



Australian Government

Department of Health and Ageing

Office of the Gene Technology Regulator

Licence for dealings involving an intentional release of a GMO into the environment

Licence No.: DIR 097

Licence holder: PPD Australia Pty Ltd

Title: Limited and controlled release of a genetically modified vaccine for prevention of selected childhood respiratory diseases

Issued:15 January 2010

More information about the decision to issue this licence is contained in the Risk Assessment and Risk Management Plan prepared in connection with the assessment of the application for the licence. This document can be obtained from the Office of the Gene Technology Regulator website at <<http://www.ogtr.gov.au>>, or by telephoning the Office on 1800 181 030.

Gene Technology Regulation in Australia

Australia's gene technology regulatory system operates as part of an integrated legislative framework. The *Gene Technology Act 2000* (Cth) and corresponding state and territory legislation form a substantial part of a nationally consistent regulatory system controlling the development and use of genetically modified organisms (GMOs).

This licence is issued by the Gene Technology Regulator in accordance with the Gene Technology Act 2000 and, as applicable, Corresponding State Law.

The Gene Technology Regulator is required to consult with, and take into account advice from a range of key stakeholders, including other regulatory authorities, on risks to human health and safety and to the environment in assessing applications for dealings involving the intentional release of GMOs into the Australian environment.

Other agencies that also regulate GMOs or GM products include Food Standards Australia New Zealand, Australian Pesticides and Veterinary Medicines Authority, Therapeutic Goods Administration, National Industrial Chemicals Notification and Assessment Scheme, National Health and Medical Research Council and Australian Quarantine and Inspection Service. Dealings conducted under any licence issued by the Regulator may also be subject to regulation by one or more of these agencies. It is recommended that the licence holder consult the relevant agency (or agencies) about their regulatory requirements.

The licence authorises the licence holder and persons covered by the licence to conduct specified dealings with the genetically modified organism(s) listed in Attachment B of this licence.

Dealings permitted by this licence may also be subject to the operation of State legislation declaring areas to be GM, GM free, or both, for marketing purposes.

Section 1 Interpretations and Definitions

1. This licence does not authorise dealings with GMOs that are otherwise prohibited as a result of the operation of State legislation declaring areas to be GM, GM free, or both, for marketing purposes.
2. In this licence:
 - (a) unless defined otherwise in this licence, words and phrases used in this licence have the same meaning as they do in the Act and the Regulations;
 - (b) words importing a gender include any other gender;
 - (c) words in the singular include the plural and words in the plural include the singular;
 - (d) words importing persons include a partnership and a body whether corporate or otherwise;
 - (e) references to any statute or other legislation (whether primary or subordinate) are a reference to a statute or other legislation of the Commonwealth of Australia as amended or replaced from time to time and equivalent provisions, if any, in corresponding State law, unless the contrary intention appears;
 - (f) where any word or phrase is given a defined meaning, any other part of speech or other grammatical form in respect of that word has a corresponding meaning;
 - (g) specific conditions prevail over standard conditions to the extent of any inconsistency.
3. In this licence:

'Act' means the *Gene Technology Act 2000* (Cth) or the corresponding State legislation under which this licence is issued.

'Annual Report' means a written report provided to the Regulator within ninety (90) days of each anniversary of issue of this licence containing all the information required by this licence to be provided in the Annual Report.

'Dealings' in relation to a GMO, means the following:

- (a) conduct experiments with the GMO;
- (b) import the GMO;
- (c) transport the GMO;
- (d) dispose of the GMO;

and includes the possession, supply or use of the GMO for the purposes of, or in the course of, a dealing mentioned in any of paragraphs (a) to (d).

'Destroy', (or **'Destroyed'** or **'Destruction'**) means, as the case requires, killed by one or more of the following methods:

- (a) treatment with chemical disinfectant
- (b) autoclaving
- (c) incineration

Note: 'As the case requires' has the effect that, depending on the circumstances, one or more of these techniques may not be appropriate.

'GM' means genetically modified.

'GMOs' means the genetically modified organisms the subject of the dealings authorised by this licence.

'ICH-GCP' means the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use, guidelines for Good Clinical Practice.

'Material' means non-biological material used in conjunction with the GMO, such as syringes, swabs, vials, gloves or for cleanup of spills.

'OGTR' means the Office of the Gene Technology Regulator.

'Personal Information' means information or an opinion (including information forming part of a database), whether true or not, and whether recorded in a material form or not, about an individual whose identity is apparent, or can reasonably be ascertained, from the information or opinion.

'Regulations' means the *Gene Technology Regulations 2001*

'Regulator' means the Gene Technology Regulator.

'Sample' means any biological material collected from trial subjects for subsequent analysis.

'TGA GCP Guidelines' means the TGA Note for Guidance on Good Clinical Practice designated CPMP/ICH/135/95.

'WHO Universal Precautions' means World Health Organisation universal precautions for the prevention of transmission of infectious agents in healthcare settings.

Section 2 General conditions

Duration of Licence

4. This licence remains in force until 31 March 2012 unless it is suspended, cancelled or surrendered. No dealings with the GMO are authorised during any period of suspension.

Holder of Licence

5. The holder of this licence ('the licence holder') is PPD Australia Pty Ltd.

Project Supervisor

6. The Project Supervisor in respect of this licence is the person named in Attachment A of the licence.
7. The licence holder must immediately notify the Regulator in writing if any of the contact details of the Project Supervisor change.

No dealings with the GMOs except as authorised by this licence

8. Persons covered by this licence must not deal with the GMO except as expressly permitted by this licence.

Persons covered by this GMO licence

9. The persons covered by this licence are the licence holder and employees, agents or contractors of the licence holder and other persons who are, or have been, engaged or otherwise authorised by the licence holder to undertake any activity in connection with the dealings authorised by this licence.
10. Prior to commencing the clinical trial with the GMOs, the licence holder must provide to the Regulator:
 - (a) a list of the names of all organisations or natural persons who will be persons covered by this licence. Where a name of a person is not known at the time of submitting the list, the function or position of the person to be covered must be provided; and
 - (b) a description of the responsibilities of the licence holder and of each person covered by the licence in relation to the requirements of this licence.

Note: Examples of functions or positions are 'site manager', 'clinical research assistant' etc.

11. Where any of the details provided under the immediately preceding condition change, the Regulator must be notified of the changes within fourteen (14) days of the change occurring.

Informing people of their obligations

12. The licence holder must inform any person covered by this licence, to whom a particular condition of this licence applies, of the following:
 - (a) the particular condition (including any variations of it);
 - (b) the cancellation or suspension of the licence;
 - (c) the surrender of the licence.
13. If a particular condition, including any variation of it, applies to a person with respect to a particular dealing, the licence holder must not permit a person covered by this licence to conduct that dealing unless,
 - (a) the person has been informed of the condition, including any variation of it, and

- (b) the licence holder has obtained from the person a signed and dated statement that the person,
 - i) has been informed by the licence holder of the condition and, when applicable, its variation;
 - ii) has understood and agreed to be bound by the condition, or its variation; and
 - iii) has not conducted the dealing without being informed of the condition, or its variation

14. The licence holder must provide the Regulator, on the Regulator's request, with copies of the signed and dated statements referred to in the immediately preceding condition.

15. Prior to commencement of the trial with the GMO the licence holder must provide to the Regulator an explanation of how the licence holder has informed, or proposes to inform, each person intended to be covered by the licence of the conditions of this licence including conditions related to the collection of Personal Information by the licence holder from the person intended to be covered by the licence.

16. Where any of the details provided under the immediately preceding condition change, the Regulator must be notified of the changes within fourteen (14) days of the change occurring.

17. The licence holder must notify the project supervisor and all persons covered by a licence that Personal Information collected by the licence holder which is relevant to the administration and/or enforcement of the licence may be released to the Regulator.

Licence holder must provide information on matters related to suitability

18. The licence holder must immediately, by notice in writing, inform the Regulator of:

- (a) any relevant conviction of the licence holder occurring after the commencement of this licence;
- (b) any revocation or suspension of a licence or permit held by the licence holder under a law of the Australian Government, a State or a foreign country, being a law relating to the health and safety of people or the environment;
- (c) any event or circumstances occurring after the commencement of this licence that would affect the capacity of the holder of this licence to meet the conditions in the licence.

19. The licence holder must provide information related to the licence holder's ongoing suitability to hold a licence when requested to do so in writing by the Regulator and must provide the information within a time period stipulated by the Regulator.

Additional information to be given to the Regulator

20. It is a condition of this licence that the licence holder informs the Regulator if the licence holder:

- (a) becomes aware of additional information as to any risks to the health and safety of people, or to the environment, associated with the dealings authorised by the licence; or
- (b) becomes aware of any contraventions of the licence by a person covered by the licence; or
- (c) becomes aware of any unintended effects of the dealings authorised by the licence.

Note: The Act requires, for the purposes of the above condition that:

- (a) the licence holder will be taken to have become aware of additional information if he or she was reckless as to whether such information existed; and*
- (b) the licence holder will be taken to have become aware of contraventions, or unintended effects, if he or she was reckless as to whether such contraventions had occurred, or such unintended effects existed.*

21. The licence holder must provide the information required by paragraphs (a), (b) and (c) of the immediately preceding condition to the Regulator as soon as practically and reasonably possible, and must also include the information in the Annual Report.

People dealing with GMOs must allow auditing and monitoring of the dealing

22. If a person is authorised by this licence to deal with the GMOs and a particular condition of this licence applies to the dealing by that person, the person must allow the Regulator, or a person authorised by the Regulator, to enter premises where the dealing is being undertaken, for the purposes of auditing or monitoring the dealing.

23. The licence holder must be able to access and control all clinical facilities specified in Table 1 to the extent necessary to comply with this licence, for the duration of the life of the licence.

24. Where any of the details provided under the immediately preceding condition change, the Regulator must be notified of the changes within fourteen (14) days of the change occurring.

Remaining an Accredited organisation

25. The licence holder must, at all times, remain an accredited organisation in accordance with the Act and comply with its instrument of accreditation.

Notices

26. The licence holder must provide all notices to the Regulator required to be given by this licence and each notice must be provided in the manner required by Section 5 of this licence.

Section 3 The GMO

GMO covered by this licence

27. The GMO covered by this licence is GM *Bovine parainfluenza virus* (MEDI 534) and is described in Attachment B of the licence.

Permitted dealings

28. The permitted dealings with the GMO are to:

- (a) conduct experiments with the GMO;
- (b) import the GMO;
- (c) transport the GMO;
- (d) dispose of the GMO;

and includes the possession, supply or use of the GMO for the purposes of, or in the course of, a dealing mentioned in any of paragraphs (a) to (d).

29. The only experiments that may be conducted with the GMO are:

- (a) inoculation of trial participants with the GMO; and
- (b) collection of samples that may contain the GMO from trial participants.

Limits - Locations, timing and size of trial

30. Subject to other conditions in this licence which provide to the contrary, dealings are to take place at the clinical facilities listed in Table 1.

31. The GMO may be stored at Cryosite facilities ([South Granville](#), NSW) prior to distribution within Australia or export from Australia.

32. A maximum total of 70 individuals may be inoculated with the GMO.

33. Table 1: Clinical facilities at which permitted dealings may occur.

Clinical Facility	Local Government Area	Locality
Women's and Children's Hospital, Adelaide	The city of Adelaide	Adelaide, SA
Royal Children's Hospital	The City of Brisbane	Herston, Qld
The Canberra Hospital	n/a	Garran ACT
Princess Margaret Hospital for Children	City of Subiaco	Subiaco, WA
Royal Children's Hospital	Melbourne City Council	Parkville, Vic
Sydney Children's Hospital	Randwick City council	Randwick, NSW

34. Samples from trial participants that may contain GMO may be collected at locations other than clinical facilities listed in Table 1.

Control measures

35. The trial must be conducted according to the **ICH-GCP** and **TGA GCP Guidelines** and **WHO Universal Precautions** for the prevention of transmission of infectious agents in healthcare settings.

36. The licence holder must not inoculate trial participants whom the licence holder knows, or should know, will, within 28 days of each vaccination with the GMO, come into contact with individuals at risk from exposure to the GMO. This restriction includes, but is not limited to individuals who are:

- (a) living in the same home, enrolled in the same classroom at day care or likely to come into close contact with infants less than 6 months of age; or
- (b) in contact with a pregnant caregiver; or
- (c) in contact with a person who is immuno-compromised; or
- (d) in contact with a health care provider for immuno-compromised patients or a day care provider for infants under the age of 6 months.

37. The licence holder must not enrol a trial participant for the trial without first ascertaining whether or not the participant will come into contact with individuals at risk from exposure to the GMOs.

Work practices

38. When undertaking a dealing with a GMO permitted by this licence, including storage, persons covered by this licence must employ work practices and behaviours which:

- (a) ensures containment of the GMO within the clinical facilities, during import, transport and disposal of the GMO; and
- (b) will not pose a risk to the health and safety of people undertaking the dealing.

Containment measures

39. All dealings permitted under this licence must be conducted within clinical facilities listed in Table 1, except for:

- (a) import;
- (b) storage;
- (c) transport; and
- (d) disposal.

40. All samples or Materials, including waste, that may contain the GMO must be treated as if they were the GMO.

41. During storage of the GMO:

- (a) The GMO must be contained within a sealed primary container that is wholly contained within a sealed secondary container;

- (b) The primary or the secondary container must be unbreakable;
- (c) The outermost container must be clearly labelled to indicate that it contains the GMO; and
- (d) Access to the GMO must be restricted to persons covered by the licence

42. Following completion of inoculation, used vaccine syringes must be destroyed or stored in accordance with the previous condition.

43. Waste generated during the study must be discarded into biohazard containers and destroyed.

44. Surplus GMO must be returned to the Cryosite storage depot, exported or destroyed.

Section 4 Transport and Disposal

45. All transport of the GMO must be according to Parts 2.1 and 2.2 of the Regulator's *Guidelines for the Transport of GMOs* version 2.1. Routes, methods and procedures used for this transportation must be documented and provided to the Regulator on request.

46. Before the expiration of this licence, all GMOs must be destroyed by autoclaving; chemical treatment; high temperature incineration or any other method approved in writing by the Regulator.

Note: GMOs may be destroyed during or at the completion of the clinical trial.

Section 5 Reporting and Documentation Requirements

Contingency Plans

47. Within thirty (30) days of the date of issue of this licence, a written Contingency Plan must be submitted to the Regulator detailing measures to be taken in the event of the unintended presence of the GMO.

48. The Contingency Plan must include details of procedures to:

- (a) ensure the Regulator is notified immediately if the licence holder becomes aware of the event;
- (b) inspect for and destroy any of the GMO that may exist as a result of the event; and
- (c) if there is a spill of the GMO, such as during inoculation, import, transport, storage or disposal implement the following measures:
 - containment of the GMO to prevent further dispersal; and
 - decontamination of the exposed area with an appropriate chemical disinfectant against the GMO.

Notice of commencement and completion of the trial

49. The licence holder must notify the Regulator in writing of the first inoculation of a trial participant within fourteen (14) days.

50. The licence holder must notify the Regulator in writing of the final inoculation of a trial participant within fourteen (14) days.

Annual Report

51. The licence holder must provide an Annual Report to the Regulator that includes the number of trial participants inoculated with the GMO.

Testing methodology

52. The licence holder must provide written document to the Regulator describing an experimental method that is capable of reliably detecting the presence of the GMO and the presence of the genetic modifications described in this licence in a recipient organism. The detection method should be capable of reliably distinguishing between GMO described in this licence and the parent organism. The document must be provided within 30 days of the issuing of this licence.

ATTACHMENT A

DIR No: 097

Full Title: Limited and controlled release of a genetically modified vaccine for prevention of selected childhood respiratory diseases

Organisation Details

Postal address: PPD Australia
Floor 9
5 Queens Road
Melbourne VIC 3004
Australia

Phone No: 03 9804 5211

Project Supervisor Details

Surname: *[Personal Information Redacted]*

First Name: *[Personal Information Redacted]*

Title: *[Personal Information Redacted]*

Phone No: *[Personal Information Redacted]*

Fax: *[Personal Information Redacted]*

Email Address: *[Personal Information Redacted]*

Position: *[Personal Information Redacted]*

Organisation: *[Personal Information Redacted]*

Postal Address: *[Personal Information Redacted]*

[Personal Information Redacted]

[Personal Information Redacted]

IBC Details

IBC Name: Children, Youth and Women's Health Service IBC

GMO Description**GMOs covered by this licence:**

Bovine parainfluenza virus containing the Respiratory syncytial virus F gene (as described in the table below) and in which the endogenous genes F and HN have been replaced by the homologous F and HN genes from Human parainfluenza virus (as described in the table below).

***Parent Organism:**

Common Name: Bovine parainfluenza virus (Medi 534)

Scientific Names: *Bovine parainfluenza virus type 3*

***Modified traits:**

Categories: Attenuation
Foreign antigen expression

Description: *Bovine parainfluenza virus* has been engineered so that two endogenous genes, (Fusion and Hemagglutinin-Neuraminidase) have been replaced with homologous genes from the related organism *Human parainfluenza virus*. In addition the GMO has been engineered to contain the Fusion gene from *Respiratory syncytial virus*.

Purpose of the dealings with the GMOs:

PPD Australia has applied for a licence to conduct a clinical trial of a genetically modified vaccine in up to 70 children at clinical locations around Australia. The purpose of the clinical trial is to evaluate the safety and efficacy of the vaccine against the common childhood respiratory pathogens *Human parainfluenza virus* and *Respiratory syncytial virus*.

Genetic elements responsible for conferring the modified traits:

Gene	Function of protein	Source	Intended purpose
hPIV3 HN	Haemagglutinin-Neuraminidase protein mediates the adsorption to, and release of virus from the host cell	hPIV3/Texas/12084/1983	Elicit an immune antibody response against hPIV3
hPIV3 F	Fusion protein mediates fusion of the viral envelope membrane with the host cell membrane	hPIV3/Texas/12084/1983	Elicit an immune antibody response against hPIV3
RSV F	Fusion protein mediates fusion of the viral envelope membrane with the host cell membrane	RSV A2 C4G	Elicit an immune antibody response against RSV