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

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TECHNICAL SUMMARY OF THE RISK ASSESSMENT AND RISK MANAGEMENT PLAN
FOR
APPLICATION NO. DIR 098
FROM
SANOFI PASTEUR PTY LTD

Introduction

The Gene Technology Regulator (the Regulator) has made a decision to issue a licence in response to a licence application (DIR 098) from Sanofi Pasteur Pty Ltd (Sanofi) for a commercial release of a genetically modified (GM) vaccine.

The *Gene Technology Act 2000* (the Act), the Gene Technology Regulations 2001 and corresponding state and territory law govern the comprehensive and highly consultative process undertaken by the Regulator before making a decision whether or not to issue a licence to deal with a genetically modified organism (GMO). The decision is based upon a Risk Assessment and Risk Management Plan (RARMP) prepared by the Regulator in accordance with requirements of the legislation. RARMPs apply the *Risk Analysis Framework* and are finalised following consultation with a wide range of experts, agencies and authorities, and the public[1].

The application

The Regulator received an application from Sanofi for a licence for dealings involving the intentional release of a live genetically modified (GM) viral vaccine for the prevention of Japanese Encephalitis.

The GM vaccine is based on *Yellow fever virus* vaccine strain YF 17D which has been modified to contain genes from *Japanese encephalitis virus* (JEV) vaccine strain JE SA14-14-2. Expression of these genes has been shown to elicit a protective immune response in vaccinated people.

Sanofi proposed a commercial release of this vaccine in medical facilities throughout Australia. The vaccine is intended for people travelling to, or resident in, areas where the disease occurs and will be prescribed by registered medical practitioners and administered in medical facilities.

Risk assessment

The risk assessment took into account information in the application, previous approvals, relevant scientific/technical knowledge and issues relating to risks to human health and safety and the environment raised in submissions received from consultation with a wide range of prescribed experts, agencies and authorities (included in Appendices B and C of the RARMP) as well as the public (included in Appendix D of the RARMP). The risk context for this assessment considered the dealings import, transport and disposal associated with the

[1] More information on the process for assessment of licence applications to release a genetically modified organism (GMO) into the environment is available from the Office of the Gene Technology Regulator (OGTR) (Free call 1800 181 030 or at OGTR Website), and in the Regulator's *Risk Analysis Framework* (OGTR 2009).

commercial release. No new risks to people or the environment were identified from the advice received on the consultation RARMP.

Initially, risk identification was used to postulate potential pathways that might lead to harm to people or the environment as a result of gene technology (risk scenarios) and determine those that warrant detailed characterisation.

Five risk scenarios were identified. This included consideration of whether, or not, expression of the introduced genes could result in products that are toxic or allergenic to people or other organisms; alter characteristics that may impact on the disease burden due to the GM virus; or produce unintended changes in its characteristics. The opportunity for gene transfer to other organisms and its effects if this occurred was also assessed.

A **risk** is only identified when a risk scenario is considered to have some chance of causing harm. Pathways that do not lead to an adverse outcome, or could not reasonably occur, do not advance in the risk assessment process.

The characterisation of the five risk scenarios in relation to both the seriousness and likelihood of harm did not give rise to any identified risks that required further assessment. The principal reasons for this include the:

- long history of safe use of the parent vaccine viruses containing the same proteins or sequences encoded by the introduced genes with no evidence of harm to otherwise healthy people
- limited ability of the GM virus to replicate in humans and other animals
- limited ability of the GM virus to replicate in mosquito vectors
- limited ability and opportunity for the GM vaccine to transfer the introduced genes

Any risks of harm to the health and safety of people or the environment from the dealings associated with the proposed release, which are the import, transport and disposal of the GM vaccine, are assessed to be **negligible**. Hence, the Regulator considers that the dealings involved in this commercial release **do not pose a significant risk** to either people or the environment.

Risk management plan

Risk management is used to protect the health and safety of people and to protect the environment by controlling or mitigating risk. Risk management includes the preparation of a risk management plan to evaluate and treat identified risks, apply general risk management measures, and propose licence conditions.

As none of the five risk scenarios characterised in the risk assessment are considered to give rise to an identified risk that requires further assessment, the level of risk from the proposed dealings is assessed to be **negligible**. The Regulator's Risk Analysis Framework defines negligible risks as insubstantial, with no present need to invoke actions for their mitigation in the risk management plan. Nonetheless, as part of the Regulator’s oversight of licensed dealings involving the release of genetically modified organisms, the licence 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.

Other regulatory considerations

Australia's gene technology regulatory system operates as part of an integrated legislative framework that avoids duplication and enhances coordinated decision making. Dealings conducted under a licence issued by the Regulator may also be subject to regulation by other agencies that also regulate GMOs or GM products including Food Standards Australia New Zealand (FSANZ), Australian Pesticides and Veterinary Medicines Authority (APVMA), Therapeutic Goods Administration (TGA), National Industrial Chemicals Notification and Assessment Scheme (NICNAS) and Australian Quarantine Inspection Service (AQIS)[2].

The TGA is responsible for assessing the quality, safety and efficacy of medicines and other therapeutic goods for use in Australia. The TGA has registered the GM vaccine for use in Australia, as a prescription medicine, for people over the age of 12 months.

Suitability of the applicant

The Regulator determined, at the commencement of the assessment process for this application, that Sanofi was suitable to hold a DIR licence under the requirements of section 58 of the Act. The Regulator is satisfied that Sanofi remains suitable as no relevant convictions have been recorded, and no licences or permits have been cancelled or suspended under laws relating to the health and safety of people or the environment.

Conclusions of the consultation RARMP

The risk assessment concluded that the dealings associated with this commercial release of the GM vaccine as a prescription medicine pose **negligible** risks to the health and safety of people or the environment as a result of gene technology.

The risk management plan concluded that these **negligible** risks do not require specific risk treatment measures. However, licence conditions have been imposed to allow appropriate oversight of the ongoing release.

[2] More information on Australia's integrated regulatory framework for gene technology is contained in the *Risk Analysis Framework* (OGTR 2009) available from the Office of the Gene Technology Regulator (OGTR) website or Free call 1800 181 030.