Australian Government
Department of Health
Office of the Gene Technology Regulator

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

Licence No.: DIR-137

Licence holder: AstraZeneca Pty Ltd

Commercial supply of attenuated GM influenza vaccines

Issued: 14 January 2016

Varied 23 November 2018

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 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 and the Department of Agriculture and Water Resources. 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 A 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. 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 Gene Technology Regulations 2001;

   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.

2. 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 in accordance with condition 20 of this licence, provided to the Regulator each year within 90 days of the European data lock point (DLP) for the GMOs in effect at the time of the report.

Note: the DLP is used to align the OGTR reporting period with that covered by the Periodic Safety Update Report (PSUR) required by the European Medicines Agency. The DLP for the GMOs is currently 31 August, and the Annual Report must therefore be provided by 29 November each year unless the DLP changes.

'ARTG' means the Australian Register of Therapeutic Goods.

'Data lock point' (DLP) means the cut-off point for data to be included in the Periodic Safety Update Report (PSUR) required by the European Medicines Agency at defined time points after the authorisation of a medicine.

Note: DLPs are published in the European Union Reference Dates (EURD) list, which is updated monthly, and changes become legally binding six months after publication.

'GM' means genetically modified.

'GMOs' means the genetically modified organisms contained in the influenza vaccines that are the subject of the dealings authorised by this licence.

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

'Regulator' means the Gene Technology Regulator.

Section 2 Licence conditions and obligations

3. The holder of this licence ('the licence holder') is AstraZeneca Pty Ltd.

4. The GMOs covered by this licence are described in Attachment A of the licence.

5. The dealings authorised by this licence are to:

a) import the GMOs;

b) transport the GMOs;

c) dispose of the GMOs

and the possession (including storage) and supply of the GMOs for the purposes of, or in the course, of any of these dealings.

Note: Use of the GMOs for therapeutic purposes is not regulated under the Gene Technology Act 2000 and this licence neither authorises nor limits such use. The GMOs (live attenuated GM influenza viruses) are subject to regulation by other federal and state departments and agencies, including the Therapeutic Goods Administration and the Department of Agriculture and Water Resources. These departments and agencies may impose further requirements for, or limitations on, the authorised dealings.

6. The permitted dealings with the GMOs may be conducted in all areas of Australia.

7. 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.

8. Any person, including the licence holder, may conduct any permitted dealing(s) with the GMOs.

9. This licence remains in force until it is suspended, cancelled or surrendered. No dealings with the GMOs are authorised during any period of suspension.

2.1 Obligations of the Licence Holder

Prior to issuing a licence, the Regulator considers suitability of the applicant to hold a licence. The following conditions address ongoing suitability of the licence holder.

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

11. The licence holder must:

a) inform the Regulator immediately in writing of:

i. any relevant conviction of the licence holder occurring after the commencement of this licence; and

ii. 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; and

iii. 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 it; and

b) provide any information related to the licence holder's ongoing suitability to hold a licence, if requested, within the stipulated timeframe.

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; and

c) the surrender of the licence.

2.2 Provision of new information to the Regulator

Licence conditions are based on the risk assessment and risk management plan developed in relation to the application using information available at the time of assessment. The following condition requires that any new information that may affect the risk assessment is communicated to the Regulator.

13. The licence holder must inform the Regulator if the licence holder becomes aware of:

a) 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) any contraventions of the licence by a person covered by the licence; or

c) 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 of a kind mentioned in paragraph 13(a) 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, of a kind mentioned in paragraph 13(b), if he or she was reckless as to whether such contraventions had occurred, or such unintended effects existed.

Note: Contraventions of the licence may occur through the action or inaction of a person.

14. If the licence holder is required to inform the Regulator under the immediately preceding condition, the Regulator must be informed without delay.

Note: An example of informing without delay is contact made at the time of the incident via the OGTR free call phone number 1800 181 030, which provides emergency numbers for incidents that occur out of business hours. Notification without delay will allow the OGTR to conduct a risk assessment on the incident and attend the location if required.

15. If at any time the Regulator requests the licence holder to collect and provide information about any matter to do with the progress of the dealings authorised by this licence, including but not confined to:

a) 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, whether or not the licence holder has provided information to the Regulator under condition 13(a);

b) any contraventions of the licence by a person covered by the licence, whether or not the licence holder has provided information to the Regulator under condition 13(b);

c) any unintended effects of the dealings authorised by the licence, whether or not the licence holder has provided information to the Regulator under condition 13(c);

d) research, including by way of survey, to verify predictions of the risk assessment, or for any purpose related to risks to the health and safety of people, or to the environment;

e) scientific literature and reports in respect of the GMOs authorised by this licence, for a nominated period;

f) details of any refusals of applications for licences or permits (however described) to deal with the GMOs made pursuant to the regulatory laws of a foreign country;

and the request is reasonable, having regard to consistency with the Act and relevance to its purpose, then the licence holder must collect the information and provide it to the Regulator at a time and in the manner requested by the Regulator.

Note: The Regulator may invite the licence holder to make a submission on the reasonability of a request by the Regulator to collect and provide information relevant the progress of the GMOs.

2.3 Obligations of persons covered by the licence

16. Persons covered by this licence must not deal with the GMOs except as expressly permitted by this licence.

17. 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.

Section 3 Reporting and Documentation

3.1 Notification of Authorisation by the Therapeutic Goods Administration

18. If the GMOs are included on the ARTG, the licence holder must notify the Regulator in writing within 14 days of registration.

19. The licence holder must notify the Regulator in writing of any subsequent amendments to the conditions of the ARTG registration involving the pattern of usage, handling, storage, transport or disposal of the GMOs, within 14 days of the change occurring.

3.2 Annual Report

20. The licence holder must provide an Annual Report to the Regulator that includes:

a) information about any adverse impacts, unintended effects, or new information relating to risks, to human health and safety or the environment caused by the GMOs or material from the GMOs during the 12 months prior to the most recent DLP; and

b) information about the number of the FluMist® doses imported and sold in each State and Territory during the previous Australian financial year.

3.3 Testing methodology

21. Prior to conducting any dealings with the GMOs, the licence holder must provide to the Regulator a written methodology to reliably detect the GMOs and the presence of the genetic modifications described in this licence in a recipient organism. The detection method must be capable of reliably distinguishing between GMOs described in this licence and the parent organism.

ATTACHMENT A

DIR No: 137

Full Title: Commercial supply of attenuated GM influenza vaccines

Organisation Details

Postal address: AstraZeneca Pty Ltd
PO Box 131, North Ryde, NSW 1670
Alma Road, North Ryde, NSW, 2113

Phone No: (02) 9978 3500

IBC Details

IBC Name: Clinical Network Services Institutional Biosafety Committee

Description of GMOs

GMOs covered by this licence

Influenza A viruses and influenza B viruses with the following genetic modifications:

- replacement of entire haemagglutinin segment with the equivalent segment from a target strain advised by the Australian Influenza Vaccine Committee (AIVC)
- replacement of entire neuraminidase segment with the equivalent segment from a target strain advised by the AIVC

Parent Organism

Common Name: Influenza virus

Scientific Name: Human *influenza A virus,* cold-adapted (derived from A/Ann Arbour/6/60)
Human *influenza B virus,* cold-adapted (derived from B/Ann Arbour/1/66)

Modified traits

Category: Altered immune response

Description: The GMOs are live attenuated cold-adapted influenza A and influenza B viruses, modified to elicit an immune response to targeted flu strains. These GMOs are generated using reverse genetics.

Nucleic acid responsible for conferring the modified traits:

Source	• Contemporary influenza virus strains for targeting with influenza vaccines as advised by the AIVC. These strains would be obtained from the WHO's Global Influenza Surveillance and Response System (GISRS).
Identity	• Entire haemagglutinin gemome segment • Entire neuraminidase genome segment
Function	• Haemagglutinin – receptor binding, fusion of viral and host endosomal membranes; antigenic determinant • Neuraminidase – hydrolysis of glycosidic bond between sialic acid and galactose; antigenic determinant
Modification	• For seasonal GM vaccines: no modifications • For pandemic GM vaccines: removal of polybasic site, should it be present, from gene encoding haemagglutinin

Purpose of the dealings with the GM vaccines

The permitted dealings are for the commercial supply of attenuated GM influenza vaccines for use as human therapeutics Australia-wide. The permitted dealings under the licence are import, transport, storage and disposal of the GM vaccines. The licence does not authorise the manufacture of the GM influenza vaccines in Australia.