ENVIRONMENTAL RISK MANAGEMENT AUTHORITY DECISION

Amended under section 67A of the HSNO Act on 2 April 2013

Date signed: 14 April 2008

Application code:	GMC04015
Application category:	Import into Containment any New Organism under the Hazardous Substances and New Organisms (HSNO) Act 1996
Applicant:	Invitrogen New Zealand Limited
Purpose:	The purpose of this application is to import genetically modified non-pathogenic *Escherichia coli*, bacteriophage, and yeast strains, and insect and mammalian cell lines for storage and use in research or diagnostics
Date received	4 March 2008
Consideration date	11 April 2008
Considered by	A Committee of the Environmental Risk Management Authority

1 Summary of decision

1.1 Application GMC04015 to import into containment genetically modified non-pathogenic laboratory strains of *Escherichia coli*, bacteriophage lambda and yeast (Order Saccharomycetales), and insect and mammalian cell lines as described in Table 1 of this decision for storage and use in research or diagnostics is **approved, with controls** (specified in Appendix 1 of this decision), having been considered in accordance with the relevant provisions of the Hazardous Substances and New Organisms (HSNO) Act 1996 (the Act) and of the HSNO (Methodology) Order 1998 (the Methodology).

The organisms approved are:

1.2 The organisms approved for importation are the genetically modified organisms described in Table 1:

Table 1: Organisms as recorded on ERMA New Zealand

Host organism	Modified by:	Containment level
Escherichia coli (Migula 1895) Castellani & Chalmers 1919 non pathogenic laboratory strains	**Changes to the microorganism genome:** Standard non-conjugative plasmid vectors used for site-directed or random mutagenesis (eg using suicide vectors or transposons to mediate gene knockouts).	PC1
Bacteriophage lambda (ICTV approved name is Enterobacteria phage λ) non-pathogenic laboratory strains	Standard non-conjugative plasmid vectors or viral sequences (eg bacteriophage) used to stably integrate genetic sequences into the genome.	PC1
Saccharomycetales (Order) non-pathogenic commercially available laboratory strains[1]	**Exogenous cloning or expression plasmid vectors or other constructs:** Standard non-conjugative cloning and expression plasmid vectors or other cloning constructs including bacteriophage, bacteriophage-derived vectors, bacterial artificial chromosomes (BACs), P1 based artificial chromosomes (PACs) and yeast artificial chromosomes (YACs).	PC1
Commercially available mammalian[2] and insect cell lines from: • *Homo sapiens*[3] Linnaeus 1758 • *Mus musculus* Linnaeus 1758 • *Rattus norvegicus* Berkenhout 1769 • *Rattus rattus* Linnaeus 1758	The donor genetic material may be sourced from a wide range of organisms (including plants, animals, bacteria, fungi and viruses) but may **not** be sourced from: • CITES species. • Persons of Maori descent. • Native or valued flora and fauna. • Uncharacterised genetic material from pathogenic organisms. The genetic material will not be sourced directly from humans unless the appropriate ethical approval was obtained.	PC1

[1] Such as laboratory strains of *Saccharomyces cerevisae, Pichia pastoris* and *Pichia methanolica.*
[2] Excluding mammalian cell lines that contain active viruses or infectious agents able to cause disease in humans.
[3] Excluding primary cell lines, human embryonic stem cell lines or cells derived from persons of Māori descent.

• *Chlorocebus aethiops* Linnaeus 1758 • *Cricetulus griseus* Milne-Edwards 1867 • *Mesocricetus auratus* Waterhouse 1839 • *Spodoptera frugiperda* Smith and Abbot 1797 • *Trichoplusia ni* Hübner 1802	The sequences can include RNAi or similar sequences. The genetically modified organisms imported **must not have**: • Modifications that result in the production of vertebrate toxins. • Modifications that result in the production of pharmacologically active forms of biologically active molecules with LD_{50} < 100 µg/kg. • Modifications that result in the production of infectious particles (with the exception of infectious bacteriophage lambda). • Modifications that enhance the pathogenicity, virulence or infectivity of the host organism or enhance the ability of the organism to escape containment. Vectors can contain standard and commercially available inducible, constitutive or tissue-specific promoters or other regulatory elements, reporter and selectable marker genes, origins of replication and protein purification tags.	PC1

2 Legislative criteria for application

2.1 The application was lodged by Invitrogen New Zealand Limited pursuant to section 40(1)(a) of the Act. The decision was made in accordance with section 45 of the Act taking into account additional matters to be considered under section 44, and other matters relevant to the purpose of the Act, as specified under Part II of the Act. Unless otherwise stated, references to section numbers in this decision refer to sections of the Act.

2.2 Consideration of the application followed the relevant provisions of the Methodology, as specified in more detail below. Unless otherwise stated, references to clauses in this decision refer to clauses of the Methodology.

3 Application Process

Application Receipt

3.1 The application was determined to be in compliance with section 40(2) of the Act and was formally received on 4 March 2008.

Notification

3.2 The Environmental Risk Management Authority (the Authority) has discretion, upon the receipt of applications to import into containment any new organism, to decide whether or not the application is publicly notified (as per section 53(2) of the Act). Application GMC04015 was not notified as it was considered that there would not be significant public interest in the application.

3.3 In accordance with sections 53(4) and 58(1)(c) of the Act and clauses 2(2)(e) and 5 of the Methodology, the Ministry of Agriculture and Forestry Biosecurity New Zealand (MAF BNZ) was notified and provided with the opportunity to comment on the application. Comments from MAF BNZ were taken into consideration.

Decision Making Committee

In accordance with section 19(2)(b) of the Act and clause 43 of the First Schedule to the Act, the Authority appointed a committee ("the Committee") of its members to hear and determine the application. The Committee comprised: Kieran Elborough (Chair), Max Suckling and Val Orchard.

Information available for the consideration

3.4 The information available for the consideration comprised:

- Application GMC04015 (Form NO2G) submitted by Invitrogen New Zealand Limited (the applicant);
- A memo from the Agency to the Committee to assist and support the Committee's decision making; and
- Comments received from MAF

4 Sequence of the consideration

4.1 In accordance with clause 24 of the Methodology, the Committee considered the information provided by the sources listed above. The approach adopted by the Committee was to look sequentially at identification, assessment and the combined evaluation of risks and of costs and benefits. Techniques for identifying and assessing information on risks, costs and benefits were based on internal procedures as specified in the ERMA New Zealand Technical Guide publications. Those risks identified as potentially significant were assessed in accordance with clause 12 of the Methodology. Management techniques were considered in relation to the assessed

risks. Costs and benefits were assessed in accordance with clause 13 of the Methodology. Qualitative scales used by the Committee to measure likelihood and magnitude of risks, costs and benefits are provided in Appendix 2 of this decision.

4.2 In carrying out its consideration, the Committee considered the adequacy of containment in accordance with section 45(1)(a)(iii) of the Act, and the magnitude and probability of the risks, costs and benefits alongside each other and in an integrated fashion. This is because the former interacts with the latter and this is recognized in clause 12(d) of the Methodology and in section 45(1)(a)(ii) of the Act.

4.3 The Committee set controls to satisfactorily provide for the matters in the Third Schedule (Part I) of the Act (see Appendix 1 of this decision).

4.4 Benefits associated with these applications were considered in accordance with clauses 9, 10, 13 and 14 of the Methodology and section 6(e) of the Act.

4.5 Finally, taking account of the risk characteristics established in accordance with clause 33 of the Methodology, the combined impact of risks, costs and benefits was evaluated in accordance with clause 34.

5 Purpose of application and scope of the approval

5.1 In accordance with section 40(1)(a) of the Act, Invitrogen New Zealand Limited (Invitrogen) seeks approval to import into containment genetically modified non-pathogenic laboratory strains of *E. coli*, bacteriophage lambda, and yeast from the Order Saccharomycetales, and insect and mammalian cell lines (as described in Table 1 of this decision) for storage or use in research or diagnostics.

5.2 The Committee noted that as the use of this approval has not been limited to Invitrogen, others could use this approval provided that their intended imports are covered by the organism description and meet the purpose of this approval (for storage or use in research or diagnostics) and the organisms are maintained as per the containment controls placed on this approval. As this approval is not limited to the applicant, additional control 8.1 has been imposed requiring any person using this approval for the first time to notify ERMA New Zealand and the MAF Inspector responsible for supervision of the facility of their intention to do so in writing.

5.3 The Committee noted that as this approval is to import genetically modified organisms (GMOs), if the organisms are to be developed further (ie will be genetic modified further), additional approvals will be required.

5.4 The Committee noted that the Hazardous Substances and New Organisms (Organisms Not Genetically Modified) Regulations 1998 (non-GM Regulations) describe when organisms are not to be regarded as genetically modified under the Act. For example, organisms modified solely by the movement of nucleic acids using physiological processes including conjugation, transduction and transformation are not classed as genetically modified as long as the nucleic acids have not be produced using *in vitro*

manipulation. The Committee noted that any organisms that fall under the non-GM Regulations but are still "new organisms" cannot be imported using this HSNO Act approval.

5.5 In accordance with section 45(1)(a)(i), the Committee is satisfied that the purpose of this application falls within the scope of section 39(1)(h) of the Act: *"such purposes as the Authority sees fit."*

6 Adequacy of the containment regime

6.1 In assessing the ability of the genetically modified non-pathogenic laboratory strains of *E. coli*, bacteriophage lambda, and yeast from the Order Saccharomycetales, and insect and mammalian cell lines to escape from containment, the Committee considered the:

- biological characteristics of the organisms;
- proposed containment regime; and
- potential pathways for the escape of the organisms from the containment facility.

Biological characteristics of the organisms

Escherichia coli

6.2 *E. coli* are rod shaped Gram negative bacteria that inhabit the gut of humans and other mammals. Non-pathogenic laboratory strains of *E. coli* (for example K12 and B strains) were derived from isolates of *E. coli*. K12 strains of *E. coli* have been shown to be non-pathogenic and not to infect or colonise humans while *E. coli* B and C strains are considered to be non-pathogenic (Smith, 1975; Kuhnert et al, 1997; Chart et al, 2000).

6.3 The Committee noted that pathogenic forms of *E. coli* (such as *E. coli* O157) exist and therefore the Committee limited the *E. coli* strains to be imported to non-pathogenic laboratory strains only (Table 1 of this decision).

6.4 The Committee noted that non-pathogenic *E coli* strains require specialised conditions to grow (for example specialised media and temperatures are required) and would not survive or form a self-sustaining population in the open environment.

Bacteriophage lambda

6.5 Bacteriophage are viruses that infect bacteria. Bacteriophage lambda is a double-stranded DNA phage that can infect permissive *E. coli* strains. Bacteriophage lambda is an important tool used in molecular biology to construct genomic libraries and cosmids.

6.6 The Committee noted that bacteriophage require specialised conditions to grow (for example requires a permissible host to be present) and would not survive or form a self-sustaining population in the open environment.

Yeasts (Order Sacharomycetales)

6.7 The term "yeasts" in this decision are members of the Order Saccharomycetales (of the class currently known as Ascomycetes) which are generally unicellular and reproduce by budding or fission. The Order Saccharyomycetales[4] includes the genus *Saccharomyces* (which includes *Saccharomyces cerevisae*) and *Pichia* (which includes *Pichia pastoris*).

6.8 The Committee noted that the approval of host organisms at Order level rather than at species level was requested to allow for the approval to cover members of the Order which may in the future be developed as model systems or as protein expression systems. The Committee noted that while all yeasts are expected to be non-pathogenic, this cannot be guaranteed. Therefore, the Committee limited the host organisms to non-pathogenic commercially available strains of the Order Saccharyomycetales (Table 1 of this decision).

6.9 The Committee also considered that although the production of aerially dispersed propagules during the handling of the yeasts is unlikely, due to the broad host organism description a control should be imposed stipulating that all open container manipulations of the yeasts are to be conducted in a biological safety cabinet operated in accordance with the requirements of AS/NZS Standard 2243.3:2002 except where the user of the approval has assessed and documented, including test methods and results, that aerially dispersed propagules are not formed by the isolate being manipulated. Such documents are to be held by the user of the approval and be available for auditing purposes (additional control 8.2).

Mammalian and insect cell lines

6.10 The cell lines listed in Table 1 are derived from human (*Homo sapiens*), mouse (*Mus musculus*), brown rat (*Rattus norvegicus)*, black rat (*Rattus rattus*), vervet monkey (*Chlorocebus aethiops*), Chinese hamster (*Cricetulus griseus*), golden hamster (*Mesocricetus auratus*), fall armyworm (*Spodoptera frugiperda*) and cabbage looper (*Trichoplusia ni*). All the genetically modified cell lines imported will be derived from commercially available cell lines.

6.11 The Committee noted that cell lines require highly specialised conditions to grow (for example specialised media, sterile conditions and a highly regulated environment) and would not survive or form a self-sustaining population in the open environment.

[4] This Order contains the genus described in Kirk et al, 2001: *Ainsworth & Bisby's Dictionary of the Fungi, Ninth Edition* which are *Arxiozyma, Clavispora, Cyniclomyces, Debaryomyces, Dekkera, Dipodascus, Endomyces, Galactomyces, Hanseniaspora, Issatchenkia, Kluyveromyces, Metschnikowia, Pichia, Saccharomyces, Saccharomycodes, Torulaspora, Williopsis, Yarrowia* and *Zygosaccharomyces*.

6.12 The Committee noted that primary human cell lines, cell lines derived from human embryonic stem cells or from persons of Māori descent are excluded from this approval. In addition, mammalian cell lines that contain active viruses or infectious agents able to cause disease in humans are also excluded as host organisms (Table 1 of this decision).

Summary of host organisms' characteristics

6.13 The Committee noted that the non-pathogenic laboratory strains of *E. coli*, bacteriophage lambda and the Order Saccharomycetales, and the insect and mammalian cell lines as described above do not normally cause disease in humans, animals, plants or fungi, do not contain infectious agents normally able to cause disease in humans, animals, plants or fungi, do not normally infect, colonise or establish in humans and are characterized to the extent that their main biological characteristics are known.

Genetic modification

6.14 The Committee noted that the proposed range of genetic modifications is very broad and involves changes to the genome of the host organism as well as the organisms to carry plasmids vectors (or in the case of *E. coli*, bacteriophage lambda). Therefore, the Committee considered the type of modifications, the source of the genetic material and the range of the genetic modifications and, after identifying any potential risks, imposed exclusions on the approved organism description.

Types of modifications

6.15 The Committee noted that standard molecular biology techniques can be used for the site-directed or random mutagenesis of the host organism (eg using suicide vectors or transposons to mediate gene knockouts) or to stably integrate specific sequences into the genome (eg an IPTG-inducible T7 RNA polymerase integrated into the *E. coli* genome or the large T antigen gene from SV40 integrated into the genome of mammalian cell lines to induce immortality).

6.16 The Committee noted that this approval also covers the importation of host organisms that carry gene constructs that do not integrate into the genome of the host organisms. This would include standard non-conjugative cloning and expression plasmid vectors or other constructs including bacteriophage vectors, bacterial artificial chromosomes (BACs), P1 based artificial chromosomes (PACs) and yeast artificial chromosomes (YACs).

Source of genetic material

6.17 The Committee noted that as this application has a very broad purpose (for storage and use in research or diagnostics), the applicant asked for genetic material to be sourced from a wide range of organisms including plants, animals, bacteria, fungi and viruses and the exact genes or other sequences to be used were not specified.

6.18 The Committee considered that as no specific consultation with Māori has been undertaken, the importation of genetically modified organisms containing genetic material from persons of Māori descent or native or valued flora or fauna is excluded from this approval (Table 1 of this decision).

6.19 The Committee considered that the importation of genetically modified organisms containing genetic material sourced directly from humans (compared to from sources such as genebanks) should be excluded from this approval unless the appropriate ethical approval had been obtained in the country where the genetically modified organism was produced (Table 1 of this decision).

6.20 The Committee noted that persons using this approval to import genetically modified organisms containing any human genetic material will need to justify for auditing or biosecurity purposes that (a) the genetic material was commercially sourced; or (b) provide evidence that production of the genetically modified organism containing human genetic material had appropriate ethical approval.

Gene sequences used

6.21 The Committee noted that as this application has a very broad purpose (for storage and use in research or diagnostics), the exact genes or other sequences to be used were not specified.

6.22 As the intent of this application is to allow the import of genetically modified organisms into PC1 containment, the Committee has excluded from the organism description genetic modifications that would require the organism to be maintained at a higher level of containment.

6.23 The Committee noted that modifications that result in the production of vertebrate toxins or pharmacologically active forms of biologically active molecules with LD_{50} < 100 µg/kg would require greater than PC1 containment and specific containment protocols. Therefore, the Committee excluded the use of sequences that would result in the production of vertebrate toxins or pharmacologically active forms of biologically active molecules with LD_{50} < 100 µg/kg (Table 1 of this decision).

6.24 The Committee noted that modifications that result in the production of infectious particles would require greater than PC1 containment and specific containment protocols. The Committee noted that as infectious particles from bacteriophage lambda only infect specific strains of *E. coli*, that these organisms could be contained at PC1. Therefore, the Committee excluded the use of sequences that would result in the production of infectious particles (except infectious bacteriophage lambda) (Table 1 of this decision).

6.25 The Committee noted that there are other modifications that could enhance the pathogenicity, virulence or infectivity of the host organisms or enhance the ability of the organism to escape (such as expression of genes that will enhance the pathogenicity of a previously non-pathogenic organism, or the mutagenesis or deletion of an endogenous gene that enhances virulence). As it would not be possible to produce a comprehensive list that would apply for now and in the future, the Authority has excluded from this approval genetically modified organisms whose modifications enhance the pathogenicity, virulence or infectivity of the host organism or enhance the ability of the host organism to escape containment (Table 1 of this decision).

6.26 To remove any uncertainty about whether genetically modified organisms could be imported that contain uncharacterised sequences that inadvertently cause the production of toxins or infectious particles or increase the pathogenicity, virulence or infectivity of the host organism or enhance the ability to escape containment, the Committee excluded the use of uncharacterised genetic material from pathogenic organisms (Table 1 of this decision).

6.27 The Committee noted that the vectors used will be standard non-conjugative plasmid vectors and will include standard and commercially available inducible, constitutive or tissue specific promoters and other regulatory elements, reporter and selectable marker genes, origins of replication and protein purification tags.

6.28 The Committee expects that all persons using this approval will need to carefully consider whether the genetically modified organisms they wish to import conform to the organism description in Table 1 of this decision. Furthermore, persons using this approval need to be able to justify how the genetically modified organisms conform to the organism description when required for auditing or biosecurity purposes.

Summary

6.29 The Committee considered, after taking into account the exclusions stated in Table 1, that the genetically modified organisms do not have characteristics that will enhance their pathogenicity, virulence or infectivity or enhance their ability to escape from containment. The Committee noted that the genetically modified organisms described in Table 1 of this decision are unlikely to remain viable if they are stored inappropriately.

Containment regime

6.30 The genetically modified non-pathogenic laboratory strains of *E. coli*, bacteriophage lambda and yeast (Order Saccharomycetales), and insect and mammalian cell lines as listed in Table of this decision are to be contained within a minimum of a Physical Containment level 1 facility (PC1).

6.31 The facility to be used shall be approved and registered as a containment facility under section 39 of the Biosecurity Act, in accordance with the MAF/ERMA New Zealand Standard *Facilities for Microorganisms and Cell Cultures: 2007* (the Standard). The minimum requirements for PC1 containment are specified in the Australian/New Zealand Standard 2243.3:2002: *Safety in Laboratories Part 3: Microbiological aspects and containment facilities*, fifth edition 2002 (AS/NZS 2243.3:2002).

6.32 The Committee noted that the Standard requires the facility to be constructed and operated in a manner to ensure that the organisms are securely contained and held only within the facility. The provisions in the Standard that ensure that containment is maintained cover access to the facility, staff training, safe handling, contingency plans, waste disposal, record keeping and packaging for organisms in transit. The Committee also noted that to prevent the likelihood of spread of aerially dispersed spores from yeast, that all open container manipulations of the yeasts are to be conducted in a biological safety cabinet unless the applicant can provide evidence that aerially dispersed propagules are not formed by the genetically modified organism being manipulated (additional control 8.2).

6.33 In summary, the Committee is satisfied that the containment regime described in Appendix 1 will be effective in containing the genetically modified non-pathogenic laboratory strains of *E. coli*, bacteriophage lambda and yeast (Order Saccharomycetales), and insect and mammalian cell lines.

Potential pathways for escape of organisms from the containment facility

6.34 The Committee considered the following potential pathways of escape of the genetically modified non-pathogenic laboratory strains of *E. coli*, bacteriophage lambda and yeast (Order Saccharomycetales), and insect and mammalian cell lines:

a) Escape in transit to the storage facility or from the storage facility to the customer

b) Escape due to unintentional release by personnel

c) Escape due to intentional release (ie sabotage)

d) Escape form a containment facility via malfunction in storage units (i.e freezer thawing out)

e) Escape during fire, flood or natural disaster

6.35 The Committee concluded that escape of the organisms via pathways i - iv is **highly improbable**.

6.36 This conclusion was formed based on the biological characteristics of the genetically modified non-pathogenic laboratory strains of *E. coli*, bacteriophage lambda and yeast (Order Saccharomycetales), and insect and mammalian cell lines, and on the basis of the provisions of the Standard and the AS/NZS 2243.3:2002 imposed by control 1.4 that relate to packaging of the organisms for transport, waste disposal, management of the facility (including access to the facility and staff training) and contingency plans. To enhance staff training, the Committee imposed control 1.2 that requires the person responsible for the facility, or particular research area of the facility, to ensure that all staff are aware of the containment controls for this approval.

6.37 The Committee noted that all organisms transported to and within New Zealand will be packaged as described in the IATA Dangerous Goods Regulations No.650 and the packaging requirements of the Standard and AS/NZS 2243.3:2002.

6.38 The Standard requires contingency plans to be in place for use in the event of accidental release of new organisms outside the facility and for fire and other emergencies. The Committee further enhanced this measure with controls that require the contingency plan to be implemented immediately following any breach of containment (control 5.3) and notification to the MAF Inspector of that facility following such an occurrence (control 5.2).

6.39 The containment facility will be run in accordance with the principles of AS/NZS 2243.3:2002, which contains provisions relating to good laboratory procedure (control 1.2, Appendix 1 of this decision). The Committee noted that adherence to this standard requires that where there is a significant risk from the production of aerosols from open container manipulations (whereby the culture is exposed to the atmosphere and includes plating and subculturing), manipulations should be conducted in a biological safety cabinet operated in accordance with the requirements of AS/NZS Standard 2243.3:2002.

6.40 The Committee imposed a control which stipulates that all open container manipulations of the yeasts are to be conducted in a biological safety cabinet except where the user of the approval has documentation that aerial dispersed propagules are not formed by the organism being manipulated (additional control 8.2).

6.41 The Committee noted that this approval allows the small scale fermentation of the organisms. ERMA New Zealand Policy Series: Protocol 3, April 2005, page 39 states that fermentations over 10 L in volume require a separate development approval. As large scale fermentations present additional risks with regards to escape from containment, due to the large volumes involved, the Committee imposed additional control 8.3 which limits the fermentation of organisms held under this approval to a volume of 10 L.

Conclusion on adequacy of the containment regime

6.42 The Committee considered the ability of the genetically modified non-pathogenic laboratory strains of *E. coli*, bacteriophage lambda and yeast (Order Saccharomycetales), and insect and mammalian cell lines to escape from containment, the containment regime (as described in Appendix 1), the biological characteristics of the organism and the potential pathways of escape. Taking all of these into consideration the Committee concluded that it is **highly improbable** that the genetically modified non-pathogenic laboratory strains of *E. coli*, bacteriophage lambda and and yeast (Order Saccharomycetales), and insect and mammalian cell lines would be able to escape from containment. The Committee noted that due to the characteristics described in sections 6.2- 6.29, even in the event of an escape, these organisms would be unable to survive in the environment without human intervention.

7 Ability of the organisms to establish a self-sustaining population and ease of eradication

7.1 In accordance with sections 44 and 37 and clause 10(e), the Committee considered the ability of genetically modified non-pathogenic laboratory strains of *E. coli*, bacteriophage lambda and yeast (Order Saccharomycetales), and insect and mammalian cell lines to form a self-sustaining population should they escape from containment and the ease of eradication of such populations.

7.2 The genetically modified non-pathogenic laboratory strains of *E. coli*, bacteriophage lambda and yeast (Order Saccharomycetales), and insect and mammalian cell lines all require highly specialised growth conditions (eg temperature, media, carbon dioxide level). Therefore, the Committee considered that in the **highly improbable** event that an escape occurred (section 6.42 of this decision) it is at least **highly improbable** that a self-sustaining population would form.

7.3 In the highly improbable event that the genetically modified non-pathogenic laboratory strains of *E. coli*, bacteriophage lambda and yeast (Order Saccharomycetales), and insect and mammalian cell lines did escape and form a self-sustaining population, the ease of eradication would depend on the characteristics of the micro-organisms. As micro-organisms would be difficult to detect they would be difficult to completely eliminate.

8 Identification and assessment of potentially significant adverse and beneficial effects (risks, costs and benefits)

8.1 The Committee considered the potential risks, costs and benefits relating to the application. In accordance with sections 5 and 6 of the Act, and clause 9 of the Methodology, the potential adverse effects of these applications were categorised and considered in terms of their area of impact on the environment, on human health and safety, Māori and their culture and traditions, the market economy and society and the community.

8.2 The potential risks, costs and benefits assessed here are those identified as significant, having regard for those matters set out in clauses 9 and 10 of the Methodology, which reflect sections 5, 6, 8 and 44 of the Act. Risks were considered in terms of the requirements of section 45(4) of the Act and clause 12 of the Methodology, including the assessment of consequences and probabilities, the impact of uncertainty and the impact of risk management. Costs and benefits were considered in terms of clause 13 of the Methodology. A "cost" is defined in clause 2 as "the value of a particular adverse effect expressed in monetary or non-monetary terms". Therefore, these have been assessed in an integrated fashion together with the risks of those adverse effects in the following assessment.

Adverse effects

The environment

8.3 The Committee considered the potential for the genetically modified organisms to have an adverse effect on the environment.

8.4 The Committee noted that some uncertainty may be generated by the wide range of genetically modified organisms to be imported. However, the Committee considered that this uncertainty is mitigated by the fact that the genetically modified organisms imported under this approval (Table 1 of this decision) will not be animal pathogens and the genetic modifications to these organisms will not enhance the infectivity, virulence or pathogenicity of these organisms or enhance the ability of the organisms to escape containment or survive in the environment. The uncertainty related to the broad organism description is also mitigated by the containment regime described in Appendix 1.

8.5 Furthermore, the Committee noted that for the organisms to have any potential adverse effects on the environment, the organisms would first need to escape containment and form a self sustaining population. The Committee considered that as it is **highly improbable** that these organisms could escape from containment and survive (section 6.42 of this decision), it is considered to be **highly improbable** that they would have an adverse effect on the environment. Therefore, the Committee considered that this effect is **negligible**.

Human health and safety

8.6 The Committee considered the potential for the genetically modified organisms to have an adverse effect on human health and safety.

8.7 The Committee noted that some uncertainty may be generated by the wide range of genetically modified organisms to be imported. However, the Committee considered that this uncertainty is mitigated by the fact that the genetically modified organisms imported under this approval will not be human pathogens and the genetic modifications to these organisms will not enhance the infectivity, virulence or pathogenicity of these organisms or enhance the ability of the organisms to escape

containment (Table 1 of this decision). The uncertainty related to the broad organism description is also mitigated by the containment regime described in Appendix 1.

8.8 The Committee noted that for the organisms to have any adverse effects on the public, the organisms would first need to escape containment and form a self-sustaining population. The Committee considered that as it is **highly improbable** that these organisms could escape from containment (section 6.42 of this decision), it is considered to be **highly improbable** that they would have an adverse effect on the public. Therefore, the Committee considered that this effect is **negligible**.

8.9 In addition, the Committee noted that as it is **highly improbable** that the organisms will escape from containment, the main group for any potential adverse effects is the laboratory workers involved in handling the organisms. The Committee noted that the containment regime described in Appendix 1, which includes controls for the use of biological safety cabinets for working with yeasts (unless proven that this is not necessary) (additional control 8.2) and the characteristics of the imported genetically modified organisms, would mean that it is **highly improbable** that they would have an adverse effect on human health and safety. Therefore, the Committee considered that this effect is **negligible**.

Māori culture and traditions

8.10 The Committee considered the potential Māori cultural effects of these applications in accordance with clauses 9(b)(i) and 9(c)(iv) of the Methodology and sections 6(d) and 8 of the Act. In addition, the Committee used the assessment framework contained in the ERMA New Zealand User Guide "Working with Māori under the HSNO Act 1996", and the ERMA New Zealand revised protocol "Incorporating Māori perspectives in Part V Decision-making", as guides in assessing the information contained in these applications.

8.11 Although recognising that iwi/Māori maintain an ongoing interest and concern in the potential long term cultural implications of genetic modification generally, the committee noted that genetic material from humans of Maori descent, or from native flora and fauna are excluded from this application. Taking into account the assessment of the potential adverse environmental effects associated with this application, the Committee considers that this application presents negligible risk to Māori culture or traditional relationships with ancestral lands, water, sites, wāhi tapu, valued flora and fauna or other taonga. This assessment is made on the condition that the organisms are, transported, handled, stored, and used in accordance with the explicitly stated controls (in Appendix 1 of this decision).

Market economy

8.12 The Committee considered that there are no adverse effects on the market economy of approving the importation of genetically modified non-pathogenic laboratory strains of *E. coli*, bacteriophage lambda and yeast (Order Saccharomycetales), and insect and mammalian cell lines.

Society and the community

8.13 The Committee considered that there are no adverse effects on society and the community of approving the importation of genetically modified non-pathogenic laboratory strains of *E. coli*, bacteriophage lambda and yeast (Order Saccharomycetales), and insect and mammalian cell lines.

Beneficial effects

8.14 The Committee considered the potential beneficial effects associated with this application, in accordance with sections 5 and 6(e) of the Act and clauses 9, 10, 13, and 14 of the Methodology.

8.15 The Committee considered that there are no beneficial effects on the environment, human health and safety or on Māori culture and traditions of approving the importation of genetically modified non-pathogenic laboratory strains of *E. coli*, bacteriophage lambda and yeast (Order Saccharomycetales), and insect and mammalian cell lines.

Market economy

8.16 The Committee considered that the importation of genetically modified non-pathogenic laboratory strains of *E. coli*, bacteriophage lambda and yeast (Order Saccharomycetales), and insect and mammalian cell lines for later sale is **likely.** While this effect would be of **minor** magnitude to Invitrogen through reduction of freight costs and delivery times, overall it would be of **minimal** magnitude to New Zealand's market economy. Nethertheless, the Committee considers that the benefit to the market economy is **non-negligible.**

Society and the community

8.17 The Committee considered that the importation of genetically modified non-pathogenic laboratory strains of *E. coli*, bacteriophage lambda and yeast (Order Saccharomycetales), and insect and mammalian cell lines is **likely** to have a **minor** magnitude to researchers leading to improved research productivity through reduced delivery times, but that it would be of **minimal** magnitude to the New Zealand society as a whole. Nethertheless, the Committee considers that the benefit to society and the community is **non-negligible**.

8.18 This Committee also noted that this approval will reduce compliance costs and time for researchers as this approval will allow researchers to import a broad range of low-risk GMOs without the need to apply for a separate import approval for each organism. The Committee noted that to further develop any of the organisms, the researchers will need to apply for additional HSNO Act approvals.

9 Overall evaluation of risk, costs and benefits

Precautionary approach

9.1 Section 7 of the Act requires the Committee to take into account the need for caution in managing adverse effects where there is scientific and technical uncertainty about those effects. The Committee used scenarios to set upper and lower bounds on the assessment of risks and the evaluation was based on the higher value of the risk. Clause 29 of the Methodology notes that where there is scientific and technical uncertainty the Authority must consider the materiality of the uncertainty to the decision. Since none of the risks were assessed as being non-negligible, the Committee concluded that this uncertainty was not material to the decision.

Approach to risk

9.2 Clause 33 of the Methodology requires the Authority to have regard for the extent to which a specified set of risk characteristics exist when considering applications. This provision provides a route for determining how cautious or risk averse the Authority should be in weighing up risks and costs against benefits. In the present application clause 33 is influenced by the applications being "in containment" and the conclusion that the containment provisions and controls will reduce most biological and physical risks to a low level.

9.3 The Committee considers that, as the identified biological, physical, or human health risks were assessed as being negligible, caution in addition to that required by section 7 of the Act is not warranted.

Aggregation and comparison of risks, costs and benefits

9.4 The overall evaluation of risks, costs and benefits was carried out in accordance with section 45 of the Act and clause 26 of the Methodology, having regard to clauses 22 and 34 of the Methodology.

9.5 As any potential adverse effects are related to the micro-organisms escaping containment and forming a self-sustaining population, these events were considered to be highly improbable, the adverse risks of importing these organisms were considered to be not significant. In contrast, the benefits of approving this application were considered to be significant.

9.6 We therefore believe that the identified benefits outweigh any potential adverse effects.

9.7 The Committee was unable to find common units of measurement with which to combine risks, costs, and benefits in accordance with clause 34(a) and there were no dominant sources of risk (clause 34(b)). Because the risks individually and as a whole are negligible, the decision is made in accordance with clause 26 (not clause 27) of the Methodology.

10 Decision

10.1 Pursuant to section 45(1)(a)(i) of the Act, the Committee is satisfied that this application is for a purpose specified in section 39(1) of the Act, namely section 39(1)(h) of the Act: *"such purposes as the Authority sees fit."*

10.2 The Committee is satisfied that the containment regime, as set out in Appendix 1 of this decision, will adequately contain the organisms as required by section 45(1)(a)(iii) of the Act.

10.3 The Committee evaluated the potential of imported genetically modified non-pathogenic laboratory strains of *E. coli*, bacteriophage lambda and yeast (Order Saccharomycetales), and insect and mammalian cell lines to escape from containment in accordance with section 44(b) of the Act. Having considered the proposed containment regime, the biological characteristics of the organisms and the potential pathways for escape from containment, the Committee concluded that it is **highly improbable** that the organisms would escape from containment.

10.4 The Committee evaluated the potential of the organism to establish an undesirable self-sustaining population should it escape containment in accordance with section 37 of the Act. The Committee considered that it is **highly improbable** that an undesirable self-sustaining population of genetically modified non-pathogenic laboratory strains of *E. coli*, bacteriophage lambda and yeast (Order Saccharomycetales), and insect and mammalian cell lines could establish. In the event that a population did establish, it would be difficult to detect and almost impossible to eradicate.

10.5 Having considered all the possible effects in accordance with sections 45(1)(a)(ii), 45(4) and 44 and pursuant to clause 26 of the Methodology, and based on consideration and analysis of the information provided and taking into account the application of risk management controls specified in Appendix 1 of this decision, the view of the Committee is that the risks (or costs) of adverse effects associated with the importation into containment genetically modified *E. coli*, bacteriophage, and yeast strains, and insect and mammalian cell lines, are outweighed by the benefits.

10.6 In accordance with clause 36(2)(b) of the Methodology the Committee records that, in reaching this conclusion, it has applied the balancing tests in section 45 of the Act and clause 26 of the Methodology and has relied in particular on the criteria set out in the following sections of the Act:

- section 44 additional matters to be considered;
- section 45 determination of application;
- section 37 additional matters to be considered; and
- the Third Schedule (Part I) matters to be addressed by containment controls for [importing, developing or field testing] of genetically modified organisms.

10.7 The Committee has also applied the following criteria in the Methodology:

- clause 9 – equivalent of sections 5, 6 and 8;
- clause 10 – equivalent of sections 36 and 37;
- clause 12 – evaluation of assessment of risks;
- clause 13 – evaluation of assessment of costs and benefits;
- clause 20 – information produced from other bodies;
- clause 21 – the decision accords with the requirements of the Act and regulations;
- clause 22 – the evaluation of risks, costs and benefits – relevant considerations;
- clause 24 – the use of recognized risk identification, assessment, evaluation and management techniques;
- clause 25 – the evaluation of risks;
- clause 26 – the risks are negligible and it is evident benefits outweigh costs;
- clause 29 and 32 – considering uncertainty;
- clause 33 – the risk characteristics; and
- clause 34 – the aggregation and comparison of risks, costs and benefits.

10.8 The application GMC04015 to import into containment genetically modified non-pathogenic laboratory strains of *E. coli*, bacteriophage lambda and yeast (Order Saccharomycetales), and insect and mammalian cell lines as described in Table 1 of this decision for storage and use in research or diagnostics, is thus **approved**, **with controls**, in accordance with section 45(1)(a) of the Act. As required under section 45(2) the approval is subject to the controls listed in Appendix 1 of this decision.

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Kieran Elborough Date: 14 April 2008

Chair New Organisms (GMO) Committee

Amended in April 2013

A technical drafting error in footnote 3 of Table 1 was corrected ("*human embryonic cell lines*" was changed to "*human embryonic stem cell lines*").

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Dr Deborah Read Date: **2 April 2013**

Chair of the Decision-making Committee

Approval numbers and BCH numbers for Organisms in Application GMC04015

Approval Code	Organism	BCH number
GMC001340	Escherichia coli (Migula 1895) Castellani & Chalmers 1919 (GMC04015)	44745
GMC001337	Bacteriophage lambda (ICTV approved name is Enterobacteria phage λ) (GMC04015)	44746
GMC001346	Saccharomycetale (GMC04015)	44747
GMC001341	Homo sapiens (Linnaeus, 1758) (GMC04015)	44748
GMC001343	Mus musculus Linnaeus, 1758 (GMC04015)	44749
GMC001344	Rattus norvegicus (Berkenhout, 1769) (GMC04015)	44750
GMC001345	Rattus rattus (Linnaeus, 1758) (GMC04015)	44751
GMC001338	Chlorocebus aethiops (Linnaeus,1758) (GMC04015)	44752
GMC001339	Cricetulus griseus (Milne Edwards,1857) (GMC04015)	44753
GMC001342	Mesocricetus auratus (Waterhouse,1839) (GMC04015)	44754
GMC001348	Trichoplusia ni (Huebner, 1803) (GMC04015)	44755
GMC001347	Spodoptera frugiperda (Smith, 1797) (GMC04015)	44756

References

Chart, H, Smith, HR, La Ragione, RM, Woodward, MJ 2000. An investigation into the pathogenic properties of *Escherichia coli* strains BLR, BL21, DH5α and EQ1. *Journal of Applied Microbiology* 89: 1048-1058.

Kuhnert, P, Hacker J, Mühldorfer, I, Burnens, AP, Nicolet, J, Frey, J 1997. Detection system for *Escherichia coli*-specific virulence genes: absence of virulence determinants in B and C strains. *Applied and Environmental Microbiology* 63: 703-709.

Kirk, PM, Cannon, PF, David, JC, Stalpers, JA (eds) 2001. *Ainsworth & Bisby's Dictionary of the Fungi, Ninth Edition*. CABI Publishing, Wallingford, UK.

Smith, HW 1975. Survival of orally administered *E. coli* K12 in alimentary tract of man. *Nature* 255: 500-502.

Appendix 1: Controls Required by this Approval

In order to provide for the matters detailed in Part I of the Third Schedule of the Act[5], *Containment Controls for Importation, Development and Field Testing of Genetically Modified Organisms,* and other matters in order to give effect to the purpose of the Act, the approved organisms are subject to the following controls:

1 To limit the likelihood of any accidental release of any organism or any viable genetic material[6].

1.1 The approved organism shall be imported into and maintained within a containment facility which complies with these controls.

1.2 The person responsible for a particular research area and/or the person responsible for the operation of the containment facility shall inform all personnel involved in the handling of the organism of the Authority's controls.

1.3 The facility shall be approved and registered by MAF as a containment facility under section 39 of the Biosecurity Act, in accordance with the MAF/ERMA New Zealand Standard (below), and controls imposed by the Authority (as follows):

1.4 The construction, operation and management of the containment facility shall be in accordance with the:

1.4.1 MAF/ERMA New Zealand Standard *Facilities for Microorganisms and Cell Cultures: 2007*[7]; and

1.4.2 Australian/New Zealand Standard AS/NZS 2243.3:2002[7] *Safety in laboratories: Part 3: Microbiological aspects and containment facilities*; and

1.4.3 Physical Containment level 1 (PC1) requirements of the above Standards.

2 To exclude unauthorised people from the facility.

2.1 Construction and operation of the containment facility shall comply with the requirements of the standards listed in control 1.4 relating to the identification of

[5] Bold headings in the following text refer to Matters to be Addressed by Containment Controls for Import, Development and Field Testing of Genetically Modified Organisms, specified in the Third Schedule of the Act.

[6] Viable Genetic Material is biological material that can be resuscitated to grow into tissues or organisms. It can be defined to mean biological material capable of growth even though resuscitation procedures may be required, e.g. when organisms or parts thereof are sub-lethally damaged by being frozen, dried, heated, or affected by chemical.

[7] Any reference to this standard in these controls refers to any subsequent version approved or endorsed by ERMA New Zealand.

entrances, numbers of and access to entrances and security requirements for the entrances and the facility.

3 To exclude other organisms from the facility and to control undesirable and unwanted organisms within the facility.

3.1 Construction and operation of the containment facility shall comply with the requirements of the standards listed in control 1.4 relating to the exclusion of other organisms from the facility and the control of undesirable and unwanted organisms within the facility.

4 To prevent unintended release of the organism by experimenters working with the organism.

4.1 Construction and operation of the containment facility shall comply with the requirements of the standards listed in control 1.4 relating to the prevention of unintended release of the organism by experimenters working with the organism.

5 To control the effects of any accidental release or escape of an organism.

5.1 Construction and operation of the containment facility shall comply with the requirements of the standards listed in control 1.4 relating to controlling the effects of any accidental release or escape of an organism.

5.2 If a breach of containment occurs, the facility operator must ensure that the MAF Inspector responsible for supervision of the facility has received notification of the breach within 24 hours.

5.3 In the event of any breach of containment of the organism, the contingency plan for the attempted retrieval or destruction of any viable material of the organism that has escaped shall be implemented immediately. The contingency plan shall be included in the containment manual in accordance with the requirements of standards listed in control 1.4.

6 Inspection and monitoring requirements for containment facilities.

6.1 The operation of the containment facilities shall comply with the requirements contained in the standards listed in control 1.4 relating to the inspection and monitoring requirements for containment facilities.

6.2 The containment manual shall be updated, as necessary, to address the implementation of the controls imposed by this approval, in accordance with the standards listed in control 1.4.

7 Qualifications required of the persons responsible for implementing those controls.

7.1 The training of personnel working in the facility shall be in compliance with the standards listed in control 1.4.

8 Additional controls

8.1 Any person using this approval for the first time shall notify ERMA New Zealand and the MAF Inspector responsible for supervision of the facility of their intention to do so in writing.

8.2 All 'open container' manipulations involving organisms of the Order Saccharomycetales shall be performed in a biological safety cabinet operated in accordance with the requirements of the Australia/New Zealand Standard 2243.3:2002: Safety in Laboratories Part 3: Microbiological aspects and containment facilities, until such time that the user has assessed and documented (including test methods and results) that aerial dispersed propagules are not formed by the organism being examined. Once such evidence is documented the tested organism may be manipulated outside of the biological safety cabinet. The evidence of these assessments shall be kept by the approval holder and made available for auditing purposes.

8.3 For fermentations involving these organisms the volume of liquid culture shall not exceed 10 L.