



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 179

Licence holder: Novotech (Australia) Pty Limited

**Clinical trial with a genetically modified *Vaccinia virus* based treatment
for solid cancerous tumours**

Issued: 14 April 2021

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 (the Regulator) in accordance with the *Gene Technology Act 2000* and, as applicable, corresponding State law.

The 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 genetically modified organisms into the Australian 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 179

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.

Section 1 Interpretations and Definitions

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 trial facility and associated pharmacy, which are 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 Condition 35, 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 GMOs, or Sample analysis other than at a Clinical trial site, and who is not undertaking any dealings with the GMOs that are not for those purposes.

'Excluded persons' means:

- persons who display any evidence of an active infection or any immunosuppressive disorder, including HIV infection;
- women who are breastfeeding or who are pregnant; and
- persons who have a history of significant skin disease, such as atopic dermatitis.

'GM' means genetically modified.

'GMO' means the genetically modified organisms that are the subject of the dealings authorised by this licence.

'NLRD' is a Notifiable low risk dealing. Dealings conducted as an NLRD must be assessed by an institutional biosafety committee (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.

'Pharmacy' means a location within the Clinical trial site, where authorised staff stores, prepares, and dispenses medications in a medical environment.

'Regulator' means the Gene Technology Regulator.

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

'Sample' means any biological material collected from an inoculated trial participant for analysis as part of the trial, and which may reasonably be expected to contain GMOs.

'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.

Section 2 General conditions and obligations

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 duration of preparation and administration of the GMOs is restricted in accordance with Condition 19.

Description of GMOs covered

6. The GMO covered by this licence is a GM *Vaccinia virus*, as described in Attachment A of the Licence.

Dealings authorised by this licence

7. The dealings authorised by this licence are to:
- (a) import the GMOs;
 - (b) conduct the following experiments with the GMOs:
 - i) prepare the GMO for administration to trial participants;
 - ii) administer the GMO to clinical trial participants by intratumoural injection or by intravenous infusion;
 - iii) collect Samples from trial participants;
 - iv) analyse the Samples described in 7(b)iii);
 - (c) transport the GMOs; and
 - (d) dispose of the GMOs

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

8. 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 GMOs. This is likely to be an NLRD or a licence issued by the Regulator.

9. To the extent that any activity by a trial participant may be considered a dealing for the purposes of the Act, that dealing is authorised by this licence.

Persons covered by the licence

10. 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.

Obligations of the licence holder

11. The licence holder must inform any person covered by this licence, to whom a particular condition of the licence applies, of the following:
- (a) the particular condition (including any variations of it); and
 - (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 11 does not apply to trial participants.

12. 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.

13. 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 licence conditions, or its variation; and
 - iii) has been trained by the licence holder in a manner which enables them to safely conduct the dealings in accordance with the conditions of this licence.

14. 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.

15. 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.

16. The licence holder must ensure that a copy of the licence is 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.

Obligations of persons covered by the 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 the 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 Limits and control measures

Limits on clinical trials conducted under this licence

18. A maximum of 150 trial participants may be inoculated with the GMO under the licence.

19. The preparation and administration of the GMO must be completed within 5 years from the date of issuing of the licence.

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

- (a) preparation of the GMO for administration to trial participants; and
- (b) administration of the GMO to trial participants.

Note: Before any of these activities take place, the details of each Clinical trial site must have been notified to the Regulator in accordance with Condition 39(a).

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

Control measures

General conduct of clinical trials

22. 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.

23. The licence holder must ensure that procedures are in place to account for the GMO from import to use or destruction, and records must be made available to the Regulator on request.

Work practices at Clinical trial sites

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

- (a) preparation of the GMO must be conducted in a Class II biosafety cabinet, or alternative containment equipment approved in writing by the Regulator;
- (b) persons preparing or administering the GMO or collecting Samples from trial participants post-GMO administration must wear personal protective equipment including a gown, gloves, mask and eye protection;
- (c) instruct Excluded persons as defined in this licence not to prepare, handle or administer the GMO and to avoid direct contact with areas, equipment or Samples potentially contaminated with the GMO. In addition, direct post-care treatment of the trial participants must not be carried out by these persons for at least seven days after each treatment or if lesions are present;
- (d) any broken skin (e.g. cuts, scratches, dermatitis) of persons conducting dealings not covered by PPE or clothing must be covered with a waterproof dressing;
- (e) all work surfaces must be decontaminated before and immediately after they have been used for conducting dealings authorised by this licence with a decontaminant that is known to be effective against the GMO;
- (f) equipment used for dealings with the GMOs must be decontaminated after use with a decontaminant that is known to be effective against the GMO;
- (g) preparation and administration of the GMO must be conducted by suitably qualified and trained medical staff; and
- (h) after the GMO has been administered to the trial participant by intravenous injection or by intratumoural infusion, the intravenous injection/intratoural infusion site must be covered with an occlusive dressing.

Conditions relating to trial participants

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

- (a) Excluded persons as defined in this licence;
- (b) those having received a prior treatment with an oncolytic virus;
- (c) those having received live vaccines, which are compatible for recombination with *Vaccinia virus*, 30 days prior to the first treatment with the GMO; and
- (d) those intending to become pregnant during the first six weeks following the last treatment with the GMO.

26. Before inoculating any trial participant with the GMOs, the licence holder must obtain written agreement from the trial participant that they will:

- (a) forgo any vaccination with live vaccines, which are compatible for recombination with *Vaccinia virus*, while participating in the trial, and have been informed by the licence holder of such compatible vaccines; and
- (b) use barrier contraception for six weeks after each treatment with the GMO; and
- (c) not donate blood, sperm, tissues or organs while participating in the trial and for six weeks after their last treatment with the GMO.

Preventive practices required post-administration

27. The licence holder must also obtain trial participant's written agreement that:

- (a) while undergoing treatment with the GMO, they will implement hygiene measures intended to prevent transmission of the GMO to other people and to animals, including, but not limited to, frequent hand washing with soap or hand disinfectant, respiratory hygiene and cough etiquette (for two weeks after each round of treatment);

Note 1: For the purposes of this licence, animals also include pets, native wildlife and birds.

Note 2: People who come into contact with livestock or other animals should wash their hands thoroughly before caring for animals or handling equipment such as food/water bowls, bridles or buckets.

- (b) they will avoid direct physical contact with children under 12 months of age and Excluded persons as defined in this licence, from the time of each treatment with the GMO until after the respective follow-up visit to the clinical trial site that occurs on or after day 7 post-GMO administration;

Note: Direct physical contact means contact of any kind between a trial participant and children under 12 months of age and Excluded persons as defined in this licence.

- (c) should they develop GMO-related lesions during the trial, they will, until such time as a clinician has determined that the lesions have healed:
 - i) continue to avoid direct physical contact with children under 12 months of age and Excluded persons as defined in this licence; and
 - ii) keep skin lesions covered with a dressing; and
 - iii) treat any item that comes into contact with the lesion or the dressing, including the outer surface of the dressing while in place, as potentially contaminated with the GMO; and
 - iv) follow instructions provided by the licence holder for disinfection of contaminated clothing, towels, linens etc. (e.g. laundering with antimicrobial detergent and/or treatment with bleach); and
 - v) if oral lesions are present, wear a mask in the presence of other people or animals and refrain from sharing items such as toothbrushes and eating utensils; and
 - vi) prevent all direct physical contact (by both people and animals) with lesions, dressings, or with any potentially contaminated material except where necessary for patient care; and

Note: Preventing physical contact by animals includes such measures as:

- *preventing animals from sniffing or otherwise contacting a lesion, scab, or dressings, clothing, towels, sheets etc. that have been in direct contact with a lesion or scab; and*
- *keeping pets out of the room while changing dressings or clothes, and sealing the used dressing inside a primary and secondary container before allowing the pet back into the room.*

- vii) ensure persons caring for lesions, wear disposable gloves and wash or disinfect their hands immediately afterwards; and
 - viii) seal used dressings and other materials used in caring for the lesion in a primary container (e.g. a press-sealed bag), place these within a secondary container (e.g. a biohazard bin) provided by the Clinical trial site, and store the secondary container such that it is inaccessible to children and animals until it is returned to the Clinical trial site; and
 - ix) return the secondary container referred to above, and its contents, to the Clinical trial site for disposal as clinical waste; and
- (d) they will inform the Clinical trial site as soon as reasonably possible if they suspect that transmission, such as physical contact of a lesion, to another person or to an animal may have occurred.

28. Trial participants must be assessed for the presence of GMO-related lesions at each follow-up visit to the Clinical trial site. If any GMO-related lesion is found, the licence holder must instruct the trial participant to follow the behavioural practices as described in Condition 27(c).

29. The licence holder must ensure all trial participants, from the time of GMO administration, are provided with a supply of unbreakable secondary containers appropriate for transporting waste back to the Clinical trial site, labelled to indicate the contact details for the Clinical trial site; that it contains GMOs; and that it must be destroyed by autoclaving, chemical treatment or high-temperature incineration.

Note: Unbreakable means able to withstand all reasonably expected conditions of storage and transport such as: the forces, shocks and impacts expected during handling; or changes of temperature, humidity or air pressure.

Transport, storage and disposal of the GMOs

30. Unless covered by an NLRD, the licence holder must ensure that transport of the GMOs must only be for the purposes of, or in the course of, another dealing permitted by this licence, for supply in accordance with Condition 8, or for export.

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

- (a) prior to disposal, unless the method of disposal is also a method of decontamination; and
- (b) before or upon suspension, cancellation or surrender of the licence, unless covered by another authorisation under the Act, or exported; and
- (c) by autoclaving, chemical treatment or high-temperature incineration; and

32. The licence holder must ensure that transport and storage of the GMOs within the Clinical trial site or transport of Samples to an Analytical facility follows these sub-conditions:

- (a) GMOs are contained within sealed, unbreakable primary and secondary containers, with the outer packaging labelled to indicate at least:
 - i) that it contains GMOs; and
 - ii) that it contains biohazardous material as designated by a biohazard label; and
 - iii) the contact details for the licence holder; and
 - iv) instructions to notify the licence holder in case of loss or spill of the GMOs; and
 - v) instructions on how to clean up a spill, as per the contingency plan in Condition 36; and
- (b) external surface of the primary and secondary container must be decontaminated prior to and after transport; and

- (c) procedures must be in place to ensure that GMOs can be accounted for and that a loss of GMOs during transport or failure of delivery can be detected; and
- (d) access to the GMOs is restricted to authorised persons for whom Condition 12 has been met (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; and

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; and

Note: When transporting and storing with coolants, it is preferable for coolants to be used outside of the secondary container.

- (f) a consolidated record of all GMOs being stored under this condition is maintained and made available to the Regulator upon request.
- (g) For the purposes of transport entirely within a building, and the GMOs are accompanied by authorised persons for whom Condition 12 has been met, Conditions 32(a)iii), 32(a)iv) and 32(c) do not apply.

33. For the purpose of import or export and transport between the border and the Clinical trial site, the licence holder must ensure the GMO is packaged, labelled, stored and transported in line with IATA classification UN 3373 [Category B].

34. Where transport is conducted by External service providers for the purpose of disposal, the licence holder must ensure that the GMO, or waste reasonably expected to contain the GMO, enters the clinical waste stream for decontamination via autoclaving or high-temperature incineration.

Note: In the event of a spill during transport by an External service provider, compliance with relevant State or Territory legislation and regulations to manage clinical or biohazardous spills is sufficient.

Contingency plans

35. At least 14 days prior to first administering the GMO at each Clinical trial site, the licence holder must provide to the Regulator a written Contingency Plan applicable to that Clinical trial site detailing measures to be taken in the event of:

- (a) the unintentional release of the GMOs, such as a spill of the GMO within a Clinical trial site; and
- (b) suspected or confirmed transmission of the GMOs to persons other than trial participants or to animals; and
- (c) a person exposed to the GMOs (including a trial participant) developing a Serious adverse event linked to the GMOs, including those known to result from infection with *Vaccinia virus*.

Note: A Contingency Plan may be applicable to more than one Clinical trial site.

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

- (a) ensure the Regulator is notified as soon as reasonably possible after the licence holder becomes aware of the event; and
- (b) if there is a spill of the GMO, such as during transport and storage within a Clinical trial site, implement the following measures:
 - i) contain the GMOs to prevent further dispersal; and

- ii) decontaminate the exposed area with an appropriate chemical disinfectant effective against the GMOs; and
- (c) if transmission of the GMOs to people other than trial participants is suspected or confirmed, provide medical treatment to affected persons as necessary; and
- (d) if a person exposed to the GMO exhibits symptoms of a Severe adverse event:
 - i) provide appropriate medical treatment to the affected person; and
 - ii) implement measures to prevent the spread or persistence of the GMO.

37. If any of the events described in Condition 35 occur, the licence holder must ensure that the appropriate procedure(s) from the Contingency Plan are implemented.

Section 4 Reporting and Documentation

The following licence conditions are imposed to demonstrate compliance with other conditions and facilitate monitoring of compliance by staff of the OGTR.

Notifications to the Regulator

38. General notifications must be sent to the Regulator as follows:

Note: Please send all correspondence related to the licence to OGTR.M&C@health.gov.au.

Notice	Content of notice	Timeframe
(a) Changes to contact details	Changes to any of the contact details of the contact person(s) for the licence or project supervisor(s) from that notified in the licence application or subsequently.	As soon as practicable.
(b) Ongoing suitability to hold a licence	<ul style="list-style-type: none"> i) The licence holder must inform the Regulator of: ii) any relevant conviction of the licence holder; or iii) 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; or iv) any event or circumstances that would affect the capacity of the licence holder to meet the conditions of the licence; and 	Immediately after any of these events occur.
	<ul style="list-style-type: none"> v) any information related to the licence holder's ongoing suitability to hold a licence, that is requested by the Regulator. 	Within the timeframe stipulated by the Regulator.
(c) People covered by the licence	<ul style="list-style-type: none"> i) names of all organisations and persons, or functions or positions of the persons, who will be covered by the licence, with a description of their responsibilities; <i>Note 1: Examples of functions or positions are 'project supervisor', 'pharmacist', 'waste contractor', etc.</i> ii) details of how the persons covered by the licence will be informed of licence conditions; <i>Note 2: This may include a description of any contracts, training, labelling, contractual agreements with other organisations or persons</i> iii) contact details of the project supervisor(s) for the licence. 	At least 14 days prior to conducting any dealings with the GMOs (to be updated within 14 days if the notified details change).
(d) Contingency Plan(s)	Contingency Plan(s), required under Condition 35, including the details specified in Condition 36.	At least 14 days prior to first administering the GMO at each Clinical trial site

Notice	Content of notice	Timeframe
(e) Training records	Copies of the signed and dated statements referred to in Condition 13.	Within the timeframe stipulated by the Regulator.
(f) Additional information required by the Act	<p>The licence holder must inform the Regulator, if the licence holder becomes aware of:</p> <ul style="list-style-type: none"> i) 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 ii) any contraventions of the licence by a person covered by the licence; or iii) any unintended effects of the dealings authorised by the licence. <p><i>Note 1: The Act requires, for the purposes of the Condition 38(f), that:</i></p> <ul style="list-style-type: none"> – the licence holder will be taken to have become aware of additional information of a kind mentioned in Condition 38(f) if he or she was reckless as to whether such information existed; and – the licence holder will be taken to have become aware of contraventions, or unintended effects, of a kind mentioned in Condition 38(f), if he or she was reckless as to whether such contraventions had occurred, or such unintended effects existed. <p><i>Note 2: Contraventions of the licence may occur through the action or inaction of a person.</i></p> <p><i>Note 3: Additional information includes any changes at a Clinical trial site, which might increase the likelihood of dispersal of the GMOs.</i></p>	<p>Without delay after becoming aware of any new information.</p> <p><i>Note: An example of notification without delay is contact made within a day 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.</i></p>
(g) Further details regarding additional information	Any further details requested by the Regulator in relation to information provided under Condition 38(f).	Within the timeframe stipulated by the Regulator.
(h) Notification of Serious adverse event	In the event of a trial participant experiencing a Serious adverse event, which may potentially be related to the GMO, the licence holder must notify the Regulator.	As soon as reasonably possible.
(i) Notification of loss or spill, or exposure of persons	The licence holder must notify the Regulator if they are notified or otherwise become aware of a loss or spill of the GMO, or of the exposure of a person other than a trial participant to the GMO.	As soon as reasonably possible.
(j) Signed records or documentation	Upon request from the Regulator, the licence holder must provide any signed records or documents collected under a condition of this licence.	Within the timeframe stipulated by the Regulator.

39. Notifications relating to each Clinical trial site must be sent to the Regulator as follows:

Note: please send all correspondence related to the licence to OGTR.M&C@health.gov.au.

Notice	Content of notice	Timeframe
(a) Compliance Management Plan	<p>A written Compliance Management Plan must be submitted for each Clinical trial site, detailing to the satisfaction of the Regulator:</p> <ul style="list-style-type: none"> i) the name, address and description of the Clinical trial site, including any associated Pharmacies/storage areas/Analytical facilities; ii) the key persons responsible for the management of the trial at the site; 	At least 14 days before first administration of the GMO at that particular Clinical trial site.

Notice	Content of notice	Timeframe
	<ul style="list-style-type: none"> iii) that the Institutional Biosafety Committee (IBC) associated with the site (if any) has been notified of the trial; iv) the proposed reporting structure for the trial at the site and how the reporting structure enables the licence holder to become aware of any self-reported incidents for the purposes of Conditions 38(h) and (i); v) 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; vi) the person(s) or class of persons administering the GMO; vii) where, within the site, the GMO is expected to be administered; viii) expected date of first administration; and ix) how compliance with Condition 22 will be achieved in relation to preparation of participant Samples for analysis subsequent to administering the GMO. <p><i>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.</i></p>	
(b) Notification of final GMO administration	Provide notification to the Regulator, in writing, of the final GMO administration of the last trial participant at each Clinical trial site.	Within 30 days of the decision to cease GMO administration at that particular Clinical trial site.

DIR No: 179

Full Title: Clinical trial with a genetically modified *Vaccinia virus* based treatment for solid cancerous tumours

Organisation Details

Postal address: Novotech (Australia) Pty Limited
Level 2
381 MacArthur Avenue
HAMILTON QLD 4007

Phone No: (07) 3719 6000

IBC Details

IBC Name: BioDesk Institutional Biosafety Committee

GMO Description

GMOs covered by this licence:

Vaccinia virus genetically modified by introduction or deletion of only the genes or genetic elements listed below.

Parent Organisms:

Common Name: *Vaccinia virus*

Scientific Name: *Vaccinia virus* (Copenhagen strain)

Modified traits:

Categories: Human therapeutic

Description: The GMO, known as TBio-6517, is a live *Vaccinia virus* treatment derived from the Copenhagen strain, modified to selectively replicate in cancerous cells and to enhance the human immune response to the target cancerous tumour cells. Modified genes are listed in Table 1.

Table 1. Nucleic acid responsible for conferring the modified traits

Identity	<ul style="list-style-type: none"> • Anti- Cytotoxic T-lymphocyte-Associated protein 4 (anti-CTLA-4) antibody gene • FMS-like tyrosine kinase 3 ligand (FLT3L) gene • Membrane-bound interleukin-12 p35 subunit (IL-12p35) gene
Modifications	<ul style="list-style-type: none"> • Insertion of the above genes • Deletion and disruption of multiple genes including virulence factors
Function	<ul style="list-style-type: none"> • anti-CTLA-4 – immunomodulatory • FLT3L – immunomodulatory • IL-12p35 – immunomodulatory • Deletion and disruption of multiple genes – selective replication and improved destruction of human tumour cells

Purpose of the dealings with the GMOs:

To conduct clinical trials assessing the safety, tolerability and efficacy of a genetically modified *Vaccinia virus* in patients with advanced solid tumours.