THE UNIVERSITY OF SYDNEY

1. Decision making processes need to be embedded in the Scheme

An important part of the OGTR's remit is to take community submissions and to consult with stakeholders when issues or developments arise. A good example of this is the call for submissions in response to the 2016-2017 Technical Review of the Gene Technology Regulations 2001, which canvassed four options related to emerging site-directed nuclease (SDN) techniques.

Because of their utility and broad applicability, SDN and related technologies have spread rapidly since they first appeared. Lab-based CRISPR-Cas genome manipulation, for example, only became possible in 2013 and the technologies are now finding widespread application in fields as diverse as human medicine and agriculture.

Although the development of technologies as powerful as CRISPR has been rare, it can be expected that the pace of change in the field will accelerate and that technology developments will continue to appear. To avoid prolonged regulatory uncertainty when important developments appear it is critical that decision making processes are sufficiently responsive and agile.

The OGTR regularly considers input from a range of Commonwealth portfolios, all States and Territories and numerous other stakeholders and so coming to a position on issues such as the definition and use of SDN technologies is perhaps inevitably going to be slow and fraught with difficulties. However, if the decision making processes incorporated in the National Gene Technology Scheme lag behind the pace of technological change, the problems associated with regulatory uncertainty will inevitably compound, potentially leading to a dysfunctional Scheme.

An agile and effective Scheme requires that systems appropriately reflect their environment. With the advent of CRISPR and other technological breakthroughs the environment has changed.

The University of Sydney IBC proposes that the Review reassesses the decision-making processes embedded in the Scheme so that they are agile enough to reflect a changing technological environment. It may be possible for example to adopt a system similar to that found in other government departments where the Regulator is given the authority to write rules or to directly seek Ministerial approval for rule changes under certain circumstances.

2. Introduce a more risk based approach to the facility certification process

According to Division 3, Section 14 of the Gene Technology Regulations, the Regulator is to decide whether to grant Certification of a facility within 90 working days (approximately four months). This is regardless of whether the facility is to be certified as PC1, PC2, PC3 or PC4. Having to wait four months after completion of the necessary paperwork for the Certification of a new space significantly holds up teaching and research, impacts negatively on business continuity and is very costly to organisations.

For the low level risk facilities, namely PC1 and PC2, the IBC and appropriately experienced person/people are responsible for determining the facility's initial physical containment level, conducting an inspection of the facility to ensure that the facility complies with the OGTR requirements, completing the application paperwork and forwarding the information to the OGTR. For the legislation to then allow four months for the processing of that application is not consistent with an agile and effective scheme, and is not proportionate to the level of risk.

The University of Sydney IBC proposes a change to the legislative framework to allow for work to commence in low risk facilities as soon as the paperwork for Certification of the facility is received by the

OGTR. The IBC could then provide provisional approval for GMO dealings approved by the IBC to commence in the facility while waiting for the OGTR to formally process the application. Any issues identified by the OGTR in the application could then be addressed and the OGTR could provide final Certification within a specified timeframe.

3. Introduce a more effective process for variations to existing Certifications

There are currently no specified OGTR timeframes for the OGTR to process requests for variations of existing Certified facilities. This means that even for lower risk certified physical containment facilities (PC1 and PC2) a request as simple as adding a new room adjoining an existing certified space could take months for the OGTR to process.

A further demonstration of the scheme not being able to be agile and effective is exampled by physical modification(s) within a currently OGTR certified space. This is a regular occurrence at our University and the current process is burdensome and untimely. If a certified facility requires an internal modification, the current process requires that a request must be sent to the OGTR for the entire facility certification to be placed on hold (thereby resulting in an immediate stop to research) and an application to vary the certification to remove the part of the facility that needs the modification must be submitted. After this request is processed, a new variation needs to be sent to the OGTR to add the changed/modified space back into the Certification instrument. Without any legislated timeframes for processing requests for variations to existing facilities, this process can potentially take months.

Given that all certified facilities within our University are either PC1 or PC2 facilities, the level of risk to containment or safety associated with variations to a facility does not seem to justify the length of time to process these applications or the disruption to research.

The University of Sydney IBC proposes that the Scheme incorporate a more effective way to manage variations to facility Certifications in low risk facilities.

4. Review of the classification category for low risk work with genetically modified laboratory mice and rats

The University of Sydney IBC proposes consideration of easing the classification category of genetically modified laboratory mice and rats that are currently defined under Schedule 3 Part 1.1a as 'Notifiable Low Risk Dealings' (NLRD) requiring certified PC1 containment.

The majority of dealings with GM/transgenic animals in widespread use by researchers fall under the current NLRD classification for PC1 containment. However, the vast majority do not involve infectious dealings with GM animals (i.e. present no microbiological hazards) or modifications that confer an advantage on the animals. Most dealings involving GM animals or the creation of GM animals involve inactivation, over-expression or mutation(s) to an endogenous gene and therefore do not involve any contact between infectious agents and mammalian cells.

Laboratory animals with germline transgenic modifications to a wide range of genes have been used by the biomedical research community for more than two decades without apparent biohazard problems. The ability to use transgenic laboratory mice (i.e. those that confer no selective advantage and do not produce infectious agents) in non-certified PC1 laboratory environments would significantly facilitate physiological research that increasingly relies on testing the influence of an endogenous gene on a physiological process.

The current regulations requiring certified PC1 containment facilities place significant constraints on the

THE UNIVERSITY OF SYDNEY

ability to use these GM animals (or unfixed tissue from them) in laboratories and facilities that are not currently certified as PC1 and/or where PC1 certification is problematic as it presents unnecessary administrative and procedural burdens for compliance.

In light of the above, we propose that consideration be given to modify the Regulations and re-classify dealings with GM animals that are non-infectious and do not confer an advantage on the animal, as 'Exempt' rather than the current NLRD classification, thus allowing the dealings to be conducted under non-certified PC1 conditions. This approach would be similar to the current classification for work with genetically modified *Caenorhabditis elegans*, which is classified as an Exempt Dealing, item 2.