



15 January 2010

**TECHNICAL 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 application (DIR 097) from Pharmaceutical Product Development Australia Pty Ltd (PPD). The licence authorises dealings involving the limited and controlled release of genetically modified (GM) *Bovine parainfluenza virus* type 3.

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 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<sup>1</sup>.

***The application***

PPD has applied for a licence for dealings involving the intentional release of a GM vaccine for prevention of selected childhood respiratory diseases into the Australian environment which qualifies as a limited and controlled release under section 50A of the Act.

The GM candidate vaccine is based on *Bovine parainfluenza virus* (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 would involve a maximum of 70 children aged 2 – 24 months. Once underway the trial is expected to be completed by 31 March 2012.

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<sup>1</sup> 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 2007) at <<http://www.ogtr.gov.au/internet/ogtr/publishing.nsf/Content/riskassessments-1>>.

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

### ***Confidential Commercial Information***

Some details, including vector maps and unpublished results from related 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 considered information in the application, current scientific 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 Appendix B of the RARMP) as well as the public (included in Appendix C of the RARMP).

The risk assessment begins with a risk scenario identification process to consider what harm to the health and safety of people or the environment could arise during this release of GMOs due to gene technology, and how it could happen, in comparison to the non-GM parent organism and in the context of the proposed receiving environment.

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, in the context of the control measures proposed by the applicant, did not give rise to any identified risks that required further assessment. The principal reasons for this include:

- limits on the number of trial participants and the locations proposed by PPD;
- suitability of controls proposed by PPD to restrict exposure to the GM virus; and
- widespread presence of the same or similar gene sequences and proteins encoded by the introduced genes in the environment.

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 release **do not pose a significant risk** to either people or the environment<sup>2</sup>.

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<sup>2</sup> As none of the proposed dealings are considered to pose a significant risk to people or the environment, section 52(2)(d)(ii) of the *Gene Technology Act 2000* mandates a minimum period of 30 days for consultation

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

## ***Licence conditions***

The Regulator has imposed a number of licence conditions including requirements to:

- limit the release to a maximum of 70 trial participants inoculated with the GM virus
- restrict exposure of at-risk individuals by specific exclusion criteria
- ensure that inoculations be performed by trained nurses and/or physicians at clinical facilities in accordance with standard universal precautions and ICH-GCP<sup>3</sup>
- store and transport all GM virus, including any waste or samples containing GM vaccine, in accordance with relevant regulations<sup>4</sup>
- dispose of all waste in accordance with standard clinical waste disposal practices

The Regulator has issued guidelines and policies for the transport, supply and storage of GMOs (*Guidelines for the transport of GMOs, Policy on transport and supply of GMOs*). Licence conditions based on these guidelines and policies have also been imposed to control possession, use or disposal of the GMOs for the purposes of, or in the course of, the authorised dealings.

## ***Other regulatory considerations***

Australia's gene technology regulatory system operates as an integrated legislative framework involving the Regulator and other regulatory agencies 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),

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on the RARMP. However, the Regulator has allowed up to 6 weeks for the receipt of submissions from prescribed experts, agencies and authorities and the public.

<sup>3</sup> The international conference on harmonisation of technical requirements for registration of pharmaceuticals for human use, guidelines for good clinical practice

<sup>4</sup> OGTR *Guidelines for the Transport of Genetically Modified Organisms*, IATA Transportation Regulations

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) and Australian Quarantine Inspection Service (AQIS)<sup>5</sup>.

TGA is responsible for human safety assessment of the participants in clinical trials. The clinical trial of the GM vaccine has been approved by TGA under the Clinical Trial Exemption (CTX) scheme. The OGTR liaised with TGA during the assessment of this licence application.

### ***Identification of issues to be addressed for future releases***

Additional information has been identified that may be required to assess an application for a large scale or commercial release of the GM virus, or to justify a reduction in containment conditions. This would include:

- the potential shedding of GM virus from seronegative trial subjects;
- data on the GMO's capacity to infect or cause disease in animals; and
- data on the genetic stability of the GMO.

### ***Conclusions of the consultation RARMP***

The risk assessment concludes that this limited and controlled release of 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 concludes that these **negligible** risks do not require specific risk treatment measures. However, conditions are imposed to limit and control the release as these were important considerations in establishing the context for assessing the risks.

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<sup>5</sup> 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). Free call 1800 181 030 or at <<http://www.ogtr.gov.au/internet/ogtr/publishing.nsf/Content/riskassessments-1>>.