Institutional Biological Safety Committee decision form[1] to develop a low-risk genetically modified organism in containment

ERMA Office use only

Application Code:	GMD08004
Application Approval Code(s):	GMD004880 - 95
BCH Number[2] (if applicable):	43638 - 53

Institutional Biological Safety Committee:	The University of Auckland Biological Safety Committee
IBSC Institution Code:	GMO07-UA018
Application type:	To develop in containment a genetically modified organism under section 40(1)(b) of the Hazardous Substances and New Organisms (HSNO) Act
Applicant:	The University of Auckland
Purpose:	To develop potential therapies for cancer by identifying human proteins targeted by the immune system.
Date application received:	4 December 2007
Considered by:	Quorate Committee consisting of: Plant pathologist, molecular biologists, human immunologist, microbiologists, cellular and molecular biologist, Biological Safety Officer, Maori representatives, lay member.
Consideration date:	4 December 2007, Revised 19 December 2007.

Summary of the decision:

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

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

Sequence of the consideration

In accordance with sections 42 and 42A of the HSNO 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 HSNO (Low-Risk

[1] This decision form should be used in conjunction with the checklist.
[2] Biosafety Clearing House record identification number.

Genetic Modification) Regulations 2003 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. Organism description Table(s)

The organism description can be specific to individual GMOs or it can encompass a project description[3]. HOWEVER, the organism description needs to CLEARLY describe the full range of GMOs permitted by this approval so ERMA New Zealand can be satisfied that it conforms with 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 strains or strains K 12 or B.

The organism(s) for development are:

Name of the host organism:	*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 *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) *Drosophila melanogaster* Meigen 1830 (fruit fly) *Trichoplusia ni* Hubner (cabbage looper) *Spodoptera frugiperda* Smith (fall army worm)	
Specify the category of **host organism** **e.g. Category 1 or 2[4]**	Category 1	
What the organism is modified with: Please specify vector and 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	

[3] As described in our "Policy documents relating to New Organisms" (ER-PO-NO-01). For more guidance refer to ERMA New Zealand User Guide *"Making an application for Rapid Assessment to Develop in Containment a Project of Low Risk Genetically Modified Organisms".*

[4] According to the HSNO (Low-Risk Genetic Modification) Regulations 2003.

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 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 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	
Please specify the category of genetic modification e.g. **Category A or B**[5]	Category A	
Containment level e.g. PC1/PC2[6]	PC1	
Approved/declined	Approved	

4. Use of special genetic material

Human Genes or Native introduced flora and fauna:	YES	NO
Does the proposed development use genetic material from native flora and/or fauna; or flora and/or fauna valued by Māori ?		X
Does the proposed development involve human cell lines or human genetic material of Māori whakapapa or origin ?		X

[5] According to the HSNO (Low-Risk Genetic Modification) Regulations 2003.
[6] As in the Australian/New Zealand Standard 2243.3:2002 with modifications referred to in the MAF Biosecurity Authority ERMA NZ Containment Standards.

If "YES" to either of the above please clearly record evidence that appropriate Māori consultation has occurred with local iwi regarding this approval (i.e. who was consulted, their status, and the results of the consultation).

5. Identification and assessment of the significant risks and costs of the organism

Describe any significant (non-negligible) risks identified, along with the Committee's assessment of the risks. Describe and justify any additional controls applied to manage the risks.

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.

6. Containment

Describe the containment system (physical and operational).

PC1 laboratory within a MAF approved Containment Facility. In most cases a Class 2 Biohazard cabinet will provide primary level of containment..

7. Controls

In considering all the matters to be addressed detailed in the Third Schedule Part I "*Containment Controls for Importing, Developing or Field Testing of Genetically Modified Organisms"* of the HSNO Act, this approval is subject to the following controls:

1. The operation, management and construction of the containment facility[7] shall be in accordance with the:
   - The MAF Biosecurity Authority/ERMA New Zealand Standard *Facilities for Microorganisms and Cell Cultures: 2007*, and
   - The Australian/New Zealand Standard 2243.3:2002 Safety in laboratories: Microbiological aspects and containment facilities, at Physical Containment Level PC1 as amended by the MAF Biosecurity Authority/ERMA New Zealand Standard *Facilities for Microorganisms and Cell Cultures: 2007*
2. If for any reason a breach of containment occurs the applicant shall notify the facility Supervisor and ERMA New Zealand immediately the event is noticed (and at least within 24 hours of the breach being detected) and shall immediately implement a contingency plan for the recovery and eradication of any organisms or viable material that has escaped.
3. The Authority or its authorised agent or properly authorised enforcement officers, may inspect the facilities at any reasonable time.

[7] Containment facility means a facility registered under section 39 of the Biosecurity Act 1993

Standard University of Auckland controls

1. The Biological Safety Officer will be notified of any accident or incident involving GMOs.
2. The Principal Investigator in charge of this project has the responsibility to ensure work practices in the laboratory meet AS/NZS 2243.3:2003 "Safety in the Laboratory: Microbiology".

Additional controls

List any additional controls –

1. No work involving the expression of oncogenes by viral vectors will be undertaken.
2. 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.

Signed: ……..…… Date …….
(on behalf of the institution)

Name:

Position: **Chair,**
The University of Auckland Biological Safety Committee.

Checklist

NB- this checklist should be completed by the IBSC, and signed and dated by the Chair of the IBSC and returned to ERMA New Zealand with the decision form.

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

		Yes/No/ N/A
1	***Legislative criteria for the application***	
1.1	The application was lodged pursuant to section 40(1)(b) of the Act.	Y
1.2	The application was considered in accordance with section 42 and 42A and matters relevant to the purpose of the Act.	Y
2	***Consideration of the application***	
2.1	The IBSC holds delegation from the Authority as provided under section 19(2)(a) of the HSNO Act.	Y
2.2	The purpose is provided for under section 39(1)(a) of the Act i.e. *The development of any genetically modified organism*.	Y
2.3	Does the IBSC consider the information provided by the applicant is relevant and appropriate to the scale and significance of the risks, costs, and benefits associated with the application (clause 8)?	Y
2.4	If NO – <please explain>	
2.5	Was any expert advice sought (clause 17)?	N
2.6	If YES – name of the expert(s) and the nature of the advice sought: <text in here>	
2.7	If YES – was the applicant informed (clause 18)?	
3	***Assessment against the criteria for low risk genetic modifications***	
3.1	Is the IBSC satisfied that each of the genetically modified organisms described in the application meet the criteria for a low-risk genetic modification specified in the criteria made under section 41 of the Act, being the HSNO (Low-Risk Genetic Modification) Regulations 2003? <If not, give details>	Y

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? (Please ensure section 4 of decision form is complete.)	N
4	***Applications involving human genetic material or human cells***	
4.2	Does the application use any genetic material or cells obtained directly from human beings?	Y
4.3	If YES, has approval from an Ethics Committee been obtained?	Y
4.4	Does the application involve the use of human cells or human genetic material sourced directly from individuals of Māori whakapapa or origin?	N
4.5	If YES, please record details in section 4 of the decision (who was consulted, their status and the results of the consultation).	
5	***Identification of significant risks[8]***	
5.1	Are there any significant risks or costs to the environment, including the sustainability of all native and valued introduced flora and fauna?	N
5.2	Are there any significant risks to the intrinsic value of ecosystems?	N
5.3	Are there any significant risks or costs to human health, including public health? *Refer to section 5 of decision for further explanation*	N
5.4	Are there any significant risks to Māori and their taonga?	N
5.5	Are there any significant economic risks or costs?	N
5.6	Are there any risks to New Zealand's international obligations, including DNA derived from CITES species or use of CITES species as host organisms?	N
	If YES is checked in any of 5.1-5.6, please list the significant risks identified in section 5 of the decision form and discuss how they were assessed in terms of likelihood and consequence, and what controls were imposed to manage them.[9]	

6	***Containment of the organisms***	
6.1	Has the IBSC considered the adequacy of containment in accordance with section 42 or 42A, and whether the modification may result in (a) GMO(s) having a greater ability to escape from containment than the unmodified organism(s)?	Y

[8] See Annex A
[9] Clauses 12 and 13 of the Methodology.

	Please record details in section 6 of the decision. Please ensure the containment controls have been specified. Note that controls relevant to the physical containment level set in the Regulations cannot be removed.	
6.2	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.	Y
6.3	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.	N
7	***Decision*** In this section YES confirms approval – if any of the answers to 7.1-7.4 are NO, then the application is declined.	
7.1	The IBSC is satisfied that the application is for one of the purposes specified in section 39(1) of the Act, being section 39(1)(a): *The development of any genetically modified organism*?	Y
7.2	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 IBSC that the organism(s) meet the criteria for rapid assessment (as per section 42(2)).	Y
7.3	The IBSC is satisfied that the proposed containment regime together with any additional controls imposed will adequately contain the organism(s) as required by section 42(2) of the Act.	Y
7.4	In accordance with clause 36(2)(b) of the Methodology the IBSC records that, in reaching this conclusion, it has applied the relevant criteria from the Methodology.	Y
7.5	The application for development of a genetically modified organism (detailed) is thus approved, with controls as detailed on the decision document.	

Signed: ……..…… Date …….
(on behalf of the institution)

Name:

Position: **Chair,**
The University of Auckland Biological Safety Committee.