December 2016

**SUBMISSION: DISCUSSION PAPER ON OPTIONS FOR REGULATING NEW TECHNOLOGIES**

Summary:

Monash University would like to thank the OGTR for the opportunity to provide comment on the Technical Review of the Gene Technology Regulations. It is clear from previous reviews that the OGTR is not only committed to receiving stakeholder feedback but is sympathetic to the impact the Regulations have on the research community and has taken decisive action to develop a robust framework for the review of activities involving recombinant DNA technologies within the Australian jurisdiction.

Monash University has always followed the philosophy that any organism with an altered genome that was created via human intervention using recombinant DNA techniques, including enzyme modification, would be included under the Gene Technology Regulations and the level of regulation be described there. Monash University therefore would prefer that the Gene Technology Regulations be amended to incorporate any emerging technologies as opposed to comparing the resulting GMO phenotype with naturally occurring organisms.

The comments below form our response to the questions posed by the OGTR as part of this Technical Review. Overall, Monash University has found the review and approval framework of current Regulations very workable and looks forward to further improvements.

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

   With the development of new technologies some clarity around where they fit within the regulatory framework is required. There are two questions being asked; Whether these new technologies should be included in the Gene Technology Regulations and what level of regulation is required based on the level of risk? Schedule 1A and Schedule 1 of the Regulations identify a number of techniques and organisms that are included in the Regulations for clarity but excluded from any regulatory processes. Schedule 2 describes a number of techniques and resulting genetically modified organisms which, when considering the level of risk to people and the environment, no longer warrant inclusion in the regulatory processes for approval.

   Monash University has always understood that the Gene Technology Regulations were in place to control the development of new organisms that were developed using recombinant DNA technologies. The technologies in question utilise DNA/RNA guides or the introduction of specific enzymes, or both, to modify the genetic sequence of the resulting organism and therefore should be included in the Gene Technology regulations for clarity. Monash University supports *Option 2: Regulate certain new technologies*. What needs to be resolved is the level of risk commensurate with the technology and how the Regulations will control their use.

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

   Monash University's experience of applying the Gene Technology Regulations over the last 15 years has demonstrated that many researchers are challenged with both the interpretation and application of the Regulations to their work and therefore seek assistance via the Institutional Biosafety Committee. The technologies in question are currently being reviewed and approved by the IBC. The inclusion of the technologies in the Gene Technology Regulations would formalize this and avoid future confusion.

   However, there is a risk of creating confusion and additional compliance burden should an approach as described in Option 4 be adopted. Furthermore, it's possible that the guide sequences to be used in some of these new technologies may have been derived via other

regulated dealings. Should these be regulated or should the dealing be split into the generation of the guides via recombinant DNA technology from the end creation of the GMO with similar genotype to the naturally occurring mutation? Given the difficulties experienced by researchers in interpreting the current Regulations, an assessment of any organisms obtained from collaborators would be required to establish whether they would be regulated or not, before applying for IBC approval.

The administrative risk and confusion could stem from the scenario that two knock out lines, both with identical phenotypes, one created by homologous recombination and the insertion of antibiotic resistance cassettes and one via oligo-directed mutagenesis, could be regulated differently; one requiring containment and one not. It is a differentiation the IBC could make and one many researchers would make but not one the animal technicians providing husbandry could make.

Furthermore, given the challenges sometimes faced by researchers in the interpretation of the current regulations as they stand, should organisms resulting from oligo-directed mutagenesis, SDN-1 or SDN-2 be excluded from Regulation, we believe we would need to impose close monitoring of such activities to ensure researchers have not inadvertently exposed themselves to breaking the law by misclassifying their work. From a practical perspective, within a University/Research Institute environment, the nature of the research adopting these techniques would be conducted within contained facilities. Therefore, altering the way oligo directed mutagenesis is regulated would have little impact on how and where the research would be conducted.

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?

   We are not aware of any. However, the introduction of such divisions may lead to further questioning from the research community in relation to other regulated activities which also pose levels of risk similar to the technologies. The introduction of a fluorescent tag, naturally occurring elsewhere, to functionally silence a gene poses a similar level of risk to using site directed mutagenesis.

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

   It is unclear that any option would change the regulatory burden for Monash University. The level of review would continue to be required to ensure the correct classification of the work. The research facilities where this work would be conducted is likely to also be used to conduct work using other recombinant DNA technologies and therefore still required certification. At this stage, we believe it is unlikely that the introduction of these options will alter the regulatory burden.

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

   The most common application of Item 1 Schedule 1 has been in classifying naturally occurring mutations in mice, such as the SCID, RAG, NOD and Nude mice. Researchers often use these animals in conjunction with other regulated organisms and include them in applications.

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.

   We have no experience with gene drive organisms and therefore are not in the position to 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.

The predominant use of RNA interference is using either shRNA, siRNA or sgRNA incorporated into retroviral delivery mechanisms. We do not believe the techniques have unclear regulatory status.

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.

Keeping with the intent of this Technical Review, providing clarity to GM organisms and how they are appropriately classified under the Gene Technology Regulations, we would encourage the OGTR to give further guidance as to how GM viruses, alone, are classified.

We have on numerous occasions needed dealings in place to take possession of GM virus particles without immediate plans for use. Classifying the generation of such GM viruses is clear under the current regulations. Likewise, using the GM viruses to infect hosts is also clearly classified. However, being in possession of a GM virus, not generating it nor using it with a host is not covered under the regulations. We currently have two options, approve a dealing including the generation of the virus, which runs the risk of being inaccurate as details about the generation are often not shared for various legitimate reasons, or approve a dealing for hypothetical work using the virus in a host which may or may not happen and if it does the dealing needs to be altered to accurately reflect the work.

Ideally, the Gene Technology Regulations could provide a category for GM viruses similar to the way GM mice, rabbits, rats and guinea pigs are classified. A classification for the GM organism, without needing to establish its initial generation or any specific future modification.