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

5 October 2012

EXECUTIVE SUMMARY OF THE RISK ASSESSMENT AND RISK MANAGEMENT PLAN
FOR
APPLICATION NO. DIR 116
FROM
PPD AUSTRALIA PTY LTD

Introduction

The Gene Technology Regulator (the Regulator) has made a decision to issue a licence in respect of licence application (DIR 116) from PPD Australia Pty Ltd (PPD). The licence authorises dealings involving the limited and controlled release of genetically modified (GM) live viral vaccines against prostate cancer.

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 Gene Technology Regulator (the Regulator) before making a decision whether 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

PPD has applied for a licence for dealings involving the intentional release into the Australian environment of two genetically modified (GM) vaccines for the treatment of prostate cancer on a limited scale and under controlled conditions.

The GM candidate vaccines are based on *Vaccinia virus* vaccine strain New York City Board of Health (NYCBH) and *Fowlpox virus* vaccine strain POXVAC-TC, which have each been modified to contain the same four human genes. Expression of these genes is expected to induce immune responses against the *prostate-specific antigen* (PSA) and to stimulate the immune system to attack and destroy cancer cells expressing PSA.

[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>.

The trial in Australia would form part of an international clinical trial involving 1200 patients in approximately 22 countries. The purpose of the trial is to evaluate the effectiveness of the viral vaccines in treating prostate cancer. The trial is proposed to take place in specified hospitals and health care facilities in ACT, NSW, QLD, SA, VIC and WA. Once underway the trial is expected to be completed within five years.

The applicant proposed a number of control measures to restrict exposure to the GM vaccines that were considered during the evaluation of this application.

Confidential Commercial Information

Some information, including details of the genetic construct used to create the GMOs and unpublished data from previous clinical have been declared Confidential Commercial Information (CCI) under section 185 of the Act. The confidential information was made available, in accordance with section 187 of the Act, to the prescribed experts and agencies 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. Advice relating to risks to human health and safety and the environment provided in submissions received during consultation on the RARMP was also considered. No new risks to people or the environment were identified from the advice received on the consultation RARMP.

Initially, potential pathways that might lead to harm to people or the environment as a result of gene technology are postulated (risk scenarios), and those that warrant detailed characterisation are determined. This process is described as risk identification.

Seven risk scenarios were postulated, including 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 viruses; or produce unintended changes in viral characteristics. The opportunity for gene flow to other organisms, and its effects if it were to occur, was also assessed.

A risk is only identified for further assessment 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 seven risk scenarios in relation to both the seriousness and likelihood of harm, in the context of the control measures proposed by the applicant and considering both the short and the long term, 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 viral vaccines into the environment are assessed to be negligible.

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. The risk management plan evaluates and treats identified risks, evaluates controls and limits proposed by the applicant, and considers general risk management measures. The risk management plan is given effect through licence conditions.

As none of the seven risk scenarios characterised in the risk assessment 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 have been imposed to restrict exposure to the GMOs and its genetic material in the

environment and to limit the trial to the size and locations proposed in the application as these were important considerations in establishing the context for assessing the risks.

The licence conditions require PPD to limit the dealings to suitable adult male participants at clinical facilities between October 2012 and December 2017. The control measures include administration of the GM vaccines by trained staff, containment provisions at the clinical site, educating trial participants in injection site bandaging and care, destroying GM vaccines not required for further studies; transporting the GM vaccines in accordance with the Regulator's transport guidelines and other specific conditions.

Conclusions of the RARMP

The risk assessment concluded that the limited and controlled release of GM virus to take place in hospitals in ACT, NSW, QLD, SA, VIC and WA, involving up to 1200 trial participants and expected to run for up to five years, 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 limit the trial in size, locations and duration, and to require controls in line with those proposed by the applicant, as these were important considerations in establishing the context for assessing the risks.