Australian National University

Submission to the Office of the Gene Technology Regulator regarding the proposed amendments to the Gene Technology Regulations

The Australian National University welcomes this opportunity to provide feedback relating to the proposed amendments to the Gene Technology Regulations as proposed in the Consultation Regulation Impact Statement (RIS). Responses to the Consultation questions are provided below.

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

ANU prefers Option 2 – Amend the Gene Technology Regulations as Proposed, with two possible exceptions outlined in Item 2 below. The proposed amendments dealing with new technologies for genetic modification will remove existing uncertainties and provide greater regulatory clarity for researchers in preparation of their applications for approval and for IBCs in their assessment of applications. The proposed amendments are important steps toward improving the operation of the Gene Technology scheme within the bounds of the existing Gene Technology legislation. They could have gone further and for this reason remain unsatisfactory in some areas e.g. where different technologies can generate the same outcomes with differing efficiencies but the amendments only ease restrictions on the least efficient. Nevertheless, apart from the minor inconsistencies outlined in Item 2 below, the proposed amendments are sensible, well-justified changes that we strongly endorse.

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?

The draft amendments do implement clearly the measures described in Section 3 of the Consultation RIS, with two possible exceptions.

First, in the amendments to Schedule 1, there is an inconsistency between Items 4 and 8 with respect to some specific outcomes that were presumably intended to be exempt. To illustrate; a descendent of a GM plant that carried a Cas9 transgene and a guide-RNA transgene and has not inherited these transgenes (consistent with item 8) but carries a mutation arising from unguided repair of a targeted break in the genomic DNA of the plant (consistent with item 4) would nevertheless not be exempt because the descendent carried a trait that arose in the initial transgenic plant because of gene technology. Presumably this is not the intended outcome, nor should it be. We suggest adding the words “apart from traits described in Item 4” to the wording of Item 8 so that it reads “An organism that is descended from a genetically-modified organism (the initial organism), but which has not inherited any traits that occurred in the initial organism because of gene technology, apart from traits described in Item 4.”

Secondly, although the word order has changed in the draft amendment, there still remains a lack of clarity in Schedule 2, Part 2, Item 10, Column 3 (Vectors) that indicates further amendment is required. This section now reads "Any of the following: Ri plasmids, or non-tumorigenic disarmed Ti plasmids, in *Agrobacterium radiobacter*, *Agrobacterium rhizogenes* (disarmed strains only) or *Agrobacterium tumefaciens* (disarmed strains only)". There is an inconsistency here. There is no specification that the Ri plasmid be a non-rhizogenic disarmed Ri plasmid. Transfer of a Ri plasmid that is not a non-rhizogenic disarmed Ri plasmid would covert *Agrobacterium radiobacter* or a disarmed strain of *Agrobacterium tumefaciens* into *Agrobacterium rhizogenes* (armed and rhizogenic) and transfer into a disarmed strain *of Agrobacterium rhizogenes* would in fact re-arm it. The distinction between *radiobacter*, *rhizogenes* and *tumefaciens* is a plasmid-borne trait and the allowed use of an Ri plasmid negates the intended restriction to use only disarmed strains of *Agrobacterium* and vice versa. Given that Item 10 is currently restricted to transformation of plant cell cultures or isolated plant tissues or organs in tissue culture, there is no point in restricting the vectors to disarmed vectors or the *Agrobacterium* strains to disarmed *Agrobacterium* strains. It is a needless and inconsistent qualification. If the rest of Item 10 remains unchanged, this section should be amended to read "Any of the following: Ri plasmids or Ti plasmids, in *Agrobacterium radiobacter*, *Agrobacterium rhizogenes* or *Agrobacterium tumefaciens*".

The same problem applies to Schedule 2 Part 1 Item 5 where the same strains of *Agrobacterium* are considered hosts and the same plasmids are considered vectors.

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

Not applicable.

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)**

  We do not see a cost associated with greater clarity, providing the attempts to improve clarity do not open up new areas of confusion. A lack of clarity about genome-editing techniques has been a source of confusion for both ANU researchers and members of the ANU IBC. For example, some researchers had assumed that organisms generated using SDN-1 were exempt because the outcome was the same as radiation- or chemical-induced mutagenesis and they needed to be reminded that under the current Regulations this was not the case. This confusion slowed down NLRD application and approval processes in some instances and made them more complicated than they needed to be. Clearly, there is benefit to be gained from greater clarity from an administrative perspective. However,

given that all of the dealings with GMOs at ANU are conducted in PC2 containment, we do not anticipate much practical benefit to ANU researchers in terms of either contained dealings (as discussed in the response to item 4.3) or dealings involving release (currently we have none).

- **4.2 Repeal of Schedule 1 item 1, specifically whether you currently work with organisms that are not GMOs solely because of this item**

Not applicable

- **4.3 Updating the categorisation of contained dealings with GMOs**

This would have little impact on ANU because we do not have certified PC1, PC3 or PC4 facilities; we only have certified PC2 facilities. Potentially, downgrades of some contained dealings to PC1 containment might encourage some researchers to request corresponding downgrades of their containment facilities. However, current ANU policy is to maintain the flexibility to conduct either PC1 or PC2 dealings in each of our containment facilities. Typically, ANU researchers conduct a mixture of exempt, PC1 and PC2 dealings in their certified PC2 facilities, so re-categorisation of dealings as PC1 or exempt is likely to have little practical impact. Re-categorisation of some DNIRs as NLRDs has the potential to reduce the administrative and compliance loads on both researchers and the ANU IBC. However, the re-categorisation of some NLRDs as DNIRs has the potential to do the opposite.

- **4.4 Clarifying the regulatory status of organisms derived from GMOs that are not themselves GMOs**

We see a considerable benefit with little or no cost associated with greater clarity in this area. However, as indicated in the response to item 2, we do not believe sufficient clarity has been achieved for Item 8 of Schedule 1.

- **4.5 minor administrative changes.**

We see little cost or benefit to ANU.

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?

We believe they are. We have previously expressed concerns about the potential for environmental harm arising from research involving gene drives and believe the greater scrutiny and capacity to impose safeguards provided by a DNIR classification is warranted.

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.

There are two features that we believe should be included in the amended regulations.

In Appendix D of the Consultation RIS, the addition of plants with GM plant parts to Schedule 2 has been rejected once again on the basis that insufficient information has been provided to support its implementation. We believe transformation of plant cells by *Agrobacterium* following leaf infiltration (agroinfiltration) is directly comparable to the animal scenario covered by Schedule 2 Part 1 Item 3 which describes "A dealing with an animal into which genetically modified somatic cells have been introduced, if (a) the somatic cells are not capable of giving rise to infectious agents as a result of the genetic modification; and (b) the animal is not infected with a virus that is capable of recombining with the genetically modified nucleic acid in the somatic cells". It is not clear what additional information is required by the OGTR to support the case for making agroinfiltration an exempt dealing.

One possible difference of concern in the plant versus animal comparison may be the use of disarmed strains of *Agrobacterium* to deliver transgenes into plant somatic cells. Disarmed strains of *Agrobacterium* carrying Ri plasmid vectors, or non-tumorigenic disarmed Ti plasmid vectors are already defined as exempt vectors under Schedule 2, Part 2, Item 10, Column 3 (Vectors). The question may then be whether they are considered infectious agents. Given that disarmed strains of *Agrobacterium* carrying disarmed Ti plasmids are incapable of forming tumours then they are not infectious in the sense that they could cause crown gall disease. Similarly, given that disarmed strains of *Agrobacterium* carrying disarmed Ri plasmids are incapable of inducing root formation then they are not infectious in the sense that they could cause hairy roots disease. Moreover, the prohibition on release of exempt organisms into the environment would still apply i.e. agroinfiltrated leaves would still need to be disposed of, as they already are, using a method that prevents the release of *Agrobacterium* into the environment. It would be useful to know if this is the sticking point in the OGTR's thinking.

Another possible difference of concern may be the pluripotent nature of all plant cells versus the irreversibly differentiated nature of animal somatic cells, which is not altogether true given that animals have somatic stem cells and it is becoming increasingly possible to de-differentiate and re-differentiate somatic cells. Although leaf cells may be pluripotent, they still require human intervention in most cases to regenerate into a plant. With or without such intervention, this possibility is already excluded by wording such as that used in Schedule 2, Part 2, Item 10, Column 2 (Hosts) which states "Either of the following if they are not intended, and are not likely without human intervention, to vegetatively propagate, flower or regenerate into a whole plant".

We do not understand the OGTR's reluctance to draft an amendment that would enable agroinfiltration to be defined as an exempt dealing and we feel it is incumbent upon the OGTR to explain the basis for their reluctance. Given that we do not see a convincing argument against implementation of agroinfiltration as an exempt dealing, we propose adding the following Item to Schedule 2 Part 1 – Exempt Dealings:

"Item 6. A dealing with a plant whose somatic cells have been modified *in vivo* by infiltration with a disarmed strain of *Agrobacterium* carrying a disarmed Ti or Ri plasmid vector, if
(a) the somatic cells are not capable of giving rise to infectious agents as a result of the genetic modification; and
(b) the somatic cells are not intended, and are not likely without human intervention, to vegetatively propagate, form a reproductive organ or regenerate into a whole plant."