Flinders University
Institutional Biosafety Committee

Research Services Office
Union Building
GPO Box 2100
Adelaide SA 5001
ibcadmin@flinders.edu.au
www.flinders.edu.au

16th December 2016

Dr Raj Bhula
Gene Technology Regulator
Office of the Gene Technology Regulator
GPO Box 9848
Canberra ACT 2601

Dear Dr Bhula,

RE: Technical Review of the Gene Technology Regulations 2001

The Institutional Biosafety Committee (IBC) and relevant University researchers recently met to discuss the options and questions posed in the technical review paper prepared by the Office of the Gene Technology Regulator (OGTR). The responses of our Committee and researchers to consulation questions discussed are summarised below.

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

   All agreed that Option 1 was not the preferred choice.

   Option 2 had support from some researchers as they felt that this option, whilst being the most conservative approach, provided the greatest level of clarity regarding what would be regulated. Those that supported this option suggested that lower risk techniques (e.g. SDN-1 and some SDN-2 or ODM techniques) should be regulated as exempt dealings (our IBC has chosen to assess and approve exempt dealing applications), whilst higher risk dealings (SDN-2 and ODM involving successive rounds of modification, and SDN-3) should be regulated as NLRDs (or higher where the modifications are in line with licenced dealings).

   Option 3 was the most widely supported. As described above, those that supported option 3 suggested that lower risk techniques should be regulated as exempt dealings, whilst higher risk dealings should be regulated as NLRDs or (where appropriate) licenced dealings. Researchers felt that this option presented a compromise between over- and under-regulation, and still provided enough clarity to determine whether their work would be regulated.

   Option 4 was not widely supported, mainly because there was concern that this option would be difficult to achieve under the process-driven regulatory framework, and was therefore not really an option at this time. There was support for a wider overhaul of the regulatory framework to include greater consideration of product, which would allow greater consistency in the regulation of organisms that may be genetically identical but derived by different processes. If this were achieved, then option 4 (with some caveats described below) would be supported.

   For option 4, concerns were raised about the ability to perform successive rounds of modification using SDN-2 or ODM techniques to produce significant changes to an organism without regulatory oversight. There was a detailed discussion regarding whether it would be possible to regulate based on how many ‘rounds’ of modification were proposed, however no consensus was reached on how to achieve this in practice. If successive rounds of modification using SDN-2 or ODM could be expressly regulated, then some researchers would support option 4.

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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?**

   One concern raised regarding all of the presented options was that the level of risk was framed with reference to their similarity to mutagenesis techniques, involving, e.g., chemical- or radiation-induced mutations. The researchers felt that although these mutagenesis techniques are less directed and more time-consuming to select for desired traits, the off-target changes that could be generated using mutagenesis could be more dangerous than a directed technique where the outcome is largely anticipated (disregarding research designed to introduce changes which increase pathogenicity, toxicity, etc.). Therefore, the researchers felt that without regulating mutagenesis techniques also, the regulation of genome editing technologies is largely not risk-driven.

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

   Our University IBC is currently assessing applications for any research involving genome editing technologies. Therefore, option 2 will not increase the regulatory burden on our Committee, and options 3-4 could potentially reduce the burden, provided that the regulations are specific and clearly outline regulation of affected techniques.

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?**

   Our researchers are not currently using or seeking to use GM gene drive organisms.

   Based on the fact that gene drives have the potential to create significant changes to populations of wild organisms, researchers at our University strongly support higher regulation of gene drive research (e.g. licenced dealings in place of NLRDs).

7. **What RNA interference techniques are you using, and are there RNA interference techniques that you believe have unclear regulatory status?**

   Researchers across our University use a range of RNA interference techniques in plants (e.g. cutting the stem and soaking in siRNA solution, spraying siRNA on leaves, germinating cells in siRNA solution) and cultured cell lines (e.g. siRNA/oligonucleotide transfection, microRNA mimics and inhibitors, short-hairpin microRNA expression).

   Researchers feel that the regulatory status of RNA interference techniques is unclear. There has been confusion arising from the apparent de-regulation of some of these techniques when used in whole animals or humans, as implied under Schedule 1, Item 2. For researchers, this appears to create a level of regulation that is not commensurate with risk for research conducted in, for example, cultured cell lines if the equivalent research conducted in a whole animal or human is non-regulated.

   We have also had a situation arise where the use of these techniques has been assessed as a NLRD (at the advice of the OGTR) because the intended host (microalgae) is not an exempt host. In this case, our IBC specifically sought advice on our interpretation from the OGTR, as there was some uncertainty about how the application should be assessed. Again, the level of risk posed by this work is considered to be

very low and the requirement to operate at PC2 level was seen by the researcher and the Committee to be non-commensurate with risk.

Additionally, as some of these techniques result in only temporary expression of siRNA in cells or organisms without modification of the genome, there have been issues with setting a time-period for which the dealing is actually regulated. Although assessed as being a dealing only for the duration that the nucleic acids are in the host, confirming that the nucleic acids have degraded by a certain time period is too difficult and therefore both the IBC and the researchers elect to treat the work as a regulated dealing from start to finish. Again, this leads to a level of regulation that is non-commensurate with risk.

Submitted on behalf of Flinders University and its researchers, by the Institutional Biosafety Committee.