



Australian Government

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

April 2025

Summary of the Risk Assessment and Risk Management Plan for Licence Application No. DIR 210

Decision

Influenza is an acute respiratory viral infection caused by influenza A or B viruses, with up to 650,000 deaths worldwide annually. For most healthy adults, seasonal influenza is a self-limited illness from which complete recovery is expected. Understanding the physiological and immunological responses of humans to these viruses is critical to develop vaccines and antiviral drugs for the control of influenza.

Doherty Clinical Trials Ltd (DCT) is seeking approval to use genetically modified (GM) influenza viruses similar to naturally circulating influenza viruses to better understand influenza infection and test the efficacy of potential vaccines and therapeutic drugs. The GM influenza viruses are made using gene technology and are considered GMOs. Healthy volunteers will receive a dose of the GM influenza viruses within a clinical facility in combination with or without a potential vaccine or therapeutic drug. The study will be conducted under strict ethical guidelines and safety protocols in an approved clinical trial facility, considering OGTR and good clinical practice guidelines. In addition, the applicant has proposed control strategies to restrict the spread and persistence of the GMO(s) in the environment.

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

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 clinical trial poses negligible to moderate risk to human health and safety and the environment, based on the current pathogenicity of circulating influenza and that any risks posed by the dealings can be managed by imposing conditions on the release.

The application

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| <i>Project Title</i> | Clinical trials of controlled infection with seasonal influenza viruses |
| <i>Parent organism</i> | Seasonal Human influenza Virus A and B (including H1N1 and H3N2) |
| <i>Principal purpose</i> | The initial aim is to evaluate the safety and infectivity of recombinant seasonal human influenza viruses in healthy volunteers. These GM viruses will then be used to assess the effectiveness of therapeutic drugs or vaccine candidates to prevent and control influenza infection. |
| <i>Genetic modifications</i> | Recombinant influenza virus A and B produced using gene technology (reverse genetics) similar to naturally circulating strains of wild-type seasonal influenza |
| <i>Previous clinical trials</i> | One completed challenge study in the United States (NCT04978454) One ongoing challenge study in the United States (NCT06476275) |
| <i>Proposed limits and controls</i> | |
| <i>Proposed duration</i> | 5 years |
| <i>Proposed trial size</i> | Up to 150 clinical trial participants |
| <i>Proposed locations</i> | Clinical Trial Ward located in East Melbourne. |
| <i>Proposed controls</i> | <ul style="list-style-type: none"> • Trial participants will be isolated in secure rooms • Staff will be trained and experienced in preventing spread of infection • Staff will wear personal protective equipment (PPE) while conducting dealings with GMO including GMO administration, serving food, patient care, checks and monitoring as required • Trial participants will remain isolated for 7 days post administration • Waste potentially contaminated with GMOs will be disposed of in GMO-labelled bin and collected by external service providers |

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 likelihood and consequence of the 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 included exposure of people or animals to the GMOs and whether there is the potential for reassortment with other viruses. Potential harms that were considered in relation to these pathways included ill health and increased disease in people or animals.

The RARMP determined that the proposed clinical trial presents **negligible to moderate risks** to the health and safety of individuals, based on the pathogenicity of circulating influenza. Licence conditions have been implemented to mitigate the risks associated with this clinical trial.

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

- the GMOs would not be more pathogenic than circulation strain of influenza
- the trial participants will remain isolated for the duration of the contagious period
- extensive PPE would be worn by staff conducting dealings.

Risk management plan

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 RARMP determined that the proposed clinical trial presents **negligible to moderate risks** to the health and safety of individuals, based on the pathogenicity of circulating influenza. Licence conditions have been imposed to mitigate the risks associated with this clinical trial. In addition, since this is a clinical trial, the licence includes limits on the number of trial participants, the facility used, exclusion criteria, and as well as a range of controls to minimise the potential for exposure of people other than trial participants to the GMO. There are also several general conditions imposed relating to ongoing licence holder suitability, auditing and monitoring, and reporting requirements, including an obligation to report any unintended effect.