QIMR Berghofer
Medical Research Institute

QIMR Berghofer MRI submission to the Review of the National Gene Technology Scheme

1. General Comments

1.1 Current Scheme

Overall, the Scheme is working well and is fit for purpose. OGTR is well respected and is building trust with stakeholders through a positive collegial approach. The Institutional Biosafety Committees (IBCs) play an important role in the scheme and the system of assessing and approving lower risk dealings (exempt and NLRDs) is working well. There is a public confidence in the expertise/knowledge held by individual IBCs and OGTR as a whole.

1.2 Product vs Process regulation

To accommodate current and future developments in gene technology, QIMR Berghofer would suggest a change in the central policy setting of the scheme to "product trigger", from the current "processed-based trigger" (i.e. focussing on the actual change(s) in the genetic code of an organism or vector, rather than focussing solely on the process through which changes are induced). There would be multiple complexities involved in this change, and we understand that careful considerations would have to be made. Alternatively, considerations/allowances should be made within the scheme for certain new technologies based on the outcome they produce, and the risk assessment.

1.3 Cost recovery

Cost recovery is of a particular concern to QIMR Berghofer, considering our relatively large number of OGTR certified facilities, dealings and licences. It is unclear how this cost recovery model would work and be applied to our operations, but it is envisaged that it would have a significant impact on Accredited Organisations. Passing audit costs onto research organisations would have a deleterious effect on their operations, and may lead to unintended consequences.

1.4 IBCs

In order to stay up-to-date with gene technologies and complex legislative system, IBCs would benefit from structured training, support and tools from the OGTR. This engagement would increase the capacity of IBCs to take action within organisations including imposing penalties for non-compliance. The role played by IBCs within organisations and the role they play in ensuring public confidence in the Scheme would also be enhanced by structured training.

1.5 IT Solutions

There are numerous ways (suggested in specific instances below) where the existing processes could be streamlined and simplified, providing investment is made in a solid and user/regulator friendly IT system. Serious consideration should be given to investing in such a system.

1.6 Regulatory Burden

Organisations accredited with the OGTR have a number of regulatory burdens placed upon them relating to (a) facilities and (b) regulation of GM work. These are both a dollar cost to the organisation and can delay the commencement of work. Most accredited organisations have safety and ethics committees in place and these committees deal with all work, whether WT or GM, and oversee the maintenance of the facilities. Such organisations maintain safe practices for dealings, and maintain compliance of their facilities. This is not only because of the regulations, but to ensure safety of their staff and environment, and also to preserve their scientific and research reputation. However the current Scheme does not take this compliance into account and offers no benefit (such as reduced audit frequency, for example) to Accredited Organisations when

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considering dealings, audit frequency or reporting requirements. Organisations or individuals working outside the Scheme, and therefore not accredited with the OGTR, do not have any of these restraints. The review of the Scheme should allow for some of this burden to be addressed.

1.7 Transport of GMOs

Many organisations have to transport GMOs. Currently there is a lack of harmonisation of what is required on a label by different regulatory authorities (OGTR/TGA/NHMRC/IATA). This can be problematicfor license holders especially those conducting clinical trials. In addition, the process of notifying (and requirements for notifications) before transport between organisations is not clear and would benefit from a structured approach.

2. Gene Technology Act Comments

2.1 Update of Sections for transition

Division 5 section 190 and 191 of the Gene Technology Act deals with the transition of GMAC to OGTR and could now be removed, or wording changed to acknowledge this is what occurred historically.

2.2 Update to Part 5, Division 7, Gene Technology Act

Consideration should be given to IBC's assessment and recommendations of the scope of a licence variation request. Where a request for a variation to an existing license is minor and does not change the risk assessment of the DNIR (as assessed and advised by IBC), consideration should be given to identifying parameters for an expedited review period (shorter than the current 90 day review period).

Examples of such minor variations might include:

- addition of different strains of the organisms already approved on the licence;
- addition of different organisms of the similar pathogenicity/host range and the same Risk Group;
- use of a different GM mouse strains, where there is no change to the risk profile of the dealing;
- change in vector/transfection agent where the change does not alter the outcome of the transfection from that approved in the original DNIR.

Under the current Scheme, the process of licence extension/renewal is not formalised. Currently, prior to the expiry of the DNIR, the Accredited Organisation may apply to the Regulator for an extension of the DNIR. Even where the organisation states there is no change in the DNIR as previously issued, and the IBC has reviewed and approved the extension, the renewal application must be examined and signed off by the regulator and must comply with the requirement for a risk assessment and risk management plan (RARMP) as per s50-52. If the expertise of an IBC is recognised and legislatively formalised, this process could be semi-automated, thus providing efficiency to both OGTR and stakeholders.

2.3 Update to Part 7, Division 2, GT Act

2.3.1 Clarity of containment requirements

Organisations may have requirements to certify facilities both with the OGTR and with the Department of Agriculture and Water Resources. It would reduce the regulatory burden for organisations if these two regulators could agree which organisms require what type of facility. Currently QIMR Berghofer has one facility (used for imported fresh water snails carrying a parasite) classified under OGTR as an aquatic facility and as an insectary under DAWR. Inconsistencies of this nature cause design nightmares, especially where there is no clear definitions of what type of facility is required for what organisms in the relative legislations. Having to contact Regulators and await clear instructions leads to facilities that cannot be correctly certified for their

intended use, or that require adaption/modification during or after build, all of which lead to extra costs as often contracts for build commencement need to proceed within set time lines.

2.3.1 New Applications

Under the current scheme, a person applies to the regulator for certification of a facility to a particular containment level. In cases of lower containment levels (PC1 and PC2), the application is made to the regulator with a report of the facility inspection by an IBC to confirm that the facility meets requirements set in Guidelines for the Certification of Physical Containment Facilities (s90). Currently, only containment facilities at PC3 and above are inspected by OGTR prior to certification being issued. The OGTR, therefore, relies on information received from the organisation that the facility meets the criteria set out in the Guidelines.

Currently there can be long delays (90 working days) for certifications to be issued for new PC1/PC2 facilities. During this time, under the current legislation, work with GMOs in these facilities cannot commence. At the same time, wild-type organisms can be used in the facility providing an organisation's safety committee deems the facility to meets the criteria required to safely conduct the work.

Consideration should be given to allowing Accredited Organisations to commence GMO work at PC1 and PC2 containment levels once the application is verified as submitted to the OGTR (i.e. an email acknowledgement of submission has been received from the OGTR), or as soon as the Accredited Organisation has deemed the facility to comply with the requirements set in Guidelines for Certification of Physical Containment Facilities.

The benefits would be:

- promotion of compliance with the OGTR system as being Accredited will bring benefit to an organisation
- lack of delays to research, leading to improved Australian competitiveness in publications, grants and patents
- increased efficiency without compromising safety/compliance as
    a) there is no difference in safety risk to personnel or the environment from the time point when the facility is deemed to comply with Guidelines (or when the application is submitted) to when the formal certificate is issued, and
    b) dealings with WT and GM organisms (especially if they are classified as exempt and NLRDs) in most instances do not increase the safety risks to personnel or the environment

2.3.2 Extensions to certifications for PC1 and PC2 containment levels

The Act does not currently specifically address extensions to a certification instrument. Therefore, even where an IBC of an accredited organisation has undertaken an inspection and verified the facility still meets the requirements set in the certification guidelines, and there is no change to the facility, the Regulator must still assess the application before the new certification can be issued. Given that the OGTR is relying on the information provided by the organization, consideration should be given to automating this process. Perhaps the organisation would be required to state which conditions are met, (e.g. tick boxes, declarations etc.) and then the certificate would be issued.

2.3.3 New builds and refurbishments at all levels of containment

When an organisation is at the design phase of a complex build, particularly PC3 and above, or where there are multiple rooms and/or the PC3 facility is multidisciplinary (insect/animal/lab/aquarium), it would be helpful to be able to discuss the design with experts at the OGTR. OGTR staff are in a good position to provide advice as they see facilities that work well, and also issues that have arisen in built facilities. This should be considered as a role for the OGTR. This could be provided as detailed technical notes/additions to the guidelines for PC facilities or by having staff available to be consulted.

The benefits being:

- Accredited Organisation tapping into the expertise of OGTR staff during planning could save more difficult discussions post-build, providing an overall saving for all parties;
- better designed facilities which are more fit for purpose at the outset;
- fewer modifications after build;
- the Regulator having the knowledge that risks of a design have been considered and managed prior to build by OGTR staff.

2.4 Update to Part 12, Division 5, GT Act

Division 5, Section 190 and 191 of the Gene Technology Act deals with the transition of GMAC to OGTR and could now be removed, or wording changed to acknowledge this is what occurred historically.

3. Gene Technology Regulations Comments

3.1 Update to Paragraph 13(A), GT Regulations

Under the current Scheme, a person needs to apply for, and obtain, a new assessment of the dealing as a NLRD from an IBC to continue to work after the applicable day mentioned in this Paragraph. However, if the IBC has reviewed the dealing (before its 5 year expiry date) and deemed that the classification and the risk assessment is still current, considerations should be given to allow the IBC to extend the dealing and report it as such to the OGTR (and not having to report it as a new dealing). This restriction for a low risk dealing is not in line with the risk assessment. Under the current Regulations, it is deemed safe to extend high risk dealings (DNIR/DIR) through a variation request.

3.2 Update to Paragraph 13(B), GT Regulations

Often a researcher will request a variation to their approved NLRD, for instance to add a new mouse strain, change a vector, add an additional certified facility, add a piece of equipment, or notify of a change of staff. The IBC checks the appropriateness and provides approval. Under the current Scheme, a new NLRD must be generated each time these modifications are approved, which requires a new notification in the annual report to the OGTR.

Consideration should be given to removing the requirement for a new NLRD to be issued each time an existing NLRD is varied, providing the scope of the dealing does not change, and the IBC has assessed that there is no change in risk.

3.3 Update to Schedule 1A, GT Regulations

Techniques that are not gene technology:

"Somatic cell nuclear transfer, if the transfer does not involve genetically modified material."

- With the ability to synthesise nucleotide sequences of considerable length, it is currently possible to transfer these sequences into a cell. While synthesising the nucleotide is not a modification of genetic material, the resulting cell cannot be differentiated from one that was transformed by a GM nucleotide and would require control under the GT Act.
- Should this definition be changed to "*Somatic cell nuclear transfer, if the transfer does not involve the introduction of any foreign nucleic acid (that is, non-homologous DNA, usually from another species)."*
- The "risk" of the resulting somatic cell is obviously the same and the above definition would cover both synthetic and natural nucleic acids.

3.4 Update to Schedule 1, GT Regulations

Organisms that are not genetically modified organisms

Item 6. Use of CRISPR-Cas9 and site-directed nuclease (SDN) techniques allows organisms to be created which would fit this criterion and be termed non-GMOs, but considering they have been created through gene technology they would be GMOs. Clarification is needed.

Item 7. There are species that meet requirements of a) and b)(ii) and c), but do not meet b)(i) as being Risk Group 1 species. If these processes occur naturally in a Risk Group 2 organism and the particular isolate is obtained, it is not clear if this isolate would be considered a GMO.

3.5 Update to Schedule 2, Part 1, GT Regulations

Considerations should be given to moving dealings with GM laboratory guinea pigs, mice, rabbits and rats (Schedule 3, Part 1, 1.1(a)) to Schedule 2, providing the animals are held in at least PC1 facilities maintained by an OGTR accredited organisation. This would reduce the regulatory burden for accredited organisations working with GM animals. It would also provide an advantage to those organisations that are accredited through the OGTR and therefore encourage compliance with legislative requirements.

3.6 Update to Schedule 3, Part 1, GT Regulations

Consideration should be given to the addition of retroviral/lentiviral type vectors that can transduce rodent cells, but not human cells to Schedule 3, Part 1, 1.1. These vectors are inherently safer to work with as there is no potential risk to the worker, therefore they could be used in PC1 facilities.

3.7 Update to Schedule 3, Part 3, GT Regulations

Given the ability to now make synthetic nucleotides coding full length sequences of many viruses, consideration should be given to changing the wording of Schedule 3, Part 3.1(i) from genome to nucleotide sequence, to ensure there is clarity that use of synthetic nucleotides would still fall under the GT Act. This would keep legislative control over this type of work.