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

April 2026

Summary of the Risk Assessment and Risk Management Plan for Licence Application No. DIR 223

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) 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 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, Ferring Pharmaceuticals Pty Ltd (Ferring), proposes to conduct a clinical trial to evaluate the safety and efficacy of a genetically modified (GM) human adenovirus, nadofaragene firadenovec, for the treatment of Australian patients with bladder cancer.

Nadofaragene firadenovec was developed for the treatment of adult patients with high-risk Bacillus Calmette-Guérin (BCG)-unresponsive non-muscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS) with or without papillary tumours. The GM adenovirus would be manufactured overseas and imported into Australia. It would be administered by bladder instillation in up to 25 patients with non-muscle invasive bladder cancer at clinical facilities and hospitals in Australia.

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, Ferring 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. Ferring 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 trials of a genetically modified adenovirus for treatment of bladder cancer[1]
Parent organism	Human adenovirus type 5 (HAdV-C5)

[1] This application was originally submitted in 2 parts. The original titles supplied by the applicant were: "A phase 3, randomised, multi-centre, open-label trial to evaluate the safety and efficacy of intravesical nadofaragene firadenovec alone or in combination with chemotherapy (gemcitabine and docetaxel) or immunotherapy (pembrolizumab) in subjects with high-grade Bacillus Calmette-Guerin (BCG) unresponsive non-muscle invasive bladder cancer (NMIBC)"; and "A Phase 3b, Randomised, Controlled Trial of Nadofaragene Firadenovec vs. Observation in Subjects with Intermediate Risk (IR) Non-Muscle Invasive Bladder Cancer (NMIBC)".

Genetic modifications	
Introduced genes	Modified human adenovirus: • deletion of gene sequences[2] to improve safety • insertion of the human interferon alpha-2b (*hIFN-α2b*) gene to produce the protein with anticancer activities
Principal purpose	The proposed trials are Phase 3 and 3b studies designed to evaluate the safety and efficacy of a genetically modified (GM) adenovirus for the treatment of Australian patients with bladder cancer
Previous approvals	• Licence DIR 217 was issued on 17 October 2025 for dealings associated with the commercial supply of the GMO in Australia. • Clinical trials (Phases 1-3) were undertaken in the United States (US). • In December 2022, the US Food and Drug Administration approved this GMO for the treatment of high-grade bladder cancers.
Proposed limits and controls	
Locations	Clinical trial sites (medical facilities) in Australia, initially up to 9 in New South Wales and Victoria
Trial size	Up to 25 clinical trial participants in Australia across the two phases
Duration	5 years
Controls	• The GMO would be administered to trial participants within clinical trial sites • Staff handling the GMO would be trained and use personal protective equipment • Higher risk staff would be excluded from handling the GMO • The GMO would be transported and stored according to the Regulator's *Guidelines for the Transport, Storage and Disposal of GMOs*. • Waste that may contain GMO would be destroyed according to clinical trial site procedures appropriate for physical containment level 2 (PC2) GMOs.

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.

Credible pathways to potential harm that were considered include the potential exposure of people and animals to the GMO, the potential for the GMO to recombine with other similar viruses and the potential for the GMO to integrate into the host genome.

The risk assessment concludes that the trial poses negligible risks to human health and safety and to the environment. No specific risk treatment measures are required to manage these negligible risks.

Important factors in reaching the conclusions of the risk assessment included that the GMO is replication incompetent, unintended exposure to the GMO would be minimised by the limits and controls outlined in

[2] Confidential Commercial Information: Some details about the deleted DNA sequences have been declared as Confidential Commercial Information under section 185 of the Act.

the risk management plan and that the likelihood of complementation and recombination of the GMO with other adenoviruses is low.

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.

As the level of risk is considered negligible, specific risk treatment is not required. However, since this is a clinical trial, the licence includes limits on the number of trial participants, locations limited to hospitals and clinical trial sites, limits on the 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.