



15 January 2010

**EXECUTIVE SUMMARY OF THE RISK ASSESSMENT AND RISK
MANAGEMENT PLAN
FOR
APPLICATION NO. DIR 097
FROM
PPD AUSTRALIA**

Introduction

The Gene Technology Regulator (the Regulator) has made a decision to issue a licence in respect of licence application (DIR 097) from Pharmaceutical Product Development Australia Pty Ltd (PPD) involving the limited and controlled release of genetically modified (GM) *Bovine Parainfluenza virus* type 3 into the environment.

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 to issue a licence to deal with a GMO. The decision is based upon a Risk Assessment and Risk Management Plan (RARMP) prepared by the Regulator in accordance with the requirements of the legislation. RARMP's apply the *Risk Analysis Framework* and are finalised following consultation with a wide range of experts, agencies and authorities, and the public¹.

The application

PPD have applied for a licence for an intentional release of a genetically modified (GM) vaccine for prevention of selected childhood respiratory diseases into the Australian environment on a limited scale and under controlled conditions.

The GM candidate vaccine is based on *Bovine parainfluenza virus* type 3 (bPIV3) which has been modified to contain genes from two common childhood respiratory pathogens *Human parainfluenza virus* type 3 (hPIV3) and *Human respiratory syncytial virus* (RSV). Expression of these genes is expected to elicit a protective immune response in vaccinated children. PPD will conduct a clinical trial of the GM vaccine in children to evaluate its safety and efficacy against hPIV3 and RSV.

The trial will take place in six specified hospitals in ACT, NSW, QLD, SA, VIC and WA and involves a maximum of 70 children aged 2 – 24 months. The trial is expected to be completed by March 2012.

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 <<http://www.ogtr.gov.au/>>), and in the Regulator's *Risk Analysis Framework* (OGTR 2009) at <<http://www.ogtr.gov.au/internet/ogtr/publishing.nsf/Content/riskassessments-1>>.

PPD proposes a number of control measures to restrict exposure to the GM vaccine that were considered during the evaluation of this application.

Confidential Commercial Information

Some details, including vector maps and unpublished results of ongoing clinical trials, have been declared Confidential Commercial Information (CCI) under section 185 of the Act. The confidential information was made available to the prescribed experts and agencies that were consulted on the RARMP for this application.

Risk assessment

The risk assessment took into account information in the application (including proposed containment measures), relevant previous approvals and current scientific knowledge and advice relating to risks to human health and safety and the environment provided in submissions received during consultation on the RARMP. 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 viral characteristics. 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, in the context of the control measures proposed by the applicant, did not give rise to any identified risks that required further assessment.

Any risks of harm to the health and safety of people, or the environment, from the proposed release of the GM virus into the environment are assessed to be **negligible**. Hence, the Regulator considers that the dealings involved in this limited and controlled release **do not pose a significant risk** to either people or the environment.

Risk management

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. However, conditions are imposed to restrict exposure to the GMO and its genetic material in the environment and to limit the release to the size and locations requested by the applicant as these were important considerations in establishing the context for assessing the risks.

The licence conditions requires PPD to **limit** the dealings to 70 trial participants at six clinical facilities between January 2010 and 31 March 2012. The **control** measures include administration of the GM vaccine by trained staff, containment provisions at the clinical site, controls to restrict exposure of the general public to the GM vaccine, destroying GM vaccine not required for further studies and transporting the GM vaccine in accordance with the Regulator's transport guidelines.

Conclusions of the RARMP

The risk assessment concluded that this limited and controlled release of the GM vaccine involving 70 trial participants in six clinical facilities in the ACT, NSW, QLD, SA, VIC and WA poses **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 restrict the release to the number of trial participants and the locations requested by the applicant as this were important considerations in establishing the context for assessing the risks.