Australian Government

Department of Health

Office of the Gene Technology Regulator

Gene Technology Technical Advisory Committee
49th Meeting 6 June 2016, Canberra
Communiqué

This Communiqué covers matters considered at the 49th meeting of the Gene Technology Technical Advisory Committee (6 June 2016)

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 ministerial Legislative and Governance Forum on Gene Technology.

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 major issues discussed by GTTAC.

DEALINGS INVOLVING THE INTENTIONAL RELEASE OF A GMO

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

The Regulator must seek GTTAC advice during the preparation of a RARMP for DIR applications which do not qualify as limited and controlled under Section 50A of the Act. The Regulator must also seek advice from GTTAC on RARMPs that have been prepared for all DIR applications.

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 144 – Clinical trial of live attenuated genetically modified (GM) influenza vaccines

Clinical Network Services (CNS) Pty Ltd is seeking approval to conduct clinical trials to assess the safety and tolerability of a new type of GM influenza (flu) vaccine. The trials would involve administration of the GM flu vaccine to up to 500 healthy adult male volunteers over a period of five years.

GTTAC noted the key points in the RARMP, including that the risk assessment concludes that the proposed dealings with the GMO pose negligible to low risks to the health and safety of people and the environment. GTTAC also noted that the trials must meet the Therapeutic Goods Administration requirements and would require approval from a human research ethics committee at each trial site. GTTAC discussed a number of topics which are captured in the committee's advice to the Regulator below.

Resolution: GTTAC advised the Regulator that:

- The novel GM vaccines are likely to be attenuated. However, requesting additional attenuation data for unspecified vaccines is warranted considering the first-in-human trials.
- Further consideration should be given to potential transmission in ferrets to inform safety in humans.
- Further consideration should be given to potential risks to pregnant women as a result of potential shedding of vaccine virus.
- The Committee agrees with the overall conclusions of the RARMP.

OTHER ADVICE

New Technologies

GTTAC's advice was sought on technical aspects of new technologies to inform the Regulator's technical review of the Regulations. The discussion focussed on techniques often referred to as genome editing, specifically oligo-directed mutagenesis and site-directed nuclease (SDN) techniques. The committee noted that SDN applications are generally divided into three techniques, SDN-1, SDN-2 and SDN-3, that produce outcomes ranging from a single mutation to the insertion of a new gene[1].

GTTAC's advice was sought on the following questions regarding the risks to the health and safety of people and the environment posed by SDN techniques and oligo-directed mutagenesis:

- Are the risks posed by organisms altered by non-homologous end joining to repair DNA cleavage (ie SDN-1) any different to naturally mutated organisms?
- Does SDN-2 or oligo-directed mutagenesis pose any risks that are different to natural mutations, conventional breeding or mutagenesis?
- Could successive rounds of modification using SDN-2 or oligo-directed mutagenesis give rise to any new risks?
- Do the potential off-target effects of SDNs or oligo-directed mutagenesis pose different risks to the intended effects of these techniques?
- What is the evidence base available to support the assessment of the above risks?

Resolution: GTTAC advised the Regulator that:

- Risks posed by organisms altered by SDN-1 are unlikely to be different to naturally mutated organisms.
- SDN-2 and oligo-directed mutagenesis are unlikely to pose risks that are different to natural mutations, conventional breeding or mutagenesis.
- Successive rounds of modifications using SDN-2 and oligo-directed mutagenesis may pose risks similar to inserting new genes or SDN-3.
- Off target effects do pose risks different to the intended effects.
- Members recommended some experts and will send relevant evidence.

[1] Site-directed nuclease (SDN) techniques:

- SDN-1: non-homologous end joining repairs DNA cleavage, which can result in random insertions, deletions and substitutions, often of only a few nucleotides.
- SDN-2: homology-directed repair of DNA cleavage is guided by a supplied template, incorporating changes to one or a few nucleotides.
- SDN-3: homology-directed repair of DNA cleavage is guided by a supplied template, inserting a new gene or genetic element.

Generic Risk Assessment for Organisms

GTTAC was provided information on work being undertaken to develop a generic risk analysis framework for organisms (GRAFO). Members were invited to provide comments or observations on the conceptual approach and draft framework.

Members noted that the GRAFO would be intended to inform OGTR's risk assessments of different types of GMOs and to have a consistency of language and approach. The GRAFO proposes a set of risk factors that may inform risk assessments of organisms in a variety of regulatory contexts.

GTTAC discussed some of the terminology and descriptors used in the draft GRAFO and commended the OGTR on developing this new guidance document.

Revised Biology Document

Biology documents are prepared by the OGTR to provide baseline biology information relevant to the risk assessment of genetically modified forms of the species.

GTTAC reviewed the content of the updated biology document for *Brassica napus* L. (canola) and *Brassica juncea* (L.) Czern. & Coss. (Indian mustard) and suggested some minor changes. The committee commended the OGTR on maintaining up-to-date biology documents and acknowledged their value.

INFORMATION ITEMS AND REPORTS

The current membership of GTTAC expired 31 January 2017. The committee was updated on the process for appointment of members to GTTAC for the 2017-20 triennium.

GTTAC received a report from the Chair and from the Regulator that provided updates on relevant activities undertaken since the previous face-to-face GTTAC meeting (4 August 2015).

ENQUIRIES AND RISK ASSESSMENT AND RISK MANAGEMENT PLANS

For all enquiries and to obtain copies of applications or RARMPs for dealings involving the intentional release of GMOs into the environment, please call the OGTR on 1800 181 030 or email ogtr@health.gov.au. RARMPs are also available on the OGTR website.