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

October 2024

Summary of the Risk Assessment and Risk Management Plan (Consultation Version) for Licence Application No. DIR 206

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 Dealing involving the Intentional Release (DIR) of GMOs into the Australian environment under the *Gene Technology Act 2000*.

The applicant, Western Sydney Local Health District (WSLHD), proposes to conduct a clinical trial to evaluate the safety and efficacy of genetically modified (GM) bacteriophages, alone or in combination with non-GM bacteriophage therapy, for the treatment of Australian patients with mycobacterial infections.

The GMOs were modified from bacteriophages which have been shown to kill mycobacteria. The GMOs would be manufactured overseas and imported into Australia. They would be administered by various methods including via nebuliser, by intravenous injection, instillation, or topical application in Australia at clinical trial sites, hospitals and other sites under the hospital in the home (HITH) program.

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, WSLHD would also require authorisation from 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. WSLHD would also require approval from the Department of Agriculture, Fisheries and Forestry for import of the GMOs.

The Regulator has prepared a Risk Assessment and Risk Management Plan (RARMP) for this application, which concludes that the proposed clinical trial poses 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 to issue a licence.

The application

Project Title	Clinical trial of the treatment of mycobacterial infections using bacteriophages[1]
Parent organism	Bacteriophages (mycobacteriophages)
Genetic modifications	Deletion of genes including the repressor gene, rendering the bacteriophages lytic in order to destroy host bacteria.
Principal purpose	The proposed dealings are to administer genetically modified bacteriophages to treat Australian patients with mycobacterial infections.

[1] Original title: *Bacteriophages for treatment of mycobacterial infections under the STAMP protocol*

Previous clinical trials	DNIR-620 issued to the Sydney Children's Hospital Network authorised the therapeutic treatment of paediatric patients with cystic fibrosis and *Mycobacterium abscessus* disease. DNIR-655 issued to the Alfred Hospital authorised bacteriophage therapy for severe lung disease due to *Mycobacterium abscessus* infection.
Proposed limits and controls	
Proposed duration	5 years
Proposed release size	At least 3 participants would be enrolled in the trial in Australia
Proposed locations	This clinical trial would be conducted within Australia at clinical trial sites, hospitals and other sites through the Hospital In The Home (HITH) program. The number of sites and specific locations are yet to be determined.
Proposed controls	• Administration will be in-hospital or by qualified persons under the HITH program. • Qualified persons will change dressings. • Administration will only be to participants under Special Access Scheme categories A and B. • Administration will be limited to the treatment of those with mycobacterial infections.

Risk assessment

The risk assessment process considers how the genetic modification and activities conducted with the GM bacteriophages in the context of import, transport, storage, administration and disposal 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, relevant previous approvals, current scientific knowledge and advice received from a wide range of experts, agencies and authorities consulted on the preparation of the RARMP. Both the short- and long-term risks were considered.

Credible pathways to potential harm that were considered include; the potential exposure of people to the GMO; the potential exposure of animals to the GMO; and the potential for the GMO to recombine with other similar bacteriophages. The potential for the GMO to be released into the environment and its effects were also considered.

The risk assessment concludes that risks to the health and safety of people are negligible and the risks to the environment from the proposed dealings with the GM bacteriophages are negligible. Specific risk treatment measures are included in the licence to maintain the risk context.

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, as this application was assessed as a limited and control licence and limited data are available for the use of this class of GMOs in clinical trials, conditions were included in the draft licence to minimise the potential for the GMO to spread in the environment. Since this is a clinical trial, the draft licence includes limits on the inclusion criteria of trial participants and the duration of the trial. 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.