Australian Government
Department of Health
Office of the Gene Technology Regulator

June 2017

Summary of the Risk Assessment and Risk Management Plan

for

Licence Application DIR 148

Decision

The Gene Technology Regulator (the Regulator) has decided to issue a licence for this application. The licence authorises import, transport, storage and disposal of a genetically modified (GM) dengue vaccine, known as Dengvaxia, for the purpose of its commercial supply as a therapeutic product.

A Risk Assessment and Risk Management Plan (RARMP) for this application was prepared by the Regulator in accordance with the requirements of 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 concludes that this commercial release poses negligible risks to human health and safety and the environment and no specific risk treatment measures are imposed. However, general licence conditions have been imposed to ensure that there is ongoing oversight of the release.

Before Dengvaxia can be used as a therapeutic agent, Sanofi-Aventis Australia Pty Ltd (Sanofi) must also obtain regulatory approval from the Therapeutic Goods Administration (TGA). Medicines and other therapeutic goods for sale in Australia are required to be assessed for quality, safety and efficacy under the *Therapeutic Goods Act 1989* and must be included in the Australian Register of Therapeutic Goods (ARTG). The TGA consults the OGTR during the assessment of applications for therapeutic products that are, or contain, genetically modified organism (GMOs). Sanofi will also need approval from the Department of Agriculture and Water Resources for import of the GM vaccine.

The application

Application number	DIR 148
Applicant	Sanofi-Aventis Australia Pty Ltd
Project title	Commercial supply of Dengvaxia, a live attenuated GM dengue vaccine[1]
Parent organism	Yellow fever virus strain 17D (YF17D)
Modified trait	Altered antigen expression

[1] The title of the project as supplied by the applicant is 'Commercial distribution and prescription of Dengvaxia in Australia.'

Genetic modification	YF17D pre-membrane gene (*prM*) replaced with Dengue virus pre-membrane gene YF17D envelope gene (*E*) replaced with Dengue virus envelope gene
Proposed release dates	Ongoing from the date of approval
Proposed locations	Medical facilities throughout Australia including specialist travel clinics, general practitioners and those belonging to the Australia Defence Force (subject to registration by the Therapeutic Goods Administration)
Purpose	Import, storage, transport and disposal of the GM Dengvaxia vaccine associated with its commercial release as a therapeutic product (subject Therapeutic Goods Administration approval)

Risk assessment

The risk assessment concludes that risks to the health and safety of people, or the environment, from the proposed dealings, either in the short or long term, are negligible.

The risk assessment process considers how the genetic modifications and proposed activities conducted with the GM vaccine 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 impact are considered.

Credible pathways to potential harm that were considered included whether or not expression of the introduced genes and genetic modifications could alter characteristics that may impact on the disease burden from the GM vaccine strains, or produce unintended changes in viral characteristics. The opportunity for gene transfer to other organisms and its effects (if it were to occur) was also considered.

The principal reasons for the conclusion of negligible risks are that:

- exposure to Dengvaxia would be minimised by well-established clinical, import, transport, storage and disposal procedures; and
- the GM vaccine strains can survive outside of a host only for short periods, and it is susceptible to common chemical decontaminants.

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.

As the level of risk is considered negligible, specific risk treatment is not required. However, the Regulator has imposed licence conditions to ensure ongoing oversight of the release and to allow the collection of information to verify the findings of the RARMP. 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.