



Australian Government

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

Summary of the Risk Assessment and Risk Management Plan for Licence Application No. DIR 208

Decision

The Gene Technology Regulator (the Regulator) has decided to issue a licence for this application for the intentional release of a genetically modified organism (GMO) into the environment. A Risk Assessment and Risk Management Plan (RARMP) for this application has been prepared by the Regulator in accordance with the *Gene Technology Act 2000* (the Act) and corresponding state and territory legislation, and finalised following consultation with a wide range of experts, agencies and authorities, and the public. The RARMP concluded that the proposed trial poses negligible risk to human health and safety and the environment and that any risks posed by the dealings can be managed by imposing conditions on the release.

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.

Risk Assessment and Risk Management Plan (RARMP) for this application has been prepared by the Regulator in accordance with the Act and corresponding state and territory legislation, and finalised following consultation with a wide range of experts, agencies and authorities, and the public. The RARMP concludes that the proposed clinical trial pose negligible risks to human health and safety and the environment.

The application

Project Title	Clinical trial of a 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 : <ul style="list-style-type: none">• Three separate genes related to immune function of human origin, which enhance anti-tumour immune responses. Deleted genes ¹ : <ul style="list-style-type: none">• 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
Limits and controls	
Duration	5 years
Number of participants	Up to 40 clinical trial participants in Australia
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
Controls	<ul style="list-style-type: none">• Transport and storage of the GMO according to the Regulator's <i>Guidelines for the Transport, Storage and Disposal of GMOs</i>• 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.

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. CCI is not available to the public.

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

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.

As the level of risk is considered negligible, specific risk treatment is not required. However, since this is a clinical trial, the 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 effect.