Australian Government
Department of Health, Disability and Ageing
Office of the Gene Technology Regulator

February 2026

Summary of the Risk Assessment and Risk Management Plan

for

Licence Application DIR-221

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 expert, agencies and authorities, and the public. The RARMP concluded that the proposed trial poses negligible to low risks 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, Melius MicroBiomics Pty Ltd (Melius), proposes to conduct a clinical trial to evaluate the safety and efficacy of a genetically modified (GM) *Escherichia coli* for the treatment of Australian patients with ulcerative colitis. Ulcerative colitis is a type of inflammatory bowel disease (IBD) that causes the formation of sores due to inflammation that affects the lining of the large intestine (colon) and rectum.

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, Melius 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. Melius would also require approval from the Department of Agriculture, Fisheries and Forestry (DAFF) for import of the GMO into Australia.

The application

Project Title	Clinical trial with genetically modified *Escherichia Coli* for the treatment of ulcerative colitis.
Parent organism	*Escherichia coli* (Nissle strain).
Genetic modifications	*E. coli* has been modified by the: • Insertion of 2 copies of the tetrathionate reductase (*ttr*) operon from

	Salmonella enterica – survival advantage in inflammatory environment.
	• Deletion of 2 genes[1]
	  ○ Gene A - reduced survivability in the broader environment; and
	  ○ Gene B - potentially reduced ability to colonise the healthy gut compared to wild type (WT)

Principal purpose	The proposed trial is a Phase 1 study designed to evaluate the safety and efficacy of GM *E. coli*, for the treatment of Australian patients with ulcerative colitis.
Previous clinical trials	None, this is a first in human clinical trial.
Proposed limits and controls	
Proposed duration	5 years
Proposed release size	Up to 36 participants in Australia (including placebo).
Proposed locations	This clinical trial would be conducted within Australia at a hospital or clinical trial sites (medical facilities). The specific clinical trial sites are yet to be identified.

Proposed controls	• The GMO would be administered to trial participants within clinical trial sites.
	• Staff handling the GMO would be trained and would wear personal protective equipment.
	• Waste that may contain the GMO would be disposed of via the facility standard practices for disposal of biological waste.
	• Any unused doses of GMO would be disposed of at the clinical trial site at the end of the trial, in accordance with the *Transport, Storage and Disposal Guidelines*.
	• Participants would be instructed:
	  ○ on appropriate hygiene practices, including proper hand washing procedures following toilet use.
	  ○ to abstain from unprotected sex and to use a double barrier method.
	• The GMO would be transported and stored according to *Transport, Storage and Disposal Guidelines*.

Risk assessment

The risk assessment process considers how the genetic modification 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 risks are considered.

[1] Confidential Commercial Information: Some details about the modification in GM *E. coli* have been declared as Confidential Commercial Information under section 185 of the Act. This information was made available to the prescribed experts and agencies that were consulted on this application. CCI is not available to the public.

Credible pathways to potential harm that were considered include the potential exposure of people and animals to the GMO and the potential for transfer of genetic material to and from the GMO. The potential for the GMO to be released into the environment and its effects was also considered.

The risk assessment concludes that the proposed clinical trial poses negligible to low risks to human health and safety and negligible risks to the environment. Specific risk treatment measures are imposed to manage these risks to people.

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

- the parent organism has a long history of safe use as a probiotic,
- the GMO has selective replication in patients with inflammatory bowel disease,
- unintended exposure to the GMO would be minimised by the proposed limits and controls outlined in the risk management plan,
- bacterial infections usually self-resolve, but in some cases may need antibiotic or hospital treatment, and
- the likelihood of complementation and recombination of the GMO with other bacteria is unlikely to result in bacteria that is more pathogenic than the parent organism, and
- bacterial infections usually self-resolving, could be treated by antibiotics or may require specific hospital care in cases of severe infection.

Therefore, 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.

The risk management plan concludes that the identified negligible to low risks can be managed to protect the health and safety of people by imposing specific risk treatment measures. Licence conditions are imposed to minimise the exposure of the GMO or novel bacteria to other people and the 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.