Environmental Protection Authority
Te Mana Rauhī Taiao

DECISION

Institutional Biological Safety Committee Decision Form[1] to **Develop** Low-Risk Genetically Modified Organisms in Containment under section 42A of the Hazardous Substances and New Organisms (HSNO) Act

Amended under s67A of the HSNO Act on 12/07/18

Application Code:	GMD08004
Application Approval Code(s):	GMD004880 -95
Institutional Biological Safety Committee:	University of Auckland Biological Safety Committee
IBSC Institution Code:	GMO07-UA018
Application type:	To develop genetically modified organisms into containment under sections 40 and 42A of the Hazardous Substances and New Organisms (HSNO) Act.
Applicant:	University of Auckland
Date the application was formally received:	4 December 2007
The application was considered by:	Chair, Biological Safety Officer, Maori community representatives, plant molecular biologist, microbiologists, molecular biologists, cellular and molecular biologist, lay member.
The consideration date of the application:	4 December 2007, Revised 19 December 2007.

First s67A amendment

Date application received	02/07/18
Considered by	Chair, Biological Safety Officer, Maori community representatives, plant molecular biologist, microbiologists, molecular biologists, cellular and molecular biologist, lay member.
Consideration date	02/07/18

[1] This decision form should be used in conjunction with the "*Matters to be considered*" section.

1. Summary of the Decision:

The application to develop the following organism(s) is **[approved, with controls]/~~[declined]~~** having been considered in accordance with the relevant provisions of the Hazardous Substances and New Organisms (HSNO) Act 1996 (the Act), the Hazardous Substances and New Organisms (Low-Risk Genetic Modification) Regulations 2003 (the Regulations), and the HSNO (Methodology) Order 1998 (the Methodology).

The application was considered by the IBSC under delegation from the Authority as provided for under section 19(2)(a) of the Act.

2. Sequence of the Consideration

In accordance with section 42A of the Act (rapid assessment), the approach adopted by the IBSC was to identify the circumstances of the genetic modification(s), to evaluate these against the criteria set out in the Regulations established under section 41 of the Act, and to consider whether there are any residual risks of significance that require further consideration (if so, see Annex A).

3. Decision

3.1. Purpose of the approval is:

To develop potential therapies for cancer by identifying human proteins targeted by the immune system.

3.2. The genetically modified organism(s) approved for development are:

Name of the host organism (including taxonomic authority):	*Escherichia coli* (Migula 1895) Castellani and Chambers 1919 (non pathogenic laboratory adapted strains) *Saccharomyces cerevisiae* EC Hansen (1883) - non pathogenic laboratory adapted strains *Pichia pastoris* Guillerm Phaff (1956) – non pathogenic laboratory adapted strains <u>Mammalian cell lines</u> *Homo sapiens* Linnaeus 1758 *Mus musculus* Linneaus 1758 (mouse) *Mus spretus* Latase 1758 (mouse) *Rattus norvegicus* Berkenhout 1769 (Norway or laboratory rat) *Rattus rattus* Linnaeus 1758 (Ship rat) *Cricetus cricetus* Linnaeus 1758 (European hamster) *Cricetulus griseus* Milne Edwards 1837

	(Chinese hamster) *Canis familaris* Linnaeus 1758 (dog) *Mesocricetus auratus* Waterhouse 1839 (golden hamster) *Chlorocebus aethiops* Linneaus 1758 (monkey) <u>Insect cell lines</u> *Drosophila melanogaster* Meigen 1830 (fruit fly) *Trichoplusia ni* Hubner (cabbage looper) *Spodoptera frugiperda* Smith (fall army worm)
Specify the category of host organism eg, Category 1 or 2[2]	Category 1
What the organism is modified with Please specify vector and source and function of donor DNA	Standard commercially available *E. coli* cloning and expression vectors, most of which are non-conjugative and definitely not self transmissible. Standard *Saccharomyces* cloning vectors (including yeast 2-hybrid vectors) which are not self transmissible. Standard commercially available mammalian, Pichia and insect cell expression vectors. In some cases transformation involving replication-deficient retroviral and AAV vectors may be used. Viral vectors will not be produced and will only be used to transform cell lines. Genes sourced from man (*Homo sapiens*), mouse (*Mus musculus*, *Mus spretus*) and rat (*Rattus norvegicus*, *Rattus rattus*) encoding: Molecules expressed in specific tissues, both normal and cancerous, that may be targeted by the immune system, and molecules that are important in regulating human immune responses (with particular reference to T-cell mediated responses to cancer). To include genes encoding: • Secreted proteins such as cytokines and hormones • Plasma membrane proteins

[2] According to the Regulations.

	such as cell adhesion molecules and cell surface receptors • Signalling molecules associated with cell surface molecules • Signal transduction molecules • Cytoskeletal proteins • Proteins involved in translation • Proteins involved in post-translation processing, protein folding and protein degradation • Transcription factors • DNA damage signalling molecules, DNA repair enzymes and proteins involved in DNA replication • Proteins involved in cell cycle/cell division • Proteins involved in cellular differentiation or cell- or tissue-specific functions • Nuclear proteins • Proteins involved in the formation and destruction of extracellular matrix • Proteins involved in apoptosis • Proteins involved in the regulation of angiogenesis and formation of vasculature • Proteins involved in cellular metabolism • Tumour suppressor proteins • Products of oncogenes • Proteins associated with cellular response to hypoxia • Enzymes • Proteins encoded by genes that are annotated in the genome as encoding hypothetical proteins (on the basis of an Open Reading Frame) but not fully characterised Also to include: • Regulatory sequences associated with all of the above sets of gene families (with particular reference to genes involved in development) • Genetic elements encoding protein variants with multiple amino acid repeats or those proteins variants that may misfold

	• cDNA sequences encoding protein tags or fusion constructs (including fluorescent and reporter marker proteins) including fluorescent and reporter marker proteins from *Aequorea* spp, and corals *Discoma* spp, *Heteractis* spp and *Anthrazoa* spp to determine transgene localisation or aid protein purification (including His tags, FLAG and GST fusion proteins and c-myc tags)
	
	• Fusion genes that would mimic and/or characterise gene translocations
	
	• Sequences encoding enzymes for assay (e.g. thymidine kinase, U6 RNA polymerase)
	
	• Both sense and anti-sense constructs including nucleotide deletions and substitutions as well as RNA interference sequences
	
	To include genome-editing techniques such as Zinc Finger Nucleases, CRISPR-Cas9 and TALENS, which involve vectors or oligonucleotides for targeted gene knockdown, mutation introduction, the introduction of fluorescent proteins, or the localization of proteins or RNAs.
	
	With the following exceptions:
	• Genes will not encode toxins with an LD50 < 100ug/kg
	• Genes not encode for infectious particles
	  • Genes will not be derived from native biota and CITES protected species
	  • Human genes will not be derived from persons of Maori descent

Specify the category of genetic modification eg, Category A or B[2]	Category A

Containment level e.g. PC1/PC2[3]	PC1
Approved/Declined	Approved

3.3. Controls

In considering all the matters to be addressed detailed in Part 1 of the Third Schedule of the Act (containment controls for importing, developing or field testing of genetically modified organisms), the approved organisms and any containment facility they are contained in are subject to the following controls:

1 Requirements to meet the Standards

1. The approved organism must be developed and held within a containment facility which complies with these controls.

2. The containment facility must be operated in accordance with the: (delete where not applicable)

- MAF/ERMA New Zealand Standard Facilities for Microorganisms and Cell Cultures: 2007a

3. Please clearly distinguish where different GMOs require different containment facilities/ PC levels:

- The Australian/New Zealand Standard 2243.3:2002 Safety in laboratories: Microbiological aspects and containment facilities, at minimum Physical Containment Level 1 (PC1).
- Note: Any references in these controls to the Standards are also subject to any subsequent version approved or endorsed by the EPA.

2 Controls additional to the requirements of the Standards

2.1. If a breach of containment[4] occurs the approval holder must ensure that the MAF Inspector responsible for supervision of the facility has received notification of the breach within 24 hours.

2.2. No work involving viral vectors and oncogenes will be undertaken.

2.3 Where replication-deficient Viral Vectors are used, all work will be conducted in a certified Class 2 Biohazard Hood. Gloves will be worn when handling replication-deficient viral vector stock. All equipment that has come in contact with vector stock will be treated with hypochlorite or other UABSC approved biocide (i.e. Virkon, Trigene) within the hood.

3 Standard University of Auckland Controls

3.1 The Biological Safety Officer will be notified of any accident or incident involving GMOs.

[3] As in the Australian/New Zealand Standard 2243.3:2002 Safety in Laboratories: Microbiological aspects and containment facilities.
[4] Breach of containment includes; escape of organism (s), unauthorised entry to facility, and/or structural integrity of the facility compromised.

3.2 The Principal Investigator in charge of this project has the responsibility to ensure work practices in the laboratory meet AS/NZS 2243.3:2002 “Safety in the Laboratory: Microbiology”.

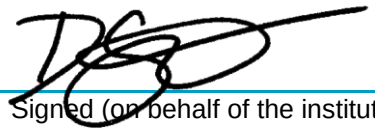
Original signature (details typed in)

Signed (on behalf of the institution)		Date
Name:	Dr John Taylor	20/12/07
Position:	Chair, University of Auckland Biological Safety Committee	

First S67A amendment

Amendment date (12/07/18)

1. To Add under heading “Inserted Genetic Material:“To include genome-editing techniques such as Zinc Finger Nucleases, CRISPR-Cas9 and TALENS, which involve vectors or oligonucleotides for targeted gene knockdown, mutation introduction, the introduction of fluorescent proteins, or the localization of proteins or RNAs.”



Signed (on behalf of the institution)		Date
Name:	Dr David Goldstone	12/07/18
Position:	Chair, University of Auckland Biological Safety Committee	

Matters to be considered

- Sections referenced in the text below indicate sections of the Hazardous Substances and New Organisms Act 1996 (the Act).
- Clauses referenced in the text below indicate clauses of the Hazardous Substances and New Organisms (Methodology) Order 1998 (the Methodology).

		Yes/No/NA
1	**Legislative criteria for the application**	
1.1	The application was lodged pursuant to section 40(1) of the Act.	Yes
1.2	The application was considered in accordance with section 42A and matters relevant to the purpose of the Act.	Yes
2	**Consideration of the application**	
2.1	Does the IBSC hold delegated authority as provided under section 19(2)(a) of the Act? If NO, the consideration cannot proceed.	Yes
2.2	Has the quorum for the Decision-making Committee (ie, the members of the IBSC that will consider this application) been reached? If NO, the consideration cannot proceed.	Yes
2.3	Does the Decision-making Committee have the appropriate expertise? If NO, the consideration cannot proceed.	Yes
2.4	Does any member of the Decision-making Committee have a conflict of interest? If YES, the consideration cannot proceed until this has been mitigated (eg, the member steps out of the room). (This should be noted in minutes.)	No
2.5	Does the Decision-making Committee consider that there is sufficient information for the formal receipt of the application using the acceptance checklist? If NO, the application cannot be considered. Please return to the applicant for further information.	Yes
2.6	Is the purpose provided for under section 39 of the Act?	Yes
2.7	Was any expert advice sought (clause 17 of the Methodology)? If YES, the name of the expert(s) and the nature of the advice sought should be recorded in the minutes. Was the applicant informed (clause 18 of the Methodology)?	No
2.8	Is the consideration of this application within 10 working days of the formal receipt of the application?	Yes
2.9	When determining an s67A amendment, was the adjustment justified to be minor in effect, or to correct a minor or technical error. *Note here any comments the*	Yes

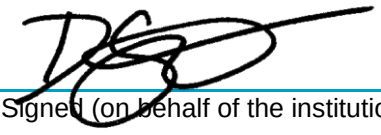
		Yes/No/NA
	Decision-making Committee made when assessing the amendment. *This amendment is minor in effect. The proposed change does not alter the risks associated with the original approval.* *Note also that additional minor amendments (apart from the proposed amendments) have also been made to the decision documents to adapt the format of this decision document from the older version of decision document template to the new template.*	
3	**Assessment against the criteria for low-risk genetic modifications**	Yes
3.1	Is the Decision-making Committee satisfied that each of the genetically modified organisms described in the application meets the criteria for a low-risk genetic modification specified in the criteria made under section 41 of the Act, being the Regulations? If NO, give details.	Yes
4	**Applications involving native flora and fauna**	
4.1	Does the application involve native or valued introduced flora and/or fauna as host organisms or as a source of genetic material? If YES, briefly summarise the results of the consultation that has occurred with local iwi regarding this application (the details of who was consulted and their status, and any specific feedback made should be recorded in the minutes).	No
5	**Applications involving human genetic material or human cells**	
5.1	Does the application involve the use any genetic material or cells obtained directly from human beings? If YES, has approval from a Human Ethics Committee been obtained? Yes. Human Ethics approval no. 010558	Yes
5.2	Does the application involve the use of human cells or human genetic material sourced directly from individuals of Māori whakapapa or origin? If YES, briefly summarise the results of the consultation that has occurred with local iwi regarding this application (the details of who was consulted and their status, and any specific feedback made should be recorded in the minutes). Note: specific exclusion that human genes will not be derived from persons of Maori descent	No
6	**Applications involving animal experimentation**	
6.1	Does the application involve animal experimentation (either in the genetic modification or subsequent use of the GMO)? If YES, has approval from an Animal Ethics Committee been obtained?	No
7	**Identification of significant risks (See Annex A)**	
7.1	Are there any significant risks or costs to the environment, including the	No

		Yes/No/NA
	sustainability of all native and valued introduced flora and fauna?	
7.2	Are there any significant risks to the intrinsic value of ecosystems?	No
7.3	Are there any significant risks or costs to human health, including public health?	No
7.4	Are there any significant risks to Māori and their taonga?	No
7.5	Are there any significant economic risks or costs?	No
7.6	Are there any risks to New Zealand's international obligations, including DNA derived from CITES species or use of CITES species as host organisms?	No
7.7	If YES is checked in 7.1-7.6, please list the significant risks identified below and discuss how they were assessed in terms of likelihood and consequence, and what controls were imposed to manage them[5]. Justify below any additional controls (in addition to the requirements in the appropriate MAF/ERMA New Zealand Standard) applied to manage the risks.	NA
8	**Containment of the organisms**	
8.1	Has the Decision-making Committee considered the adequacy of containment in accordance with section 42A of the Act? *Note here any comments the Decision-making Committee made when assessing the containment of the organisms if warranted.* Please ensure the containment controls have been specified. Note that controls relevant to the physical containment level set in the Regulations cannot be removed.	Yes
8.2	Are any additional measures proposed because of the particular nature of the organism(s)? If YES, please ensure additional controls are listed on the decision form. Discuss the reasons for imposing the additional controls here. *The committee recognised the small potential risk involved with use of replication defective viral vectors and oncogenes. An additional control was therefore placed on approval expressly prohibiting use of genes encoding oncogenes in conjunction with viral vectors. The second additional control reinforces practices involving use of replication defective viral vectors volunteered by the applicant*	Yes
8.3	Are there any other matters that may affect the adequacy of containment, such as the expected time-frame for the project, and external matters such as the potential for sabotage? If YES, please explain.	No
8.4	Is this decision restricted to a specific site (in the case of multi-site applicant organisations)? IF YES, which site and why?	No
9	**Decision:** If any of the answers to 9.1-9.4 are NO, then the application must be declined.	

[5] Clauses 12 and 13 of the Methodology.

		Yes/No/NA
9.1	The Decision-making Committee is satisfied that the application is for one of the purposes specified in section 39 of the Act.	Yes
9.2	Based on analysis of the information provided, and having considered the characteristics of the organisms and the modifications and the criteria for low-risk genetic modification detailed in the HSNO (Low-Risk Genetic Modification) Regulations 2003, it is the view of the Decision-making Committee that the organism(s) meet the criteria for rapid assessment (as per section 42A of the Act).	Yes
9.3	The Decision-making Committee is satisfied that the proposed containment regime together with any additional controls imposed will adequately contain the organism(s) as required by section 42A of the Act.	Yes
9.4	In accordance with clause 36(2)(b) of the Methodology, the Decision-making Committee records that, in reaching this conclusion, it has applied the relevant criteria from the Methodology.	Yes
9.5	The application for the development of genetically modified organism(s) is thus **[approved]/[~~declined]~~,** with controls as detailed on the decision document.	Yes
9.6	Is the Decision-making Committee's decision made by consensus?	Yes
10	**Amendment:** If any of the answers to 10.1-10.2 are NO, then the proposal must be declined.	
10.1	The Decision-making Committee is satisfied that the proposal to amend the decision meets the section 67A criteria of either a minor in effect or corrects a minor or technical error.	Yes
10.2	The Decision-making Committee is satisfied that the alteration(s) to the decision do not change the scope of the approval, or increase the risk that was initially discussed when the decision was first made. *Note here any comments from the committee made when assessing the proposal.* *Please note the commentary in s2.9*	Yes

Original details typed in



Signed (on behalf of the institution) Date

Name: Dr David Goldstone 12/07/18

Position: Chair, University of Auckland Biological Safety Committee

Administrative requirements	**Yes/No**
Confirm that the minutes record the decision-making process including the discussion of adequacy of containment and the reasons for imposing or not imposing additional controls.	Yes

Confirm that hard copies of the application and decision, the consideration documentation (such as the minutes) and any other correspondence related to this application will be maintained by the IBSC.	Yes

Organism	Approval
Escherichia coli (Migula 1895) Castellani & Chalmers 1919	GMD004885
Saccharomyces cerevisiae (Meyen ex E. C. Hansen, 1883)	GMD004893
Pichia pastoris Guillerm Phaff (1956)	GMD004890
Homo sapiens (Linnaeus, 1758)	GMD004886
Mus musculus Linnaeus, 1758	GMD004888
Mus spretus (Lataste,1883)	GMD004889
Rattus norvegicus (Berkenhout, 1769)	GMD004891
Rattus rattus (Linnaeus, 1758)	GMD004892
Cricetus cricetus (Linnaeus,1758)	GMD004883
Cricetulus griseus (Milne Edwards,1857)	GMD004882
Canis familiaris (Linnaeus, 1758)	GMD004880
Mesocricetus auratus (Waterhouse,1839)	GMD004887
Chlorocebus aethiops (Linnaeus,1758)	GMD004881
Drosophila melanogaster (Meigen, 1830)	GMD004884
Trichoplusia ni (Huebner, 1803)	GMD004895
Spodoptera frugiperda (Smith, 1797)	GMD004894

Annex A - Guidelines for dealing with significant risks

Organism description

The organism description can be specific to individual GMOs or it can be generic. HOWEVER, the organism description needs to CLEARLY describe the full range of GMOs permitted by this approval so the EPA can be satisfied that it conforms to the HSNO (Low-Risk Genetic Modification) Regulations 2003. For example: “not low-risk” modifications need to be clearly excluded from the vectors and donor nucleic acids if you are expressing uncharacterised nucleic acid sequences from pathogenic organisms, OR, for example, if using (non-pathogenic) *Escherichia coli* as a host, identify it as the non-pathogenic laboratory strains.

Assessment of Risk

Significant risks are those risks that the Decision-making Committee considers are not negligible (i.e. they require active management beyond the normal requirements of the specified physical containment level). In most circumstances the default controls will be adequate to contain the organism(s) and there will not be any significant residual risks. However, there may be some instances where the Decision-making Committee considers that this is not the case and where additional controls should be applied. In these situations, the Decision-making Committee may choose to present a full assessment of the potentially significant residual risk or contact the EPA.

Where the Decision-making Committee considers that there are potentially significant risks that require to be fully assessed, then they may decide to use the following approach to assess these risks prior to evaluating options for managing or reducing the risks.

If the Decision-making Committee deems that the organism(s) cannot be adequately contained or that the risks cannot be reduced to a negligible level by applying additional controls, then the application is not appropriate for rapid assessment and should be declined or referred to the EPA.

Assessment of the Potentially Significant Adverse Effects (Risks and Costs) of the Organism(s)

Adverse effects (risks and costs) may be grouped into categories reflecting those used in the identification section of the decision e.g., effects on, for example:

- biological and physical environment
- human welfare including health and safety
- social or community conditions
- Māori issues and concerns, and
- economic aspects.

Each potentially significant adverse effect should be discussed under a separate heading and cross-referenced to the identification section of the decision. Information provided that has been produced for other processes or jurisdictions (in New Zealand or overseas) should be discussed with reference to clause 20.

Example

Outline of the application: The applicant is proposing to import a transgenic plant where the plant will be allowed to form full shoots and roots, and the pollen will be required for scientific analysis. (For this example and simplicity, only one potentially significant risk has been identified. Occasionally, there may be more than one).

The following wording provides an example for the Identification and Assessment section of the decision form.

The risks and costs assessed were those identified as potentially significant, having regard for those matters set out in clauses 9 and 10 of the Methodology, incorporating sections 5, 6 and 8 of the HSNO Act. Risks were considered in terms of the requirements of clause 12 of the Methodology, especially the assessment of consequences and probabilities, the impact of uncertainty and the impact of risk management. Costs were considered in terms of clause 13 of the Methodology.

The Decision-making Committee identified a potentially significant risk in that the genetically modified organism may cause an adverse effect on the environment if the pollen escaped from containment and was found to hybridise with flora, forming a self sustaining population and thus constituting the release of a new organism.

The Decision-making Committee proceeded to address this potentially significant risk by the following process.

- the likelihood of escape from containment
- the likelihood of hybridisation with a plant species and the formation of a self-sustaining population.

The Decision-making Committee considered the nature of the potential adverse effect (clause 12(a)), relating to <plant species> hybridising with other <plant species> if they escaped from containment.

The Decision-making Committee was unable to determine whether hybrids occur between <plant species>, so there is uncertainty over whether hybrids with the naturalised species could occur (clause 12(e)). Since <plant species> already in New Zealand are recorded as uncommon, the Decision-making Committee considers that it is very unlikely for escaping pollen to land on receptive flowers outside of containment but the effect if it should occur would be minor-moderate, therefore the risk is low (clause 12(b)).

In order to reduce the risk, by reducing the likelihood of escape of pollen, the Decision-making Committee has proposed an additional control. In the event of initiating flowering, all pollen shall be contained by bagging and seed shall be collected. The containment manual shall be updated to reflect the process for bagging pollen and collecting seed.

The Decision-making Committee is satisfied that the <plant species> are easily identifiable due to their phenotype and easily eradicated (clause 12(d)). Eradication procedures include physical removal for small

scale infestations or by a range of common soil-applied and plant-applied herbicides, including Glyphosphate, Diuron, Metribuzin, Simazine, Chlorpropham, DCPA and Trifluralin for larger scale infestations.

The Decision-making Committee considers that the risk to the environment by the escape and hybridisation is reduced to negligible by the additional controls on pollen and seed (clause 12(c)).

Annex B - Submission of decisions

2 When submitting a decision to the EPA, the IBSC should:

3 Send an electronic copy of the decision form (Microsoft Word format) and checklist to the following email address: IBSC@epa.govt.nz

4 Post a signed copy of the completed decision form and checklist along with the application[6] to:

Environmental Protection Authority

PO Box 63 002

Wellington

5 Attention: Applications Administrator, New Organisms Group

6 Following advice from the EPA that completion of the decision form and the matters to be considered is acceptable, send a copy of the decision to the applicant.

[6] For a s67A amendment, post a signed copy of the proposal for a s67A, and the new and old decision forms and checklists.