Australian Government

Department of Health

Office of the Gene Technology Regulator

MINUTES OF THE
GENE TECHNOLOGY TECHNICAL ADVISORY COMMITTEE
23 November 2016 Meeting

About these Minutes

These minutes are intended to summarise discussion during the 50th meeting of the Gene Technology Technical Advisory Committee (GTTAC), held on 23 November 2016. They reflect key elements of the discussion, outcomes, matters agreed and actions arising, and are not intended to be a verbatim record of the meeting.

Attendance

Members

- Professor John Rasko AO (GTTAC Chair)
- A/Prof Jason Able
- E/Prof Craig Atkins
- Prof Ross Barnard
- Prof Jacqueline Batley
- Prof Gabrielle Belz
- Dr Graham Bonnett
- Ms Laura Fell
- Prof Ian Godwin
- A/Prof John Hayball
- Dr Rodney Mahon
- Dr Michael Michael
- Dr Gabrielle O'Sullivan
- Prof Marie Ranson
- Dr Kelly Shaw
- A/Prof Jason Smythe
- Dr Diane Webster
- Prof Paul Young

Apologies

- Prof Kevin Smith

Guests

- Dr Raj Bhula (Gene Technology Regulator)
- Dr Michael Dornbusch (GTTAC Secretary)

Presenters

- Dr Eong Ollis
- Dr Helen Holt
- Dr Vijay Mareddy
- Dr Brian Weir
- Dr Louisa Matthew

Secretariat

- Mr Greg Barber
- Dr Gillian Colebatch
- Mr Dimitri Kun

The meeting commenced at 09:15am (AEST)

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Agenda Item 10. Review of the Gene Technology Regulations 2001

The Chair invited Dr Louisa Matthew to provide members with an update on progress of the Regulator's technical review of the Gene Technology Regulations 2001 (the Regulations), and to seek advice on gene drives and RNA interference.

Specifically, advice was sought by the Regulator from GTTAC on the following:

1. Could contained laboratory research on GM gene drive organisms pose different risks to human health and safety and the environment to other contained research with GMOs? If so,

- what are these risks?
- what evidence is available to support the assessment of these risks?
- how could these risks be managed?

2. Please identify newly developing RNA interference (RNAi) techniques and applications you are aware of, including details of relevant technical publications where possible.

The Chair asked whether members were aware of any new RNAi techniques. Dr Michael Michael noted that using Cas9 to chop up RNA was a relatively new way of achieving similar results to RNAi techniques. He added that modified Cas9 had been used to bind GFP to RNA molecules so that they could be tracked around cells. Members referred to publications in PNAS[3] and Nature[4] on Cas9-tagetting of RNA and Prof Paul Young sent them to the OGTR via email.

The Chair recalled a recent publication involving a system similar to CRISPR/Cas9, and Prof Barnard added that there were at least 6 systems from different organisms already identified.

Moving to the question on gene drives, the Chair commented that there is a substantive difference between this technology and other biotechnology. Dr Bonnett sought clarification on whether the

[3] Price et al (2015) Cas9-mediated targeting of viral RNA in eukaryotic cells. *PNAS* 112(19):6164-9
[4] O'Connell et al (2014) Programmable RNA recognition and cleavage by CRISPR/Cas9. *Nature* 516(7530): 263-6

advice sought related to risks if a GMO with a gene drive is released, or if it stays in containment. Dr Kelly Shaw noted that the potential effects of gene drives are currently theoretical and queried whether the questions could be answered in the absence of evidence or data.

Prof Barnard considered the questions that need to be addressed are whether the current containment rules are adequate, and whether the GMO could be controlled if it escaped containment. He suggested that although the containment regulations are in place, if an organism with a gene drive was to escape containment, it could be very difficult to retrieve it. Prof Smythe agreed that current containment requirements are likely to be adequate for GMOs with a gene drive, but added that the assessment would need to look at the particular trait.

Dr O'Sullivan noted that some NLRDs can be undertaken in a PC1 facility unless the modification confers an advantage, and queried whether gene drives could sometimes confer a disadvantage. Dr Matthew clarified that any GMO with a functional gene drive is considered to have an advantage, and a minimum containment level of PC2 is required. Dr O'Sullivan commented that this may not be clear to researchers or IBCs.

> *Secretariat note:* Following the meeting, the OGTR published a guidance document for IBCs on regulatory requirements for contained research with GMOs containing engineered gene drives: http://www.ogtr.gov.au/internet/ogtr/publishing.nsf/Content/ibc-1

Prof Ross Barnard asked whether a dealing with a GMO containing a gene drive could be an exempt dealing. Mr Will Tucker responded that it is possible *Caenorhabditis elegans* with a GM gene drive could be exempt, but not any plants or animals.

> *Secretariat note:* Mr Tucker subsequently clarified that *C. elegans* with a functional gene drive should be excluded from exempt dealings, as the relevant clause (Schedule 2, Part 1, Item 2) excludes modifications which provide an advantage.

The Chair proposed that a GM gene drive organism could pose different risks to human health and the environment than other GMOs if it escaped containment. A/Prof Smythe commented that a PC2 facility is considered adequate for containment of most GM insects and plants, so these organisms can only escape containment through an unintentional or release or by someone deliberately not following containment requirements. A/Prof Smythe suggested that gene drive organisms would not pose different risks within PC2 facilities but agreed with the Chair that they may do so if they escaped containment.

Prof Ian Godwin considered it would be difficult to propose adequate limits and controls for a limited and controlled release of a GM gene drive organism. Dr Bonnett noted that some modifications included safeguards to allow appropriate levels of control of the spread of the GMO.

Leaving aside the question of what controls or containment level might be needed, the Chair asked if members agreed that GMOs with gene drives could pose different risks than other GMOs, and the committee confirmed agreement with a show of hands.

The Chair asked members to specify the risks posed by GM gene drive organisms. Dr Bonnett suggested that the main risk is harm to the environment, including destruction of a species as the most extreme consequence. Prof Kevin Smith observed that the possible effects of gene drives on populations were theoretical and there is no evidence that a population could be destroyed. Prof Barnard commented that possible effects have been extrapolated from an understanding of the mechanisms. Prof Godwin considered that the technique may not work as well as predicted theoretically. The Chair proposed the OGTR keeps watching the development of these techniques and emerging evidence of how effective they are.

Moving to the question of risk management, the Chair noted that well considered regulations and guidelines would allow any risks to be managed. Prof Barnard commented that there are already structured regulations with different categories of dealings requiring different levels of containment.

Resolution:

- Publications on Cas9-tagetting of RNA were provided to the OGTR
- Depending upon the cargo and its effects, gene drive containing organisms may pose different risks if accidentally released from appropriate containment
    - Risks include risks to people and the environment, including the potential to adversely impact on populations/ecology
    - Evidence to support assessment of these risks is currently mostly theoretical; the Regulator should keep a watching brief on emerging data and evidence
    - Risks could be managed by giving further consideration to containment measures, guidelines and appropriate regulation.