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

November 2023

Summary of the Risk Assessment and Risk Management Plan for Licence Application No. DIR 196

Decision

The Gene Technology Regulator (the Regulator) has decided to issue a licence for the import, transport, storage, and disposal of a genetically modified (GM) vaccine, Qdenga, as part of its commercial supply in Australia as a human vaccine against dengue virus. The vaccine is intended to be available under prescription for people travelling to dengue-affected areas.

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

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 commercial supply of the GM vaccine poses negligible risks to human health and safety and the environment, and no specific risk treatment measures are required. However, general licence conditions have been imposed to ensure there is ongoing oversight of the release.

The application

Project Title	Commercial supply of Qdenga, a live attenuated GM dengue vaccine
Parent organism	Dengue virus serotype 2 strain PDK-53
Modified trait	Altered antigen expression
Genetic modification	A 'strain' is a genetic variant or subtype of a microorganism. Strains of dengue virus can also be categorised into 4 distinct 'serotypes' based on their surface antigen expression. The genetic backbone for the GMOs in this application is a non-GM dengue virus serotype 2 strain that has been attenuated (weakened) through spontaneous mutations that occurred during a subculturing process in tissue culture. The vaccine contains 4 GM strains of dengue virus, known as TDV-1, TDV-2, TDV-3, and TDV-4, where the serotype 2 backbone has been modified to contain pre-membrane (*prM*) and envelope (*E*) genes from the 4 dengue serotypes. As glycoproteins prM and E are present on the surface of dengue virus particles and are recognised by the human immune system, the GM vaccine is intended to stimulate immune responses against all these serotypes.
Proposed locations	Australia-wide
Principal purpose	Commercial supply of the GM dengue vaccine

Previous approvals	The GM vaccine has not previously been approved in Australia. Internationally, the GM vaccine has been approved by health authorities in Indonesia, the European Union, Great Britain, Brazil, Argentina, and Thailand.
Proposed period of release	From issue of licence

Risk assessment

The risk assessment process considers how the genetic modification and proposed activities conducted with the GM vaccine 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 accidental exposure of people to the GMOs during transport and storage, preparation and administration of the vaccine, and during disposal of the GMOs and any associated waste. The potential for the GMOs 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 vaccine are negligible. No specific risk treatment measures are required to manage these negligible risks.

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

- the GMOs are attenuated in comparison to wildtype (WT) dengue
- the dose received through accidental exposure would be smaller than that administered during vaccination
- the GM vaccine has a favourable safety profile at doses higher than would be expected through accidental exposure
- 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.

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 vaccine containing the GMOs.

As the level of risk was assessed as negligible, specific risk treatment is not required. However, the Regulator has imposed licence conditions regarding post release review (post-market surveillance) to ensure that there is ongoing oversight of the supply of the GM dengue vaccine and to allow the collection of ongoing information to verify the findings of the RARMP. The 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.