Environmental Protection Authority
Te Mana Rauhī Taiao

New Zealand Government

Staff Assessment Report

3 February 2021

Advice to the Decision-making Committee on APP204176: Pfizer SARS-CoV-2 vaccine BNT162b2 (COMIRNATY™)

Application code:	APP204176
Application type and sub-type:	Section 26 statutory determination
Applicant:	Pfizer New Zealand Limited
Date application received:	29 January 2021
Purpose of the Application:	To determine if the SARS-CoV-2 vaccine BNT162b2 (COMIRNATY™) is a new organism for the purpose of the Hazardous Substances and New Organisms Act 1996

Executive summary and recommendation

In January 2021, Pfizer New Zealand contacted the Environmental Protection Authority (EPA) to request a determination under section 26 of the Hazardous Substances and New Organisms Act 1996 (The Act) regarding the new organism status of its SARS-CoV-2 vaccine BNT162b2, sold under the trade name COMIRNATY™. The applicant specifically requested that the EPA make a determination as to whether BNT162b2 was an organism or not.

We have reviewed the application and the relevant published literature regarding BNT162b2 and components thereof. Based on this analysis, we recommend that BNT162b2 does not meet the definition of an organism in the Act, and therefore it cannot be a new organism for the purpose of the Act.

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Introduction

Purpose of this document

1. This document has been prepared by EPA staff in the New Organisms team to advise the HSNO Decision-making Committee delegated to determine whether the SARS-CoV-2 vaccine BNT162b2 (COMIRNATY™) is to be considered as a new organism for the purpose of the Hazardous Substances and New Organisms Act (1996) (the Act). This document discusses information provided in the application as well as information from other readily available sources.

Application summary

2. This application was prepared by Pfizer New Zealand Limited (the applicant). The applicant seeks a determination under section 26 of the Act on whether the SARS-CoV-2 vaccine BNT162b2 (COMIRNATY™) is to be considered as a new organism under the Act.
3. The applicant has provided information on the BNT162b2 vaccine, pertaining to its structure, and its nature as a messenger RNA (mRNA) molecule that encodes a single protein. The applicant also provided reasoning as to why the BNT162b2 vaccine should not be considered as an organism, and therefore not a new organism for the purpose of the Act.

BNT162b2 description

4. As stated in the application, BNT162b2 consists of purified single-stranded messenger RNA (mRNA) molecules encoding the spike glycoprotein of SARS-CoV-2, the virus that causes the disease COVID-19 (ViralZone 2020; Fig 1). The spike protein is responsible for host cell binding and fusion, which allows the virus to invade mammalian cells (Masters & Perlman 2013), and it is also a major protein recognised by the immune system in its responses to SARS-CoV-2 infections

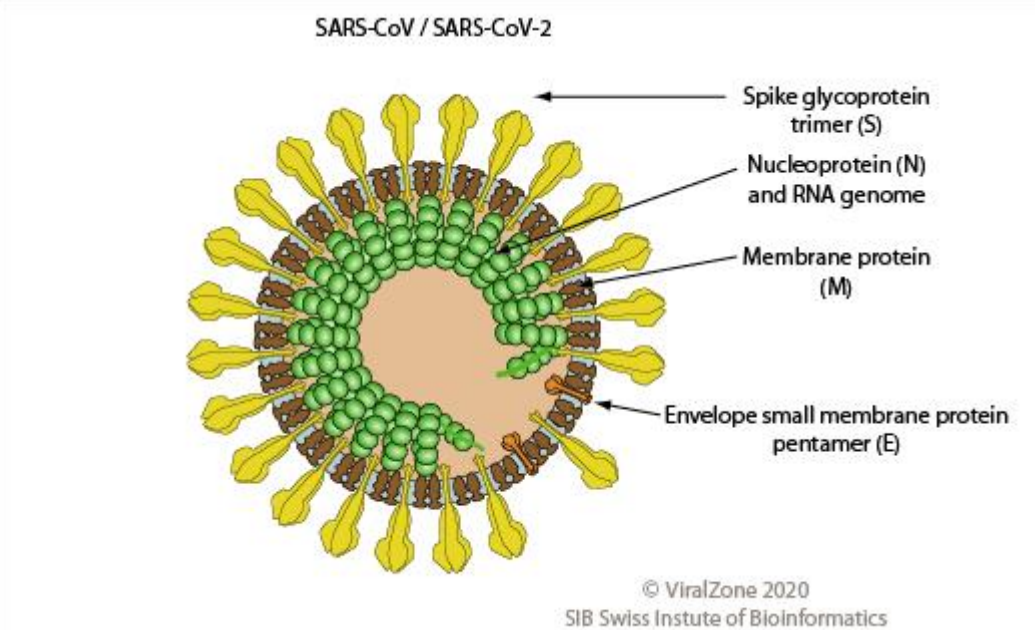

Figure 1: Generic structure of SARS-CoV and SARS-CoV-2 viruses. The gene encoded in BNT162b2 is the spike protein (S).

(Shomuradova et al, 2020).The BNT162b2 mRNA constitutes the active ingredient of the vaccine, which is packaged inside lipid nanoparticles.

5. In addition to the encoded spike protein, the BNT162b2 mRNA contains a number of other components that enable it to function as an mRNA molecule (Table 1).The various elements described in Table 1 make up the overall structure of the mRNA in a specific sequence that enable its function is such that it is recognised by ribosomes in cells of the recipients of the vaccine. The roles of the various components of an mRNA are described in the Figure 2 legend.

Table 1: Functional elements of the BNT162b2 mRNA molecule.

Element	Description	Position
cap	A modified 5'-cap1 structure (m7G+m3'-5'-ppp-5'-Am)	1-2
5'-UTR	5´-untranslated region derived from human alpha-globin RNA with an optimized Kozak sequence.	3-54
sig	S glycoprotein signal peptide (extended leader sequence), which guides translocation of the nascent polypeptide chain into the endoplasmic reticulum.	55-102
S protein_mut	Codon-optimised sequence encoding full-length SARS-CoV-2 spike (S) glycoprotein containing mutations K986P and V987P to ensure the S glycoprotein remains in an antigenically optimal pre-fusion conformation; stop codons: 3874-3879.	103-3879
3'-UTR	The 3´ untranslated region comprises two sequence elements derived from the amino-terminal enhancer of split (AES) mRNA and the mitochondrial encoded 12S ribosomal RNA to confer RNA stability and high total protein expression.	3880-4174
poly(A)	A 110-nucleotide poly(A)-tail consisting of a stretch of 30 adenosine residues, followed by a 10-nucleotide linker sequence and another 70 adenosine residues.	4175-4284

6. Ribosomes are responsible for "reading" the genetic code of the mRNA to produce a single protein (a process called translation), in this case, the SARS-CoV-2 spike protein. Ribosomes recognise mRNA molecules for translation via their cap structures (Fig 2). The BNT162b2 mRNA has a chemically synthesised cap modification (Table 1) that is similar to the naturally occurring cap structures found in mammalian cells (Hunt 2020).

7. As described in Table 1, the "sig" sequence of the BNT162b2 mRNA encodes a signal peptide that causes ribosomes to pause translation of the partially translated protein until the ribosome-mRNA is bound to the endoplasmic reticulum in the cell cytoplasm. The endoplasmic reticulum is a membranous subcellular structure in which proteins that are destined to be either secreted from the cell or to remain as an integral component of the cell membrane are translated. The sig sequence ensures that the spike protein is secreted from the cell, where it is recognised as foreign by the immune system. This causes the immune system to generate neutralising antibodies against the spike protein, which in turn provides the vaccine recipient with protection against future infection with SARS-CoV-2.

8. As further stated in the application, the mRNA contains a number of modifications that are not found in naturally occurring mRNA molecules and/or SARS-CoV-2. Specifically, the mRNA contains a non-natural nucleotide, N1-methylpseudouridine, in place of the uridine residues that would ordinarily be found in a natural mRNA molecule. Additionally, the mRNA contains two mutations that encode proline amino acid residues in place of other amino acids that are found in the naturally-occurring spike protein. The purpose of these mutations is to prevent the cleavage of the spike protein at the site of the two proline mutations. This cleavage normally occurs in the

early stages of the viral infection process, after the virus has bound to its cellular receptor. The cleavage allows the viral fusion process with the cell membrane to take place, and thus the invasion of the virus into the interior of the cell, where it begins to replicate. It is known that this cleavage alters the way the protein is presented to the immune system. This altered conformation of the spike protein results in the generation of antibodies that are less effective against the intact virus before cell binding occurs.

9. Modified nucleotides such as N1-methylpseudouridine have been demonstrated to reduce the immunogenicity of *in vitro*-transcribed mRNA molecules relative to mRNA molecules containing uridine (a nucleotide normally found in mRNA molecules). This delays the destruction of the

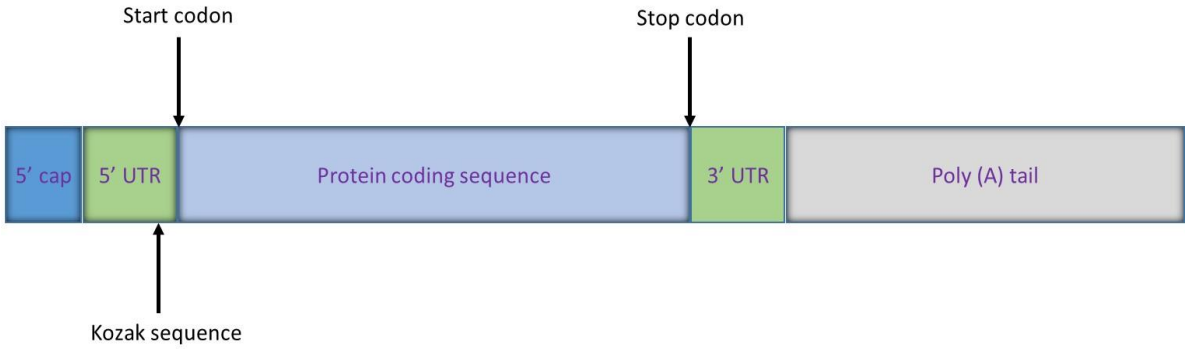

Figure 2. Generic structure of a mammalian mRNA molecule. Based on their chemical naming convention, mRNA molecules are said to have 5' and 3' ("five prime" and "three prime") ends. Recognition of the mRNA molecule by ribosomes begins at the 5' end of the molecule, by recognition of the so-called 5' cap. The ribosome then "reads' the mRNA through the 5' UTR (5' untranslated region) until it encounters a so-called Kozak sequence, which signifies the presence of the start codon for protein production. The BNT162b2 5' UTR is derived from a non-viral source, and is optimised to ensure correct translational initiation. Ribosomes use a so-called genetic code made up of 3 nucleotide codons to translate the nucleotide sequence encoded in the mRNA into the amino acid subunits that make up the protein encoded by the mRNA. The start codon encodes the first amino acid (usually methionine) in the protein's sequence. In contrast to the start codon, the stop codon does not encode an amino acid, but is recognised by the ribosome as the termination of translation. Thus, the last amino acid in a protein may be any of the 20 amino acids that make up the protein. The 3' UTR (3' untranslated region) contains sequences that help determine the stability (that is, resistance to degradation by proteins that degrade mRNAs) of the mRNA molecule (Hunt 2020). Like its 5' UTR, the BNT162b2 3' UTR was constructed to optimise the stability of the mRNA, and thereby help to optimise its translation into protein. The poly (A) tail comprises a long sequence of adenosine nucleotide residues. The poly (A) tail is bound by poly (A)-binding proteins, which also play a role in stabilisation of the mRNA (Hunt 2020).

mRNA in the recipient, which allows the production of the spike protein. This artificial nucleotide also appears to enhance the ability of N1-methylpseudouridine-substituted mRNAs to function more efficiently as templates for ribosomes to produce proteins from the genes they encode (Andries et al, 2015).

Evaluation of BNT162b2 against statutory criteria

10. We examined BNT162b2 against the statutory criteria set out in the Act to determine whether it is a "new organism". To make a determination on the status of a new organism under section 26 of the Act, we must first determine whether BNT162b2 fits the definition of an "organism".

11. The Act defines an organism as:

Organism—

(a) does not include a human being:

(ab) includes a human cell:

(b) includes a micro-organism:

(c) includes a genetic structure, other than a human cell, that is capable of replicating itself, whether that structure comprises all or only part of an entity, and whether it comprises all or only part of the total genetic structure of an entity:

(d) includes an entity (other than a human being) declared to be an organism for the purposes of the Biosecurity Act 1993:

(e) includes a reproductive cell or developmental stage of an organism

12. As BNT162b2 clearly is not a human cell, the definitions which could potentially pertain to BNT162b2 are (b), (c), (d) and (e). We considered whether BNT162b2 is a microorganism, a genetic structure capable of replicating itself, an entity declared to be an organism for the purposes of the Biosecurity Act 1993, or a reproductive cell or developmental stage of an organism.

BNT162b2 as a potential micro-organism

13. The Act does not define the term "micro-organism". However, the Oxford English Dictionary defines a micro-organism as:

    "a microscopic organism, especially a bacterium, virus, or fungus."

14. In considering whether BNT162b2 is a micro-organism, we considered whether BNT162b2, as "highly purified single-stranded messenger ribonucleic acid molecules (mRNAs) encapsulated in lipid nanoparticles", as it was described in the application, could potentially be seen to resemble a virus in some aspects. Again, there is no definition of "virus" in the Act. The Oxford English Dictionary defines a virus as:

    "an infective agent that typically consists of a nucleic acid molecule in a protein coat, is too small to be seen by light microscopy, and is able to multiply only within the living cells of a host"

15. As discussed above, the BNT162b2 mRNA is an artificial mRNA molecule that encodes the amino acid sequence of a single gene, the SARS-CoV-2 spike protein. Thus, BNT162b2 can only serve as a template for the production of the spike protein in the cells of a recipient. The spike protein is only produced in the cells of the vaccine recipient, and is not part of the structure of the BNT162b2 lipid nanoparticle. In contrast, while viruses use a host cell's own functions to help it reproduce, they contain all the genes necessary to produce new viral particles, which can then go on to infect additional cells in the host.

16. Because BNT162b2 does not encode any genes that would allow its self-replication, it cannot reproduce itself, nor any component of the vaccine's lipid nanoparticle capsule under any circumstances. Therefore, BNT162b2 is not a virus because it is unable to multiply, either within a living organism or otherwise. Therefore, the Act's definition (b) of "organism" does not apply to BNT162b2.

BNT162b2 as a potential genetic structure

17. As the active vaccine component BNT162b2 is an mRNA molecule composed of natural and artificial nucleotide residues, it could potentially be considered to be a genetic element or a genetic structure.

18. A genetic element is defined in section 2 of the Act as:

    "(a) heritable material; and

    (b) any genes, nucleic acids, or other molecules from the organism that can, without human intervention, replicate in a biological system and transfer a character or trait to another organism or to subsequent generations of the organism"

19. As the genomes of many viral species including Coronaviruses are composed of RNA (Masters & Perlman 2013), the nucleotide sequence of BNT162b2 might be considered to be "heritable material". However, as N1-methyl pseudouridine incorporated into BNT162b2 RNA is not a nucleotide that is found in nature, the *in vitro*-transcribed BNT162b2 mRNA molecule cannot be reproduced in a mammalian (including human) cell. Moreover, as discussed in the previous section, the BNT162b2 mRNA has no means to replicate itself, even if one takes into account the potential substitution of uridine for pseudouridine in a cell. For these reasons the BNT162b2 RNA neither meets the criteria of definition (a), nor definition (b) of "genetic element", as defined in the Act.

20. Unlike the term "genetic element", the term "genetic structure" mentioned in the section 2 definition of "organism" has no definition of its own. However, as with the definition of "genetic element", definition (c) of "organism" states:

    *"includes a **genetic structure**, other than a human cell, that is capable of replicating itself…"*. As with definition (b) of "genetic element", the BNT162b2 mRNA, as a genetic structure encoding only the SARS-CoV-2 spike protein, does not have the capacity to replicate itself. Therefore, the Act's definition (c) of "organism" does not apply to BNT162b2.

BNT162b2 as an entity (other than a human being) declared to be an organism for the purposes of the Biosecurity Act 1993

21. The Governor General has not declared that BNT162b2 is an organism for the purposes of the Biosecurity Act. Therefore, the Act's definition (d) does not apply to BNT162b2.

BNT162b2 as a potential developmental stage of an organism

22. As BNT162b2 mRNA encodes a viral protein, it might potentially be considered as a developmental stage of a virus. As was discussed earlier, BNT162b2 is not a virus. Furthermore, BNT162b2 as a whole is entirely artificially constructed, and the RNA component of the vaccine contains nucleotides that are not found in nature. Finally, although the SARS-CoV-2 spike protein is certainly produced during the viral infection process, it does not occur in the absence of the production of the other proteins of the virus. Furthermore, as the BNT162b2 mRNA does not possess the capacity to replicate itself, BNT162b2 cannot possibly constitute a developmental stage of an organism, because replication of the viral RNA genome is an essential part of SARS-CoV-2 replication. Therefore the Act's definition (e) of "organism" does not apply to BNT162b2.

Comments from Agencies

23. In accordance with s26(5)(b) of the Act, EPA staff advised Medsafe, the Department of Conservation (DOC) and the Ministry for Primary Industries (MPI) – as the agencies most likely to hold information relevant to this determination – of the application and asked for comment.

DOC

24. DOC noted that the application is well outside its area of expertise, and therefore did not have an official view on it. DOC further went on to note that BNT162b2 does not appear to meet the definition of a new organism or a genetically modified organism.

MPI

25. MPI provided a summary and analysis of the application (Appendix 1), and stated: "MPI is satisfied that the applicant has provided information attesting that an entity meeting the definition of an organism under the HSNO Act is not present in the COMIRNATY™ COVID vaccine."

Ministry of Health (Medsafe)

26. Medsafe stated that it had no comment on the application.

Effect on New Zealand's international obligations

27. There is no potential effect of which we are aware of this application on New Zealand's international obligations.

Recommendation

28. We recommend that the SARS-CoV-2 vaccine BNT162b2 (COMIRNATY™) does not meet the definition of "organism" in the Act, and therefore cannot be considered to be a new organism for the purpose of the Act. For your convenience, we have included the New Organisms Decision Tree and Explanatory Notes in Appendix 2 of this document to aid in your decision making.

References

Andries O, Mc Cafferty S, De Smedt SC, Weiss R, Sanders NN, Kitada T 2015. N1-methylpseudouridine-incorporated mRNA outperforms pseudouridine-incorporated mRNA by providing enhanced protein expression and reduced immunogenicity in mammalian cell lines and mice. Journal of Controlled Release 217: 337-344.

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Masters PS, Perlman S 2013. Coronaviridae. In: Knipe DM, Howley PM ed. Fields Virology. 6th ed, Wolters Kluwer|Lippincott Williams & Williams. Pp. 825-858.

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Appendix 1: Comments from the Ministry for Primary Industries

Biosecurity New Zealand
Tiakitanga Pūtaiao Aotearoa

Comments Form to the EPA for New Organism Applications

Application code(s):	APP204176
Applicant name:	Pfizer New Zealand Limited
Contact:	Kristen J. Perry
Application:	To determine whether the Pfizer/BioNTech COVID-19 Vaccine (BNT162b2 [mRNA]), tradename COMIRNATY™, is a new organism.
EPA contact:	[redacted]
Date:	02/02/2021
MPI response coordinator:	Barry Weeds (Principal Adviser Biosecurity HSNO)
Option to speak at hearing:	No

Scope of comments

MPI submits these comments for consideration to the EPA on the following basis (where relevant to the type of application):

- Clarity of information provided by the applicant;
- Information that MPI considers should be taken into consideration by the EPA;
- Adequacy of the proposed containment system, including suggestions for controls and/or amendments to proposed controls;
- Enforceability of any proposed controls; and
- Whether MPI supports / opposes the application or is neutral.

Matters relating to the application that are not within the scope of these comments may be provided to the EPA separately.

Comments

Application scope

The applicant is applying for a determination on whether the Pfizer/BioNTech COVID-19 vaccine (BNT162b2 [mRNA]), tradename COMIRNATY™, is an organism under the Hazardous Substances and New Organisms (HSNO) Act 1996.

General

MPI considers that the information provided by the applicant adequately supports the contention that the Pfizer/BioNTech COVID-19 vaccine (BNT162b2 [mRNA]), tradename COMIRNATY™, is not an organism, as defined under the HSNO Act 1996, and, therefore, should not be considered to be a new organism under that Act.

Application comments

1. The applicant has provided information on the composition of the COMIRNATY™ COVID vaccine. While it does consist of a genetic structure (single stranded mRNA), this is not able to self-replicate. The mRNA encodes a sequence based on the SARS-CoV-2 surface glycoprotein sequence which, when translated in

cells, produces the SARS-CoV-2 surface glycoprotein ('spike protein'), which generates an immune response in recipients.

2. MPI is satisfied that the applicant has provided information attesting that an entity meeting the definition of an organism under the HSNO Act is not present in the COMIRNATY™ COVID vaccine.

Appendix 2: Section 26 decision pathway

Explanatory Notes

Decision pathway for applications under Section 26 for determination as to whether an organism is a new organism

Context

This decision pathway describes the decision-making process for applications under Section 26 for determination as to whether an organism is a new organism.

Introduction

The purpose of this decision pathway is to provide the HSNO decision maker[1] with guidance so that all relevant matters in the Hazardous Substances and New Organisms Act (1996) (the *Act*) and the Hazardous Substances and New Organisms (Organisms Not Genetically Modified) Regulations (1998) (the *Regulations*) have been addressed. It does not attempt to direct the weighting that the HSNO decision maker may decide to make on individual aspects of an application.

The decision pathway has two parts –

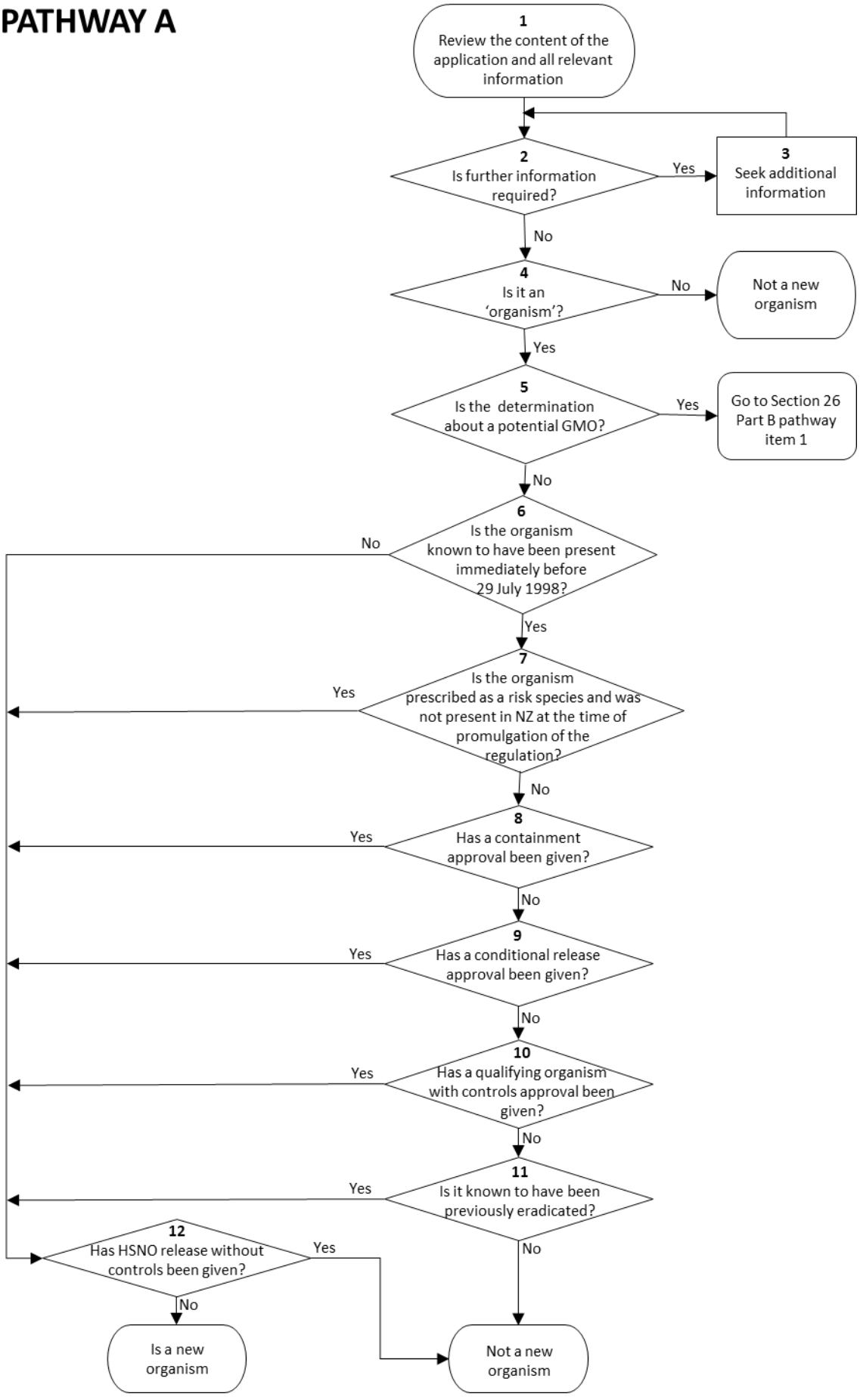
- Flowchart (a logic diagram showing the process prescribed in the HSNO Act and the Methodology to be followed in making a decision), and
- Explanatory notes (a discussion of each step of the process).

Of necessity the words in the boxes in the flowchart are brief, and key words are used to summarise the activity required. The explanatory notes provide a description of each of the numbered items in the flowchart, and describe the processes that should be followed.

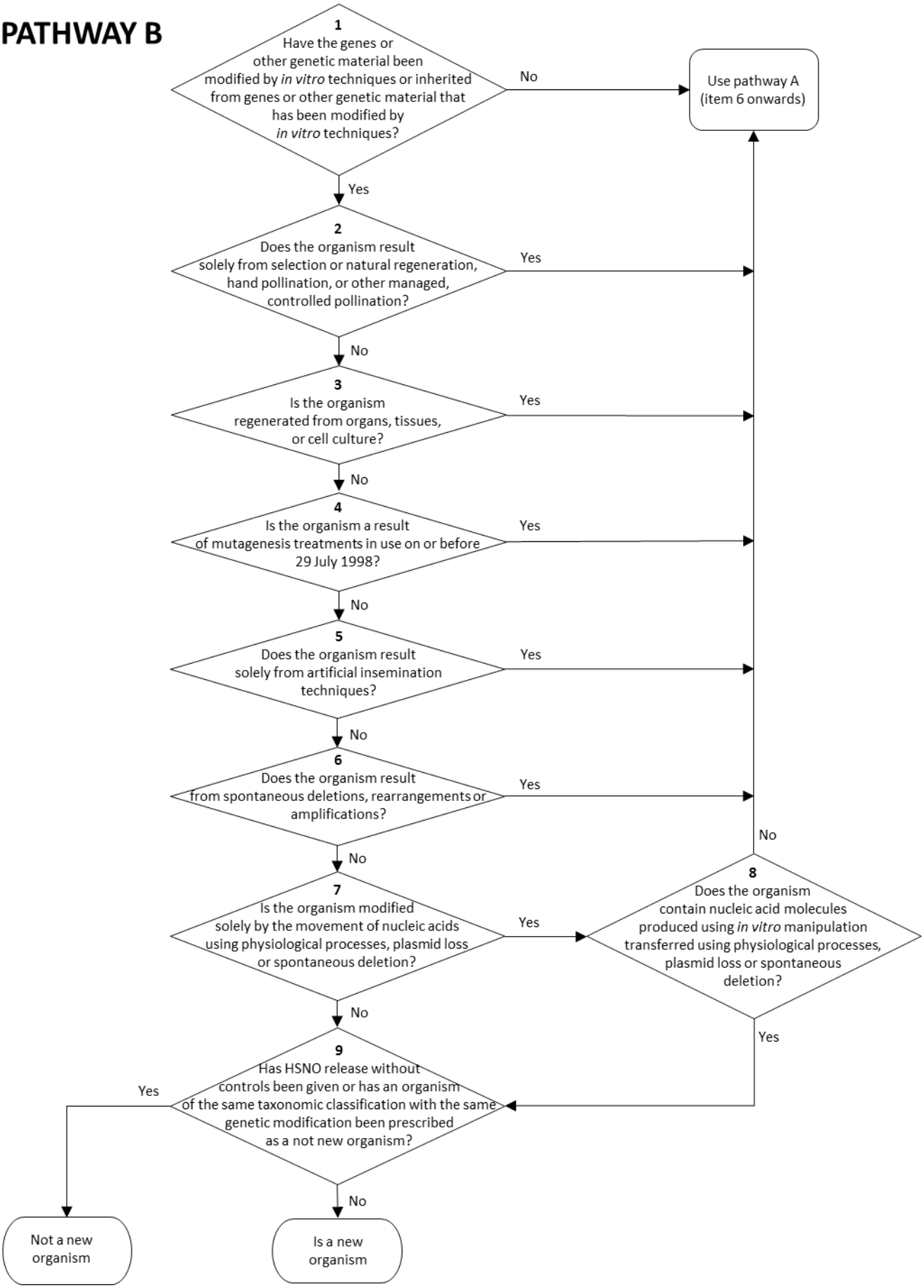
For proper interpretation of the decision pathway it is important to work through the flowchart in conjunction with the explanatory notes.

[1] The HSNO decision maker refers to either the EPA Board or any committee or persons with delegated authority from the Board.

PATHWAY A


1
Review the content of the application and all relevant information
2
Is further information required?
Yes
3
Seek additional information
No
4
Is it an 'organism'?
No
Not a new organism
Yes
5
Is the determination about a potential GMO?
Yes
Go to Section 26 Part B pathway item 1
No
6
Is the organism known to have been present immediately before 29 July 1998?
No
Yes
7
Is the organism prescribed as a risk species and was not present in NZ at the time of promulgation of the regulation?
Yes
No
8
Has a containment approval been given?
Yes
No
9
Has a conditional release approval been given?
Yes
No
10
Has a qualifying organism with controls approval been given?
Yes
No
11
Is it known to have been previously eradicated?
Yes
No
12
Has HSNO release without controls been given?
Yes
No
Is a new organism
Not a new organism

PATHWAY B


1
Have the genes or other genetic material been modified by *in vitro* techniques or inherited from genes or other genetic material that has been modified by *in vitro* techniques?
No
Use pathway A (item 6 onwards)
Yes
2
Does the organism result solely from selection or natural regeneration, hand pollination, or other managed, controlled pollination?
Yes
No
3
Is the organism regenerated from organs, tissues, or cell culture?
Yes
No
4
Is the organism a result of mutagenesis treatments in use on or before 29 July 1998?
Yes
No
5
Does the organism result solely from artificial insemination techniques?
Yes
No
6
Does the organism result from spontaneous deletions, rearrangements or amplifications?
Yes
No
7
Is the organism modified solely by the movement of nucleic acids using physiological processes, plasmid loss or spontaneous deletion?
Yes
8
Does the organism contain nucleic acid molecules produced using *in vitro* manipulation transferred using physiological processes, plasmid loss or spontaneous deletion?
No
Yes
No
9
Has HSNO release without controls been given or has an organism of the same taxonomic classification with the same genetic modification been prescribed as a not new organism?
Yes
No
Not a new organism
Is a new organism

Section 26 pathway A

Item 1	**Review the content of the application and all relevant information** Review the application, staff advice and any relevant information held by other Agencies, and advice from experts.
Item 2	**Is further information required?** Review the information and determine whether or not there is sufficient information available to make a decision.
Item 3	**Seek additional information (Section 52 and Section 58)** If the HSNO decision maker considers that further information is required, then this may be sought either from the applicant (if there is an external applicant) or from other sources. If the HSNO decision maker considers that the information may not be complete but that no additional information is currently available, then the HSNO decision maker may proceed to make a determination. If the application is not approved on the basis of lack of information (or if the organism is considered new) and further information becomes available at a later time, then the HSNO decision maker may choose to revisit this determination.
Item 4	**Is it an organism (i.e. fits the "organism" definition in Section 2)?** An organism (a) does not include a human being: (ab) includes a human cell: (b) includes a micro-organism: (c) includes a genetic structure, other than a human cell, that is capable of replicating itself, whether that structure comprises all or only part of an entity, and whether it comprises all or only part of the total genetic structure of an entity: (d) includes an entity (other than a human being) declared to be an organism for the purposes of the Biosecurity Act 1993: (e) includes a reproductive cell or developmental stage of an organism If yes, go to item 5. If no, as this is not an organism, it is not regulated under the new organism provisions of the HSNO Act.
Item 5	**Is the determination about a potential GMO (Section 2A(1)(d))?** If the determination relates to whether an organism is a potential GMO, go to pathway B. If the organism is not a GMO, go to item 6.
Item 6	**Does the organism belong to a species that was known to be present in NZ immediately before 29 July 1998 (Section 2A(1)(a))?** Determine on the basis of the available information whether on balance of probabilities the organism is known to belong to a species that was present in New Zealand immediately prior to 29 July 1998. For the purposes of making a Section 26 determination an organism is considered to be present in New Zealand if it can be established that the organism was in New Zealand: (a) immediately before 29 July 1998; and

	(b) not in contravention of the Animals Act 1967 or the Plants Act 1970 (excluding rabbit haemorrhagic disease virus, or rabbit calicivirus). If yes, go to item 7 to test the organism against the next criterion. If no, go to item 12.
Item 7	**Is the organism prescribed as a risk species and was not present in New Zealand at the time of promulgation of the relevant regulation (Section 2A(1)(b))?** Determine whether the organism belongs to a species, subspecies, infrasubspecies, variety, strain, or cultivar that has been prescribed as a risk species by regulation established under Section 140(1)(h) of the Act. If the organism is prescribed as a risk species, determine whether it was present in New Zealand when it was prescribed. The organism is a new organism if it was not present in New Zealand at the time of the promulgation of the relevant regulation. Note: at this point it may become apparent that the organism is an unwanted organism under the Biosecurity Act. If this is the case, then MPI and DOC may be advised (they may already have been consulted under items 1, 2 and 3). If yes, go 12. If no, go to item 8 to test the organism against the next criterion.
Item 8	**Has a containment approval been given for the organism under the Act (Section 2A(1)(c))?** For the purposes of making a Section 26 determination, this will also include the following organisms which are "deemed" to be new organisms with containment approvals under the HSNO Act: (a) animals lawfully imported under the Animals Act 1967 before 29 July 1998 pursuant to Section 254 of the HSNO Act; (b) animals lawfully present in New Zealand in a place that was registered as a zoo or circus under the Zoological Garden Regulations 1977 pursuant to Section 255 of the HSNO Act (except where other organisms of the same taxonomic classification were lawfully present outside of a zoo or circus –see section 2A(2)(c)); (c) hamsters lawfully imported under the Hamster Importation and Control Regulations 1972 pursuant to Section 256 of the HSNO Act; or (d) plants lawfully imported under the Plants Act 1970 before 29 July 1998 pursuant to Section 258 of the HSNO Act. If yes, go to item 12. If no, go to item 9 to test the organism against the next criterion.
Item 9	**Has a conditional release approval been given for the organism (Section 2A(1)(ca))?** If yes, go to item 12. If no, go to item 10 to test the organism against the next criterion.
Item 10	**Has a qualifying organism with controls approval been given for the organism (Section 2A(1)(cb))?** A "qualifying organism" is an organism that is or is contained in a "qualifying medicine" or "qualifying veterinary medicine". These terms are defined in Section 2 of the HSNO Act. If yes, go to item 12. If no, go to item 11 to test the organism against the next criterion.
Item 11	**Is the organism known to have been previously eradicated (Section 2A(1)(e))?**

	Determine whether the organism belongs to a species, subspecies, infrasubspecies, variety, strain, or cultivar that is known to have been previously eradicated. Eradication does not include extinction by natural means but is considered to be the result of a deliberate act. If yes, go to item 12. **If no, then the organism is not a new organism.**
Item 12	**Has HSNO release approval without controls been given for an organism of the same taxonomic classification under Sections 35, 38 or 38I of the Act or has an organism of the same taxonomic classification been prescribed as a not new organism (Section 2A(2)(a))?** If a release approval has been given for an organism of the same taxonomic classification under Section 35 or 38 of the Act then the organism is not a new organism. If a release approval has been given for an organism of the same taxonomic classification under Section 38I of the Act **without controls** then the organism is not a new organism, however, if this approval has been given **with controls** then it is a new organism. If an organism of the same taxonomic classification has been prescribed by regulations as not a new organism[2] then it is not a new organism. **If yes, the organism is not a new organism.** **If no, the organism is a new organism.**

[2] The HSNO decision maker refers to either the EPA Board or any committee or persons with delegated authority from the Board.
lation.govt.nz/regulation/public/2009/0143/latest/whole.html#DLM2011201

Section 26 pathway B

Item 1	**Have the genes or other genetic material been modified by *in vitro* techniques or inherited from genes or other genetic material that has been modified by *in vitro* techniques?** If yes, go to item 2. If no, the organism is not a genetically modified organism. However, you must check whether it meets the other new organism criteria so go to Pathway A item 6 onwards.
Item 2	**Does the organism result solely from selection or natural regeneration, hand pollination, or other managed, controlled pollination (Regulation 3(1)(a) of the Regulations)?** Is the organisms solely the result of selection or natural regeneration, hand pollination, or other managed, controlled pollination? If yes, the organism is not a GMO. However, you must check whether it meets the other new organism criteria so go to Pathway A item 6 onwards. If no, go to item 3.
Item 3	**Is the organism regenerated from organs, tissues, or cell culture (Regulation 3(1)(b) of the Regulations)?** Is the organism regenerated from organs, tissues, or cell culture, using any of the following techniques: selection and propagation of somaclonal variants, embryo rescue, and cell fusion (including protoplast fusion)? If yes, the organism is not a GMO. However, you must check whether it meets the other new organism criteria so go to Pathway A item 6 onwards. If no, go to item 4.
Item 4	**Is the organism a result of mutagenesis treatments in use on or before 29 July 1998 (Regulation 3(1)(ba) of the Regulations)?** Is the organisms the result of mutagenesis that uses a chemical or radiation treatment that was in use on or before 29 July 1998? If yes, the organism is not a GMO. However, you must check whether it meets the other new organism criteria so go to Pathway A item 6 onwards. If no, go to item 5.
Item 5	**Does the organism result solely from artificial insemination techniques (Regulation 3(1)(c) of the Regulations)?** Is the organism solely the result of artificial insemination, superovulation, embryo transfer, or embryo splitting? If yes, the organism is not a GMO. However, you must check whether it meets the other new organism criteria so go to Pathway A item 6 onwards. If no, go to item 6.
Item 6	**Does the organism result from spontaneous deletions, rearrangements or amplifications (Regulation 3(1)(e) of the Regulations)?** Is the organism a result of spontaneous deletions, rearrangements, and amplifications within a single genome, including its extrachromosomal elements? If yes, the organism is not a GMO. However, you must check whether it meets the other new organism criteria so go to Pathway A item 6 onwards. If no, go to item 7.

Item 7	**Is the organism modified solely by the movement of nucleic acids using physiological processes, plasmid loss or spontaneous deletion (Regulation 3(1)(d) of the Regulations)?** Is the organism modified solely by the movement of nucleic acids using physiological processes, including conjugation, transduction, and transformation, or by plasmid loss or spontaneous deletion? If yes, go to item 8. If no, go to item 9.
Item 8	**Does the organism contain nucleic acid molecules produced using in vitro manipulation transferred using physiological processes, plasmid loss or spontaneous deletion (Regulation 3(2) of the Regulations)?** Are nucleic acid molecules produced using in vitro manipulation transferred using any of the techniques referred to in item 7? If yes, go to item 9. If no, the organism is not a GMO. However, you must check whether it meets the other new organism criteria so go to Pathway A item 6 onwards.
Item 9	**Has HSNO release approval without controls been given or has an organism of the same taxonomic classification with the same genetic modification been prescribed as a not new organism (Section 2A(2)(b))?** If a release approval has been given for an organism of the same taxonomic classification with the same genetic modification under Section 38 of the HSNO Act then the organism is not a new organism. If a release approval has been given for an organism of the same taxonomic classification with the same genetic modification under section 38I of the HSNO Act **without controls** then the organism is not a new organism, however, if this approval has been given **with controls** then it is a new organism. If an organism of the same taxonomic classification with the same genetic modification has been prescribed by regulations as not a new organism[3] then it is not a new organism. **If yes, the organism is not a new organism.** **If no, the organism is a new organism.**

[3] http://www.legislation.govt.nz/regulation/public/2009/0143/latest/whole.html#DLM2011201