



**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 161**

**Licence holder: Novotech (Australia) Pty Ltd**

**Title: A genetically modified respiratory syncytial virus (RSV) vaccine for use in clinical trials**

Issued: 16 July 2018

Transferred to Novotech (Australia) Pty Ltd: 18 March 2021

**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 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 activities involving 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, the Australian Pesticides and Veterinary Medicines Authority, the Therapeutic Goods Administration, the 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.

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.

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.

## Interpretations and definitions

1. In this licence:
  - (a) unless defined otherwise, words and phrases used 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.
2. In this licence:

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

**'Analytical facility'** means a laboratory in Australia accredited to undertake testing of human diagnostic samples, such as a medical testing laboratory accredited by the National Pathology Accreditation Advisory Council (NPAAC), and conforming to the AS/NZS 2243.3:2010 Safety in Laboratories: Microbiological Safety and Containment, particularly in relation to the handling of human diagnostic specimens.

**'Annual Report'** means a written report provided to the Regulator by the end of September each year, containing all the information required by this licence to be provided in the Annual Report for the preceding financial year.

**'Clinical Trial Site'** means a clinical trial facility or hospital, in Australia, that is notified to the Regulator for the purposes of conducting clinical trials authorised by this licence.

**'Contingency Plan'** means a written plan detailing measures to be taken if and when certain events, as specified in Condition 20, occur.

**'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) high-temperature incineration; and
- d) any other methods used by Clinical Trial Sites for disposal of infectious clinical waste.

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

**'Excluded Persons'** means

- women who are or may be pregnant;
- persons with immunodeficiency or immunosuppression that result in a full or partial impairment of the immune system;

**'GM'** means genetically modified.

**'GMO'** means the genetically modified organism that is the subject of the dealings authorised by this licence.

**'ICH-GCP'** means the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – *Guideline for Good Clinical Practice*, as current at the time experiments with the GMO are conducted under this licence.

**'Medical staff'** means qualified and registered physician, surgeon or nurse.

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

**'Personal Information'** means information or an opinion about an identified individual, or an individual who is reasonably identifiable:

- (a) whether the information or opinion is true or not; and
- (b) whether the information or opinion is recorded in a material form or not.

**'Regulations'** means the Gene Technology Regulations 2001 (Commonwealth) or the corresponding State law under which this licence is issued.

**'Regulator'** means the Gene Technology Regulator.

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

**'Serious adverse event'** means any untoward medical occurrence that at any dose:

- results in death;
- is life-threatening;
- requires inpatient hospitalisation or prolongation of existing hospitalisation;
- results in persistent or significant disability/incapacity;
- is a congenital anomaly/birth defect; or
- is a medically important event or reaction.

**'Storage facility'** means a distribution centre or pharmacy where the GMO is stored.

**'TGA'** means Therapeutic Goods Administration.

**'TGA-annotated ICH-GCP'** means the ICH-GCP annotated with TGA comments as [published on the TGA website](#) as current at the time experiments with the GMO are conducted under this licence.

**'WHO Universal Standard Precautions'** means World Health Organisation *Standard Precautions in health care* (2007) as published on the [WHO website](#).

## General conditions and obligations

### Holder of licence

3. The holder of this licence ('the licence holder') is [Novotech \(Australia\) Pty Ltd](#).

### Validity of licence

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

### Description of GMOs covered

5. The GMO covered by this licence is GM *respiratory syncytial virus* (RSV), as described in Attachment A of the licence.

### Dealings authorised by this licence

6. The dealings authorised by this licence are to:
  - a) import the GMO;
  - b) conduct the following experiments with the GMO:
    - i. administer the GMO to trial participants by intranasal inoculation
    - ii. collect samples that may reasonably be expected to contain the GMO from trial participants; and
    - iii. analyse *in vitro* the samples mentioned in (b)(ii)
  - c) transport the GMO;
  - d) dispose of the GMO;and to possess, store, supply and use the GMO in the course of any of these dealings.
7. To the extent that any activity by a trial participant may be considered to be a dealing for purposes of the Act, that dealing is authorised by this licence.
8. 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.

### Persons covered by this 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.

### Obligations of the Licence Holder

#### Contact person for the licence

10. The licence holder must notify the Regulator in writing as soon as reasonably possible if any of the details of the contact person(s) for the licence change from that notified in the licence application or subsequently.

*Note: Please address correspondence to [OGTR.Applications@health.gov.au](mailto:OGTR.Applications@health.gov.au).*

## Ongoing suitability of the licence holder

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

11. The licence holder must, at all times, remain an accredited organisation in accordance with the Act and must comply with its instrument of accreditation.
12. 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.
13. The licence holder must be able to access and control the areas or rooms, where dealings with the GMO are undertaken, at a Clinical Trial Site(s) to the extent necessary to comply with this licence, for the duration of the licence.

*Note: This may involve written contracts, agreements or other enforceable arrangements with Clinical Trial Site(s).*

## 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.*

14. 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 14(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 14(b) or 14(c) 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.*

15. If the licence holder is required to inform the Regulator under Condition 14, the Regulator must be informed without delay.

*Note: An example of informing without delay is contact made within a day of the incident via the OGTR free call phone number 1800 181 030. This number is monitored 24 hours per day, seven days a week. Notification without delay will allow the OGTR to conduct a risk assessment on the incident and attend the location if required.*

16. If the licence holder informs the Regulator under Condition 14 and the Regulator requests further information, such information must be provided in a manner, and within the time period, stipulated by the Regulator.

### **Informing people covered by the licence of licence conditions and obligations**

*The following conditions seek to ensure that persons conducting the dealings are aware of the licence conditions, and appropriate processes are in place to ensure they meet their obligations.*

17. 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.

*Note 1: No particular conditions of this licence apply to trial participants, therefore trial participants need not be informed of licence conditions.*

*Note 2: No particular conditions of this licence apply to persons analysing and transporting patient samples, therefore such persons need not be informed of licence conditions. However, the licence holder must ensure that analysis of participant samples reasonably likely to contain the GMOs takes place in suitable facilities in accordance with Condition 32.*

*Note 3: Information required under Condition 17 may be provided to external service providers who are engaged solely for the transport and/or disposal of the GMOs through labelling the outermost container of the GMO in accordance with Condition 49.*

18. If a particular condition, including any variation of it, applies to a person with respect to a particular dealing, other than import, transport or disposal by external service providers in accordance with Condition 49, the licence holder must not permit a person covered by this licence to conduct that dealing with the GMO 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; and
    - ii. has understood and agreed to be bound by the condition, or its variation; and
    - iii. has been trained in accordance with paragraph (c) below; and
  - c) the person has been trained in a manner which enables them to:
    - i. safely conduct the dealings in accordance with the conditions of this licence; and
    - ii. meet the work practices and behavioural requirements for conducting the dealings at Clinical Trial Sites; and
19. The licence holder must:
  - a) inform the persons covered by this licence that any Personal Information relevant to the administration and/or enforcement of the licence may be released to the Regulator; and

- b) provide the Regulator, if requested, with copies of the signed and dated statements referred to in Condition 18.

### Contingency planning

- 20. At least 14 days before commencing any dealings with the GMO authorised by this licence, the licence holder must provide the Regulator with documents detailing:
  - a) methodology to reliably detect the GMO, and the presence of the genetic modifications in a recipient organism, and which is able to distinguish between the GMO and the unmodified parent organism; and
  - b) a Contingency Plan detailing measures to be undertaken in the event of:
    - i. the unintentional release of the GMO, such as a spill within or outside Clinical Trial Site; or
    - ii. suspected or confirmed transmission to any persons other than trial participants; or
    - iii. a person (including a trial participant) developing a Serious adverse event which may be related to exposure to the GMO, including events known to result from infection with *respiratory syncytial virus*.

*Note: Serious adverse events which may be related to exposure to the GMOs must also be summarised in the Annual Report to the Regulator (see Condition 27).*

- 21. The licence holder must ensure that if any of the events described in Condition 20(b) occur, the appropriate procedure(s) from the Contingency Plan must be implemented.

*Note: Condition 20(b) lists events which the Contingency Plan must address, while Condition 22 specifies content for the Contingency Plan.*

- 22. The Contingency Plan must include details of procedures to be implemented:
  - a) if there is a spill of the GMO outside of a Clinical Trial Site, such as during import, transport, storage or disposal, procedures to:
    - i. contain the GMO to prevent further dispersal; and
    - ii. decontaminate the exposed area with a chemical disinfectant demonstrated to be effective against the GMO.
  - b) if transmission of the GMO to people other than trial participants is suspected or confirmed, procedures to:
    - i. provide appropriate medical treatment to affected persons; and
    - ii. provide relevant information about the GMO to the clinician(s);
    - iii. take steps to prevent the further spread or persistence of the GMO; and
    - iv. identify the pathway of exposure.
  - c) if a person (including a trial participant) experiences a Serious adverse event which may be related to exposure to the GMO, including events known to result from infection with *respiratory syncytial virus*, procedures to:
    - i. provide appropriate medical treatment to the affected person; and
    - ii. take steps to prevent the spread or persistence of the GMO.
  - d) ensure the Regulator is notified without delay if the licence holder becomes aware of any of the events described in paragraphs (a)-(c) above.



## Reporting

23. At least seven days before commencing dealings with the GMO at each Clinical Trial Site, the licence holder must provide the Regulator with:
- a) the names of all organisations and persons (other than trial participants), or functions or positions of persons, who will be covered by the licence at that Clinical Trial Site, with a description of their responsibilities;  
*Note: Examples of functions or positions include 'Principal Investigator', 'Clinical research assistant' and Pharmacist.*
  - b) details of how persons covered by the licence will be informed of licence conditions that applies to them with respect to a particular dealing; and  
*Note: This may include how training in licence conditions will be conducted, how the GMO to be transported will be labelled, and contractual agreements with other organisations such as clinical waste treatment providers or courier companies.*
  - c) details of how the licence holder will ensure compliance with licence conditions at Clinical Trial Sites over the period that dealings are conducted at that location.  
*Note: This may include a description of local reporting structures, positions of persons involved in research governance, contracts, agreements, or other enforceable arrangements.*
24. Any changes to the information provided under Condition 23 must be communicated to the Regulator in writing and within 14 days of the changes occurring.
25. The licence holder must notify the Regulator of the following:
- a) the name, address and description of each storage facility, at least 7 days before storage commences at the facility; and
  - b) the name, address and description of each Clinical Trial Site, at least 7 days before dealings with the GMO commence at that site; and
  - c) the date of the first inoculation of the first trial participant at each Clinical Trial Site, no later than 7 days after the event; and
  - d) the date of the final inoculation of the last trial participant at each Clinical Trial Site, within 30 days of the decision to cease inoculations at that location.
26. The GMO may only be stored at Clinical Trial Sites or storage facilities notified to the Regulator under Condition 25(a).
27. The licence holder must provide an Annual Report to the Regulator that includes:
- a) the number of trial participants inoculated with the GMO at each Clinical Trial Site under this licence; and
  - b) a summary of all investigations and outcomes relating to any Serious adverse events required to be reported by the Contingency Plan under Condition 22 d).

*Note: Attachment B contains a checklist of documents and notifications that must be maintained and/or sent to the Regulator.*

## Obligations of persons covered by the licence

28. Persons covered by this licence must not deal with the GMO except as expressly permitted by this licence.
29. 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.

## Limits and control measures

*The following licence conditions maintain the risk assessment context within which the application was assessed by imposing limits on where and when experiments with the GMOs may be performed, and controls on how activities can be undertaken.*

### Limits on clinical trials conducted under this licence

30. The GMO may be administered to a maximum of 350 healthy adults over the life of the licence. Inoculation of trial participants must be completed by 16 July 2023.
31. The GMO may only be administered to, and samples collected from, trial participants at Clinical Trial Sites.

*Note: The details of a Clinical Trial Site must have been provided to the Regulator under Condition 25(b) prior commencement of dealings at that site.*

### Selection of Facilities

32. The licence holder must ensure that dealings (other than import and transport carried out by external service providers) are only conducted at facilities that employ work practices and adhere to standards which:
  - a) maintain containment of the GMO; and
  - b) do not compromise the health and safety of people; and
  - c) minimise exposure of persons undertaking the dealings to the GMO, other than intended exposure of trial participants.

*Note: Suitable facilities are Clinical Trial Sites and Analytical facilities which adhere to appropriate standards (National Safety and Quality Health Service (NSQHS) Standards, Australia/New Zealand Standard 2243.3:2010 Safety in Laboratories Part 3: Microbiological Safety and Containment) and guidelines (the Australian Guidelines for the Prevention and Control of Infection in Healthcare and the National Pathology Accreditation Advisory Council (NPAAC)).*

### General conduct of clinical trials

33. The licence holder must ensure that a copy of the licence is available and readily accessible to persons conducting dealings at Clinical Trial Sites.
34. The licence holder must ensure that the clinical trials are conducted according to ICH-GCP and TGA-annotated ICH-GCP Guidelines, and that clinical trial staff follow WHO Universal Standard Precautions.
35. The licence holder must ensure that procedures are in place to account for the contents of all vials containing GMOs that are imported into Australia under this licence. The GMO must be accounted for from import to use or destruction, and records must be made available to the Regulator on request.
36. The licence holder must ensure that procedures are in place and implemented at each Clinical Trial Site to track the dispensation, return and destruction of the containers described in Conditions 44 and 47, and records must be made available to the Regulator on request.

37. Staff at Clinical Trial Sites must:
- a) while dispensing the GMO:
    - i. be suitably qualified and trained pharmacist or medical staff; and
    - ii. not use sharps; and

*Note: 'sharps' includes any object (in its intact or broken form) able to pierce human skin.*

    - iii. use a Class II biosafety cabinet, or other aerosol-containment equipment approved in writing by the Regulator, to prepare the inoculum; and
    - iv. wear personal protective equipment including a long-sleeved laboratory coat or gown and gloves
  - b) while administering the GMO:
    - i. be suitably qualified and trained medical staff; and
    - ii. not use sharps; and

*Note: 'sharps' includes any object (in its intact or broken form) able to pierce human skin.*

    - iii. wear personal protective equipment including a laboratory coat or gown, gloves, eye protection and a surgical mask protecting the nose and mouth; and
    - iv. ensure that only the trial participant and two clinical staff are in the room during administration.
38. The licence holder must ensure that Excluded Persons, as defined in this licence, are excluded from directly handling the GMO, dispensing the GMO, administering it to trial participants or caring for trial participants at Clinical Trial Sites as part of the clinical trial. This must be documented in writing and records made available to the Regulator on request.
39. The licence holder must educate staff handling the GMO, dispensing the GMO, administering it to trial participants or caring for trial participants at Clinical Trial Sites as part of the clinical trial on the potential for transmission of the GMO to people who are at risk of severe RSV infection including children aged 2 years or younger and the elderly. This must be documented in writing for each staff and records made available to the Regulator on request.

### **Conditions relating to trial participants**

40. Only adults may be inoculated with the GMO.
41. The licence holder must ensure that exclusion criteria used in selecting trial participants include (but need not be limited to) the following:
- a) Excluded Persons as defined in this licence;
  - b) persons who care for children aged 2 years or younger;
  - c) residents of aged care facilities;
  - d) persons with risk factors for more severe clinical RSV disease e.g. those with cardiovascular or pulmonary disorders;
  - e) women not willing to use effective contraception while participating in the study, or who are breastfeeding; and
  - f) persons who are unable or unwilling to comply with the requirements listed in Condition 44.

42. The licence holder must ensure that persons are not enrolled in the trial unless they have indicated that they are not likely to come into contact with Excluded Persons, children aged 2 years or younger and residents of aged care facilities for 14 days following each inoculation with the GMO.
43. The licence holder must ensure that trial participants are educated about the potential for transmission of the GMO to other people especially those who are at risk of severe RSV infection including children aged 2 years or younger and the elderly, and about measures to prevent transmission of the GMO.
44. The licence holder must obtain trial participants' written agreement that they will:
  - a) for 14 days following each inoculation of the GMO:
    - i. implement hygiene measures intended to prevent interpersonal transmission of the GMO, including but not limited to frequent hand washing with soap or hand disinfectant, and practicing respiratory hygiene and cough etiquette;
    - ii. avoid contact with Excluded persons;
    - iii. avoid contact with residents of aged care facilities;
    - iv. avoid contact with children aged 2 years or younger;
    - v. seal used tissues and other materials used to collect respiratory secretions in a primary container (e.g. a sealable plastic bag), place these within a secondary container provided by the Clinical Trial Site, and store secondary containers such that they are inaccessible to children and animals until they are returned to the Clinical Trial Site.
  - b) return all secondary containers referred to in Condition 44(a)(v) to the Clinical Trial Site for disposal as clinical waste; and
  - c) refrain from donating blood, blood products, tissues or organs from the time of their first inoculation with the GMO until 6 months after their final inoculation.
45. At least 30 days before the first clinical trial commences, the Participant Information and Informed Consent Form (PIICF) must be submitted to, the Regulator for approval. Any changes to the PIICF required by the Regulator to address Conditions 41 to 44 must be made within the time period specified by the Regulator.
46. Records of trial participants' agreements as required under Condition 44 must be made available to the Regulator on request.
47. The licence holder must ensure that, for each inoculation with the GMO, each trial participant is provided with a supply of primary and secondary containers appropriate for storing and transporting waste back to Clinical Trial Sites. Secondary containers must be labelled:
  - a) to indicate that they contain GMOs;
  - b) to indicate that it must be destroyed as infectious clinical waste; and
  - c) with contact details for the Clinical Trial Site.

### **Storage of the GMO**

48. Storage of GMO stock solutions at Clinical Trial Sites or storage facilities, notified to the Regulator under Condition 25, must be in accordance with Part 2.1 of the Regulator's *Guidelines for the Transport, Storage and Disposal of GMOs*, as current at the time of storage, with the following modifications:
  - a) the relevant Security requirement (item 2.1.15 in version 1.1 of these guidelines) does not apply;

*Note: Item 2.1.15 is exempted as it refers specifically to an IBC record of assessment for an NLRD, rather than to this licence. It is replaced with the following sub-condition.*

- b) access to the GMOs during transport must be restricted to authorised persons (i.e. the GMOs are within a locked unit or an area which has restricted access). This includes situations where containers are left for collection in a holding area, or left unattended prior to decontamination or disposal.

### **Transport and Disposal of the GMO**

- 49. Transport by service providers external to a Clinical Trial Site, and engaged solely for import, transport and/or disposal of the GMO (other than those that may be contained within a patient sample), must be conducted in accordance with one of the following:
  - (a) for transport in the course of import or export, or between the Australian border and the premises of the addressee or sender, the GMO must be packaged and transported according to IATA requirements for classification UN 3373 (Biological Substance, Category B), as current at the time of transportation; or
  - (b) for transport entirely within Australia, the GMO must be contained within a sealed, unbreakable primary container, with the outer packaging labelled to indicate at least:
    - i. that it contains GMOs; and
    - ii. the contact details for the licence holder; and
    - iii. instructions to notify the licence holder in case of loss or spill of the GMO; and
    - iv. where transport is for the purpose of disposal, that the GMO must be disposed of as infectious clinical waste.
- 50. For all other transport, including within a Clinical Trial Site, the GMO (other than those that may be contained within a patient sample) must be transported according to Part 1.2 of the Regulator's *Guidelines for the Transport, Storage and Disposal of GMOs* as current at the time of transportation, with the following modifications:
  - (a) the relevant Security requirement (item 1.2.1.5 in version 1.1 of these guidelines) does not apply;

*Note: Item 1.2.1.5 is exempted as it refers specifically to an IBC record of assessment for an NLRD, rather than to this licence. It is replaced with the following sub-condition.*

- (b) access to the GMOs during transport must be restricted to authorised persons (i.e. the GMOs are within a locked unit or an area which has restricted access). This includes situations where containers are left for collection in a holding area, or left unattended prior to disposal.

*Note: This Condition does not apply to transport of waste by trial participants. Under Condition 44 trial participants must agree to return waste to Clinical Trial Sites in the containers provided but such transport is not subject to any condition.*

- 51. Waste containing the GMO, including unused GMO stocks, that is disposed of from Clinical Trial Sites must be disposed of as infectious clinical waste.
- 52. Unless covered by another authorisation, stocks of the GMO must be used or destroyed on or before the date specified in Condition 30.

*Note: Condition 35 requires the licence holder to account for all vials of GMO imported under this licence from import to use or destruction, and to make records available to the Regulator on request.*

**DIR No: 161**

**Full Title:** A genetically modified respiratory syncytial virus (RSV) vaccine for use in clinical trials

**Organisation Details**

Postal address: Novotech (Australia) Pty Ltd  
Level 2, 381 MacArthur Ave  
Hamilton QLD 4007

Phone No (07) 3719 6000

**IBC Details**

IBC Name: BioDesk Institutional Biosafety Committee

**GMO Description**

**GMO covered by this licence:**

A genetically modified *Human respiratory syncytial virus* known as MinL4.0 RSV, modified by codon pair deoptimisation in the L open reading frame (ORF), synonymous codon changes in the SH ORF, specific single codon changes in each of the L, N, P and M2-1 genes, and deletion of part of the non-coding region of SH gene (as specified in the table below).

**Parent Organism:**

Common Name: Respiratory syncytial virus (RSV)  
Scientific Name: *Human respiratory syncytial virus*

**Modified traits:**

Categories: human therapeutic – attenuation  
Description: The GMO is a live RSV vaccine derived from RSV A2 strain, modified to attenuate the virus, while retaining the ability to elicit an immune response.

**Purpose of the dealings with the GMO:**

To conduct clinical trials assessing the safety, tolerability and efficacy of a genetically modified RSV vaccine in healthy adults.

**Table 1. Nucleic acid responsible for conferring the modified traits:**

Source	<ul style="list-style-type: none"> <li>• RSV A2 strain</li> </ul>
Identity	<ul style="list-style-type: none"> <li>• RNA-dependent RNA polymerase (L) ORF</li> <li>• Nucleocapsid (N) gene</li> <li>• Phosphoprotein (P) gene</li> <li>• Second Matrix (M2-1) gene</li> <li>• Small hydrophobic (SH) ORF</li> </ul>
Function	<ul style="list-style-type: none"> <li>• L – viral transcription</li> <li>• N – viral RNA binding protein; transcription and replication of the viral genomic RNA</li> <li>• P – component of the viral RNA-dependent RNA polymerase complex; transcription and replication factor</li> <li>• M2-1 – transcription factor</li> <li>• SH – cell-to-cell fusion; ion channel</li> </ul>
Modifications	<ul style="list-style-type: none"> <li>• L ORF was modified by incorporating 1,378 synonymous nucleotide substitutions (i.e. changes to the nucleotide sequence that don't change the encoded amino acids).</li> <li>• Nucleotide substitutions to encode the following single amino acid changes: <ul style="list-style-type: none"> <li>○ N - K136R</li> <li>○ P - E114V</li> <li>○ M2-1 - N88K</li> <li>○ L - T1166I.</li> </ul> </li> <li>• Deleted 112 nucleotide fragment of the downstream non-coding region of the SH gene and synonymous nucleotide substitutions in the last three codons of the SH ORF.</li> </ul>

## ATTACHMENT B

### Checklist of documents and notifications that must be maintained and/or sent to the Regulator:

When	What	Condition	Specific timeframe
Before commencing dealings with the GMO (including storage)	PIICF must be submitted to the Regulator. Any changes required must be made within the time period specified by the Regulator.	45	At least 30 days before the first trial commences
	Methodology to reliably detect the GMO, and the genetic modifications in a recipient organism	20	At least 14 days before commencing any GMO dealings
	Contingency Plan		
	Names of all organisations and persons who will be covered by the licence at each Clinical Trial Site, with a description of their responsibilities	23	At least 7 days before commencing dealings at each Clinical Trial Site
	Details of how persons covered by the licence will be informed of licence conditions		
	Details of how the licence holder will ensure compliance with licence conditions at Clinical Trial Sites over the period that dealings are conducted at that location		
	Name, address and description of each Storage facility	25	At least 7 days before commencing storage
	Name, address and description of each Clinical Trial Site		At least 7 days before commencing dealings
Following first inoculation at each Clinical Trial Site	Date of the first inoculation of the first trial participant at each Clinical Trial Site	25	No later than 7 days after the event
When inoculations cease at each Clinical Trial Site	Date of the final inoculation of the last trial participant at each Clinical Trial Site	25	Within 30 days of the decision to cease inoculations at that location
Any time after issue of licence	Any relevant conviction of the licence holder occurring after the commencement of this licence	12	Immediately
	Any revocation or suspension of a licence or permit held under a law relating to the health and safety of people or the environment		
	Any event or circumstances occurring after the issue of this licence that would affect the capacity of the holder of this licence to meet the conditions in it.		
	Any information related to the licence holder's ongoing suitability to hold a licence		
	Additional information as to risks to the health and safety of people or to the environment associated with the dealings	14	Without delay
			If and when requested



When	What	Condition	Specific timeframe
	Any contraventions of the licence by a person covered by the licence		
	Any unintended effects of the dealings		
	Events described in Condition 22 a)-c) (Contingency plan)	22 d)	Without delay
	Any changes to the information provided under Condition 23	24	Within 14 days of the changes occurring
	Copies of the signed and dated statements referred to in Condition 18	19 b)	If requested
	Procedures to account for the contents of all vials containing GMOs from import to use or destruction	35	
	Procedures at each Clinical Trial Site to track the dispensation, return and destruction of the containers described in Condition 47 (waste containers provided to Trial participants)	36	
	Records of Excluded Persons being excluded from directly handling the GMO, administering it to trial participants or caring for trial participants	38	
	Records of education of clinical trial staff on the potential for transmission of the GMO to people who are at risk of severe RSV infection	39	
	Records of trial participants' agreements as required under Condition 44	46	
	Annual Report	27	