



Australian Government

Department of Health and Aged Care
Office of the Gene Technology Regulator

Gene Technology Technical Advisory Committee

2 August 2023

Communiqué

This Communiqué covers matters considered at the 34th videoconference of the Gene Technology Technical Advisory Committee (2 August 2023)

The Gene Technology Technical Advisory Committee (GTTAC) is a statutory advisory committee established under the *Gene Technology Act 2000* (the Act) to provide scientific and technical advice to the Gene Technology Regulator (the Regulator) and the Gene Technology Ministers' Meeting.

The Regulator seeks advice from GTTAC on licence applications to work with Genetically Modified Organisms (GMOs) and on Risk Assessment and Risk Management Plans (RARMPs) prepared for applications. The purpose of this Communiqué is to provide a brief overview of GTTAC's consideration of applications and RARMPs and, in accordance with the Gene Technology Regulations 2001, to publish committee resolutions given to the Regulator. The Communiqué also provides an overview of any other deliberations of the committee. It does not include information which is treated as Confidential Commercial Information in accordance with the Act.

DEALINGS INVOLVING THE INTENTIONAL RELEASE OF A GMO

Dealings involving the Intentional Release (DIR) of a GMO into the environment can involve a limited and controlled release (clinical trial or field trial) or a commercial (general) release.

For commercial releases, the Regulator must seek GTTAC advice twice. The first consultation is on matters to consider when preparing the RARMP and the second is on the RARMP itself. For limited and controlled releases, the Regulator must seek GTTAC advice only once on the RARMP.

The RARMP for every DIR licence application is issued for public consultation. Information on how to obtain copies of DIR applications and RARMPs is provided at the end of this document.

ADVICE ON CONSULTATION RARMPs – LIMITED AND CONTROLLED RELEASE

DIR 197 – Clinical trial of genetically modified *Lactobacillus brevis* for treatment of inflammatory bowel disease

Licence application DIR 197 from Novotech (Australia) Pty Ltd is for a clinical trial of genetically modified (GM) *Lactobacillus brevis* for treatment of inflammatory bowel disease.

GTTAC discussed the likelihood assessment of the identified plausible pathways for shedding of the GMO into the environment. GTTAC suggested clarifying in the RARMP how the risk levels of the individual events link to the overall conclusion.

GTTAC noted a lack of data on the growth rate of the GMO, which would inform assessment of the likelihood of the GMO persisting in the environment. Members suggested a comparison of the GMO and native strain bacterial growth rates would be highly informative.

GTTAC considered more data was needed on the levels of the human vasoactive intestinal peptide (VIP) produced by the GMO. GTTAC discussed the potential for a systemic infection in trial participants, noting that ulcerative colitis is associated with inflammation and ulceration of the large intestine, which can lead to bacteraemia.

Resolutions

- While the committee agreed that all risk scenarios were identified, they expressed concern with the individual and collective likelihood assessment of the release pathways of the GMO into the environment based on uncertainty in relation to a number of areas including the growth rate of the GMO, VIP expression levels, persistence of the GMO in the gastrointestinal tract, and the replication and competition potential of the GMO in the environment.
- The committee recommended the office revise the RARMP to address these concerns and to ensure the consistency of the risk communication.

DEALINGS NOT INVOLVING THE INTENTIONAL RELEASE OF A GMO

The Regulator may seek GTTAC advice on RARMPs prepared for an application for Dealings Not involving an Intentional Release (DNIR) into the environment. DNIR licences include research work with GMOs undertaken in physical containment facilities (e.g. certified by the Regulator) and clinical trials undertaken in clinical facilities.

ADVICE ON DNIR RARMPs

DNIR 670 – Gene Drive *Anopheles farauti*

QIMR Berghofer Medical Research Institute has applied for a licence to conduct laboratory-contained research to develop a gene drive mosquito to control the spread of malaria.

GTTAC discussed and sought clarification on whether the antibodies intended to be expressed by the GMOs (three single-chained antibodies, scFvs) cross-react with human antigens. GTTAC suggested that if so, this may impact the risk assessment.

GTTAC discussed the role of melittin and magainin in potential anaphylaxis and suggested that the consequence assessment could be reduced.

Resolutions

- The Committee agreed that all plausible risk scenarios were identified but requested the office consider the issue of the potential human cross-reactivity of the scFVs and revise the RARMP accordingly.
- The Committee agreed that the risk of anaphylaxis from single or repeated exposure of people involved in the trial to melittin and/or magainin is likely to be negligible to low in the context of the proposed containment measures.
- The Committee did not identify additional information that should be considered.
- The Committee agreed with overall conclusion of the RARMP.

DNIR-671 – Clinical trial with a genetically modified *Salmonella* Typhimurium in patients with advanced solid tumours

DNIR-671 is a licence application from Novotech for a clinical trial to evaluate the safety and preliminary anti-tumour activity of GM *Salmonella* Typhimurium in patients with metastatic or unresectable solid tumours.

GTTAC discussed the characteristics and distribution of the GMO in different biological samples and requested that the OGTR provide further clarification on this matter.

Other key topics discussed by the Committee included:

- the presence of the GMO in target tissues
- whether the protein expressed in the GMO is membrane bound.

Resolutions

- The Committee agreed that the risk assessment identified all plausible risk scenarios. It recommended that the office further address in the RARMP implications of the characteristics and distribution of the GMO in tissues.
- Clarification is also sought on whether the expressed protein is soluble or membrane bound.
- The Committee agreed that the proposed licence conditions are appropriate for the dealings.
- There is no additional relevant information that should be considered.
- The Committee agreed with the overall conclusion of the RARMP.

ENQUIRIES

For all enquiries, please call the OGTR on 1800 181 030 or email ogtr@health.gov.au.