Response to the Technical Review of the Gene Technology Regulations 2001

On behalf of the Davies Research Centre (DRC) of the University of Adelaide I appreciate the opportunity to respond to the review. The DRC is focussed on ruminant science, from basic research to applications to improve productivity, animal health and welfare. The DRC is initiating projects to assess the use of gene editing, specifically to improve the efficiency of editing approaches and applying these to test the transfer of gene variants that already occur naturally in the target species and are welfare positive, e.g. to mitigate heat stress or to avoid the need for manual removal of horns.

We believe that the editing approach could have a positive effect on genetics of livestock species to improve productivity, food supply, environmental impact, animal health and welfare for a secure food supply. The gene editing approach will allow breeders to achieve significant positive results in a single generation. Conventional breeding strategies would take several generations to achieve the same result, which in a species with a long generation interval, such as cattle, may be decades. In addition, conventional breeding is more focussed on production traits and e.g. welfare traits are generally not included and hence little progress is made in these important area. A gene editing approach could underpin improvement in traits that are not the main genetic selection targets in elite genetic lines thus achieving additional genetic gain in socially important traits.

Consultation questions

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

The Davies Research Centre supports Option 4 for livestock applications, which would exclude new technologies from regulation dependent on the result they produce.

This may differ from the preferred option for plants where the issues differ, containment of pollen from plants is difficult whereas edited animals can be tagged and breeding from these animals controlled. Animal breeding has been, and will continue to be focused of selection naturally occurring variation, while plant breeding has routinely used mutagenesis.

The use of traditional mutagenesis generally introduces (uncontrolled) point, or simple mutations, which generally are not pre-existing in the species. Thus gene editing represents an advance in-so-far as it allows for point mutations to be created at pre-determined sites. This would be covered under Option 3.

In livestock, however, editing will be used to introduce existing alleles with predicted phenotypic outcomes. These alleles may differ by several bases and require guide DNA to ensure accurate creation of the desired change. The cloning approaches used in creation of edited livestock provide the opportunity to verify the variation made, by embryo biopsy and sequencing prior to implantation, and hence the edited sequence in livestock would be verified before live animals are born.

In livestock breeding and genetic selection scenarios, animals that are edited will be extensively tested by the industry in “progeny test” programmes where any unexpected detrimental effects will be identified, and only edited animals with positive effects used in

subsequent breeding. Given the nature of animal breeding, edited animals will be identified and tracked and their progeny also identified and phenotypes recorded. Thus, breeding from edited individuals will be monitored and controlled. This is in contrast to edited plants which will escape in an uncontrolled fashion into the environment.

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

The review is based on the current technology and does take into account that this is a rapidly moving field where techniques are changing to become more efficient and flexible and have increasing accuracy. Setting regulatory parameters based on the technical approaches is therefore likely to be shortsighted and regulations rapidly superseded. It would be more appropriate if regulations were based on the outcomes of the process and accuracy with which it is achieved.

As the editing methods improve further, it becomes more important to evaluate the motivation and intended outcomes. In particular, if the variations that will be introduced are pre-existing in the target species and if resulting phenotypes are characterized should be taken into account in deciding the regulatory requirement.

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 indicated in responses to previous questions: Options 2-3 do not appropriately address the issues associated with the use of gene editing for livestock where pre-existing alleles in the same species, which are not simple point variations, and with known effects would be introduced to new populations (breeds). Only Option 4 would cover this approach.

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

The regulatory change proposed related to Option 4 would require proof of prior knowledge of alleles within the target species and information on their effects. Such information would be a prerequisite for embarking on the editing work. Hence the exemption from regulatory requirement would be based on preparative work routinely done prior to initiating the editing programme.

Other Options, specifically Option 3 would place much of the genome editing for known allele with in the same species under regulatory control. This would be a significant burden for the livestock industry which would exploit this technology, and may create a competitive disadvantage for Australia vs other countries where such approaches were allowed. Given that edited individuals would be indistinguishable from the natural variations, import of germplasm from edited individuals into Australia may occur, thus placing a further disadvantage on the competitiveness of the Australian industries.

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

Item 1 Schedule 1 is detailed on the University of Adelaide website http://www.adelaide.edu.au/rb/oreci/gene-tech/gmo-dealings/#schedules and is consulted by researchers when deciding whether they are required to submit a Dealing Application to the IBC. Changes to this Schedule would be updated so that researchers have access to current regulations.

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?

Gene drive organisms do present different risks compared with gene editing for natural variation as discussed above. The current PC2 level containment for gene drive technology is more than adequate. Gene drives may prove to be important technological tools to contain invasive animal species, the PC2 containment level allows research into their functionality to be undertaken. Proposals for release into the environment should be elevated through DIR-level dealing regulation but should be assessed liberally and not subjected to excessive precautionary regulation that would inhibit development and adoption.

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.

No comment, the Davies Centre is not currently using RNAi

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.

It is important to have public confidence in the regulatory system but also to prevent unnecessary barriers to innovation and competitiveness. It is essential that there is transparency, coordination, predictability and efficiency of the system, while protecting health and the environment. A distinction should be made between editing with predictable outcomes, such as introduction of existing variations within species using guide sequences, which would fall under Option 4, and editing with unpredictable outcome, even those that may fit under Option 3, where randomly selected sites can be targeted and NHJ introduce unpredictable variations. It is therefore important to focus on the outcome and not the technique *per se*.

In summary, the regulations may need to be different for plants and animals depending upon the outcome. The regulations may also need to be different where there is potential for uncontrolled release into the environment (eg plants and flies) versus species that can be that are contained (eg livestock).

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