers that non-GMO is a "mutant organism" in which the mutational event did not involve the introduction of foreign nucleic acid. A strict interpretation of this item would mean that any directed mutagenesis technique that involves the introduction of a short nucleic acid guide molecule would be classed as a GMO. It should be considered whether transient expression of a CRISPR-Cas9 system that leaves no residual exogenous DNA (like radiation or chemical mutagenesis, but directed) be classified differently than one where the same mutagenic system is used but where vectors integrate exogenous DNA into the genome.

6. Might contained laboratory research on GM gene driven 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 comment.

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.
We use shRNA in plasmid or viral vectors, siRNA, miRNA (potentially other small RNAs). Potentially, shRNA integrated via a RV/LV system that knocks down a tumour suppressor, for instance, would have continued oncogenic capacity whereas transiently delivered RNA interference components against the same genes would have the same effect for a much shorter timeframe, and hence would be much safer (to the researcher). The half-life of RNA interference components may also wish to be considered – current siRNA half-lives are relatively short but conceivably, with modifications, they could greatly increase in half-life. Further, the vectors used to introduce these RNAi reagents (especially *in vivo*) might need to be considered, particularly with the advent of nanoparticles which in theory could be highly efficiently directed at almost any cell type or species – would nanoparticles that selectively target rodents be classified differently than ones that target human cell types (*cf.* retroviral Ecotropic versus Amphotropic envelopes)?

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.