Email Submission: Paul Thomas

1. What is your preferred option? Please explain why.

I am advocating Option 3. Specifically, I am writing to provide feedback on the proposed changes regarding "gene drive" regulation (Item 69).

2. Do the draft amendments clearly implement the measures described in Section 3 of the Consultation RIS? If not, which areas of the draft amendments do you think require additional clarification, and what clarification is needed?

Yes, apart from the amendments relating to dealings with Gene Drive GMOs (Schedule 3, 3.1 (r) & (s)).

*Gene drive **function** is context-dependent, and depends not only on the genetic composition of the gene drive GMO but also the sexual partner that is used to generate offspring. Further clarification is required to clearly delineate what is classified as a **functional** gene drive versus a **non-functional** gene drive.*

Gene drives could, in some circumstances, spread through wild populations. Indeed, this potential for population-level genetic modification has stimulated enormous interest in their development across a range of species to deliver health, conservation and agricultural benefits. However, there is also legitimate concern that unintentional release or spread of a gene drive GMO could have significant and unfortunate environmental consequences. It is clearly important that all stakeholders, including the general public, have total confidence in regulation of this powerful technology. It is therefore imperative that appropriate safeguards are employed during development of gene drives in the laboratory. Apart from physical and environmental containment, scientists have advocated the use of "molecular containment" (Akbari et al (2015) Science) strategies. The two main approaches are:

1. Split drives. Here the gene drive components (gRNA- and CAS9-expression cassettes) are located onto separate chromosomes. The gene drive can no longer function as a single self-replicating unit.

2. Synthetic target sequence. Here the target sequence ("landing pad") of the gene drive is engineered in the laboratory strain of the GMO, ensuring that the drive would not have any activity in wild/unmodified populations.

*Section 3 states that "**Non-functional** gene drives do not continue to be preferentially inherited, therefore the proposed amendment is focused only on functional gene drive GMOs." However, it is not clear if gene drive **function** relates to their activity in **wild type organisms (i.e. wild populations or unmodified laboratory strains)** or in the **modified laboratory strains** used for the experimental analysis. Given that the purpose of molecular safeguards is to prevent spread of the gene drive into the environment (and at the same time allow collection of data relating to gene drive activity in a laboratory setting) it seems sensible to consider the functional impact on **unmodified/wild populations** as the key criterion. The alternative possibility, that a functional gene drive is one that is preferentially inherited in a modified laboratory strain, would essentially apply to all gene drive experimentation, regardless of the molecular safeguards employed. Using this definition, there would be little incentive to incorporate the recommended safeguards into gene drive experimentation as a licence would be required for all gene drive dealings. Indeed, there would be a disincentive to incorporate molecular safeguards because split-drives and synthetic*

target sequences can take months and possibly years to engineer and validate, depending on the species. In my view, this is counterproductive and will hinder responsible development of the technology.

3. If your preferred option is Option 3, please indicate which amendments (or parts thereof) you support being progressed and why.

Apart from the section relating to gene drive dealings, I support the proposed amendments.

4. What are the costs and benefits to you or your organisation from the proposed amendments? Please describe these compared to current arrangements, for each area of amendment:
    4.1 Clarifying the GT Regulations to take technological developments into account (i.e. in relation to SDN-1, SDN-2, ODM and RNAi)
    4.2 Repeal of Schedule 1 item 1, specifically whether you currently work with organisms that are not GMOs solely because of this item
    4.3 Updating the categorisation of contained dealings with GMOs
    4.4 Clarifying the regulatory status of organisms derived from GMOs that are not themselves GMOs
    4.5 minor administrative changes.

*It seems reasonable that dealings that involve a gene drive GMO that is **functional when mated with unmodified/wild type version of the species** in question should be strictly regulated and I support the proposed requirement for a licenced dealing under these circumstances. However, if a licence is required for gene drive dealing/experimentation that incorporates molecular safeguards such as split drives and synthetic target sequences, this will impose a significant administrative and regulatory burden on the growing group of researchers who are interested in developing this technology. Although there is no direct financial cost associated with application for a Licenced Dealing, the time and effort required for the Licence application is much much higher than a NLRD. Notably, an NLRD for a "safe experimental" gene drive GMO would still enable the OGTR to gather information on gene drive experimental due to the requirement for mandatory notification of NLRD projects.*

5. Are the proposals to change the classification of certain NLRDs and exempt dealings (identified in **Appendix B** of the Consultation RIS) commensurate with any risks to the health and safety of people and the environment posed by the dealings?

Yes, but only for a gene drive GMO that is functional in the unmodified/wild type versions of the species.

6. Are there any features in the options presented that you have concerns with? Or, are there any particular features that you believe should be included? Please explain why and give substantiating evidence where possible.

No further comments.

The Regulator is consulting on these proposals to amend NLRDs and exempt dealings under Section 142 of the *Gene Technology Act 2000*.