Australian Government

Department of Health and Aged Care

Office of the Gene Technology Regulator

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

Licence No.: DIR 181

Licence holder: Novotech (Australia) Pty Limited

Clinical trial of a genetically modified Herpes virus for the treatment of cystic fibrosis

Issued: 7 July 2021

Varied: 14 December 2021

Varied: 1 July 2022

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.

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

In assessing applications for dealings involving the intentional release of genetically modified organisms into the Australian environment, 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.

Other agencies that also regulate genetically modified organisms or GM products include Food Standards Australia New Zealand, Australian Pesticides and Veterinary Medicines Authority, Therapeutic Goods Administration, Australian Industrial Chemicals Introduction Scheme, and the Department of Agriculture, Water and the Environment. 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.

Further information on licence DIR 181

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 (OGTR) website or by telephoning the Office on 1800 181 030.

CONDITIONS OF THIS LICENCE

1. In this licence:

    (a) unless defined otherwise, words and phrases used in this licence have the same meaning as they do in the Act and the Regulations;

    (b) words denoting a gender include any other gender;

    (c) words in the singular include the plural and words in the plural include the singular;

    (d) words denoting 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 general 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.

'Clinical trial site' means a medical facility in Australia such as a clinical research facility or hospital, and associated Pharmacy, which is notified in writing to the Regulator for the purposes of conducting this clinical trial.

'Contingency Plan' means a written plan detailing measures to be taken if certain events, as specified in Conditions 43-44, occur.

'Decontaminate' (or ***'Decontamination'***) means, as the case requires, kill the GMOs by one or more of the following methods:

(a) chemical treatment;

(b) autoclaving;

(c) high-temperature incineration; or

(d) a method approved in writing by the Regulator.

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

'External service provider' means a person engaged by the licence holder solely in relation to transport, storage and/or disposal of the GMO other than at a Storage facility or Clinical trial site, or Sample analysis other than at a Clinical trial site, and who is not undertaking any dealings with the GMO that are not for those purposes.

'GM' means genetically modified.

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

'IBC' means an institutional biosafety committee.

'NLRD' is a Notifiable low risk dealing. Dealings conducted as an NLRD must be assessed by an IBC before commencement and must comply with the requirements of the *Gene Technology Regulations 2001*.

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

'Personal information' has the same meaning as in the *Privacy Act 1988*. 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 a treated trial participant for subsequent analysis as part of the trial, and which may reasonably be expected to contain the GMO.

'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 third party facility offering logistical services and distribution of clinical supplies.

Holder of licence

3. The licence holder is Novotech (Australia) Pty Limited.

Remaining an Accredited Organisation

4. The licence holder must, at all times, remain an accredited organisation.

Validity of licence

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

Note: Although this licence has no expiry date, the period during which the GMO may be administered is restricted in accordance with condition 23.

Persons covered by this licence

6. The persons covered by this licence are the licence holder, and any employees, agents or External service providers of the licence holder, or the project supervisor(s), or other persons who

are, or have been, engaged or otherwise authorised by the licence holder or the project supervisor to conduct any of the dealings authorised by this licence.

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. The licence holder must keep a record of all organisations and persons covered by this licence, with a description of their responsibilities.

Note: Where External service providers are used, it is sufficient to record the company name and the position or job title of the person(s) conducting the dealing.

9. The licence holder must provide information related to the persons covered by the licence when requested to do so in writing by the Regulator and must provide the information within a time period stipulated by the Regulator.

Description of GMOs covered

10. The dealings authorised by this licence are only permitted to be conducted in respect of the GMOs identified and described in **Attachment A**.

Dealings authorised by this licence

11. 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 adult clinical trial participants by inhalation into the lungs;

ii) collect Samples from trial participants;

iii) analyse the Samples described in 11(b)ii);

(c) transport the GMO;

(d) dispose of the GMO;

and may possess, supply, use or store the GMO for the purposes of, or in the course of, any of these dealings.

12. Supply of the GMO for the purposes of dealings by a person or organisation not covered by this licence is only authorised by this licence if the Regulator provides prior written approval to the licence holder.

Note: For approval to be granted, the receiving person or organisation must have an appropriate authorisation to conduct dealings with the GMO. This is likely to be an NLRD, or a licence issued by the Regulator.

Conditions imposed by the Act

Note: The Act mandates the following 3 conditions.

Informing people of licence conditions (section 63)

13. The licence holder must inform any person covered by the licence, to whom a particular condition of the 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.

Note: No particular conditions of this licence apply to trial participants; therefore, condition 13 does not apply to trial participants.

Monitoring and audits (section 64)

14. If a person is authorised by this licence to deal with the GMO 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.

Additional information to be given to the Regulator (section 65)

15. The licence holder must inform the Regulator if he or she:

(a) becomes aware of additional information about 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: For the purposes of this condition:

(a) The licence holder is 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 is 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.

Informing the Regulator of any material changes of circumstance

16. 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 after the commencement of this licence, of a licence or permit held by the licence holder under a law of the Commonwealth, 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 licence holder to meet the conditions in it.

17. 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.

Further conditions with respect to informing persons covered by the licence

18. If a particular condition, including any variation of it, applies to a person with respect to any dealing, the licence holder must not permit a person covered by this licence to conduct that dealing unless the person has been informed of the condition, including any variation of it.

Note: Information required under condition 18 may be provided to External service providers who are engaged solely for storage and transport of the GMO through labelling of the outermost container of the GMOs in accordance with condition 39 or condition 40.

19. If a particular condition, including any variation of it, applies to a person with respect to any dealing, other than to an External service provider, the licence holder must not permit a person covered by this licence to conduct that dealing unless:

(a) 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 (b) below; and

(b) the licence holder has trained that person in a manner which enables them to conduct the dealings in accordance with the conditions of this licence.

20. The licence holder must notify all persons covered by the licence, from whom Personal information relevant to the administration and/or enforcement of the licence is collected by the licence holder, that such Personal information may be disclosed to the Regulator.

21. The licence holder must ensure that a copy of the licence conditions are readily available to all persons covered by the licence, other than External service providers, who are conducting dealings with the GMO.

Note: The licence may be made available electronically.

Limits on clinical trials conducted under this licence

22. The GMO may be administered to a maximum of 15 trial participants under this licence.

23. Administration of the GMO must be completed within 3 years from the date of issuing of the licence.

Conditions about trial participants

24. The licence holder must notify each trial participant, from whom Personal information relevant to the administration and/or enforcement of the licence is collected by the licence holder, that such Personal information may be disclosed to the Regulator.

25. The licence holder must ensure that criteria used in selecting trial participants include (though are not limited to) the following:

(a) Trial participants must be aged at least 18 years; and

(b) Trial participants must be willing to attend all study visits and complete all procedures required by the clinical trial protocol.

26. Before administering the first GMO dose to any trial participant, the licence holder must obtain written agreement from the trial participant that they will not donate blood or organs for 90 days after the last dose of the GMO.

27. Before administering the first GMO dose to any trial participant, the licence holder must obtain the trial participant's written agreement that following each administration of the GMO they will, for at least 48 hours or a lesser period approved in writing by the Regulator:

(a) implement hygiene measures intended to prevent transmission of the GMO to other people and to animals susceptible to infection with HSV-1 (e.g. pet rabbits), including but not limited to:

i. wearing a surgical mask;

ii. avoiding direct and indirect oral contact e.g. kissing, sharing food, utensils, cups and plates;

iii. refraining from coughing or sneezing in close proximity to other people and animals; and

iv. following standard hygiene practices including hand washing after coughing or sneezing or touching nasal secretions, and avoiding touching the face until doing so.

(b) collect all nasal secretions in tissues and seal contaminated tissues in a press seal plastic bag or other container supplied by the Clinical trial site, then wash their hands thoroughly with soap and water; and

(c) return the sealed plastic bag or container holding the tissues to the Clinical trial site at their next visit.

Note: For a lesser period to be approved by the Regulator, the licence holder must have demonstrated experimentally that the requested period is sufficient for inactivation of the GMO to occur under extracellular conditions simulating the human body.

28. Before administering the first GMO dose to any trial participant, the licence holder must obtain the trial participant's written agreement that from the time of their first GMO treatment until the end of the 36th day after their final GMO treatment, they will implement the following hygiene measures:

(a) avoid their saliva coming into direct or indirect contact with other people e.g., through kissing; engaging in oral sex without barrier protection; sharing food, utensils, cups and plates, or tooth brushes;

(b) avoid sharing towels or other personal items; and

(c) when in a space shared with other people, wash or sanitise hands after touching their mouth or eyes.

Note: Conditions 27 and 28 can be undertaken simultaneously during periods to which both apply.

29. The licence holder must ensure that during administration of the GMO, trial participants wear PPE including gloves, an impermeable full length gown, impermeable hair covering and shoe coverings. This PPE must be removed before leaving the treatment room and disposed of into the clinical waste bin.

30. The licence holder must ensure that before each trial participant leaves the Clinical trial site following administration of the GMO, the participant is provided with sealable bags or a container suitable for storing contaminated tissues and transporting them back to the Clinical trial site, and labelled to indicate contact details for the Clinical trial site, that it contains GMOs, and that it must be destroyed by autoclaving or high-temperature incineration.

Conditions related to the conduct of the dealings

31. Conditions that apply to dealings with GMOs do not apply to Samples collected from trial participants, or other materials or waste, that are reasonably expected not to contain the GMO. The licence holder must provide to the Regulator upon request, a written justification for this expectation.

32. The licence holder must ensure that dealings are only conducted in a manner which:

(a) does not compromise the health and safety of people; and

(b) minimises the exposure of persons conducting the dealings to the GMO, other than intended exposure of trial participants.

Note: The licence holder may achieve this by only engaging or otherwise authorising persons to conduct dealings who are required to adhere to appropriate standards and guidelines. For example standards developed by the National Pathology Accreditation Advisory Council for pathology practices, the Australian Guidelines for the Prevention and Control of Infection in Healthcare, Guidelines for Good Clinical Practice and the National Safety and Quality Health Service (NSQHS) Standards, or the behavioural requirements for dealings conducted in OGTR certified facilities.

33. The licence holder must ensure that facilities where dealings occur (other than import, transport and disposal) employ work practices and adhere to standards consistent with condition 32.

Storage and administration of the GMO, and collection of samples

34. All persons handling the GMO, including as supplied in sealed vials, must wear protective clothing including gloves.

35. Administration of the GMO into human trial participants must not commence prior to approval by a Human Research Ethics Committee.

36. The following activities must occur within a Clinical trial site:

(a) administration of the GMO to trial participants.

Note: Before this activity takes place, the details of each Clinical trial site must have been notified to the Regulator in accordance with condition 46(a).

37. The licence holder must ensure that the following work practices and behaviours, where applicable, are followed during administration of the GMO:

(a) the GMO must be administered to trial participants by clinical staff qualified to carry out the procedure;

(b) the GMO must be administered to trial participants in an enclosed space containing (at a maximum) only the furniture and equipment required for the procedure, any post-administration testing and waste disposal;

(c) all surfaces (excepting the ceiling) in the space used to administer the GMO must be smooth, impermeable to water, easily cleanable and resistant to damage by the cleaning agents and disinfectants that will be used in accordance with condition 37(h)(i) and 37(h) (iii);

(d) in addition to the trial participant, a maximum of one person may be present in the administration area while the GMO is being nebulised and during post-administration testing;

(e) clinical trial staff administering the GMO and assisting with post-administration tests must follow the aerosol protection plan approved for their Clinical trial site in accordance with condition 47;

(f) in addition to following condition 37 (e), clinical trial staff present in the treatment area while the GMO is being nebulised must wear personal protective equipment (PPE) including gloves, an impermeable full length gown, a splash barrier in front of the face, an impermeable hair cover and shoe covers. This PPE must be removed before leaving the treatment area and either Decontaminated if reusable (e.g. face shield or powered air-purifying respirator) or disposed of into a clinical waste bin;

(g) before the treatment room is reused for a different purpose, either the room must be left unused with the door(s) closed for a minimum of 72 hours OR the following items (at a minimum) must be Decontaminated:

i) all work surfaces used while administering the GMO;

ii) all re-usable equipment potentially contaminated with the GMO; and

iii) all readily accessible surfaces including, but not limited to, chairs, door handles, floors, and walls to a height reachable by an adult.

Transport, storage and disposal of the GMOs

38. The licence holder must ensure that transport of the GMOs is conducted only for the purposes of, or in the course of, another dealing permitted by this licence, for supply in accordance with condition 12, or for export.

39. For the purposes of import, subsequent transport to either a Storage facility or a Clinical trial site, and export, the licence holder must ensure that the GMO is packaged, labelled and transported in accordance with IATA shipping classification UN 3245.

40. The licence holder must ensure that transport and storage of the GMO within a Storage facility or Clinical trial site, and any transport between a Storage facility and a Clinical trial site, follows these sub-conditions:

(a) The GMO is contained within sealed, unbreakable container, labelled to indicate at least:

i) that it contains a GMO;

ii) that it contains biohazardous material as designated by a biohazard label;

iii) the contact details for the licence holder;

iv) instructions on how to clean up a spill, as per the contingency plan in condition 44; and

v) instructions to notify the licence holder in case of loss or spill of the GMO.

(b) the external surface of the container must be decontaminated before and after transport;

(c) procedures must be in place to ensure that GMO can be accounted for and that a loss of any GMO during transport or failure of delivery can be detected;

(d) access to the GMO is restricted to authorised persons for whom condition 18 has been met (i.e. the GMO is 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;

Note: All stored GMOs remain the responsibility of the licence holder.

(e) if the GMO is being transported or stored with a coolant (e.g. dry ice, liquid nitrogen or any other coolant) which will release a gas, a mechanism to allow the escape of the gas must be included. If water ice is used as a coolant then the outer packaging should be constructed so as to prevent any leakage. All containers must be able to withstand the temperatures to which they will be subjected;

(f) a consolidated record of all GMOs being stored under this condition is maintained and made available to the Regulator upon request; and

(g) where transport takes place entirely within a building, and the GMO is accompanied by authorised persons for whom condition 18 has been met, conditions 40(a)iii), 40(a)iv) and 40(c) do not apply.

41. The licence holder must ensure that all GMO and all waste reasonably expected to contain the GMO are Decontaminated:

(a) prior to disposal, unless the method of disposal is also a method of decontamination;

(b) before or upon suspension, cancellation or surrender of the licence, unless covered by another authorisation under the Act; and

(c) by autoclaving, chemical treatment, or high-temperature incineration.

42. Where Decontamination is carried out by an External service provider, the licence holder must ensure that the GMO, or waste reasonably expected to contain the GMO, enters the clinical waste stream and is decontaminated by autoclaving or high-temperature incineration.

Contingency plans

43. The licence holder must ensure that any person (other than a trial participant) exposed to the GMO is offered prompt medical advice. The clinician must be provided with any relevant information about the GMO.

44. If there is a spill or an unintentional release of GMO at a Storage facility or Clinical trial site, the following measures must be implemented:

(a) the GMO must be contained to prevent further dispersal;

(b) persons cleaning up the GMO must wear protective clothing;

(c) the exposed area must be decontaminated with an appropriate chemical disinfectant effective against the GMO such as 1% hypochlorite solution;

(d) any material used to clean up the spill or personal protective clothing worn during clean-up of the spill must be decontaminated; and

(e) the licence holder must be notified as soon as reasonably possible.

Notification and reporting

*Note: Notices and reports may be emailed to OGTR.M&C@health.gov.au. A summary of notification and reporting requirements is provided at **Attachment B**.*

45. The licence holder must notify the Regulator, in writing, of the name and address of each Storage facility before commencement of dealings at that location.

46. Before first administering the GMO at each Clinical trial site, the licence holder must provide the Regulator with a Compliance Management Plan for that Clinical trial site, specifying:

(a) the name, address and description of the Clinical trial site, including any associated storage areas/Analytical facilities;

(b) the key persons or roles responsible for management of the trial at the site;

(c) the measures implemented at the Clinical trial site to ensure the licence holder can meet the reporting requirements and time frame specified in subconditions 50(b), (c) and (d);

(d) that the IBC associated with the site (if any) has been notified of the trial;

(e) details of how the persons covered by the licence (for that type of dealing) will be informed of licence conditions applicable to them and how they will be trained to safely conduct the dealings;

(f) the person(s) or class of persons administering the GMO;

(g) where, within the site, the GMO is expected to be administered;

(h) the expected date of first administration; and

(i) how the site will comply with subconditions 37 (b), (c), (d), (e) and (h).

Note: For the purpose of finding out whether the Act has been complied with, an OGTR inspector may, if entry is at a reasonable time, enter a facility occupied by the licence holder or a person covered by the licence and exercise monitoring powers.

47. Before first administering the GMO at each Clinical trial site, the licence holder must provide the Regulator with, for that site, a detailed plan for effective protection from aerosols to the mouth, nose and eyes of staff administering nebulised GMO to trial participants. Each plan must be approved in writing by the Regulator before administration of the GMO at the corresponding site commences.

Note: Aerosol protection measures for staff administering the GMO may include, but are not limited to, physical isolation of the trial participant from the staff member e.g. through use of a sealed mist tent or separate room with communication via a glass panel or webcam, or use of a powered air-purifying respirator (PAPR).

48. Before first administering the GMO at each Clinical trial site, the licence holder must provide the Regulator with, for that site, an exposure management plan detailing how exposure to the GMO of people not involved in the clinical trial will be minimised. Each plan must be prepared in consultation with the corresponding Clinical trial site and, where relevant, approved by the IBC associated with the site.

Note 1: people not involved in the clinical trial include, but are not limited to, users of adjoining rooms, corridors or rooms connected to the treatment room via the ventilation system.

Note 2: exposure management strategies could include, but are not limited to, use of a negative-pressured, HEPA-filtered environment, such as a mist tent, isolation room or suitably ventilated laboratory; limiting the use of adjoining or connected rooms/corridors during and after the procedure; considering air circulation between rooms via the ventilation system; and allowing sufficient time for aerosolised GMO to settle out before opening the treatment room door.

49. The licence holder must notify the Regulator, in writing, of the final inoculation of the last trial participant at each Clinical trial site, within 30 days of the decision to cease inoculations.

50. The licence holder must inform the Regulator as soon as reasonably possible:

(a) in the event of a trial participant experiencing a serious adverse event which may be related to the GMO;

(b) if they are notified or otherwise become aware of a loss or spill of the GMO;

(c) if they are notified or otherwise become aware that a trial participant has not followed the procedures described in conditions 27 and 28; and

(d) if they are notified or otherwise become aware of the exposure of a person other than a trial participant to the GMO.

51. Upon request from the Regulator, the licence holder must provide any signed records or documentation collected under a condition of this licence, within a time period stipulated by the Regulator.

Attachment A

DIR No: 181

Title	Clinical trial of a genetically modified Herpes virus for the treatment of cystic fibrosis

Organisation Details

Postal address:	Novotech (Australia) Pty Limited Level 2 381 MacArthur Avenue HAMILTON QLD 4007
Phone No:	(07) 3719 6000

GMO Description

GMOs covered by this licence:

Herpes simplex virus-1 modified by deletion and introduction of the genes and genetic elements listed in Table 1 below.

Parent Organism

Common Name:	*Herpes virus*
Scientific Name:	*Herpes simplex virus-1* (HSV-1)

Modified traits

Categories:	Human therapeutic – replication incompetent, protein expression
Description:	The GMO is modified such that it cannot replicate, and expresses two copies of the full length *human cystic fibrosis transmembrane conductance regulator* (CFTR) gene. These are intended to replace the dysfunctional CFTR gene in patients with cystic fibrosis.

Table 1. Nucleic acid responsible for conferring the modified traits

Identity, nature of modification	Modified trait, description
• Genes involved in viral replication replaced with an expression cassette comprising:	Replication-incompetent
➢ a constitutively active promoter;	Constitutive transgene expression
➢ coding sequence of human cystic fibrosis transmembrane conductance regulator (CFTR) gene; and	Expression of human CFTR protein in transduced cells
➢ other regulatory elements	Transgene expression

Purpose of the dealings with the GMOs

To conduct an initial study of genetically modified HSV-1 expressing the human CFTR protein, intended to assess safety and efficacy in a small group of cystic fibrosis patients.

Attachment B

Prior to the commencement of the trial at a given location	Condition	Timeframe for reporting
The name and address of each Storage facility	45	Before commencement of dealings at that location
A Compliance Management Plan for each trial site, including: • the name, address and description of the Clinical trial site, including any associated storage areas/Analytical facilities; • the key persons or roles responsible for the management of the trial at the site; • the measures implemented at the Clinical trial site to ensure the licence holder can meet the reporting requirements and time frame specified in subconditions 50(b), 50(c) and 50 (d); • that the IBC associated with the site (if any) has been notified of the trial; • details of how the persons covered by the licence (for that type of dealing) will be informed of licence conditions applicable to them and how they will be trained to safely conduct the dealings; • the person(s) or class of persons administering the GMO; • where, within the site, the GMO is expected to be administered; • expected date of first administration; and • how the site will comply with subconditions 37 (b), (c), (d), (e) and (h)	46	Before the first administration of the GMO at the relevant Clinical trial site
For each Clinical trial site, a detailed plan for effective protection from aerosols to the mouth, nose and eyes of staff administering nebulised GMO to trial participants. **Each plan must be approved in writing by the Regulator before administration of the GMO at the corresponding site commences.**	47	Before the first administration of the GMO at the relevant Clinical trial site
Information to be provided at any time during the Clinical trial		
Any additional information related to the health and safety of people and the environment associated with the dealing covered by the licence, or any unintended effect of the dealing authorised by the licence	15(a), (c)	As soon as the licence holder becomes aware
Information related to any contravention of the licence by a person covered by the licence	15(b)	As soon as the licence holder becomes aware
Any relevant conviction of the licence holder	16(a)	Immediately
Any revocation or suspension of a licence or permit held by the licence holder under a law of the Commonwealth, a State or a foreign country	16(b)	Immediately
Any event or circumstances that would impact the licence holder capacity to meet the licence conditions	16(c)	Immediately
Any Serious adverse event which may be related to the GMO	50(a)	As soon as reasonably possible
Any loss or spill of the GMO, or exposure of a person other than the trial participant to the GMO	50(b), (d)	As soon as reasonably possible after becoming aware of the event

Prior to the commencement of the trial at a given location	Condition	Timeframe for reporting
Any event where a trial participant has not followed the procedures described in the instruction provided by the licence holder	50(c)	As soon as reasonably possible after becoming aware of the event
Information to be provided on request by the Regulator		
Information related to the persons covered by the licence	9	Within a timeframe stipulated by the Regulator
Information related to the licence holder's ongoing suitability to hold a licence	17	Within a timeframe stipulated by the Regulator
Any signed records or documentation collected under a condition of this licence	51	Within a timeframe stipulated by the Regulator