

# **ANU IBC response to the OGTR Discussion paper: Options for regulating new technologies.**

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

Everyone in our IBC supported Option 4 'Exclude certain new technologies from regulation based on the outcomes they produce'. The regulations should exclude organisms indistinguishable from those generated by non-GM techniques such as chemical or radiation mutagenesis because they do not pose risks different to organisms generated by non-GM techniques and because they cannot be readily identified as having a history of genetic modification, making their regulation both futile and difficult.

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

No obvious additional risks or benefits.

## **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?**

None apart from those already identified in the discussion paper:

- 1) risks arising from the unintentional release of GMOs modified by SDN-1 or SDN-2 for the purposes of developing gene-drive technology. There is also a risk of inadvertent gene drive arising from the unintentional release of GMOs that retain active SDN-1 or SDN-2 systems in organisms modified by SDN-1 or SDN-2 for the purposes of investigating gene function. The risk assessment/regulatory issues associated with gene drive are addressed in the response to question 6.
- 2) risks arising from the use of successive rounds of modification using SDN-2 or oligonucleotide-directed mutagenesis to accumulate sequence changes in a single gene. For example, these technologies could be used to replace the coding sequence of a gene with an altered coding sequence containing multiple non-synonymous mutations. The question arises, at what point does the altered gene qualify as foreign DNA necessitating classification as a PC2 GMO? Multiple base substitutions can arise naturally over evolutionary time scales but are unlikely to be generated by conventional mutagens. One possible evaluation tool might be to look at the similarity of the protein encoded by the variant gene compared to that encoded by the original gene e.g. using BlastP homology searches of protein sequence databases. For example, if the variant protein is more similar to a protein from another genus or more divergent than the nearest relative from another genus, then the variant gene could perhaps be considered foreign and the organism be classified as a PC2 GMO.

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

From an IBC perspective, it would remain much the same unless dealings involving the development of gene-drive technology were to become DNIRs rather than NLRDs. The creation of additional classes of exempt dealing would have only a minor impact.

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

Schedule 1 is used as a benchmark for what constitutes a genetic modification and would benefit from greater clarity as outlined in 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? Supporting information and science-based arguments should be provided where possible.**

Yes, gene-drive organisms will pose different risks to other GMOs, but risks will vary according to:

- 1) the mode of sexual reproduction. For example, gene-drive experiments in an outcrossing plant with wind-borne pollen would pose a higher risk (and require more stringent containment measures) than gene-drive experiments in a self-fertilising plant with heavy pollen or insect-borne pollen, and, in the case of the latter, the risk would also depend on the nature of the pollinating insect. For example, bees are easier to exclude from plant containment facilities than thrips.
- 2) the nature of the organism. For example, gene-drive experiments in a self-incompatible, sexually-reproducing fungal pathogen of plants may entail more risk than gene-drive experiments in a non-pathogen because the consequences may not be limited to the target species but could potentially affect its host plant.
- 3) the nature of the gene targeted. For example, gene-drive experiments affecting genes essential for reproduction, may entail greater risk to species viability, than a gene affecting a phenotypic trait unrelated to reproduction. Pest species are often considered targets for reproductive gene-drive to eliminate or drastically reduce the pest population. However, the concept of what constitutes a pest is very subjective, with species considered a pest in one context often seen differently in another. The risk is that reproductive gene drive could affect both and thereby cause harm as well as benefit.
- 4) the location of the containment facility relative to the host range of the gene-drive target. For example, gene-drive experiments in insect vectors of diseases conducted in a containment facility located within the insect vector's range might pose a greater risk than the same experiments conducted in a containment facility outside that range. As a specific example, gene-drive experiments conducted on mosquito vectors such as *Aedes aegypti* in a North Queensland facility could pose a greater risk than the same experiments conducted in a containment facility in Melbourne.
- 5) the potential to spread in the local environment following an unintentional release. For example, gene-drive experiments conducted in a species isolate well adapted to the local environment would pose a greater risk than a laboratory-bred isolate poorly adapted to the local environment, with a consequent low likelihood of survival and/or a poor chance of mating with local isolates.
- 6) any safeguards/controls built into the SDN delivery system. For example, inadvertent gene drive could be avoided by using inducible SDN or segregating away the inciting SDN construct or using transient delivery systems

Overall, the risks to the environment of using gene drives could be managed by developing and using a threshold to determine when an NLRD should become a DNIR. This threshold could be determined/defined via an enhanced environmental risk assessment that would involve ecologists, population geneticists, and species-specific experts etc. to assess the possible risks that the gene-drive GMO would pose if it were unintentionally released into the environment. A gene drive with the potential to spread in a local environment in the event of an unintentional release should require DNIR approval because of the increased risk to the environment.

**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.**

Our organisation uses RNAi delivered by both gene constructs and direct application of RNA. We believe that the use of RNAi poses minimal risk in animals or plants on the basis that, even if inherited, loss of gene function would already have occurred in nature and accumulated in the host

organism if it conferred a selective advantage relative to the unmodified organism. The delivery of RNAi by direct application of RNA should not therefore be subject to regulation and the delivery of RNAi by gene constructs should only be subject to regulation to the extent that the inciting gene construct remains present in the progeny of the primary GMO. The one possible exception is the potential hazard to workers using viral delivery of RNAi that could target and down regulate genes known to be important in controlling cancer. However we note that a) it would be very unlikely that such a vector could infect more than a few cells following accidental exposure, and b) targeting a single gene alone would pose a negligible risk. In principle, the regulation of such RNAi should be the same as over-expression of oncogenes and this can be done as an NLRD for defective viral vectors if the host is mentioned in Part 2 of Schedule 2.

**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.**

We agree that plants with parts grafted onto non-GM parts should be classified as GM plants, but should be classified as exempt unless the GM part is capable of giving rise to a whole transformed plant by vegetative or sexual propagation.

We also agree that null segregants should be classified as non-GMO.

We also agree that plants with leaves modified by agro-infiltration should be classified as GM, but should be classified as exempt unless there is the intention of using/allowing the agro-infiltrated material to generate a whole transformed plant.