# Questions & Answers on licence application DIR 196 – commercial supply of a genetically modified (GM) dengue vaccine, Qdenga

**What is this application for?**

Takeda Pharmaceuticals Australia Pty Ltd is seeking approval for the import, storage, transport, and disposal of a genetically modified (GM) dengue vaccine, Qdenga, as part of its commercial supply in Australia as a human vaccine against dengue virus.

**What is dengue?**

Dengue is a mosquito-borne disease caused by dengue viruses. 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 proteins on the surface of the viral particle that are recognised by the immune system. People infected for the first time can develop sudden and painful fever. The infection usually resolves after a week and the person has life-long immunity to that particular serotype of dengue virus. However, a subsequent infection with a different serotype of dengue virus can potentially lead to life-threatening dengue haemorrhagic fever or dengue shock syndrome.

**How has the dengue vaccine been genetically modified?**

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.

**Why is the dengue vaccine being supplied in Australia?**

Dengue is exotic to Australia, but Australians can be infected when they travel to neighbouring tropical regions where dengue is endemic. When a person infected with dengue returns, the disease is brought into Australia and sporadic outbreaks occur in the warmer parts of Australia, where the disease-transmitting *Aedes* mosquito lives.

**What regulatory processes apply to this commercial supply?**

The Gene Technology Regulator (the Regulator) has specific responsibility to protect the health and safety of people, and to protect the environment from any risks posed by gene technology. For this type of application, the activities assessed by the Regulator are the import, transport, storage, and disposal of the GM vaccine.

The use of the vaccine in people will also require approval by the Therapeutic Goods Administration (TGA). The TGA considers the safety and efficacy of the vaccine in people being vaccinated as part of their approval process, and also determines conditions for the use of the vaccine.

The import of the vaccine will also require a permit from the Department of Agriculture, Fisheries and Forestry (DAFF).

**Has Qdenga been used previously?**

Qdenga has not previously been approved for commercial use in Australia.

Internationally, Qdenga has been approved by health authorities in Indonesia, the European Union, Great Britain, Brazil, Argentina, and Thailand.

**What controls are proposed for this commercial supply?**

The licence application proposes an ongoing commercial supply of the GM vaccine. The Gene Technology Regulator has prepared a consultation Risk Assessment and Risk Management Plan (RARMP), which finds that the proposed commercial supply of this GM vaccine poses negligible risk to the health and safety of people or the environment. However, licence conditions drafted in the consultation RARMP ensure that there is ongoing oversight of the commercial supply.

**How can I comment on this application?**

The full consultation RARMP and a summary of the RARMP for application DIR 196 are available on the OGTR website or via the contacts listed below. You are invited to submit your written comments (including email) on the consultation version of the RARMP, related to any risks to the health and safety of people or to the environment from the proposed commercial supply. Please note that issues such as **patient safety, quality and efficacy of therapeutic products, and marketability and trade implications** do **NOT** fall within the scope of the evaluations conducted under the *Gene Technology Act 2000* as these are the responsibility of other agencies and authorities. Comments must be received by the close of the consultation period on **18 October 2023**.

**What are the next steps in the evaluation process?**

The RARMP will be finalised, taking into account submissions related to the protection of people or the environment. A de-identified summary of all comments received and consideration of those comments is included in the Appendices to the final RARMP. The finalised RARMP will inform the Regulator's decision on whether or not to issue a licence.

**The Office of the Gene Technology Regulator**

**OGTR Website**

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