Submission on Technical Review of the Gene Technology Regulations 2001

To whom it may concern,

Please find a number of submissions from scientists at OGTR. Because of the nature of their submissions I have not been able to collate them to provide a single cohesive submission. Please let me know if you need clarification on any of the views put forward.

Kind Regards

Helen

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Submission 1- H Leonard

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

There is no doubt that we need greater clarity as members of IBCs as to where some of these technologies fall when attempting to classify new dealings so I believe option 1 is not a desired outcome.

The new technologies would not produce GMOs by a method that would fit with the list of organisms that are not GMOs in Schedule 1, however some of the GMOs resulting from use of CRSPR or interfering RNAs might be difficult to detect from "mutants" that might occur in nature if these organisms were to be released.

It is clear from early papers that bystander and off target effects are being seen and that some of these are difficult to predict so the consequences of the changes cannot be determined. Changes in host range or ability to grow in different environments may occur. Some of these changes will give the new GMO and advantage over WT organisms.

Once the GMO can be investigated in contained facilities and shown to be "safe" for release than conditions can be included in the approved for it to be so. So low level regulation for contained dealings with higher for released dealings unless the new GMO is characterised would be appropriate.

Where a new technology is generates a single nucleotide random change it will generate mutants similar to random occurrences in nature and be no different and difficult to detect.

I therefore think that a graded approach might be the best way to proceed and provide an appropriate way to monitor and limit the risk of the new technology.

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

Dealings under option 3 where the resulting material is the same as what could occur in nature and is

- kept in contained facilities, (e.g. only in tissue culture or similar situations)
- where there is no possibility of accidental release
- where the organism could not survive outside a facility

could be given a lower classification.

Option 3 because it regulates by exclusion may again fall behind new practice and not be as easy to keep on track with the changes so this is a disadvantage.

Where the work is contained, if regulated and within contained dealings, so not for release than all the work is low risk. The risk of a change in an organism making it more virulent/ increasing its host range / for a plant spreading faster surviving better in the wild is not a problem if all work is conducted within certified facilities.

Dealings where whole animals are for release or plants with field trials could be regulated at a higher level at least until fully characterised.

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

AN IBC has to assess it anyway so whether exempt or NLRD it is not an issue

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

It is used as part of classification especially for new types of dealings where a committee might be unsure and if it were changes the changes would be taken into account

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.
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.

QIMR has submitted a separate request for clarification on the use of a micro RNA linked with an Adeno vector for clarification in December 2016 – for ease I have copied the request and the response here

about the dealings with AAV microRNA, miR-941.

You queried what classification in the Gene Technology Regulations 2001 the following dealings/experiments fall under that involve timed mating between male mice (injected with AAV encoding miR-941) and wild-type females, and collecting embryos at pre-implantation stage (blastocyst) to check for presence of miR-941.

From your description, it appears that the miR-941 is likely to be present in the sperm of the male mice injected with AAV encoding miR-941 which could be transmitted to the female mice it was mated with, and to the embryo. Therefore, we agree with your IBC that the dealings involving the live mice including the female mice mated with would fall under Schedule 3 Part 2.1(k) up to the point where the animal is euthanised and embryos are collected. Classification of dealings with collected embryos (which may contain mir-91) would depend on the procedures/experiments done with them:

- *If the embryos are digested / made non-viable to isolate mir-91 – this may be classified as exempt dealings under item 4 of Part 2 (Host/vector system) of Schedule 2;*
- *If the embryos are cultured in vitro, these dealings may fall under Schedule 3 Part 1.1(c) (PC1 NLRD), given that isolated mice embryos are classified as exempt under item 4 of Part 2 of Schedule 2;*
- *If the embryos are transplanted back or pregnancy is progressed to full term and mice pups are born, this may fall under Schedule 3 Part 2.1(k) up to the point where the pups are euthanised to the collect tissues/organs;*
- *Analysis for the presence of miR-941 in various body tissues of the newborn mice pups may fall under Schedule 3 Part 1.1(c) (PC1 NLRD) if they are cultured in vitro, or exempt under item 4 of Part 2 of Schedule 2 if the isolated cells, tissues or organs are digested / made non-viable to isolate mir-91.*

In another type of research we have a library of mutant Plasmodium where the mutations are due to insertions and each parasite mutant is individually tagged, but a researcher uses all the mutants in the same single infection of a mouse at once. This was new technology to our committee.

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.

Not at this stage

Submission 2

I have looked over the options and I would suggest either option 2 or 3.

Submission 3

A few comments:

1. I think Option 3 is the optimal one as it follows the policy framework of regulating procedure rather than outcome. Within option 3, it is stated under 'Cons' that regulation under this option could impede commercialisation. I think this is an issue with all regulation but it should be clear that safety must always be the first concern. Regulations should not be concerned with commercialisation unless/until all safety concerns are first met. In addition, no figures are provided for how the regulations will affect commercialisation. It seems to be a bit of a 'throw-away' line without numbers to back it.

2. Another 'Con' for option 3 is that it may subject genetically identical organisms that were derived by different processes to different regulations. But I think this is an inevitability of a policy that regulates process over outcome. As indicated, to change this and use other options would really require a change of policy, not regulation under the current policy.

3. It is also suggested that reliably detecting organisms that are indistinguishable from naturally occurring mutants is a great challenge to enforcing compliance. But I think that the aim of the policy is upfront clarity for researchers, not as a form of policing. Sticking with a regulatory option 3 that continues to follow the policy of regulating procedure rather than outcome helps to maintain that clarity for researchers.

4. Overall, I think that option 3 provides the coverage to regulate with clarity procedures that may generate non-normal mutations.

5. Option 4 proposes to exclude organisms from regulation that are indistinguishable from conventional breeding and simple mutagenesis. However, this option is only available 'after the fact' and moves away from the policy of regulating procedure.

Submission 4

I am Option 2. It's one of those areas where technologies are developing at light speed. Probably best to regulate certain new technologies until it is determined that there are no adverse downstream effects rather than under-regulate and have something detrimental happen.