THE UNIVERSITY OF WESTERN AUSTRALIA

Government of Western Australia
Department of Health
South Metropolitan Health Service

Royal Perth Bentley Group

HARRY PERKINS INSTITUTE
OF MEDICAL RESEARCH

GENE TECHNOLOGY LEGISLATIVE REVIEW

JOINT SUBMISSION

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The University of Western Australia would like to join with Harry Perkins Institute of Medical Research and the Government of Western Australia, Department of Health, South Metropolitan Health Service, Royal Perth Bentley Group in supporting the submission of the Association of Biosafety for Australia and New Zealand. This comprehensive submission has taken into account the learned and experienced opinions of Biosafety Professionals across Australia. Specifically, we would like to join in the submission for the following changes.

General Comments

Reduction of administrative process and duplication between government departments should be of paramount importance. 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.

Existing standards and guidelines should be consulted to ensure that any issued Guidelines from the OGTR do not conflict with already issued and practiced Guidelines from other entities.

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.

Should this definition be changed 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).

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 both facilities and regulation of actual work with GM organisms. Regulation represents both a dollar cost and a delay to commencement of work. Most accredited organisations as a matter of business 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.

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.

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.

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), as well as state level Biosecurity. It would be helpful if these regulators could agree on a standard type of facility for organisms, or had a mechanism for decision making in this area. Inconsistencies in the facility requirements can and do 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

GT Act 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 of 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.

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 of clinical trials.

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 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 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.

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 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) and what it must include is written within the Act (s49.50-52). This leads to delays in issuing the new DNIR and work for staff/time and costs to OGTR in preparing the documentation. Consideration should be given to an automatic approval system where there is no change in any of the conditions of the license.

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

Addition or removal of facilities of the same containment level eg PC2 laboratory

Dealings

Given the ability to now make synthetic nucleotides coding full length sequences of many viruses, consideration should be given to the wording of Schedule 3 part 3.1(i) from *genome* to *nucleotide sequence*, to ensure there is clarity and flexibility for future technological advances.

DIRs

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.

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.

Section 13A Time Limit for stopping notifiable low risk dealings

The frame work for assessing dealings is meant to use a risk based approach. Consideration could be given to an IBC being able to extend an NLRD providing it has been reviewed, and that the risk level has not altered.

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.

Proposed change to a dealing type

There are now available retroviral –lenti type vectors that can transduce rodent cells but not human cells. These vectors are inherently safer to work with as there can be no potential exposure to the worker. Could this dealing be added to:

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.

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 gagpol, rev and an envelope protein gene, or a subset of these

Exempt dealing

Consideration should be given to moving 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.