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

September 2023

Summary of the Risk Assessment and Risk Management Plan

for

Licence Application DIR 197

Decision

The Gene Technology Regulator (the Regulator) has decided to issue a licence for a clinical trial using a genetically modified organism (GMO). It qualifies as Dealings involving the Intentional Release (DIR) of genetically modified organisms into the Australian environment under the *Gene Technology Act 2000* (the Act).

The applicant, Novotech (Australia) Pty Limited (Novotech) proposes to conduct a first-in-human clinical trial of genetically modified (GM) *Lactobacillus brevis* bacteria for treatment of inflammatory bowel disease. The GMO would be administered orally and is designed to have anti-inflammatory effects in the gastrointestinal tract.

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 will 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 will also require approval from the Department of Agriculture, Fisheries and Forestry for import of the GM treatment.

The Regulator has prepared a Risk Assessment and Risk Management Plan (RARMP) for this application, which was finalised following consultation with a wide range of experts, agencies and authorities, and the public. The RARMP concludes that the proposed clinical trial poses negligible to moderate risks to human health and safety and the environment, and that the risks posed by the dealings can be managed by imposing conditions on the release.

The licence

Project title	Clinical trial of genetically modified *Lactobacillus brevis* for treatment of inflammatory bowel disease
Parent organism	*Lactobacillus brevis*
Genetic modifications[1]	• Introduction of gene encoding human vasoactive intestinal peptide (VIP) to reduce inflammation
Principal purpose	To assess the safety of single and multiple ascending doses of the GMO in healthy clinical trial participants
Previous clinical trials	None

[1] Information about genetic modifications other than the introduction of the VIP gene is protected as Confidential Commercial Information (CCI). Under Section 185 of the Act, the confidential information was made available to the prescribed experts and agencies that were consulted on the RARMP for this application.

Limits and controls	
Duration	7 years
Release size	Up to 28 trial participants will be treated with the GMO
Locations	Medical facilities and the homes of clinical trial participants in Melbourne, Victoria
Controls	• importing the GMO in a form that is double packaged and ready for administration • tracking GMO doses dispensed to clinical trial participants and destroying any GMO doses that remain unused at the end of the trial • issuing spill kits to trial participants to clean up any spill of GMO that occurs at home • instructing clinical trial participants in appropriate hygiene measures

Risk assessment

The risk assessment concludes that the proposed clinical trial poses negligible to moderate risks to human health and safety and the environment. Specific risk treatment measures are included in the licence to manage these risks.

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 the short- and long-term impact are considered.

Credible pathways to potential harm that were considered include potential exposure to the GMO through accidental ingestion or through shedding from trial participants; the potential for the introduced gene to be transferred to other bacteria; and the potential for the GMO to spread in the environment and enter food and feed.

Important factors in reaching the conclusions of the risk assessment included:

- the GMO is not expected to colonise human or animal guts;
- the small scale of the clinical trial minimises the likelihood of horizontal gene transfer events;
- there are plausible pathways for release of the GMO into the outdoor environment;
- there is uncertainty regarding the ability of the GMO to establish and spread in the environment;
- VIP is capable of causing adverse health effects at sufficiently high levels of exposure.

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.

The risk management plan concludes that the identified negligible to moderate risks can be managed to protect the health and safety of people and the environment by imposing specific risk treatment measures. A number of licence conditions are imposed to restrict release of the GMO into the outdoor environment.

The licence includes limits on the number of trial participants and 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.