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

12 December 2024

Summary of the Risk Assessment and Risk Management Plan (Consultation Version) for Licence Application No. DIR 208

Introduction

The Gene Technology Regulator (the Regulator) has received a licence application to conduct a clinical trial using a genetically modified organism (GMO). It qualifies as a DIR licence application under the *Gene Technology Act 2000* (the Act).

The applicant, Novotech (Australia) Pty Limited (Novotech), proposes to conduct a clinical trial to evaluate the safety and efficacy of a genetically modified (GM) vaccinia virus (VACV), for the treatment of solid tumours.

The proposed GM VACV has been designed to preferentially replicate in, and kill cancer cells. The GM VACV would be manufactured overseas and imported into Australia. It would be administered by intravenous infusion in up to 40 patients with solid tumours at clinical facilities and hospitals in Australia.

Clinical trials in Australia are conducted in accordance with requirements of the *Therapeutic Goods Act 1989*, which is administered by the Therapeutic Goods Administration (TGA). Therefore, in addition to approval by the Regulator, Novotech would require authorisation from the TGA before the trial commences. Clinical trials conducted in Australia must also be conducted in accordance with the *National Statement on Ethical Conduct in Human Research* and with the *Guidelines for Good Clinical Practice* of the International Council for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use. Novotech would also require approval from the Department of Agriculture, Fisheries and Forestry (DAFF) for import of the GMO into Australia. In addition, they may require approval from the Chief Inspector of Stock before bringing the GMO into South Australia; an authorisation from the Department of Jobs, Skills, Industry and Regions - Agriculture Victoria in Victoria and a Prohibited Matter Permit from New South Wales, Queensland and Western Australia if they wish to conduct dealings in those states.

The Regulator has prepared a Risk Assessment and Risk Management Plan (RARMP) for this application, which concludes that the proposed clinical trials pose negligible risks to human health and safety and the environment. Licence conditions have been drafted for the proposed clinical trial. The Regulator invites submissions on the RARMP, including draft licence conditions, to inform the decision on whether or not to issue a licence.

The application

Project Title	Clinical trial of GM vaccinia virus for the treatment of solid tumours
Parent organism	Vaccinia virus (VACV)
Principal purpose	The proposed trial is a Phase 1 study designed to evaluate the safety and efficacy of a genetically modified (GM) vaccinia virus, for the treatment of patients with solid tumours.
Genetic modifications	Introduced genes[1]: • Three separate genes related to immune function of human origin, which enhance anti-tumour immune responses. Deleted genes[1]: • The deletion of three VACV genes, which improves the efficacy and safety of the GMO.
Previous clinical trials	This is a first in human clinical trial using this GMO
Proposed limits and controls	
Proposed duration	5 years
Proposed number of participants	Up to 40 clinical trial participants in Australia
Proposed locations	The proposed trial would be conducted at a number of hospitals and clinics across Australia. The exact clinical trial sites are yet to be identified
Proposed controls	• Transport and storage of the GMO according to the Regulator's *Guidelines for the Transport, Storage and Disposal of GMOs* • Require staff handling the GMO to be trained and to use personal protective equipment • Staff with immunosuppressive disorders are excluded from handling the GMO • Disposal of waste that may contain GMO according to clinical site procedures appropriate for risk group 2 organisms • Provide patients with detailed instructions regarding the care of any skin-related reactions post-treatment and the use of good hygiene practices

Risk assessment

The risk assessment process considers how the genetic modifications and proposed activities conducted with the GMO might lead to harm to people or the environment. Risks are characterised in relation to both the seriousness and likelihood of harm, taking into account information in the application (including proposed controls), relevant previous approvals and current scientific/technical knowledge. Both short- and long-term impacts are considered.

Credible pathways to potential harm that were considered included the; potential exposure of people or animals to the GMO; and the potential for the GMO to transfer or acquire genetic material from other viruses. The potential for the GMO to be released into the environment and its effects were also considered.

The risk assessment concludes that the trial poses negligible risks to human health and safety and to the environment. No specific risk treatment measures are required to manage these negligible risks.

[1] Confidential Commercial Information (CCI): Some details about the inserted and deleted genes have been declared as CCI under section 185 of the Act. This information will be made available to the prescribed experts and agencies that will be consulted on this application. CCI is not available to the public.

Important factors in reaching the conclusions of the risk assessment included that the GM VACV treatment selectively replicates in cancer cells, and unintended exposure to the GMOs would be minimised by the limits and controls.

As risks to the health and safety of people, or the environment, from the proposed trial of the GMO treatment have been assessed as negligible, the Regulator considers that the dealings involved do not pose a significant risk to either people or the environment.

Risk management

The risk management plan describes measures to protect the health and safety of people and to protect the environment by controlling or mitigating risk. The risk management plan is given effect through licence conditions. Draft licence conditions are detailed in Chapter 4 of the RARMP.

As the level of risk is considered negligible, specific risk treatment is not required. However, since this is a clinical trial, the draft licence includes limits on the number of trial participants, types of facilities used, limits on the duration of the trial, as well as a range of controls to minimise the potential for the GMO to spread in the environment. In addition, there are several general conditions relating to ongoing licence holder suitability, auditing and monitoring, and reporting requirements which include an obligation to report any unintended effects.