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

July 2025

Summary of the Risk Assessment and Risk Management Plan

Consultation Version

for

Licence Application No. DIR 217

Introduction

The Gene Technology Regulator (the Regulator) has received a licence application for the import, transport, storage, and disposal of a non-replicating adenoviral vector-based therapeutic product, nadofaragene firadenovec, as part of its commercial supply in Australia as a treatment for high-grade Bacillus Calmette-Guérin (BCG)-unresponsive non-muscle invasive bladder cancer (NMIBC).

Before nadofaragene firadenovec can be registered as a therapeutic, its quality, safety, and efficacy must be assessed by the Therapeutic Goods Administration (TGA). If registered as a human therapeutic, the TGA may impose conditions relating to the use and labelling of the GM therapeutic. As nadofaragene firadenovec is manufactured overseas, a permit from the Department of Agriculture, Fisheries and Forestry will be required for its import into Australia.

The Regulator has prepared a draft Risk Assessment and Risk Management Plan (RARMP) for this application, which concludes that the proposed supply of the GM therapeutic poses negligible risks to human health and safety and the environment, and no specific risk treatment measures are proposed. Licence conditions have been drafted for the proposed dealings. The Regulator invites submissions on the RARMP, including draft licence conditions, to inform the decision on whether or not to issue a licence.

The application

Application number	DIR 217
Applicant	Ferring Pharmaceuticals Pty Ltd
Project Title	Commercial supply of nadofaragene firadenovec for bladder cancer treatment[1]
Parent organism	Human adenovirus C serotype 5 (HAd5)
Modified trait	Replication incompetent HAd5 expressing a human interferon alfa-2b (*hIFN-α2b*) gene
Genetic modification	• deletion of gene sequences[2] to improve safety • insertion of the *hIFN-α2b* gene to produce the protein with anticancer activities
Proposed locations	Australia-wide
Principal purpose	Commercial supply of the GM therapeutic

[1] The original title supplied by the applicant is: *Gene therapy for bladder cancer.*

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

Previous approvals	The GM therapeutic has not previously been approved in Australia. Internationally, the GM therapeutic has been approved by the Food and Drug Administration (FDA) in the USA.
Proposed period of release	Ongoing from issue of licence

Risk assessment

The risk assessment process considers how the genetic modification and proposed activities conducted with the GM therapeutic in the context of import, transport, storage, and disposal 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, relevant previous approvals, current scientific knowledge and advice received from a wide range of experts, agencies and authorities consulted on the preparation of the RARMP. Both the short and long term risks were considered.

Credible pathways to potential harm that were considered include the potential for accidental exposure of people to the GMO during transport and storage, preparation and administration of the GMO, and during disposal of the GMO and any associated waste; the potential for the GMO to recombine with other similar viruses; the potential for the GMO to integrate into the host genome and the potential for the GMO to be released into the environment and its effects were also considered.

The risk assessment concludes that risks to the health and safety of people and to the environment from the proposed supply of the GM therapeutic are negligible. No specific risk treatment measures are proposed to manage these negligible risks.

The principal reasons for the conclusion of negligible risks associated with the import, transport, storage and disposal of the GMO are:

- the GMO is replication incompetent and susceptible to clearance by the host immune system and, in comparison to wildtype (WT) adenovirus, is unlikely to infect humans and cause disease
- the dose received through accidental exposure would be smaller than that administered to patients
- import, transport, storage, and disposal will follow well established procedures.

Risk management

Risk management is used to protect the health and safety of people and to protect the environment by controlling or mitigating risk. The risk management plan evaluates and treats identified risks and considers general risk management measures. The risk management plan is given effect through licence conditions. Draft licence conditions are detailed in Chapter 4 of the RARMP.

The risk management plan concludes that risks from the proposed dealings can be managed so that people and the environment are protected by imposing general conditions to ensure that there is ongoing oversight of the therapeutic containing the GMO.

As the level of risk was assessed as negligible, specific risk treatment is not required. However, the Regulator has drafted licence conditions regarding post release review (post-market surveillance) to ensure that there is ongoing oversight of the supply of the GM therapeutic and to allow the collection of ongoing information to verify the findings of the RARMP. The draft licence also contains a number of general conditions relating to ongoing licence holder suitability, auditing and monitoring, and reporting requirements, which include an obligation to report any unintended effects.