Submission to the Gene Technology Legislative Review
Association of Biosafety for Australia and New Zealand

General comments

Any review of the Gene Technology Act should consider areas where there may already be duplication between the Gene Technology Act and other intersecting regulatory schemes and to the extent possible reduce such duplication. In addition, requirements under the Act that are based on bureaucratic processes as opposed to evidence that has determined the need for risk mitigation should be minimized.

To the extent possible, the revisions of the Act should recognize the need for the Regulator to issue Guidelines but not where these guidelines are not required because they would depart from the requirements of existing standards or guidelines.

Use of industry experts for guideline development

Where possible, the Regulator should consider the use of external industry experts to provide advice or comment on the development of guidelines prior to construction and certainly prior to consultation. This would ensure that proposed guidelines meet community expectations and that an external viewpoint from those that work in the discipline, and that will consequently be subject to any imposition, is received and incorporated before the major consultation period. Peak bodies such as ABSANZ could be used to source industry experts.

Update of Sections for transition

Division 5 section 190 and 191 of the Gene Technology Act (The Act) deals with the transition of GMAC to OGTR.

ABSANZ Recommendation 1
Reference to the transition of GMAC to OGTR should be removed from S190-191 of the Act.

Description of 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 now possible to transfer these into a cell within a nanoparticle and alter it. 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.

ABSANZ Recommendation 2
Consideration should be given to changing the definition of somatic cell nuclear transfer to:

"Somatic cell nuclear transfer, if the transfer did not involve the introduction of any foreign nucleic acid (that is, non-homologous DNA, usually from another species, and which includes synthetic or artificially synthesised DNA)."

The "risk" of resulting somatic cell is obviously the same and the above definition would cover both synthetic and natural nucleic acids.

Regulatory requirements for organisations that have quality systems in place

Organisations accredited by the OGTR are subject to regulation in a number of ways that relate to (a) facilities and (b) regulation of GM work. Regulation represents both a dollar cost and a delay to commencement of work. Most accredited organisations as a matter of buisness already maintain safe practices for dealings as well as maintain their facilities to ensure safety of their staff and environment, and also to preserve their scientific and research reputation. However the legislation as written does not take this compliance into account and offers no benefit to Accredited Organisations when considering dealings, or 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 constraints.

ABSANZ Recommendation 3

a) The review of the Act should consider the practices that are already in place especially for low risk and NLRD dealings. There is very little evidence that releases that may occur from low level facilities have any impact on human health and safety or that of the environment, in which case regulation is not really risk based.

b) Consideration of pre-existing quality systems as a surrogate for regulatory oversight should be considered.

Standardisation of Requirements for Transport of GMOs

Many organisations have to transport GMOs. Currently there is a lack of standardisation of what is required on a label between different regulatory authorities (OGTR /TGA /NHMRC/IATA) which causes issues with license holders especially those conducting clinical trials.

ABSANZ Recommendation 4

Where possible, standardise GMO transport labelling requirements.

Certification of Facilities

Clarity of containment requirements

Organisations may have requirements to certify facilities both with the OGTR and with the Department of Agriculture and Water Resources (DAWR). It would be helpful if these two regulators could agree

which organisms require what type of facility. For example a facility used with imported fresh water snails carrying a parasite is classified by OGTR as an aquatic facility and as an insectary by DAWR. Inconsistencies of this nature cause design problems, especially where there is no clear definitions of what type of facility is required for what organisms in the relative legislations.

Certifications of PC1/PC2 facilities

Section 84: When the Regulator may certify the facility

(a) The Regulator may, by written instrument, certify the facility to a specified containment level if the facility meets the containment requirements specified in guidelines issued by the Regulator under section 90.

New Applications

Facilities must comply with OGTR guidelines in order to be certified, but only containment facilities at PC3 and above are audited by OGTR prior to certification being issued. For certification of lower PC level facilities, the OGTR therefore rely on information received from the organisation in addition to the ability for OGTR staff to randomly audit some or all of the PC1/PC2 certified facilities if it chooses to do so.

Currently there can be long delays for accredited organisations for certification to be issued on new PC1/PC2 facilities. During this time under the legislation, work with GMs where the dealing must be conducted at either PC1 or PC2 cannot commence. However Wild type organisms can be used in the facility if an organisation's safety committee deems the facility meets the criteria required to safely conduct the work.

Given that the OGTR rely on the audit undertaken by delegates of the IBC to ensure that facility meets the OGTR guidelines for certification consideration could be given to allowing Accredited Organisations to commence GM work at PC1 and PC2 containment levels, once the application is verified as submitted to OGTR (i.e email notification has been received that OGTR have received the application). This is analogous to the mechanism used by the TGA for the commencement fo clinical trials, which is significantly more risk than the use of PC1 or PC2 organisms in a containment facility.

Possible advantages of this approach:

- Lack of delays to commencement of research, leading to improved Australian competitiveness in publications, grants and patents;
- Reduction in frustration of scientists and members of IBCs; and
- No cost to OGTR in terms of time commitment of its staff over what is already undertaken.

ABSANZ Recommendation 5

Consideration could be given to allowing Accredited Organisations to commence GM work at PC1 and PC2 containment levels, once the application is verified as submitted to OGTR.

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 audit and verified the facility is still compliant with the certification guidelines and there is no change to the facility, the Regulator (sic) must still assess the application before the new certification can be issued. Given that the OGTR is relying on the information provided to it by the organisation consideration should be given to implementation of a notification mechanism whereby organisations could be responsible for notification of such compliance to the Regulator in an effort to reduce double handling and unnecessary oversight. it should be possible to automate this process in an electronic age. Maybe the organisation would be required to state a number of conditions are met, (say through tick boxes) and then the certificate can be issued.

ABSANZ Recommendation 6

Consideration should be given to implementation of a notification mechanism whereby organisations could be responsible for notification of facility compliance of facilities requiring extension, to the Regulator, rather than have to undergo through what appears to be an unnecessary process.

Dealing with GMOs

DNIRs

Applications

Under the current legislation a DNIR is issued for a 3 year period. Prior to the expiry of the DNIR, the Accredited Organisation may apply to the Regulator for an extension of the DNIR.

Even in instances 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 comply with the requirement for a risk assessment and risk management plan (RARMP). The information required for this approval is articulated within s49-s52 of the Act. This can lead to delays in issuing the new DNIR and work for staff/time and costs to OGTR in preparing the documentation.

ABSANZ Recommendation 7

a) ***Consideration should be given to an automatic approval system for a DNIR extension where there are no other changes to the DNIR or in any of the conditions of the license.***
b) ***Where a request for a variation to an existing license is minor and does not change the risk assessment of the DNIR, consideration should be given to identifying parameters for this to occur within a shorter time frame than the current 90 day review period.***

Examples might include

- ***Addition/ change of strain of the same organism classified in the AS/NZS 2243.3 Standard as being of the same risk group and not altered in pathogenicity/host range or similar classification.***
- ***Use of a different GMO mouse***
- ***Change in vector/transfection agent where the change does not alter the outcome of the transfection from that approved in the original DNIR.***

Dealings

Given the ability to now make synthetic nucleotides coding full length sequences of many viruses, consideration should be given to change 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 Act. This would ensure legislative control over this type of work.

(i) a dealing involving use of a viral or viroid genome, or fragments of a viral or viroid genome, to produce a novel replication competent virus with an increased capacity to cause harm compared to the capacity of the parent or donor organism;

Example: A dealing would comply with paragraph (i) if it produces a novel replication competent virus that has a higher capacity to cause harm to any potential host species than the parent organism because the new virus has:

(a) an advantage; or

(b) a new potential host species or mode of transmissibility; or

(c) increased virulence, pathogenicity or transmissibility.

ABSANZ Recommendation 8

Consideration should be given to change 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 Act.

DIRs

Staff of OGTR acknowledged at the recent IBC forum (May 2017) that the DIR application form was developed for work with plants and so some questions are not relevant to applications for clinical trials. A separate application form should be established for clinical trial applications. Expertise could be sought to develop this form.

ABSANZ Recommendation 9

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NLRDs

The majority of the review work for members of IBCs is in assessing low risk dealings whether with wild type or GM organisms. By definition these are from risk group 1 or 2 organisms as defined by

AS/NZS2243.3, the organism being unlikely to cause serious health or environmental damage if accidently released or an incident occurs in the facility where staff may be exposed.

S 13A Time Limit for stopping notifiable low risk dealings

The frame work for assessing dealings is meant to use a risk based approach. What is the risk of extending an NLRD? Consideration should be given to an IBC being able to extend an NLRD providing it has been reviewed.

ABSANZ Recommendation 10

Consideration should be given to an IBC being able to extend an NLRD providing it has been reviewed.

S 13B Requirements for Institutional Biosafety Committees about records of assessments of notifiable low risk dealing proposals

Often a researcher will request a variation to their approved work, for instance to add a new mouse strain, change a vector, add a different certified facility so they can use some piece of equipment, they may wish to notify of a change of staff. For wildtype organisms the IBC checks the appropriateness and notes the varied approval.

However if it is an NLRD, then a new NLRD must be generated with a new record of assessment. This then 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 it is varied, providing the scope of the dealing does not change, and the IBC has assessed that there is no change in risk.

ABSANZ Recommendation 11

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

Proposed change to a dealing type

Retroviral – lenti type vectors that can transduce rodent cells but not human cells are now available. These vectors are inherently safer to work with as there can be no potential exposure to the worker. Consideration could be given to adding this dealing as an NLRD suitable for conduct at PC1

Part 1—Notifiable low risk dealings suitable for at least physical containment level 1

Note: Because of subregulation 12 (1), a dealing mentioned in this Part is not a notifiable low risk dealing if it is also a dealing of a kind mentioned in Part 3.

ABSANZ Recommendation 12

Consideration could be given to adding dealings involving the use of safe lentiviral vectors as an NLRD suitable for conduct at PC1.

1.1 Kinds of dealings suitable for at least physical containment level 1

A dealing involving the introduction of a replication defective retroviral vector able to transduce rodent cells into a host mentioned in Part 2 of Schedule 2, if:

(i) all viral genes have been removed from the retroviral vector so that it cannot replicate or assemble into a virion without these functions being supplied in trans; and

(ii) viral genes needed for virion production in the packaging cell line are expressed from independent, unlinked loci with minimal sequence overlap with the vector to limit or prevent recombination; and

(iii) either:

(A) the retroviral vector includes a deletion in the Long Terminal Repeat sequence of DNA that prevents transcription of genomic RNA following integration into the host cell DNA; or

(B) the packaging cell line and packaging plasmids express only viral genes ga, gpol, rev and an envelope protein gene, or a subset of these

Exempt dealings

Consideration should be given to reassessing all GM laboratory mice and rats to exempt dealings providing they are kept in contained facilities of at least PC1 containment level and are held 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.

ABSANZ Recommendation 13

Consideration should be given to reassessing all GM laboratory mice and rats to exempt dealings providing they are kept in contained facilities of at least PC1 containment level and are held by an OGTR accredited organisation.