Australian Government
Department of Health
Office of the Gene Technology Regulator

08 February 2021

Summary of Licence Application DIR 183

The Westmead Institute for Medical Research has made an application under the *Gene Technology Act 2000* (the Act) to conduct clinical trials using genetically modified organisms (GMOs).

Project Title	Clinical trial with genetically modified *E.coli* to reduce antibiotic resistance
Parent organism	*Escherichia coli* (Nissle strain) and human gut bacteria
Genetic modifications	
Introduced genes	Two antibiotic resistance plasmids (bacterial circular DNA packages) were modified by • Deletion of genes responsible for the resistance to multiple classes of antibiotics • Deletion of genes that enable plasmids to persist in bacteria • Introduction of genes for resistance to specific antibiotics (fosfomycin and tetracycline) to enable selection for the GMO
Principal purpose	The proposed trial is designed to evaluate the safety and efficacy of GM *E.coli* to deliver genes to gut bacteria that restore sensitivity to antibiotics
Previous clinical trials	This is a first-in-human clinical trial using these GMOs.
Proposed limits	
Proposed location/s	The proposed trial would be conducted at Westmead Hospital
Proposed release size	Less than 100 participants per year
Proposed period of the clinical trial	5 years
Proposed controls	• Administration of GMO would be conducted in a clinical setting. • Eligible participants would remain in a clinical setting for a minimum of 7 days after administration of the GMO. • Any consumables potentially contaminated with the GMO will be disposed of through the clinical waste streams.

The application

Most people carry bacteria in their gut that are resistant to certain antibiotics, but experience no ill effects. However, in some circumstances these gut bacteria can make medical treatments less effective. The proposed trial is designed to evaluate the safety and efficacy of GM *E.coli* delivering genes to gut bacteria that restore sensitivity to antibiotics.

The application is for a limited and controlled release under section 50A of the Act, as the Regulator was satisfied that its principal purpose is to enable the applicant to conduct the trial, and the proposed limits and controls are such that consultation with prescribed experts, agencies and jurisdictions is not required at this stage. The proposed clinical trial would need approval from a registered Human Research Ethics Committee prior to commencement.

Next steps

The Gene Technology legislation sets out what the Regulator must do, as well as what the Regulator can or must consider, before deciding whether or not to issue a licence for this application.

The Regulator's staff will prepare a consultation version of the Risk Assessment and Risk Management Plan (RARMP) considering aspects of the application including the proposed limits and controls in accordance with the legislation.

The Regulator will seek comment on the consultation RARMP from the public, as well as a wide range of experts, agencies and authorities. The public and experts will be invited to provide submissions on the risks to human health and safety, and on risks to the environment from the proposed release.

At this stage, the consultation RARMP is expected to be released for public comment in late April 2021.

After consultation, the Regulator's staff will finalise the RARMP, taking into account advice on relevant matters. The finalised RARMP will form the basis of the Regulator's decision whether or not to issue a licence. The consultation and final versions of the RARMP and associated documents will be available on the OGTR website when they are released.

Other information available from the OGTR website:

- information on Australia's national scheme for regulation of gene technology and
- information on the DIR application process.

Please use the contact details below, if you

- would like a copy of the application. Please include the identifier DIR 183.
- have any questions about the application or the legislated evaluation process or
- wish to register on the mailing list.

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