

**THE SINGAPORE BIOSAFETY GUIDELINES
FOR RESEARCH ON
GENETICALLY MODIFIED ORGANISMS (GMOs)**



May 2006

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SECTION 1: INTRODUCTION

1.1 BACKGROUND

GMAC was set up in April 1999 to oversee and advise on the issues relating to genetic modification (GM) and genetically modified organisms (GMOs).

GMAC's primary objective is to ensure public and environmental safety, while allowing for the commercial use of GMO and GMO-derived products by companies and research institutions, in compliance with international standards.

These guidelines were drawn up after a review of relevant guidelines, regulations and publications including those from Australia, United States of America (USA), Europe, World Health Organization (WHO) and United Nations Environment Programme (UNEP). A list of all relevant documents and references are listed in Appendix 1.

All communications with GMAC should be addressed to the Secretariat.

Secretariat, Genetic Modification Advisory Committee (GMAC)

20 Biopolis Way # 08-01 Centros, Singapore 138668

Tel : +65-6826-6111

DID : +65 6826 6358

Fax : +65 6478 9581

Email : info@gmac.gov.sg

Website: <http://www.gmac.gov.sg>

1.2 OBJECTIVES OF GUIDELINES

These guidelines are established to ensure the safe containment, handling and transport of genetically modified organisms used in research and to provide a common framework for assessment and notification of research on GMOs.

1.3 SCOPE OF GUIDELINES

The scope of the Singapore Biosafety Guidelines for Research on GMOs covers experiments that involve the construction and/or propagation of all biological entities (cells, organisms, prions, viroids or viruses) which have been made by genetic manipulation and are of a novel genotype and which are unlikely to occur naturally or which could cause public health or environmental hazards

1.4 DEFINITIONS OF ABBREVIATIONS

For purposes of these Guidelines, the following abbreviations shall be defined as follows.

- “GMOs” refers to Genetically Modified Organisms
- “GMAC” refers to the Genetic Modification Advisory Committee of Singapore.
- “AVA” refers to the Agri-Food and Veterinary Authority of Singapore
- “MOH” refers to the Ministry of Health
- “NEA” refers to the National Environment Agency
- “MOM” refers to the Ministry of Manpower
- “OSH Guidelines” refers to the Occupational Safety and Health Guidelines (Biomedical Sciences) issued by MOM
- “BATA” refers to the Biological Agents and Toxins Act 2005 (Act 36 of 2005), regulated by the Ministry of Health
- “IBC” refers to the Institutional Biosafety Committee
- “NACLAR” refers to the National Advisory Committee for Laboratory Animal Research
- “BAC” refers to the Bioethics Advisory Committee
- IBC refers to Institutional Biosafety Committee

A detailed glossary of terms can be found in Appendix 20.

SECTION 2: PURVIEW - EXTENT AND EXEMPTIONS

2.1 EXTENT OF GUIDELINES

- 2.1.1 These guidelines cover experiments that involve the construction and/or propagation of all biological entities (cells, organisms, prions, viroids or viruses) which have been made by genetic manipulation and are of a novel genotype* and which are unlikely to occur naturally, or which could cause public health or environmental hazards.**

The categories of experiments which fall under these guidelines are described in Section 3. A list of other relevant documents is included in Appendix 1.

- 2.1.2 Intentional release of genetically manipulated organisms must adhere to the "Singapore Guidelines on the Release of Agriculture-related Genetically Modified Organisms" (GMAC).
- 2.1.3 Work with GMOs derived from biological agents and toxins known to be hazardous to human health are regulated, under Section 2(c) of the Biological Agents and Toxins Act (Act 36 of 2005).
- 2.1.4 Work in the field of human health such as gene therapy, or other genetic manipulations on humans involving stem cells, whole organs or individuals will be assessed by MOH or its designated agency(ies). These investigations include the introduction of nucleic acids (genetically manipulated or chemically synthesised and their derivatives), or genetically manipulated micro-organisms, or cells into human subjects for the purposes of gene therapy, cell marking, or for stimulating an immune response against a subject's own cells, as used for the treatment of some cancers. For exemptions, refer to 2.1.6.
- 2.1.5 Research proposals where the introduction into human subjects of nucleic acids (genetically manipulated or chemically synthesised), or genetically manipulated micro-organisms, or cells, is designed to stimulate an immune response to antigenic determinants of infectious agents, as in the case of classical vaccine, should be submitted to the appropriate Bioethics committees. If necessary, advice from GMAC could also be obtained.
- 2.1.6 Vaccines which have been approved for use in Singapore, as well as the transfer of non-genetically manipulated autologous host cells, organ and tissue transplants are exempt from Sections 2.1.4, and 2.1.5.
- 2.1.7 If an investigator is unsure whether their research proposal falls within these guidelines, a description of their proposed research should be submitted, in writing, to their Institutional Biosafety Committee(s) (IBC) for clarification, before the commencement of their research work.

The responsibilities of GMAC, IBCs and principal investigators (laboratory leaders) are defined in Section 5.

* In the case of multicellular organisms, 'novel genotype' refers to any of the cells which make up the organism.

2.2 EXEMPTIONS

2.2.1 The following classes of experiments ((i) - (vii)) are exempt from the guidelines unless they fall within Categories A or B in Section 4. Such experiments exempt from the guidelines are classified as Category C (refer also to 4.3).

- (i) Experiments involving the fusion of mammalian cells which generate a non-viable organism, for example, the construction of hybridomas to make monoclonal antibodies.
- (ii) Fusion of protoplasts between non-pathogenic micro-organisms.
- (iii) Protoplast fusion, embryo-rescue, *in vitro* fertilisation or zygote implantation in plant cells.
- (iv) Experiments involving the breeding or use of gene 'knockout' mice (i.e. mice in which the genetic modification involves deletion or inactivation of a specific gene), independent of whether the mice carry a selectable marker gene, provided that the marker gene does not confer an advantage on the animal. If further genetic manipulations are performed on these 'knockout' mice, these are not exempt from the guidelines and falls within Category B(i) (Risk Group 2).
- (v) Research involving the introduction of naked nucleic acids into plants or animals (other than humans), unless the nucleic acid is both recombinant and able to give rise to infectious agents.
- (vi) Work involving the introduction of genetically manipulated somatic cells into animals, unless they are able to give rise to infectious agents.
- (vii) Experiments involving approved host/vector systems (refer to Appendix 2) provided that the donor DNA:
 - is not derived from plant or animal pathogens and that the DNA to be introduced is characterised fully and will not increase host or vector virulence;
 - is derived from mammalian sources and is used to construct shot-gun libraries in an approved host/vector system mentioned in Appendix 2;
 - does not code for a vertebrate toxin having a LD50 of less than 100 µg/kg;
 - does not represent or comprise more than two-thirds of a viral genome, and is not being used in any experiment in which missing segments of the viral genome that are essential for infection are available in the host cell or will become available by further breeding processes.

- 2.2.2 All experiments, whether exempt or not, should be carried out under conditions of standard microbiological laboratory practice. When pathogenic organisms are used, appropriate containment levels should be used and the personnel should be properly trained and have had the recommended vaccinations as stipulated in the guidelines issued or recommended by regulatory authorities such as MOH and AVA, e.g. Laboratory Biosafety Manual, 3rd Ed, World Health Organization.
- 2.2.3 Exemptions under Sections 2.2.1 (i) – 2.2.1 (viii) **do not apply** should the experiments involve intentional releases of genetically manipulated organisms, which include contained field trials. Such experiments must adhere to the Singapore Guidelines on the Release of Agriculture-related Genetically Modified Organisms.
- 2.2.4 Exemption from these guidelines does not equal exemption from statutory provisions applying to any aspect of a project involving genetic manipulation (e.g. importation, quarantine legislation).

2.3 REGULATORY AGENCIES

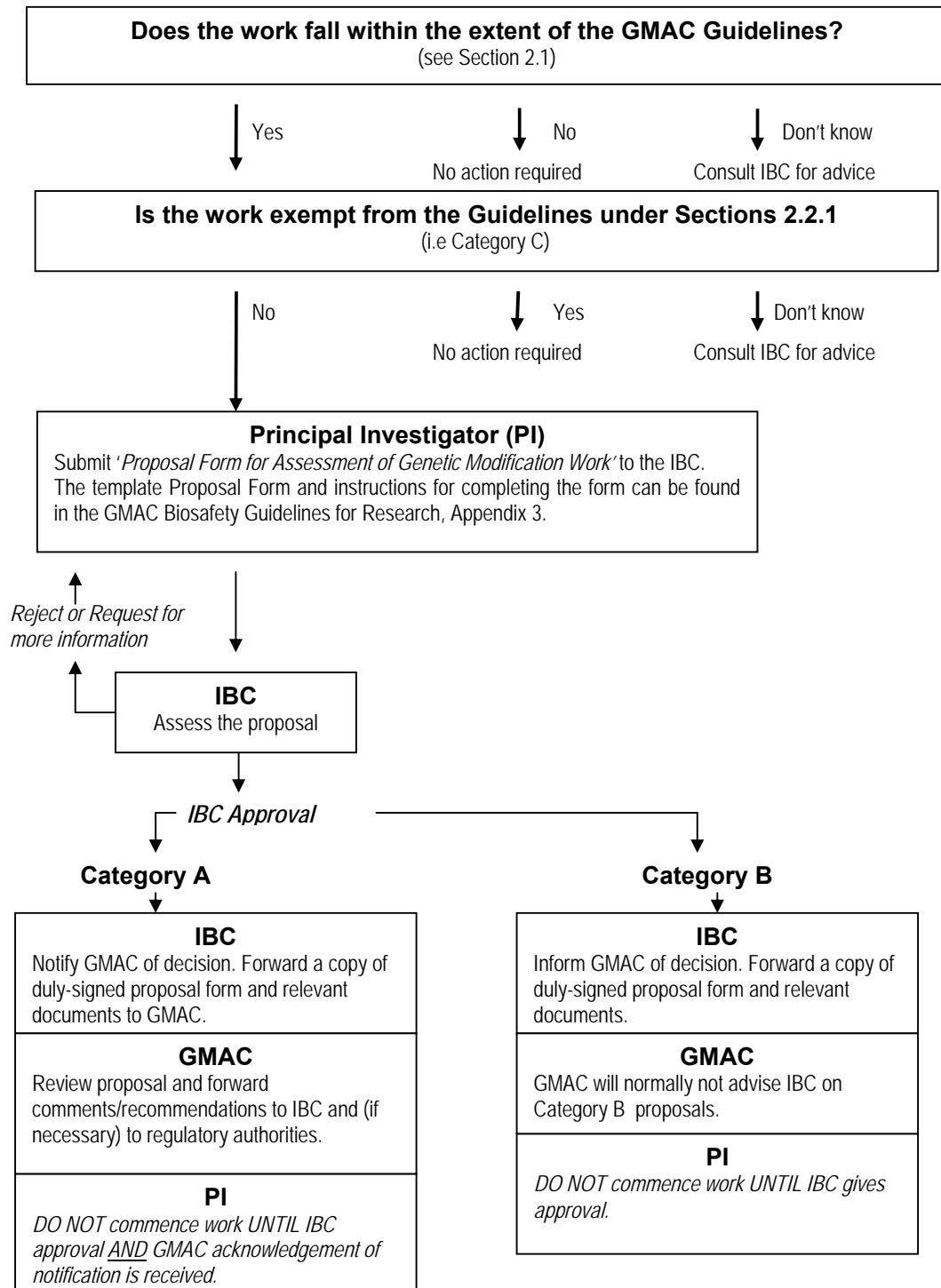
The national agencies responsible for the various aspects of regulatory affairs on behalf of the GMAC are:

- Regulation of laboratories dealing with GMO research, involving animal pathogens and plant pests – AVA
- Importation of organisms including GMOs – AVA, MOH and NEA (please also see section 6)
- Certification of Safety and Health of workers – MOM
- Research Laboratory Certification - MOM
- Clinical Laboratory Certification - MOH

SECTION 3: SUMMARY OF PROCEDURES

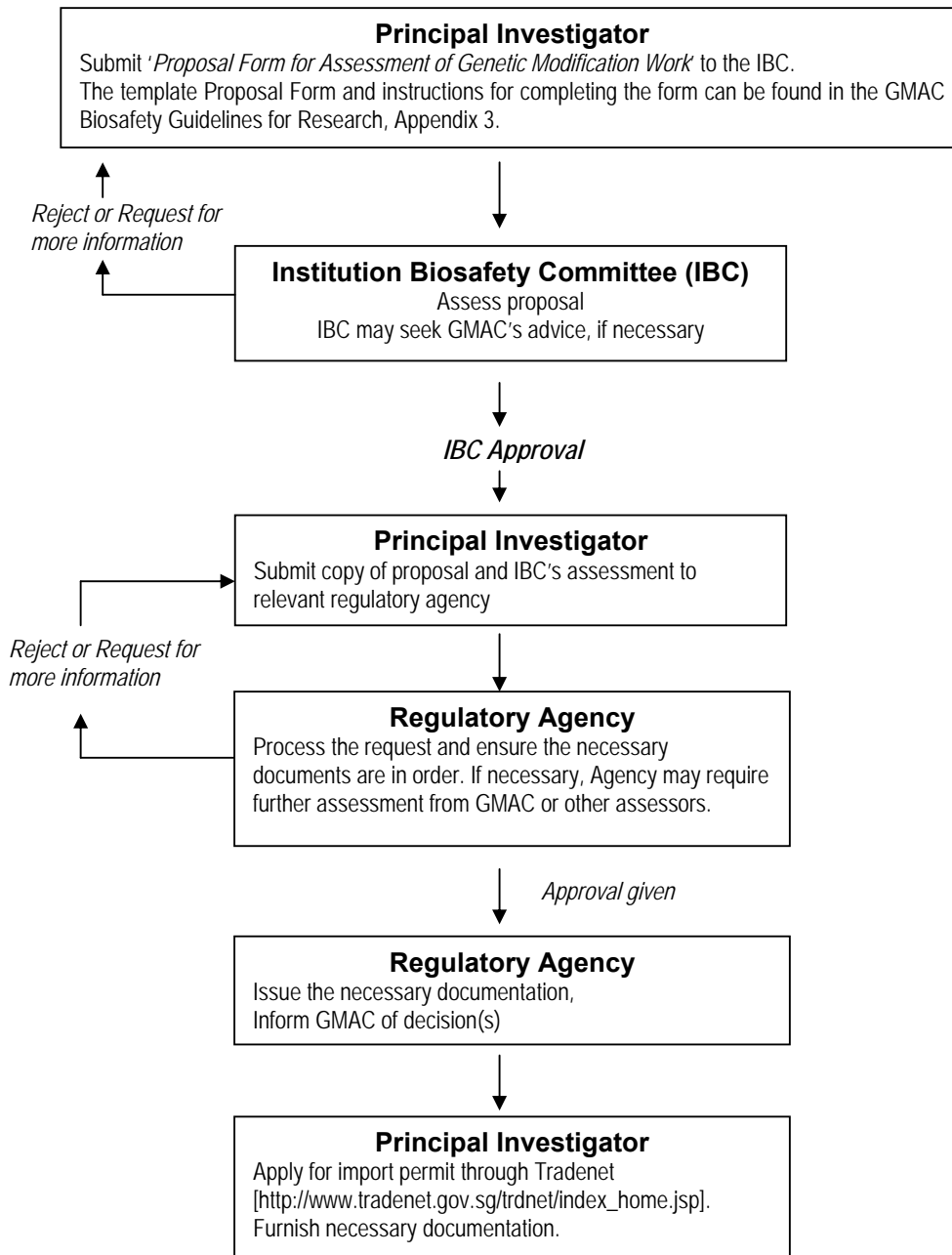
3.1 DECISION FLOW CHART FOR ASSESSMENT AND NOTIFICATION OF RESEARCH WORK

The relevant procedures for assessment and notification of research work involving genetic manipulation are detailed in Sections 3.3 – 3.6. A simplified Decision Chart is shown below for easy referral.



3.2 FLOW CHART FOR IMPORTATION OF GMOs FOR RESEARCH
(Applicable to GMOs falling under Category A and/or B)

Note that importation or possession of GMOs, not relating to human health, is regulated under Section 9 of the Animals and Birds Act (Cap 7). Additionally, importation or procurement to import specific biological agents and toxins, which is capable of causing death, disease or malfunction in a human, as those specified under First, Second, Fourth and Fifth Schedules, is regulated under the Biological Agents and Toxins Act (Act 36 of 2005).



3.3 **CATEGORY A – EXPERIMENTS REQUIRING IBC APPROVAL AND GMAC NOTIFICATION (REGULATED EXPERIMENTS WITH SIGNIFICANT RISKS)**

Please refer to Section 4.1 for a description of experiments falling into Category A.

Experiments in this category **require both IBC assessment and GMAC notification** prior to commencement. Principal investigators should **not commence work** on proposals assessed as Category A until advised by their IBC, which will not transpire until the IBC receives acknowledgement of GMAC notification.

Principal Investigators intending to conduct experiments classified as Category A should submit a 'Proposal Form for Assessment of Genetic Manipulation Work' to their respective IBCs for assessment. The IBC shall assess the proposal and determine the appropriate working and containment measures and facilities necessary.

A proposal in this category should be submitted by the Principal Investigator to the IBC for assessment on a GMAC 'Proposal Form for Assessment of Genetic Manipulation Work'. The IBC should assess the proposal and determine the appropriate working and containment conditions. Upon approval, the IBC should forward the proposal to the GMAC secretariat, together with a summary of the IBC's recommendations or comments, for notification.

Instructions for filling out the forms are included in Appendix 3. When completing the forms and assessing the experiments, the IBC and the investigator should identify potential hazards and their types, and decide upon any special procedures necessary for the proposed experiments.

The GMAC Secretariat will return a copy of the GMAC 'Proposal Form for Assessment of Genetic Manipulation Work', carrying a GMAC case reference number, to the IBC within 10 working days to acknowledge receipt of the proposal. The case reference number should be quoted in all future correspondences relating to the proposal. The acknowledgment of receipt does not imply GMAC's acknowledgement or endorsement of IBC's decision. Work must not commence until GMAC has released its acknowledgement and/or endorsement to the IBC.

3.4 **CATEGORY B – EXPERIMENTS REQUIRING IBC APPROVAL (NOTIFIABLE EXPERIMENTS WITH LOW RISKS)**

Please refer to Section 4.2 for a description of experiments falling into Category B.

Experiments in this category **require assessment by the IBC** prior to commencement. Principal investigators **should not commence Category B experiments** until advised by the IBC.

Principal Investigators intending to conduct experiments classified as Category B should submit a 'Proposal Form for Assessment of Genetic Manipulation Work' to their respective IBCs for assessment. The IBC shall assess the proposal and determine the appropriate working and containment measures and facilities necessary.

The IBC shall forward a copy of the approved proposal form, together with a summary of the IBC's recommendations, to the GMAC Secretariat. GMAC will normally not advise the IBC on Category B proposals, unless necessary.

**3.5 CATEGORY C – EXPERIMENTS EXEMPT FROM THE GUIDELINES
(EXPERIMENTS WITH NO SIGNIFICANT RISKS)**

Please refer to Section 4.3 for a description of experiments falling into Category C.

Experiments in this category are exempt from the guidelines and therefore do not require IBC assessment or GMAC notification.

Principal investigators who are unsure if their work falls under the exemptions in Sections 2.2.1 (i) – 2.2.1 (vii) should submit a proposal on a 'Proposal Form for Assessment of Genetic Manipulation Work' to their respective IBCs for assessment. The IBC shall assess the proposal and determine the appropriate categorization. GMAC will normally not advise the IBC on Category C proposals, unless necessary.

SECTION 4: EXPERIMENTS COVERED BY THE GUIDELINES

4.1 CATEGORY A – EXPERIMENTS REQUIRING IBC APPROVAL AND GMAC NOTIFICATION (REGULATED EXPERIMENTS WITH SIGNIFICANT RISKS)

This category includes experiments which may pose high risks to laboratory workers, the community or the environment. This category also includes experiments for which the type or level of hazard is unclear. The level of containment required will vary depending on the kind of experiments and their assessed hazard.

In general, experiments involving biological agents or toxins that are defined as First, Second and Fifth Schedules of the BATA and/or classified as Risk Group 3 and 4 of the OSH Guidelines will fall within this Category A.

A facility of containment of, at least, level BSL2 (as determined by the IBC and with reference to the Biosafety level detailed by the ATCC and CDC) is required.

This category of work **requires IBC assessment and approval, followed by GMAC notification before work begins**. Principal investigators **should not commence work** on proposals assessed as Category A until advised by the IBC, following IBC's receipt of GMAC acknowledgement of notification. Please refer to Section 3 for procedures for submitting proposal forms and obtaining GMAC advice.

The following classes of experiments fall within Category A:

- A(i) Experiments with toxin producers:
- Experiments using DNA which encodes a vertebrate toxin having an LD50 of less than 100 µg/kg. Appendix 4 lists some toxins falling under this sub-category.
 - Experiments in which toxin genes are expressed at a high-level, even if the LD50 is greater than 100 µg/kg. Experiments using uncharacterised DNA from toxin-producing organisms and, which therefore, could contain toxin sequences also falls under this sub-category. However, experiments using DNA which has been fully characterised and shown not to code for a toxin, from a toxin-producing organism as donor, is not included in this sub-category.
- A(ii) Experiments using viral vectors whose host range includes human cells, and where the viral vectors contain one or more inserted DNA sequences coding for a product known; to play a role in the regulation of cell growth; or to be toxic to human cells. (Special conditions for working with viral vectors encoding oncogenes are given in Appendices 5 and 6.)
- A(iii) Experiments involving introduction of DNA into microorganisms which can cause plant or animal (including human) diseases when used as host or vector, except:

- (a) microorganisms listed as approved hosts or vectors (see Appendix 2); or
- (b) if the DNA will not increase the virulence of the host or vector and the DNA is fully characterised, in which case it is classified as B(iii).

This sub-category does not include experiments using replication-defective viruses as host or vector. However, experiments using defective vector/helper virus combinations which have the potential to regenerate non-defective recombinant virus are included in this sub-category.

- A(iv) Introduction of pathogenicity genes into microorganisms other than the approved hosts included in Appendix 2. This sub-category includes those genes whose products are suspected of, or have a risk of initiating autoimmune diseases.
- A(v) Cloning or transfer of entire viral genomes, viroids, or fragments of a genome capable of giving rise to infectious particles with the capacity to infect human, animal or plant cells. Experiments involving cloning of less than two-thirds of an entire viral genome do not fall within this sub-category. Cloning of a viral genome which lacks a vital component of its replication or packaging activity that is not supplied by the experimental system, also does not fall within this sub-category.
- A(vi) Experiments involving recombination between entire viral genomes, viroids and/or complementary fragments of these genomes, where one or more fragments encode virulence or pathogenic determinants. This sub-category includes experiments that could alter the host range of pathogens or increase pathogen virulence or infectivity.
- A(vii) Experiments where a fragment of or the entire genome of a virus is injected into an embryo to produce a transgenic animal which secretes or produces infectious viral particles (see Appendix 12)
- A(viii) Experiments not falling within the A sub-categories listed above or into Category B, but which fall within the extent of the guidelines (see Section 2).

4.2 CATEGORY B – EXPERIMENTS REQUIRING IBC APPROVAL (NOTIFIABLE EXPERIMENTS WITH LOW RISKS)

This category includes experiments which may pose low-level risks to laboratory workers, the community or the environment. These experiments require at least Biosafety Level 2 physical containment (laboratory, plant house, animal house, insectary, bird house or aquarium), as determined by the IBC and with reference to the Biosafety level detailed by the ATCC and CDC. Some experiments may require additional precautions or higher containment because the donor DNA or its components are hazardous or infectious, for example special containment features are needed for the housing of transgenic animals. Recommendations for procedures for GM-BSL2 and other containment levels are in the appendices (Appendix 7 *et seq*).

IBC assessment is required before work begins on this category of experiments. Principal investigators **should not commence work** on proposals assessed as Category B until specifically advised by the IBC. Procedures for submitting proposal forms and obtaining IBC advice are in Section 2.

Category A takes precedence and Category A conditions apply if the proposed experiments fall into both Categories A and B.

The following classes of experiments fall within Category B:

- B(i) Experiments with whole animals (including non-vertebrates) which involve genetic manipulation of oocytes, zygotes or early embryos to produce a novel organism. For transgenic animal work, prior approval from the institution's bioethics committee is needed. (See Appendix 1 for other relevant documents, Appendix 12 on the relevant administrative procedures required by these Guidelines, and Appendix 13 *et seq* for transgenic animal facility requirements.)
- B(ii) Genetic manipulation experiments involving the production of modified whole plants.
- B(iii) Work with non-approved host/vector systems (i.e. other than those listed in Appendix 2) where the host or vector either:
 - (a) does not cause disease in plants, humans or animals; or
 - (b) is able to cause disease in plants, humans or animals but the introduced DNA is completely characterised and will not cause an increase in the virulence of the host or vector.
- B(iv) Experiments with approved host/vector systems, in which the gene inserted is: (a) a pathogenic determinant; or (b) DNA that is not fully characterised from microorganisms which are able to cause disease in humans, animals or plants; or (c) an oncogene. (See Appendices 5 and 6 for work with oncogenes.)

Shot-gun cloning of mammalian DNA in approved host/vector systems does not fall into this category. Approved host/vector systems are listed in Appendix 2. Investigators may request to have new host/vector systems added to the list by making a detailed submission to GMAC through their IBC.

Note that experiments not falling within B sub-categories or in Category A, but falling under the Extent in Section 1, require GMAC advice and IBC approval (see sub-category A(viii)).

**4.3 CATEGORY C – EXPERIMENTS EXEMPT FROM THE GUIDELINES
(EXPERIMENTS WITH EXTREMELY LOW RISKS)**

This category includes experiments which do not pose significant risks to laboratory workers, the community or the environment.

Experiments falling into this category include those classes of experiments as outlined in Section 2.2.1 (i) – 2.2.1 (vii).

Principal Investigators who are unsure of the categorization of their experiments are required to seek advice from their respective IBCs, by submitting a 'Proposal Form for Assessment of Genetic Manipulation Work'. The IBC shall assess the proposal and determine the appropriate categorization status.

SECTION 5: ROLES AND RESPONSIBILITIES

5.1 INSTITUTIONS

Any institution, company or organisation that carries out genetic manipulation, imports organisms arising from such work, produces such organisms, or plans to sell or release such organisms into the environment, should abide by all existing legislation and relevant guidelines, especially current GMAC Guidelines.

Such institutions, companies or organisations are required to establish an IBC and provide the resources and facilities which are necessary for safe work in laboratories. The IBC should carry out its duties adequately, and ensure, by recruitment, procedures and other measures that adequate supervision of work occurs. Institutions may consider making compliance with the GMAC Guidelines a term of their employment contracts, if appropriate. Those Institutions conducting large scale or industrial scale work should have a Biological Safety Officer.

GMAC appreciates the difficulties that small institutions and companies may have in establishing an IBC. These institutions and companies can choose to be supervised by another IBC. Such arrangements should be formalised between the institutions concerned, and the GMAC notified. A representative of the smaller institution should closely liaise with, or be a member of, the IBC.

The responsibilities of IBCs are described in Section 5.2. Institutions should recognise the essential roles of their IBC and give it the authority and support it needs to undertake its duties.

5.1.1 Recruitment and staff training

The institution should ensure that laboratory staff is informed of hazards and have adequate training to make sure that their work is carried out within these guidelines. The IBC Chair or Biological Safety Officer should be readily accessible to give advice.

5.1.2 Certification of Biosafety Level 3 (BSL3) and Biosafety Level 4 (BSL4) facilities

BSL3 and BSL4 facilities (laboratories, animal houses, plant houses, insectaries, bird houses, aquaria) are to be approved by the regulatory agency(ies). Institutions planning to conduct experiments which require BSL3 or BSL4 containment should notify the GMAC Secretariat. The necessary advice regarding the structural requirements about these BSL3 and BSL4 facilities are included in Appendices 8, 9, 11, 15 and 17. These advice may also be found in the OSH Guidelines for Laboratories and Production Facilities in the Biomedical Sciences Industry (OSH Guidelines) and the Laboratory Biosafety Manual, 3rd Ed, WHO.

Appropriate door signs and universal Biohazard signs and labels are available from laboratory and reagent suppliers.

5.2 INSTITUTIONAL BIOSAFETY COMMITTEES

IBCs are vital for executing these guidelines and thus the monitoring and surveillance of genetic manipulation work. The calibre and experience of IBC members should be such that it can competently undertake its duties. The Chair of the Committee should be of sufficient standing in the institution for decisions and advice by the IBC to be effectively carried out. Appropriate deputising arrangements should be made when the Chair is on leave.

5.2.1 Where applicable, duties and obligations in relation to biological agents and toxins, as stipulated in the Part V of the BATA legislation must be adhered to.

5.2.2 Composition

The IBC should comprise:

- individuals with requisite knowledge and expertise to evaluate and oversee work being conducted in the institution;
- the Biological Safety Officer, if appropriate;

One microbiologist, and one molecular biologist and/or a geneticist, should be included as well as a scientist with expertise relevant to the organisms being studied in the institution. Different disciplines need only be represented when work falling within that area is performed in the institution. For example, an institution working only on plants need not have an animal geneticist.

Responsibilities may be combined in the same person if appropriate.

5.2.3 Biological Safety Officer

Institutions should either appoint a Biological Safety Officer, or assign such duties to the IBC. If institutions have more than one officer, for the purposes of these Guidelines, only one name per institution is to be submitted to GMAC in the annual reporting requirements. The officer should ideally have experience in working with containment conditions and should be sufficiently trained and competent to offer advice on, or participate in staff training. Suitable deputising arrangements should be made when the officer is on leave.

The Biological Safety Officer or the IBC Chair should act as adviser to the head of the institution or company in all biosafety matters. Regular safety audits and the supervision of a regular evaluation program for relevant pieces of equipment should be carried out by the Biological Safety Officer or the IBC. The Biological Safety Officer should also consult the OSH Guidelines for additional requirements that need to be fulfilled.

5.2.4 Conflicts of Interests

To avoid any potential conflicts of interest, IBC members should not assess their own proposals that they have submitted. The IBC should have sufficient scientifically qualified members to ensure that proposals can be adequately evaluated.

IBC members who may have commercial interests on an item of the agenda being assessed should declare their interests and be excluded from the meeting.

5.2.5 Monitoring of Work

The IBC should ensure that GMAC's and its own advice on proposals are received by principal investigator(s) and, if necessary, are acted upon. The IBC should visit laboratories and facilities occasionally to monitor biosafety aspects and implementation.

In order to effect the intent of these guidelines, an IBC may draft whatever rules it considers necessary to supplement these guidelines. Furthermore, IBCs should have appropriate powers to ensure that all aspects of these guidelines are observed.

5.2.6 Duties

The main functions of the IBC are to:

- assess all research proposals it receives, (including changes to Category C projects), so as to identify potential hazards to the researchers, the public and the environment. It should also advise the investigator(s) about these hazards and their management;
- ascertain the containment level and procedures for experiments falling within GMAC Categories A and B (see Section 4), and determine the storage and transportation requirements for genetically manipulated organisms falling within these Guidelines;
- send an original typed GMAC 'Proposal Form for Assessment of Genetic Manipulation Work', together with the IBC's assessment, to the GMAC for assessment of experiments falling under Category A, and make sure that GMAC advice is followed. For Category B, an original typed proposal form, together with the IBC's assessment, should be sent to GMAC for notification. See Appendix 3 for instructions on completing proposal forms;
- inspect plant houses, animal houses, bird houses, insectaries and aquaria before they are used for genetic manipulation work. The IBC should also conduct inspections and monitor procedures in **all** the institution's containment facilities. At least annual inspections of these facilities should be carried out to make sure that they continue to meet the relevant containment standards. The detailed requirements for these facilities are in Appendices 7 *et seq*;
- monitor ongoing work within the institution from time to time and make recommendations to investigators, if appropriate;
- assess the qualifications and experience of personnel involved in research proposals, to make sure that they are adequate for good microbiological practice and the supervision of junior personnel;
- maintain a register of approved projects with their assessment as well as projects exempted under Sections 2.2.1(i) to 2.2.1 (vii) of these guidelines;
- maintain a list of the personnel who work in containment facilities, and ensure that new workers are familiar with the appropriate containment procedures and the correct use of laboratory equipment.

- take responsibility for drafting rules and making decisions about specific procedural safety matters. GMAC does not need to be consulted about these, as long as they are consistent with these guidelines.

5.2.7 Reporting Requirements

When the IBC is being set up it should provide GMAC with a completed 'Annual Report by Institutional Biosafety Committee' form. This form can be found in Appendix 3. The deadline for the annual submission is 1st January.

5.2.8 Medical History of Workers

For personnel using GM-BSL2 physical containment facilities, GMAC advises that no special arrangements are necessary outside the normal institutional practices for laboratory workers.

Many institutions doing microbiological research, routinely take serum samples from personnel at regular intervals. Such samples are stored for diagnostic tests on workers exposed to accidents or who develop unexplained illness.

For experiments requiring a physical containment level of GM-BSL3 or higher, laboratory workers should have an initial medical examination, and other requirements as stipulated under the OSH Guidelines.

5.2.9 Accidents and Incidents

The IBC or the Biological Safety Officer should record both the accident or incident and the follow-up action. If the IBC Chair is satisfied that the accident or incident was directly attributable to genetic manipulation work, and was significant, they should make a report to both the GMAC and the head of the institution. An example of such an incident could be the intentional failure to comply with these guidelines, or an incident which might have risked human health or the environment.

5.3 PRINCIPAL INVESTIGATORS

The Principal Investigator should be thoroughly familiar with the requirements of these guidelines and should ensure that, the guidelines are adhered to, for any project he/she is responsible and for which, involves the use of genetic manipulation. Specifically, he/she should:

- assess the proposal to decide if it falls within the guidelines. If unsure, the investigator should consult the IBC;
- provide all information on the proposal that the IBC may need for assessment or monitoring of the proposal;
- follow through on GMAC's and IBC's advice and recommendations;
- fill out a typed original GMAC 'Proposal Form for Assessment of Genetic Manipulation Work' and hand a copy (keeping a second copy) to their IBC, before starting work on any project which falls under these Guidelines, and ensure that work does not commence until approval is granted by the IBC;

- submit a new proposal form to the IBC before any major change is made to the experimental system of a proposal, which may result in a change of category or which may affect the exempt status of Category C projects.
- conduct experiments under the conditions of physical containment approved by the IBC or as advised by the GMAC in the case of category A proposals (see Section 4);
- ensure that students, subordinates, and other co-workers are aware of the nature of potential hazards of the work and have been given relevant training. They should also arrange for training, if needed;
- inform the IBC of any changes to the project team;
- promptly report accidents, unexplained illnesses and absences to the IBC;
- advise the IBC when intending to import biological material(s) falling within these guidelines (see also Section 6.6).

SECTION 6: TRANSPORT AND IMPORT

6.1 GENERAL CONSIDERATIONS FOR TRANSPORT AND PACKAGING OF MATERIAL

6.1.1 Basic Requirements

The basic requirements for transport of viable genetically manipulated organisms is that there should be a minimal risk to humans and the environment and that the samples should not leak if the packaging is damaged in most foreseeable accidents. Approved testing of packaging should reflect these accident scenarios and should include pressure and temperature changes and severe impact. The recipients should have facilities to contain the organisms at the required level.

6.1.2 Transport Requirements

For transport within an institution, care should be taken when transporting material likely to contain live genetically manipulated organisms. Any container of viable organisms should be transported in another closed unbreakable container which can be easily decontaminated.

For transport outside an institution, procedures must have been set up for the safe transport of biological materials by air, rail and road. Different packing and transport arrangements apply to: materials that are non-infectious; have a low probability of being infectious; are thought likely to be infectious; or contain genetically modified micro-organisms. It is the responsibility of the sender to make sure that all packaging and transport regulations are followed.

The transport of biological materials is controlled by the following regulations; current issues should be consulted:

- The International Air Transportation Association (IATA), *Dangerous Goods Regulations*; (IATA online store – <http://www.iata.org/>)

The IATA *Dangerous Good Regulations* are the most comprehensive and, in general, incorporate the provisions of the other regulations.

Locally, the BATA regulates against transportation by certain means for specified biological agents and toxins covered under the legislation.

6.1.3 Categories of Biological Materials

For the purposes of transport, infectious material is distinguished from other material as follows:

- Biological materials not harbouring known infectious agents, can be transported without restrictions.
- All biological products and diagnostic specimens with a low probability of being infectious for humans or animals must be packaged according to Packing Instructions #650 of the IATA Dangerous Goods Regulations.

- All materials that are genetically modified but thought unlikely to be infectious for animals or humans must be packaged according to Packing Instructions #913 of the IATA Dangerous Goods Regulations.
- All materials that are infectious or thought likely to be infectious for humans or animals, or are genetically modified and thought likely to be infectious for humans or animals, must be packaged according to Packaging Instructions #602 of the IATA Dangerous Goods Regulations.

The above regulations detail: the certification requirements; the maximum quantities that can be transported by cargo or passenger aircraft; the external labelling requirements (including the identifying UN number); and the details to be included in the Shipper's Declaration for Dangerous Goods.

6.1.4 Documentation

When infectious material is being transported, a Shipper's Declaration for Dangerous Goods must be completed indicating origin, contents and date of dispatch, and should be placed in a separate leak-proof bag so as to protect the declaration form from potential contamination by the contents of the package. Recipients should be informed, before delivery, of all known hazards associated with the material.

6.1.5 General

- Only accredited personnel may undertake the packaging for transport which should be done according to the above regulations.
- Facilities should be provided for after-hours delivery of samples, and night staff should be warned of any hazards.
- Procedures and precautions for unpacking should be appropriate to the type of package being unpacked.
- When infectious waste is removed from a laboratory, the relevant local public health regulations should be followed.

6.2 TRANSPORT OF TRANSGENIC ANIMALS

6.2.1 In making transport arrangement for transgenic animals, two principles are paramount:

- the need to prevent the animals from escaping, to ensure that transgenic animals will not interbreed with feral populations; all reasonable scenarios such as accidents should be considered;
- the need to ensure that the animals are properly identified, that they arrive at the intended destination, and that a competent biologist with experience in handling transgenic animals takes delivery of them. Accounting procedures should be instigated to make sure that all animals sent are delivered - whether dead or alive.

- 6.2.2 The IBC may formulate whatever rules it considers essential to meet these conditions. It may be necessary for the IBC to inspect the transport arrangements to determine that the above principles are complied with and that any additional conditions which the IBC considers appropriate have been met (see also Appendix 13).
- 6.2.3 Animal boxes should comply with IATA standards. Modifications can be made to the boxes especially for pathogen-free animals. The boxes must be escape-proof and allow easy observation during an import inspection without opening the box.
- 6.2.4 Transport of all animals should also adhere to the NAELAR Guidelines on the Care and Use of Animals for Scientific Purposes.

6.3 TRANSPORT OF TRANSGENIC INSECTS AND THEIR PATHOGENS

Genetically manipulated insects (including live insects and insect cell cultures infected with genetically manipulated pathogens)

- 6.3.1 The insects should be in a clearly labelled, unbreakable holding container, which is adequately sealed to prevent the insects escaping.
- 6.3.2 The holding container should be placed in a secondary container which is also, clearly labelled and well sealed.
- 6.3.3 Upon arrival, the insects should immediately be transferred from the holding container to a new container.
- 6.3.4 After transfer of the transported insects into new containers, all of the transport material should be decontaminated by autoclaving
- 6.3.5 Accounting procedures should be instigated to make sure that the same number of organisms and containers that are sent are delivered.

6.4 TRANSPORT OF TRANSGENIC PLANTS

- 6.4.1 Vegetative transgenic plant material should be transported within and between institutions in a primary container (for example, a plastic bag for cuttings, an envelope for seeds), which is packed in another unbreakable container.
- 6.4.2 The outer container should be labelled to indicate that it contains transgenic plant material, and the label should include the telephone number of a person to contact should the package be lost or damaged. Labels on seed packets should include the number of seeds being transported.
- 6.4.3 Whole transgenic plants should be netted and deflowered and all seed or fruit removed before transport. Plants may be transported in pots, contained in boxes or crates.
- 6.4.4 Accounting procedures should be instigated to make sure that the same number of plants and containers that are sent are delivered.

6.5 SUPPLY OF GENETICALLY MANIPULATED MATERIAL TO OTHER RESEARCH WORKERS

- 6.5.1 Investigators supplying people in Singapore with genetically manipulated material shall make sure that recipients who are unfamiliar with the genetic manipulation field are made aware of the existence of these guidelines and of the need to observe them.
- 6.5.2 When genetically manipulated organisms are supplied to investigators overseas, the requirements of Article 19.4 of the Convention on Biological Diversity (<http://www.biodiv.org/chm/conv/art.htm>), must be met. Article 19.4 stipulates that:

Each Contracting Party shall, directly or by requiring any natural or legal person under its jurisdiction providing the organisms referred to in paragraph 3 above, provide any available information about the use and safety regulations required by that Contracting Party in handling such organisms, as well as any available information on the potential adverse impact of the specific organisms concerned to the Contracting Party into which those organisms are to be introduced.*

To make sure that Singapore's responsibility as an exporter with respect to Article 19.4 is satisfied, individuals or organisations exporting genetically manipulated organisms must provide the following information to authorities in the recipient country.

- details of the risk assessments that have been carried out in Singapore, and the conditions under which the organism has been approved for use in Singapore (e.g. contained use in a BSL2 laboratory, or small scale field trial under specified conditions);
- any information known to the sender about possible adverse effects of the organism in the recipient country. (In many cases, a disclaimer that no assessment has been made of potential effects in the recipient country may be suitable.)

* 'Any living modified organism resulting from biotechnology that may have adverse effect on the conservation and sustainable use of biological diversity.'

6.6 IMPORT OF GENETICALLY MANIPULATED ORGANISMS OR MATERIAL

- 6.6.1 Importation or possession of GMOs, not relating to human health, is regulated under Section 9 of the Animals and Birds Act (Cap 7).
- 6.6.2 Importation or procurement to import specific biological agents and toxins, which is capable of causing death, disease or malfunction in a human, as those specified under the First, Second, Fourth and Fifth Schedules, is regulated under the Biological Agents and Toxins Act (Act 36 of 2005).
- 6.6.3 Work with imported genetically manipulated viral genomes, micro-organisms, plants or animals fall under the extent of these Guidelines. Investigators should seek the approval of the relevant regulatory agency for intended import and submit a proposal for assessment if appropriate. Appendix 19 contains a list of regulated organisms. These should be taken in tandem with those specified by existing legislation.
- 6.6.4 Permission should be obtained from the relevant agency to import all biological materials, including transgenic micro-organisms, plants and animals. Permission can be obtained by submitting an 'Application for Import Permit' to the appropriate quarantine officer given on the form. The form is available from:

For Plants, Animals, plant-related or animal-related pathogens and pests:

Head,
Import Export Division
Agri-Food & Veterinary Authority (AVA)
5, Maxwell Road, #02-03 Tower Block, MND Complex
Singapore 069110
Fax: 6325-7648

For Human related pathogens:

Head,
Biosafety Branch, Ministry of Health (MOH)
College of Medicine Building 16 College Road, Singapore 169685
Tel: 6325 8347 / 1341 / 8342
Fax: 6325 4679
Email: MOH_Biosafety@moh.gov.sg
Website: <http://www.biosafety.moh.gov.sg>

For Human related pests:

Head,
Environmental Health Institute, National Environment Agency (NEA)
41 Science Park Road #03-24/28 The Gemini
Singapore Science Park II
Singapore 117610
Fax: 6777 8029

6.6.5 The form should contain any relevant information about the genetically manipulated material which falls within these Guidelines. In particular, the following information should be included if appropriate:

- details of the donor organism, which is the DNA source and characteristics of the genes transferred;
- the method or vector used to transfer the DNA to the host organism;
- host organism;
- complete details should be provided if a plant or animal is infected with a genetically manipulated micro-organism.
- Risk assessment on import, handling and transport of the genetically manipulated material.

6.6.6 If appropriate, the relevant agency may make the information provided on this form available to the GMAC, or to other assessors, and may request specific information about any aspect of the genetically manipulated material. GMAC's assessment of the Application to Import will be accelerated if a small-scale proposal for the work has already been received.

APPENDICES

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APPENDIX 1: OTHER RELEVANT DOCUMENTS

Documents relevant to and mentioned in the guidelines are listed below.

1. Relevant Local Legislation

All local legislation is available on the Singapore Statutes Online [http://statutes.agc.gov.sg/]

- 1.1. Animal and Birds Act (Cap 7)
- 1.2. Biological Agents and Toxins Act 2005 (Act 36 of 2005)
- 1.3. Control of Plants Act (Cap 57A)
- 1.4. Workplace Safety and Health Act 2006 (Act 7 of 2006)

2. Relevant Local Guidelines

- 2.1. Singapore Guidelines on the Release of Agriculture-Related GMOs, GMAC

The publication is available from:

- GMAC Secretariat or
- <http://www.gmac.gov.sg>

- 2.2. *Laboratory Biosafety Manual, 3rd edition, World Health Organization, 2004, (ISBN 92-4-154650-6); relevant to the Biological Agents and Toxins Act*

Publications of the WHO can be obtained from:

*Marketing and Dissemination, World Health Organization
20 Avenue Appia, 1211 Geneva 27, Switzerland
Email:bookorders@who.int*

- 2.3. Occupational Safety and Health Guidelines for Laboratories and Production Facilities in the Biomedical Sciences Industry, Ministry of Manpower

The publication is available from:

- Occupational Safety & Health Division, Ministry of Manpower
#03-02 Havelock Road
Singapore 059764
Email: mom_oshd@mom.gov.sg OR
- <http://www.mom.gov.sg/OSHD/Resources/Guides/Guidelines/>

- 2.4. *Guidelines on the Care and Use of Animals for Scientific Purposes, NACLAR*

The publication is available from:

- The National Advisory Committee for Laboratory Animal Research
NACLAR Secretariat
20 Biopolis Way #08-01 Centros
Singapore 138668 OR
- <http://www.feedback.gov.sg>
(see e-consultation paper under National Advisory Committee for Laboratory Animal Research)

3. Worldwide guidelines specific to genetic manipulation

3.1. Australia

- i. Guidelines for Certification of Facilities/Physical Containment Requirements
- ii. Good Industrial Large Scale Practice
- iii. Guidelines for the transport of GMOs

Publications (i) – (iii) above are available from:

- Office of Gene Technology Regulator
Commonwealth Department of Health and Aging
MDP54 PO Box 100 Woden
ACT 2606 Australia
- <http://www.health.gov.au/ogtr/index.htm>

3.2. United States of America

Guidelines for Research Involving Recombinant DNA Molecules,
National Institutes of Health, Department of Health and Human Services, USA

The publication is available from:

- Office of Biotechnology Activities
National Institutes of Health, MSC 7010
6000 Executive Blvd, Suite 302
Bethesda, MD 20892-7010
United States of America
- <http://www.nih.gov/od/oba/>

3.3. European Commission

- i. Guidelines for the Risk Assessment of Operations Involving the Contained Use of Genetically Modified Micro-organisms (GMOs), September 1993
ACGM/HSE/DOE/NOTE 7
- ii. Laboratory Containment Facilities for Genetic Manipulation, June 1988
ACGM/HSE/NOTE 8

Publications (i) and (ii) above, and other 'Notes' that comprise the UK Guidelines can be obtained from:

- Advisory Committee on Genetic Modification
Health and Safety Executive
Rose Court, 2 Southwark Bridge
London SE1 9HS, United Kingdom
- Website: <http://www.hse.gov.uk/index.htm>

- iii. Safety Considerations for Biotechnology 1992, OECD, Paris, 1992

Publication (iii) above is available from:

- OECD Publications Service
2 rue André-Pascal
75775 Paris, Cedex 16
France

4. Other relevant guidelines, regulations and publications

- i. Australian Code of Good Manufacturing Practice for Therapeutic Goods – Medicinal Products
- ii. Australian Guidelines for the Registration of Drugs, Vol. 1, 2nd edition, July 1994 (Includes Appendix 17: Guidelines on clinical data to support applications for substances produced by genetic manipulation; and Appendix 18: Guidelines on clinical data to support applications for monoclonal antibodies.)

Publications (i) and (ii) above are available from:

- *Publications Officer, Therapeutic Goods Administration
PO Box 100, Woden ACT 2606
Australia*
- <http://www.health.gov.au/>

- iii. Australian Code of Practice for the Care and Use of Animals for Scientific Purposes, NHMRC, CSIRO, Australian Agricultural Council, 1997, ISBN 0-644-10292-6
- iv. NHMRC Statement on Human Experimentation and Supplementary Notes, 1992
- v. Human Gene Therapy and Related Procedures, 1994, ISBN 0-644-32916-5
- vi. National Guidelines for the Management of Clinical and Related Wastes, 1988, ISBN 0-644-08265-8

Publications (iii) – (vi) above are available from:

- *The Publications Officer
National Health and Medical Research Council
GPO Box 9848, Canberra ACT 2601
Australia*
- *Website: <http://www.health.gov.au/nhmrc>*

- vii. Laboratory Safety Guidelines that Take Account of HIV and Other Blood-Borne Diseases, ANCA Bulletin No 3, January 1990
- viii. Infection Control in the Health Care Setting - Guidelines for the Prevention of the Transmission of Infectious Diseases, April 1996

Publications (vii) – (viii) above are available from:

*Australian National Council on AIDS and Related Diseases
GPO Box 9848, Canberra ACT 2601
Australia*

- ix. AS 2243: Safety in laboratories
- x. AS/NZS 2243.1: 1997: Safety in laboratories: General
- xi. AS/NZS 2243.3: 1995: Safety in laboratories: Microbiology and Amdt 1, April 1996
- xii. AS 2252: Biological safety cabinets
- xiii. AS 2252.1: 1994: Biological safety cabinets (Class I) for personnel protection and environmental protection

- xiv. AS 2252.2: 1994: Laminar flow biological safety cabinets (Class II) for personnel, environment and product protection
- xv. AS 2647: Biological safety cabinets - installation and use, 1994
- xvi. AS 2982: Laboratory design and construction
- xvii. AS/NZS 2982.1: 1997: General requirements
- xviii. AS 1324: Air Filters for use in air conditioning and general ventilation
- xix. AS 1324.1: 1996: Construction
- xx. AS 1324.2: 1996: Tests
- xxi. AS 1807.6: Cleanroom, workstations and safety cabinets – Methods of test: Determination of integrity of terminally mounted HEPA filter installations , 1989

Publications (ix) – (xxi) above are available from:

- *Standards Association of Australia
National Sales Centre PO Box 1055
Strathfield NSW 2135
Australia*

- xxii. The requirements manual for agricultural chemicals
- xxiii. The requirements manual for veterinary chemicals

Publications (xxii) – (xxiii) above are available from:

- *AGPS Mail Order Sales
GPO Box 84, Canberra ACT 2601
Australia*

- xxiv. Vaccination of Laboratory Workers Handling Vaccinia and Related Poxviruses Infectious for Humans, 1990, Advisory Committee on Dangerous Pathogens and Advisory Committee on Genetic Modification, ISBN 0-11-885450-X
- xxv. HIV - the Causative Agent of AIDS and Related Conditions, January 1990
Advisory Committee on Dangerous Pathogens

Publications (xxiv) – (xxv) are available from:

- *Health and Safety Executive
Rose Court, 2 Southwark Bridge
London SE1 9HF, United Kingdom*
- *HMSO Publications Centre
PO Box 276, London SW8 5DT
United Kingdom*

- xxvi. Biosafety in Microbiological and Biomedical Laboratories , 4th edition, Washington DC, 1999, US Department of Health and Human Services

Publication (xxvi) – (xxv) above is available from:

- *Superintendent of Documents
US Government Printing Office
Washington DC 20402, United States of America*
- *<http://www.cdc.gov/od/ohs/biosfty/bmbl4/bmbl4toc.htm>*

- xxvii. Collins C H, *Laboratory Acquired Infections: History, Incidence, Causes and Prevention*, 3rd edition, Butterworths-Heinemann, London , 1993, ISBN 0-750606428
- xxviii. *Convention on Biological Diversity* , June 1992, United Nations Environment Programme

The above publication is available from:

- *Secretariat, Convention on Biological Diversity
United Nations Environment Programme
15 chemin des Anemones
CP 356, CII-1219 Chatelaine, Geneva
Switzerland*
- *<http://www.biodiv.org>*

- xxx. Information Systems for Biotechnology

The above publication is available from:

- *<http://gophish.biochem.vt.edu/index.html>*

APPENDIX 2: LIST OF GMAC-APPROVED HOST/VECTOR SYSTEMS

BIOLOGICAL CONTAINMENT

The objective of biological containment is to minimise both the survival of the host and vector outside the laboratory, and the transmission of the vector from the propagation host to a non-laboratory host. This Appendix lists the host/vector systems currently approved by GMAC as providing a level of biological containment.

	Host	Vector
Bacteria	<i>Escherichia coli</i> K12 or <i>E. coli</i> B derivatives which do not contain conjugative or generalised transducing phages	<ol style="list-style-type: none"> 1. Non-conjugative plasmids 2. Bacteriophage <ul style="list-style-type: none"> - lambda - lambdoid - Fd or F1 (e.g.M13)
	<i>Bacillus subtilis</i> or <i>B. licheniformis</i> Asporogenic strains with a reversion frequency of less than 10^{-7}	Indigenous <i>Bacillus</i> plasmids and phages whose host range does not include <i>B. cereus</i> or <i>B. anthracis</i>
	<i>Pseudomonas putida</i> Strain KT 2440	Certified plasmids: pKT 262, pKT 263, pKT 264
	<i>Streptomyces</i> specified species <i>S. coelicolor</i> <i>S. lividans</i> <i>S. parvulus</i> <i>S. griseus</i>	<ol style="list-style-type: none"> 1. Certified plasmids: SCP2, SLP1, SLP2 PIJ101 and derivatives 2. Actinophage phi C31 and derivatives
Fungi	<i>Neurospora crassa</i> , laboratory strains	No restriction
	<i>Saccharomyces cerevisiae</i>	No restriction
	<i>Pichia pastoris</i>	No restriction
	<i>Schizosaccharomyces pombe</i>	No restriction
Slime moulds	<i>Dictyostelium</i> species	<i>Dictyostelium</i> shuttle vectors, including those based on the endogenous plasmids Ddp1 and Ddp2

	Host	Vector
Tissue Culture	Mammalian (including human) cells	Non-viral vectors or defective viral vectors (including retrovirus or retroviral-helper combinations) that cannot infect human cells.
	Avian cells	Avipoxvirus vectors
	Plant cell cultures	Non-tumorigenic disarmed Ti plasmid vectors in <i>Agrobacterium tumefaciens</i> and non-pathogenic viral vectors
	Insect cell cultures, such as <i>Spodoptera frugiperda</i> *	Baculovirus (<i>Autographa californica</i> nuclear polyhedrosis virus)

Note:

The above approved hosts may also be used in experiments where DNA is inserted into the host cell without the use of a biological vector (for example, by mechanical, electrical or other means), provided that the DNA:

- is not derived from microorganisms able to cause disease in humans, animals or plants, unless the DNA to be introduced is fully characterised and will not increase the virulence of the host or vector;
- does not code for a toxin for vertebrates with an LD50 of less than 100 µg/kg, and is not an oncogene;
- does not comprise or represent more than two-thirds of the genome of a virus and is not being used in an experiment in which the genetic material missing from the viral genome and essential for producing infection is available in the cell into which the incomplete genome is introduced, or made available by subsequent breeding processes.
- Any commercially available Host-Vector Systems.

Such a system with an approved host and the DNA meeting these conditions would constitute an approved host/vector system for the purposes of these Guidelines, and hence would fall under exemption section 2.2.1.

* provided the recombinants are also inclusion-negative (e.g. polyhedrin minus)

APPENDIX 3: INSTRUCTIONS FOR COMPLETING GMAC PROPOSAL FORMS AND ANNUAL REPORT BY IBC

The Institutional Biosafety Committee will use the information provided in the GMAC 'Proposal Form for Assessment of Genetic Manipulation Work' to determine the category into which the project fits and the containment level. GMAC will use the information in the form to assess proposals falling into Category A. In order to enable GMAC and the IBC to carry out those functions, a clear statement of what the applicant proposes to do is needed, and if this cannot easily be fitted into the space provided, a separate description shall be attached. The following suggestions are intended to ensure that GMAC has sufficient relevant information to make a prompt decision on the application.

Title of Project and Aims

When describing the aim of the proposal, include a brief description of the main steps involved. If both immediate and long term broader aims are included, make clear which component of the work needs IBC approval (or GMAC advice) now.

If the project is complex and likely to take several years to complete, it will help if the work to be undertaken first is described separately. If recombinant DNA is ultimately to be inserted into whole animals or plants, or into bacteria not listed in Appendix 2 of these Guidelines, it may well be that approval can be given in the first instance for cloning and characterisation of specific genes or other DNA, with approval for later stages being possible only after such characterisation. If the stages are made clear to the Committee, approval or advice for the first stage may be given to enable the work to start.

If the intention is to import biological material which falls under the Guidelines, the title may read 'Intention to import...'

Source of DNA

If the DNA has already been cloned, please give details of the construct: e.g. who made it, how it was made, and what is known of its properties.

If several genes or species etc. are to be used, list all of them, because one proposal may cover them all. For example, if appropriate, request advice for chickens, ducks and other avian species. This will alleviate the need for repeated applications.

Host Organism

If more than one host is to be used, particularly if different containment levels apply, clarify when and how each is to be used. Comments made above on dividing a project into stages may be relevant. Please also complete the supplementary information form for experiments involving whole plants.

Vectors

Make the description for prokaryotic vectors as broad as is necessary to cover the intended work. For example, specify 'non-conjugative plasmids such as pBR322 and pUC9' if the project is likely to require a range of specific vectors as the project progresses. If only pBR322 and pUC9 are requested, the approval will be limited to the two vectors and will not cover the many closely related vectors which may turn out to be more useful.

The description of vectors should comprise more than a series of letters, symbols and numbers. Some description of their properties is also required.

In the case of retroviral vectors, be specific and indicate what is known about their properties, and provide details of the construct, if appropriate, on a separate sheet of paper, including a genetic map and/or a description of its construction.

Assessment of Potential Hazards

The increasing range of hosts and vectors being used makes it imperative for every applicant to assess assiduously any potential hazards associated with the proposed work and to discuss such hazards and their containment in the proposal. Failure to do so may delay assessment until after additional information has been sought and obtained from the applicant.

Details of Personnel

For the 'full details' requested, please include the extent and nature of relevant experience on a separate sheet of paper. These details need not be sent to GMAC but should be checked by the IBC.

Proposal Form

A copy of the proposal form is attached to this Appendix. The proposal form is self-duplicating and allows for sufficient copies to be made for GMAC, the IBC and the principal investigator's records. Please note that GMAC requires the originals (i.e. top copies) of forms to be submitted, and not photocopies.

PROPOSAL FORM FOR ASSESSMENT OF GENETIC MANIPULATION WORK

GMAC Ref No.: _____
(for official use only)

Name of Scientist(s) : _____

Name of Institution : _____

Type of Experimental Organisms (please tick) :

Animal Plant Others, please specify: _____

Experiment Risk Group (please tick) :

Category A Category B Category C

A. Experimental detail (attach separate sheet if necessary)

1.	Project title
2.	Research unit involved
3.	Experimental objective
4.	Rationale for the experiment
5.	Duration of the experiment

B. Organism/vector (attach separate sheet if necessary)

1.	Name and address of exporting user
2.	Date of transfer
3.	Name of organism/vector
4.	Natural host
5.	Requirement(s) to ensure containment, safe handling, storage and disposal

Prepared by:

_____	_____	_____
Name and Signature	Appointment / Laboratory	Date
Contact Details		
Address	:	_____

Tel Number	:	_____
		Fax Number : _____
Email	:	_____

Reviewed by:

_____	_____	_____
Date received	Name and Signature	Date
IBC Chairman		

Note that IBCs should provide annual reports of its composition and activities by 1st January every year.

The following section is applicable for Category A experiments only:

Please indicate if approval have been sought from relevant regulatory authority (MOH / AVA / NEA) for *use/possession/import/transport of the GMO.

If yes, please provide supplementary proof.

If no, please explain why.

**(highlight where applicable)*

For a list of regulatory contact points, please refer to Section 6.6 (page 23).

SUPPLEMENTARY INFORMATION FORM
FOR EXPERIMENTS INVOLVING WHOLE PLANTS
(Attach separate sheet if necessary)

1. Are the experimental plant noxious weeds or closely related to species which are noxious weeds?

If 'yes', please elaborate:

2. Are the microorganisms/fungi etc. involved in this work known to be harmful to humans, animals or plants?

If 'yes' :

- a) Give further information about the harmful agent:
- b) Detail the known and likely transmission modes (including carrier insects) for this agent:

3. Are the genetically manipulated plants to be grown?

If 'yes' :

- a) What developmental stage will they reach?

- b) Describe the techniques to be employed to contain plant materials (including pollen, seeds, spores, vegetative materials) during and at the completion of the experiments.
 - c) What is the proposed method of disposal of plant materials at the conclusion of the experiment?
- 4.
- a) Is soil or soil substitute to be used? (Specify.)
 - b) How will it be sterilised?
5. Describe the facility to be used for cultivation of the plants. Include information such as location, proximity to containment laboratory etc.:
6. Give any additional information which may be relevant to the assessment of this work:

ANNUAL REPORT BY INSTITUTIONAL BIOSAFETY COMMITTEE

(Please submit to GMAC Secretariat by 1st January)

Name of Institution : _____

Address of Institution : _____

Tel : _____ Fax : _____

Submitted by : _____ Date: _____

Name and Signature

A. Composition of IBC

IBC APPOINTMENT	NAME	DESIGNATION
Chairman		
Biological Safety Officer		
Committee Members		

B. List of Current Proposals for Genetic Manipulation Work (attach separate sheet if necessary)

i) Category A

ii) Category B

iii) Category C

C. Report on Significant Accident or Incident attributed to Genetic Manipulation Work
(attach separate sheet if necessary)

D. List of Additional Comments for GMAC

List of Approved Facilities for Genetic Manipulation Work

(Please complete one copy for each facility with a containment level equivalent to BSL3, and for each large scale facility.)

Name of Facility : _____

Location : _____

Manager : _____

Special features of facility :

Date of Last Inspection: _____ Date of Previous Inspection: _____

Period of room use and projects for which it has been used :

Dates of Staff Training: _____ (Cleaning Staff)

_____ (Emergency Staff)

_____ (Engineering Staff)

List of Current Manuals and Inspection Date :

Inspection Dates for :

_____ (Air handling system)

_____ (Alarms)

_____ (Biosafety Cabinet)

_____ (Building Finishes)

_____ (Centrifuges)

_____ (Cleanliness)

_____ (Decontamination Equipment)

_____ (Effluent Disposal)

_____ (HEPA filters)

_____ (Refrigeration)

_____ (Sterilisers)

Please keep all necessary documentation as proof for the above, to be provided when requested by GMAC or during on-site inspections.

APPENDIX 4: TOXINS

For work involving toxins that fall under Fifth Schedule of the BATA, prior approval for its use must be sought from the Ministry of Health.

Fifth Schedule Agents (as of 3rd January 2006)

1. Botulinum toxins (Types A, B, C, D, E, F and G)
2. *Clostridium perfringens* toxins
3. Staphylococcal Enterotoxin B
4. Shigatoxins
5. Verotoxins

Section 4.1, Category A(i), of these Guidelines requires that, for work involving the cloning of genes for toxins (or uncharacterised DNA from organisms that synthesise toxins for vertebrates) with an LD50 of less than 100 µg/kg, the IBC seek a recommendation from GMAC before giving approval for work to commence.

Below is a list of a number of toxins with an LD50 of less than 100 µg/kg. The list is not exhaustive. If it is not known whether a substance should be regarded as toxic, GMAC advice shall be sought.

SOME TOXINS WITH AN LD50 OF LESS THAN 100 µg/kg *

Abrin

Bacillus anthracis lethal factor

Bordetella pertussis toxin

Cholera - see *Vibrio cholerae*

Clostridium botulinum toxins

Clostridium perfringens epsilon toxin

Clostridium tetani toxin

Corynebacterium diphtheriae toxins

Escherichia coli heat labile (LT) enterotoxin and LT-like toxin

Oxygen-labile haemolysins such as streptolysin O

Yersinia pestis murine toxins

Pseudomonas aeruginosa exotoxin A

Ricin

Shigella dysenteriae toxin

Staphylococcus aureus determinants A, B and F, alpha and beta toxin, exfoliative toxin

Vibrio cholerae toxin and toxins neutralised by antiserum monospecific for cholera toxin (e.g. heat labile toxins of *E. coli*, *Klebsiella* and other related enterotoxins)

Yersinia enterocolitica heat stable toxin

* Information derived from the NIH Federal Register, Vol 51, No 88, May 1986 (Appendix F) and information provided by the NIH Office of Recombinant DNA Activities.

APPENDIX 5: GUIDANCE FOR WORK INVOLVING GM VIRUSES FOR GENE TRANSFER INTO ANIMAL & HUMAN CELLS IN A LABORATORY SETTING

1. General Considerations

Genetic modification of viruses is a common practice in medical research laboratories to study the biology of the viruses. Viruses are also used as efficient vehicles for gene transfer into animal and human cells.

The hazards associated with the use of genetically-modified viruses depend on the following:

- (a) The virus' host range;
- (b) Its ability for repeated rounds of infection;
- (c) Its competence for replication inside the cell;
- (d) The possibility of generating replication-competent virus from replication-defective vectors by recombination (e.g. in the case of retroviruses);
- (e) The ability of the genetic material of the virus to be integrated into the chromosome of the infected cell;
- (f) The stability of the virus inside the cell and exposed in the environment;
- (g) The means of transmission of the virus (e.g. through aerosol or skin abrasions and other physical contact);
- (h) The nature of the introduced DNA sequences or its encoded protein.

2. Approval and Consultation

Principal Investigators should seek the clearance from IBC prior to the start of any experimentation with genetically-modified viruses.

Exhaustive references for the Biosafety Level and Guidelines with regards to the use of specific animal and human-infectious viruses shall be obtained by the Principal Investigator prior to the start of the project. The following organisations provide good references for specific animal and human viruses:

- (a) American Biological Safety Association (ABSA)
www.absa.org
- (b) Center for Disease Control (CDC)
www.cdc.gov
- (c) American Tissue Culture Collection (ATCC)
www.atcc.org

3. Procedures for handling rodent and other non-human viruses

Viruses that are capable of infecting **ONLY animal (non-human and non-primate)** species are not considered to be associated with any hazard to the manipulator or other laboratory personnel. Practices associated with good tissue culture technique will be adequate in containing and handling these viruses. While the risks associated with the use of these viruses are considered negligible, solutions and contaminated cells shall be decontaminated/autoclaved before disposal to prevent accidental infection of other animal cell lines.

4. Procedures for handling viruses that can potentially infect human cells ('human infectious' viruses)

The primary hazard associated with the use of live recombinant viruses that have the capacity or that could potentially infect human cells lies on the type of the viruses and the nature of the introduced genetic sequences. Primate-infectious viruses shall be considered "potentially human-infectious". For all human-infectious viruses handled in a class II biological safety cabinet, the primary hazard to the scientist is the possibility of infection by viruses through broken skin brought about by needles and other commonly used sharps such as pipettes. The potential danger to other laboratory personnel depends on the stability and infectivity of the virus in the extracellular environment and the nature of the introduced genetic material.

For all human-infectious or potentially human-infectious viruses, the major requirement is for good virological and tissue culture practice on the part of the scientist with regard to the following precautions:

- (a) A facility of containment of level BSL2 or higher (as determined by the IBC and with reference to the Biosafety level detailed by the ATCC and CDC) will be required. All manipulations shall be conducted in a class II biological safety cabinet or equivalent. Only one individual shall use the cabinet at any one time.
- (b) Laboratory gowns, gloves and face mask shall be worn during manipulations with recombinant human-infectious viruses.
- (c) Dishes and plates of cells containing human-infectious viruses shall be handled in larger plates (or inverted lids) to provide traps for accidental spills.
- (d) All pipettes, glassware and plasticware shall be decontaminated by submersion or by placing in polyethylene bags which should subsequently be sealed and autoclaved.
- (e) For viruses which are able to persist in the environment (e.g. adenovirus, vaccinia virus, hepatitis virus, papillomavirus), decontamination and bagging of waste should be done within the biosafety cabinet prior to removal and autoclaving. Care should be taken to ensure that the amount of material held in the biosafety cabinet is minimised, in order to avoid interference with the air flow in the cabinet.
- (f) Mouth pipetting is strictly prohibited.
- (g) Open flames that could interrupt the air-flow in the biosafety cabinet should be avoided.
- (h) The use of sharp instruments (sharps) such as syringe needles, glass pipettes, razors, scissors and surgical knives, wherever possible, should be avoided, since skin abrasions represent the most likely portal of entry to the body. Where the use of sharps is unavoidable, these instruments shall be placed in separate biological disposal receptacles and sterilized before disposal.
- (i) Tissue cultures infected with human-infectious or potentially human-infectious viruses shall be kept in specially dedicated incubators.
- (j) Likewise, frozen stocks of human-infectious or potentially human-infectious viruses should be kept in specially designated and clearly marked liquid nitrogen

tanks and freezers. Laboratory personnel who leave the laboratory for new employment shall ensure that these materials are either discarded or entrusted to another worker. A central register shall be maintained which includes a record of stored cell lines and human-infectious viruses. Principal Investigators are responsible for providing information for the register and maintaining a record of the viruses and infected cell lines used in their laboratories. The maintenance of a central register for the institution/ company/organisation is the responsibility of the IBC.

- (k) Great care shall be taken to decontaminate spills immediately. The correct disinfectant to use in any given situation depends on the organism being handled and is the responsibility of the Principal Investigator in charge of the work to select an appropriate disinfectant. After each session, work surfaces shall be wiped down with an appropriate disinfectant before ultraviolet decontamination. Where a hood has been used for handling amphotropic retroviruses, subsequent use with non-amphotropic viruses can be undertaken following decontamination with a suitable disinfectant and ultraviolet decontamination.
- (l) Only trained individuals shall be permitted to handle human-infectious recombinant viruses. It is the responsibility of the Principal Investigator to ensure the proper training of personnel in consultation with the IBC.
- (m) Under no circumstances should investigators be infecting cultures of their own cells, or of their immediate relatives, or those of other members of the laboratory.
- (n) Before beginning work with human-infectious (genetically manipulated) viruses where vaccination with the corresponding virus is regarded as an effective means of preventing subsequent infection (e.g. vaccinia, hepatitis), investigators shall be vaccinated.
- (o) Before beginning work with genetically-modified viruses that are potentially able to infect human cells, investigators are advised to consider lodging a serum sample for subsequent health surveillance.

5. Infection of animals with recombinant viruses

- (a) Infectious animal viruses unable to infect human cells

Viruses of this group are not considered hazardous and accordingly good animal handling practices are appropriate. Infected animals shall be kept in separate cages and be held in the biohazard room separate from non-infected animals. Infected animals should be clearly marked. If possible, the use of micro-isolators should be encouraged to prevent cross-infection. Precautions should be taken to avoid animals escaping and coming into contact with other animals. All waste generated from animals of this group shall be autoclaved before disposal.

- (b) Viruses with the capacity to infect human cells

Animals infected with human-infectious viruses shall be kept in a separate cage which is clearly labelled as containing the particular virus in question. They should be kept in a separate biohazard room from non-infected animals. The main risk is to the handler who shall take great care to avoid being scratched, bitten or exposed to aerosols. Gloves, face mask and protective clothing must be worn to avoid direct contact with tissue and body fluids. Work place should be covered with protective paper which shall be changed regularly. Only trained

staff shall handle these infected animals under the supervision of the Principal Investigator. Precautions should be taken to avoid animals escaping and coming into contact with other animals. All waste should be autoclaved prior to disposal.

6. Gene therapy

In projects where viruses are being used to deliver genes to human subjects (gene therapy), the approval from the relevant institutional ethics committees and the Medical Clinical Research Committee (Ministry of Health) should be obtained, unless the therapy has already been established by the MOH as an approved treatment. A separate guideline governs the control of virus production and safety testing procedures in gene therapy experiments.

APPENDIX 6: PROCEDURES FOR WORK WITH HAZARDOUS FRAGMENTS OF DNA

Note for Category B (iv), Section 4.2

When working with isolated DNA molecules or amplifying DNA molecules using techniques such as the polymerase chain reaction (PCR), there are some cases where caution is warranted. Some degree of risk may exist and the extent of this is uncertain.

Such cases include:

1. DNA which encodes an active oncogene product or tumour suppressor gene product, particularly when this is associated with a gene promoter with high activity in human cells. DNA containing more than one active oncogene is associated with increased risk.
2. DNA encoding growth factors, their receptors or other substances that might directly or indirectly alter the growth patterns of human cells.
3. DNA or RNA representing complete viral genomes or fragments with the potential to regenerate live virus. Complete genomes for HIV or papilloma viruses, for example, warrant careful handling.

There is some risk that such molecules could enter the cells of the operator, the principal routes of entry being through breaks in the skin. It is therefore recommended that work of this type be carried out using gloves in order to avoid skin contact. Special care shall be taken when using needles or other sharp instruments.

Precautions for handling genetically manipulated viruses with the capacity to infect human cells are described in Appendix 5.

APPENDIX 7: REQUIREMENTS FOR GENETIC MODIFICATION BIOASFEY LEVEL 2 (GM-BSL2)

The requirements listed here for GM-BSL2 containment emphasise the procedures to be observed by the laboratory worker to ensure a basic level of laboratory safety. There are also some architectural requirements relating to laboratory design and equipment.

The requirements for Biosafety Level 2 in the Laboratory Biosafety Manual (3rd Ed, WHO) and the OSH Guidelines for Laboratories and Production Facilities in the Biomedical Sciences Industry shall apply for GM-BSL2. In addition, the following requirements must be included.

Laboratory Procedures

Many of the laboratory procedures detailed below are those that would be considered essential minimum practices in any microbiological laboratory.

1. Storage of food or drink in the laboratory or any storage unit containing genetically manipulated DNA (e.g. refrigerator) is prohibited.
2. Equipment used for handling cultures or contaminated material which is not readily steam sterilised shall be chemically disinfected after use.
3. All technical procedures shall be performed in a way that minimises the creation of aerosols. In particular, operations such as sonication or vortexing which may generate aerosols are to be done in a biological safety cabinet. A period of at least five minutes shall be allowed for aerosols to settle before opening homogeniser or sonicator containers in a biological safety cabinet.

Essential Equipment

Each laboratory shall be equipped with basin mixers for hand washing, preferably foot-operated, elbow-operated or electronically operated. Emergency drench showers and eyewash stations shall be provided.

Laboratory Signs

The laboratory shall be labelled with adhesive signs:

- on the door, with a sign designating the level of containment;
- in the laboratory, with a sign giving procedures required for work at this level of containment.

The signs for laboratories shall be put up only after inspection by the relevant regulatory agency for all higher levels of containment.

Constant Temperature Rooms

Walk-in warm rooms and cold rooms used for incubation or storage of genetically manipulated material may be certified as GM-BSL2 facilities even if they do not contain sinks or coat hooks. Work in such rooms shall otherwise follow all the procedures required for GM-BSL2 laboratories.

APPENDIX 8: REQUIREMENTS FOR GENETIC MODIFICATION BIOSAFETY LEVEL 3 (GM-BSL3)

GM-BSL 3 and 4 facilities must be approved by the relevant regulatory agency before commencement of work. The requirements for Biosafety Level 3 in the Laboratory Biosafety Manual (3rd Ed, WHO) and the OSH Guidelines for Laboratories and Production Facilities in the Biomedical Sciences Industry shall apply for GM-BSL3.

Essentially, work in laboratories at GM-BSL3 level shall conform with the procedures set out for GM-BSL2 laboratories, with the following additional requirements:

Laboratory Procedures

1. All aerosol-producing equipment such as that for sonication and vortexing shall be kept and used in the biosafety cabinet.
2. The biosafety cabinet and/or the laboratory shall be decontaminated with formaldehyde gas after major spills of contaminated material. Records of such spills and any other accidents must be kept, detailing date, time and person(s) involved with the cleaning up measures taken. Such records must be available for inspection at all times.
3. No other work is to be done simultaneously with work requiring GM-BSL3 containment.
4. While work is in progress a sign on the door shall indicate the level of containment required for that work.
5. Protective clothing shall not be worn outside the laboratory; it shall be transported to the decontamination area in sealed bags or boxes. Boxes shall have provision for penetration of steam during autoclaving.
6. No one may enter the laboratory for cleaning, servicing of equipment, repairs or other activities unless the principal investigator or the biosafety officer has been informed and laboratory surfaces have been disinfected.
7. Where a pressure steam steriliser (autoclave) is not available within the laboratory, laboratory wastes shall be bagged and placed in an unbreakable container with a secured lid for transport to the pressure steam steriliser. The surface of the container should be decontaminated with a suitable disinfectant. Wastes shall not be stored outside the facility before they are sterilised.

Laboratory Planning and Construction

8. The laboratory shall not be located adjacent to, nor open onto, corridors used by the general public.

Decontamination

9. Provision shall be made to decontaminate the biological safety cabinet(s) and the room independently with formaldehyde gas, and for the gas to be purged safely to atmosphere upon completion of the procedure.
10. Decontamination of the safety cabinet(s) shall be performed in accordance with the requirements of established International Standards (see Appendix 1) and will

require the provision of a front cover plate and exhaust duct adaptor to fit the particular cabinet.

Pest Control Program

11. A pest control program against insects, rodents, birds, etc. shall be instituted.

Signs

12. The laboratory shall be labelled on the door and wall with GM-BSL3 signs after approval by the relevant regulatory agency.

APPENDIX 9: REQUIREMENTS FOR GENETIC MODIFICATION BIOSAFETY LEVEL 4 (GM-BSL4)

GM-BSL 3 and 4 facilities must be approved by the relevant regulatory agency before commencement of work. The requirements for Biosafety Level 4 in the Laboratory Biosafety Manual (3rd Ed, WHO) and the OSH Guidelines for Laboratories and Production Facilities in the Biomedical Sciences Industry shall apply for GM-BSL4.

Essentially, work in laboratories at GM-BSL4 level shall conform with the procedures set out for GM-BSL3 laboratories, with the following additional requirements:

Laboratory Procedures

1. All street clothing, including underwear, shall be removed and retained in the outer clothing change room. Complete laboratory clothing, including shoes, shall be provided by the organisation and shall be used by all personnel entering the facility. When leaving the facility, personnel shall remove their laboratory clothing and store or discard it in the inner change room before showering.
2. Personnel entering or leaving the laboratory shall indicate, either manually or electronically, the time of each exit and entry.
3. There should always be at least two workers present (or, if only one, a second person located at an observation window or in telecommunication or video surveillance) to assist in case of an emergency.
4. The autoclave and fumigation chamber shall be decontaminated after each exposure to the laboratory environment.
5. A primary container holding viable or intact biological material shall be opened only in a flexible film isolator or a maximum containment laboratory. Containers may be opened in other laboratories only if the biological material has been rendered non-infectious or non-toxic, and the space in the primary and secondary containers has been decontaminated.

Laboratory Construction

6. A telephone or other means of outside communication shall be provided inside the laboratory unit.
7. Walls, floors and ceilings of the facility shall be constructed in such a manner as to form a sealed internal shell which facilitates easy fumigation. The internal surfaces of the shell shall be resistant to liquids and chemicals used in the facility and shall facilitate easy cleaning and decontamination. All apertures in the structures and surfaces shall be sealed to prevent vermin or insects from entering the area. Any windows shall be resistant to breakage.
8. A pass-through dunk tank, fumigation chamber or equivalent decontamination equipment shall be provided, so that materials and equipment that cannot be decontaminated in the autoclave can be rendered safe for removal from the facility.
9. A shatter-resistant observation window, or suitable alternative monitoring facilities, shall be installed so that laboratory occupants can be observed from outside the laboratory.

10. An automatically-starting emergency power source, emergency lighting and communication system shall be provided.

Signs

11. The laboratory shall be labelled on the door and wall with GM-BSL4 signs after approval by the relevant regulatory agency.

APPENDIX 10: REQUIREMENTS FOR PLANT HOUSE BIOSAFETY LEVEL 2 (GP-BSL2)

The following standard of plant house and operating procedures (GP-BSL2) is regarded as a suitable minimum for genetic manipulation work with whole plants which falls under Category B in Section 3. Most work with plants will be adequately contained in this standard of plant house.

Plant house work which falls under Category A will require at least GP-BSL2 level of containment, and additional operating procedures and/or a higher standard of construction may be recommended.

Construction

1. The plant house shall have a floor of concrete, or some other substance approved by IBC. Any openings in the walls or roof (e.g. windows, vents, and air supply and exhaust inlets and outlets) shall be screened with fine screens (thirty –gauge 30/32 mesh wire gauze). The drainage exits shall be designed to avoid entry of invertebrates, rodents and insects. Transparent sections of the plant house shall be made of impact-resistant material selected to maintain the integrity of the structure during all foreseeable impact events, including windstorm, and impacts from golf balls, stones picked up by grass mowers, hailstones and the like. If ordinary glass is used, a protective screen shall be fitted.
2. Entrances to the plant house shall be posted with a sign identifying the type of plant house and listing the procedures applicable, including emergency and maintenance procedures.
3. If the plant house is free-standing, it shall have an anteroom for entry and exit. The anteroom shall be fitted with a sticky pest strip or automatic insecticide aerosol device designed to kill arthropods which gain entry. An anteroom is not necessary if the plant house connects directly with a certified small or large scale containment facility.
4. A wash-basin shall be provided within the plant house adjacent to the entry door. Effluent should be disinfected. Where a laboratory is directly connected to the plant house, the basin may be in the laboratory.

Operating Procedures

5. The plant house shall be inspected regularly to ensure that its containment features are intact. Screens, filters and the like shall be cleaned regularly (in accord with manufacturer's specifications when provided).
6. All doors to the plant house shall be locked for the duration of the work except for those periods when personnel are actually working inside it.
7. Hands shall be washed with soap and water before leaving the plant house.
8. Only persons authorised by the IBC are to enter the plant house. All such persons shall be trained to follow normal plant house routines as well as these operating procedures.

9. All plants in the plant house shall be treated as containing genetically manipulated DNA. Work in the plant house other than that involving genetic manipulation shall be discouraged.
10. Operations which may generate aerosols shall be done in a biological safety cabinet as specified for BSL2 laboratory containment.
11. Plants and tissues taken into or out of the plant house shall be carried in closed containers. Waste plants, tissues, soil, soil substitutes and the containers shall be sterilised.
12. Living plants or tissues shall not be taken from the plant house except to a containment laboratory or, with the approval of the IBC, when they are being transferred to another organisation.
13. If the work permits, plants shall be sprayed regularly with a systemic insecticide. The plant house shall be sprayed or fumigated to kill other arthropods (especially mites) at regular intervals, and at the end of each series of experiments. The organisation shall have an effective insect and rodent control program.
14. The experimental materials shall be inspected regularly for signs of arthropod infestation. The inspection regimen shall pay particular attention to mites as they would not normally be excluded by the window and vent screens.

APPENDIX 11: REQUIREMENTS FOR PLANT HOUSE BIOSAFETY LEVEL 3 (GP-BSL2)

Note on plant houses with higher biosafety containment than GP-BSL2

GP-BSL 3 and 4 facilities must be approved by the relevant regulatory agency before commencement of work. Certain experiments may warrant the use of plant houses with additional containment features and operating procedures higher than those of GP-BSL2 (see Appendix 10). Each project will be considered on an individual basis, and additional operating procedures with a GP-BSL2 facility rather than GP-BSL3 may be recommended. The following requirements are recommended for institutions which may be planning to build plant houses providing containment greater than GP-BSL2.

The attached notes are provided so that IBCs can identify some of the requirements which need to be incorporated into the design of BSL3 containment facilities.

GP-BSL3 door signs will be provided after AVA's biosecurity inspection and certification.

The GP-BSL3 standard plant house and operating procedures shall meet all the requirements of the GM-BSL2 standard as well as those listed below. Note that references to plants or plant tissues in GP-BSL2 should be regarded as referring to all organisms when GP-BSL3 standards are being considered.

Construction

1. All structural joints in the plant house, including transparent sections, shall be fully sealed using an elastomeric sealant.
2. If the plant house is free-standing it shall have an anteroom for entry and exit. The innermost door shall have a door -closing device fitted. The anteroom shall be fitted with a sticky pest strip or automatic insecticide aerosol device designed to kill arthropods which gain entry. An anteroom is not necessary if the plant house connects directly with a certified small or large scale containment facility.

Operating Procedures

3. Personnel shall decontaminate their hands by washing with soap and warm water in the wash-basin provided on entering and leaving the plant house. When entering, personnel shall put on overshoes, covering clothes (e.g. gown/boiler suit) and a hat in the anteroom. These garments shall be removed on leaving the plant house and kept in the anteroom (or laboratory) between uses. They shall be laundered regularly.
4. Materials and equipment taken into or out of the plant house shall be treated by a technique demonstrated to be effective in destroying or removing all stages of the life-cycle of arthropods. This requirement applies to soil substitutes and where feasible to soil. Soil substitutes which can be readily decontaminated shall be used whenever possible. Use of soil is discouraged.

APPENDIX 12: PROCEDURES FOR EXPERIMENTS INVOLVING TRANSGENIC ANIMALS

Introduction

Genetic manipulation work which involves the use of animals includes:

- introduction of DNA into the fertilized oocyte or zygote or early embryo, or which may be carried out in or involve whole animals;
- introduction of a fragment of the whole genome or a virus into an embryo to produce a transgenic animal secreting infectious viral particles;
- use of genetically modified micro-organisms to infect animals.

All investigators and IBCs responsible for genetic manipulation work which involves transgenic animals should be familiar with the requirements of the NACLAR Guidelines on the Care and Use of Animals for Scientific Purposes and laboratory biosafety.

Procedures

(A) For Principal Investigators

Investigators planning work which will fall under Category B (i.e., production of transgenic animals) and which will not fall under Category A nor involve planned releases of genetically manipulated organisms should:

1. Complete a GMAC 'Proposal Form for Assessment of Genetic Manipulation Work'.
2. In addition, attach a description addressing each of the points listed in Appendix 13 (1- 8).
3. Submit the proposal to their IBC.
4. Do not initiate work involving these animals until IBC approval has been received.

(B) For Institutional Biosafety Committees

Upon receipt of a proposal for work with transgenic animals, the IBC should:

1. Assess the information provided in the proposal form and the description of the animal facilities. Points to consider in the design of facilities are laid out in Appendix 13.
2. Inspect the proposed facilities.
3. Either
 - (i) approve the proposed protocol and facilities, or
 - (ii) recommend additional precautions and give approval when these have been implemented.
4. Attach a copy of the terms of the approval if IBC approval is qualified in any way, or if additional conditions are required, and provide this advice to the investigator.

5. Ensure that the experimental protocol complies with standard requirements for experiments involving animals.
6. Notify GMAC of the IBC certification of the transgenic-animal holding facilities, and send a copy of the assessment and proposal forms, including IBC advice to relevant regulatory authorities for notification (if necessary).

APPENDIX 13: DESIGN OF ANIMAL FACILITIES

Introduction

Facilities for laboratory animals used for studies for genetic manipulation work of either an infectious or non-infectious nature should be physically separated from other activities such as animal production and animal quarantine.

Animals under experiment may be either small laboratory animals (e.g., mice, rabbits) or large domestic animals (e.g., pigs, sheep, cattle). The requirements for the housing and maintenance of the animals may differ in scale as a result, but the microbiological safety principles are similar.

Housing of transgenic animals

The particular point of concern with transgenic animals is that the result of any insertion of novel genetic material into the genome of an animal is unpredictable, both in terms of the expression of the new genetic material and regarding the effect of this material on neighbouring genes. Furthermore, any escape of the novel genetic material through either the escape of transgenic animals or through their interbreeding with wild or uncontained animals is potentially irreversible.

The containment for transgenic animals varies in different experiment systems. The nature of the containment required depend on the type of animal, the stages in the animals' life cycle that will be involved in the work, the number to be used, and the nature of the genetic manipulation.

Housing of infectious animals

Points to consider for the housing of animals in which infectious agents have been used, including transgenic animals produced by infectious agents.

1. The animal housing must comply with the NAACLAR guidelines on the care and use of animals for scientific purposes.
2. Laboratory animal facilities are an extension of the laboratory and may be integral to, and inseparable from, the laboratory.
3. As a general principle, the biological and physical containment recommended for working with infectious agents in vivo and in vitro are comparable.
4. The physical containment levels for work with infectious genetically manipulated animals follow the animal containment levels GA-BSL2 or GA-BSL3 as appropriate for the pathogen. Requirements for GA-BSL2 and GA-BSL3 animal containment facilities are set out in Appendices 14 and 15.

Points to consider

This section lists some points to consider in the design of facilities for genetic manipulation work involving the production of transgenic animals.

The containment required for transgenic animals varies among different experimental systems. The following points govern the nature of containment involved:

Details of Animal Involved

1. Class, genus and species of animal (if transgenic aquatic vertebrates are involved see Appendix 18)
2. Stages in life cycle that will be involved (embryo only to full maturity and reproduction).
3. Approximate number of animals involved at any one time.

Type of Work

4. Whether the work will involve:
 - (a) modification of germline cells;
 - (b) modification of somatic cells;
 - (c) intention to breed;
 - (d) use of genetically modified micro-organisms to infect animals;
 - (e) infectious agents used to produce transgenic animals

Details of the Genetic Manipulation

5. Depending on the type of work, the following points should be considered before deciding upon the level of animal containment (GA-BSL2 & GA-BSL3):
 - (i) nature of DNA to be inserted (origin and characterisation of DNA, references to published work, reference numbers of small-scale proposals covering preparation of the DNA);
 - (ii) method to be used for introducing the DNA (including details of the construction of any vector to be used, references to published work or reference numbers of small-scale proposals covering preparation of the vector, and containment level recommended for work with the vector);
 - (iii) likelihood of the technique to be used for introducing the DNA resulting in the animal bearing an agent potentially transmissible to animals in the same facility or to humans, and the possible routes of transmission;
 - (iv) reproductive capability of the genetically manipulated animal - is the inserted DNA likely to be heritable?

Other Work Being Performed in the Same Holding Facility

6. Are there any other animals being housed in the same facility? If so,
 - (i) how many animals are being housed?
 - (ii) are they all the same species and strain? (what other species are involved?)
 - (iii) what is the nature of any experimental work being carried out on the other animals (for example, infectious-disease work, or genetic manipulation work)? Is it likely that these experiments will interfere with the proposed work?
 - (iv) what arrangements are there to ensure that the other animals are kept separate from the transgenic animals?
 - (v) what procedures are in place for the identification of, and accounting for, individual animals?

Disposal of Animals

7. Bearing in mind the points to consider and the information provided above, consider what special precautions are needed, in addition to standard animal-house practices, regarding the disposal of animals.

Transport of Animals

8. If it is necessary to transport the animals alive from the holding facility to the laboratory or another facility, consider what precautions are needed to be taken in addition to the provisions set out in Section 6.2 of the Guidelines.

APPENDIX 14: REQUIREMENTS FOR GENETIC MODIFICATION ANIMAL BIOSAFETY LEVEL 2 (GA-BSL2)

Personnel must receive training in the handling of the animals to be used and an appropriate standard of work supervision must be maintained. The person responsible for the animal experiment must ensure that all those having contact with the animals and waste materials are familiar with the code of practice and are aware of any other precautions and procedures that may be required.

Adherence to the biosafety guidelines does not exempt researchers from practising responsible laboratory animal care and maintain basic welfare standards (useful references: Guidelines for the Care and Use of Animals for Scientific Purposes, NACLAR 2004; Guide to the Care and Use of Experimental Animals, Canadian Council on Animal Care). Researchers should also be aware that they are subject to Singapore laws that legislate against cruelty to animals. This is contained in Part IV of the Animals and Birds Act (Cap. 7).

These requirements are to be used in addition to the applicable requirements for Animal Biosafety Level 2 in the OSH Guidelines for Laboratories and Production Facilities in the Biomedical Sciences Industry and requirements for Genetic Modification Biosafety Level 2 in Appendix 7.

Construction

1. Entrance to the animal house must be posted with a sign identifying the type of animals housed and listing applicable procedures, including emergency and maintenance procedures.
2. The animal room must be constructed with impermeable and easily cleanable surfaces. Any openings in the walls or roof (e.g., windows or vents) must be screened with fine screens to prevent the entry and escape of insects and other pests. The doorway and room structure should be rodent-proof. Drainage exits in the floor should always contain water or disinfectant in the trap. Drain traps must be regularly cleaned and disinfected.
3. If the animal house is separated from the containment laboratories, an anteroom in which protective clothing and footwear can be stored is required.
4. An autoclave and/or incinerator for the sterilisation of waste materials must be available on site.

Operating Procedures

5. The animal facility must be inspected regularly by the IBC to ensure that its containment features are intact. Only people authorized by the IBC can enter the animal house. All such people should be trained in normal animal-house procedures as well as these operating procedures. A biosafety manual is prepared or adopted. Personnel are advised of special hazards, and are required to read and to follow instructions on practices and procedures. A record book should be maintained to provide an up-to-date inventory of the procedures performed.
6. Work surfaces are to be decontaminated after use and after any spill of viable material. Eating, drinking, smoking and the storage of food for human use is not

permitted in animal rooms. Personnel should wash their hands after handling cultures and animals and before leaving the animal room.

7. Suitable protective clothing, gloves and footwear should be worn. It is further recommended that such footwear and clothing not be worn in other areas. Protection against inhalation of aerosols, scratches or bites should be considered.
8. Bedding material and waste from animal cages or pens used to house animals infected with genetically modified organisms should be removed in such a manner as to minimise the creation of aerosols. This material should be autoclaved before removal from the animal containment unit.
9. Effective disinfectants must be available for immediate use.
10. Special attention should be paid to constraining animals during experiments. The prevention of their escape must be ensured.
11. Animals or animal tissue transported in or out of the animal house must be carried in closed containers. Animals involved in genetic manipulation experiments are not to be used for other purposes or to provide tissue for other purposes.
12. Cultures, tissues, or specimens of body fluids are placed in a container that prevents leakage during collection, handling, processing, storage, transport, or shipping. Live animals or animal tissue taken from the animal house must only go to another containment facility or be transferred to another organisation which has suitable animal containment facilities. (See Section 5, or requirements regarding the transfer of infectious materials.)
13. Carcasses of animals infected with genetically modified organisms must be rendered safe by sterilisation before disposal.
14. Insect and rodent control measures must be taken.
15. All incidents, including animal bites and scratches as well as spills and accidents which result in overt exposures to infectious materials are to be immediately reported to and recorded by the person responsible for the work. Medical evaluation, surveillance, and treatment are provided as appropriate and written records are maintained.
16. If genetic manipulation experiments are conducted on invertebrates or aquatic vertebrates, the following additional conditions apply:
 - (i) a mechanism should be provided to ensure that neither the organisms nor their gametes can escape into the supply or discharge system of the rearing container (e.g., tank or aquarium); the top of the rearing container should be covered to avoid escape of organisms and their gametes;
 - (ii) in the case of invertebrates that crawl, jump or fly, manipulated and non-manipulated animals should be kept apart;
 - (iii) measures should be taken to enable escaped invertebrates to be detected and recaptured or destroyed; for ticks and mites, containers should be kept over trays filled with oil;
 - (iv) all experimental cages/pens must be numbered and documented;
 - (v) used culture vessels must be decontaminated before disposal or thoroughly cleaned before reuse;

- (vi) flying or crawling arthropods should be handled on white trays to facilitate the detection of escape;
- (vii) the use of an electric insect-control unit should be considered;
- (viii) the activity of arthropods and the risk of accidental escape can be reduced by chilling.

It should be borne in mind that invertebrates can harbour infectious organisms, for example, viruses in mosquitoes, midges and biting flies in soft ticks, trypanosomes in triatomid bugs, organisms from sewage in mollusca, crustacea or echinodermata. Such invertebrates should be kept at a containment level appropriate to the risk from the human pathogens carried by these invertebrates.

APPENDIX 15: REQUIREMENTS FOR GENETIC MODIFICATION ANIMAL BIOSAFETY LEVEL 3 (GA-BSL3)

GA-BSL 3 and 4 facilities must be approved by the relevant regulatory agency before commencement of work. Personnel must be experienced in the handling of the animals to be used and a high standard of work supervision must be maintained. The person responsible for the animal experiment must ensure that all those having contact with the animals and waste materials are familiar with the code of practice and are aware of any other precautions and procedures that may be required. The requirements for GM-BSL3 laboratories also apply to animal facilities at GA-BSL3 level. In addition, the requirements for GA-BSL2 animal containment facilities shall be complied with in addition to the requirements below.

Adherence to the biosafety guidelines does not exempt researchers from practising responsible laboratory animal care and maintain basic welfare standards (useful references: Guidelines for the Care and Use of Animals for Scientific Purposes, NACLAR 2004; Guide to the Care and Use of Experimental Animals, Canadian Council on Animal Care). Researchers should also be aware that they are subject to Singapore laws that legislate against cruelty to animals. This is contained in Part IV of the Animals and Birds Act (Cap. 7).

These requirements are to be used in addition to the applicable requirements for Animal Biosafety Level 3 in the OSH Guidelines for Laboratories and Production Facilities in the Biomedical Sciences Industry and requirements for Genetic Modification Biosafety Level 3 in Appendix 8.

Construction

1. Entrance into GA-BSL3 animal facilities is limited to people aware of the potential hazards. The entrance door should be fitted key but freely accessible from inside. The door must be posted with signs identifying the facility and listing the applicable procedures. The name and telephone number of the animal-facility supervisor or another responsible person should be attached.
2. The GA-BSL3 facility must not be accessible to the general public or open onto a public thoroughfare.
3. The facility shall be constructed so that the finishes on walls, floors, ceilings and benches are smooth, impervious and easily cleanable on all surfaces and are able to withstand all relevant decontaminations.
4. All waste from the animal facility shall be decontaminated by autoclaving prior to disposal. When animals are in the room, floor drains should be sealed with an airtight plug.
5. The animal room should be sealable to permit fumigation. It should be possible to decontaminate the GA-BSL3 area independently with formaldehyde gas and for the gas to be discharged safely to the atmosphere upon completion.
6. The facility must have access to an autoclave either within the GA-BSL3 area or in the animal building.
7. The facility must have a hand basin and foot and elbow operated taps located near the exit.

8. Biological safety cabinets are to be used within the GA-BSL3 facility for containment of aerosols and control of infectious material. The cabinet should exhaust to the outside air through a HEPA filter or to the room air extract system.
9. Infected animals may be housed in isolators, safety cabinets, or containment units.

Operating Procedures

10. No other work is to be performed simultaneously with work requiring GA-BSL3 containment. The GA-BSL3 facility must be inspected at least annually by the IBC to ensure that its containment requirements are intact. Only people authorised by the IBC are to enter the animal facility and they can do so only after they have been advised of the potential hazards and meet any specific requirements (e.g., immunisation). A record should be maintained to provide an up-to-date inventory of the animals present and a chronological record of procedures performed.
11. The protective clothing and footwear must be removed before leaving the facility. Dirty clothing must be decontaminated, preferably autoclaved, before being laundered.
12. Special attention must be paid to containing animals during experiments and to the prevention of their escape.
13. Live animals must not leave the facility. Animal carcasses must be rendered safe by sterilisation before disposal. Animals used in genetic manipulation experiments are not to be used for other purposes or to provide tissue for other purposes.

APPENDIX 16: REQUIREMENTS FOR INSECTARY BIOSAFETY LEVEL 2 (GI-BSL2)

The following standards of insectary and operating procedures (GI-BSL2) are regarded as suitable minima for genetic manipulation work involving insects (and spiders/mites) which falls under Category B(i) in Section 3 of these Guidelines. Most work with *Drosophila melanogaster*, using the P-element as vector, will be adequately contained by these standards. They may also be sufficient for work with other insects and/or their pathogens where there is a high level of biological containment, e.g. only non-flying life-stages or strains of the insect, or genetically crippled strains of a pathogen are being used.

Work with genetically engineered insects, or in which insects will contain genetically engineered pathogens, which falls under Category A of these Guidelines will require at least BSL2 level of containment, and additional operating procedures and/or higher standard of construction may be recommended (see Appendix 17).

Construction

1. The insectary shall be fitted with a double self-closing door that provides a seal sufficient to contain the insect species under study. The door should preferably be unmeshed. The insectary shall also be free of other possible escape routes, e.g. false ceilings. Windows shall be closed at all times and, preferably, permanently sealed. If there are sinks, the outlets shall have water traps or other suitable measures to prevent escape.
2. Entrances shall be clearly labeled with signs stating that the room contains genetically manipulated insects.
3. Signs explaining handling procedures shall be displayed inside the room.
4. All air-conditioning inlets and outlets shall be covered with gauze of a sufficient gauge to prevent insects passing through.
5. The insectary shall be fitted with at least one electric insect trap or, for *Drosophila* work only, more than one yeast-based *Drosophila* trap. Yeast traps must be regularly replaced and the IBC must be satisfied that their number, composition and operation yield effective recapture rates that are equivalent to those of an electric trap. Similarly, for other insects, appropriate traps, e.g. pheromone/kairomone, shall be installed where necessary.

Operating procedures

6. General practices shall be as required for GM-BSL2 laboratory work.
7. Manipulated and non-manipulated insects shall be kept in separate containers except where genetic crosses have to be made. Such crosses shall be clearly labeled and treated as manipulated insects.
8. All insects shall be kept in cages or other suitable containers. All cages/containers shall be clearly labeled and a central logbook of all recombinant insect stocks kept in the laboratory. Imported recombinant insects shall be indicated as such in the logbook.

9. All containers and material wastes shall be adequately sealed before disposal and deposited in clearly labeled bins prior to decontamination using approved methods.
10. All containers that contain or have contained manipulated insects shall be decontaminated prior to disposal.
11. Material to be autoclaved shall be transported to an autoclave in an adequately sealed bag.
12. The room shall be kept free of material wastes.

APPENDIX 17: REQUIREMENTS FOR INSECTARY BIOSAFETY LEVEL 3 (GI-BSL3)

Note on insectaries with higher containment than GI-BSL2

GI-BSL 3 and 4 facilities must be approved by the relevant regulatory agency before commencement of work. Certain experiments with genetically engineered insects (Category B(i) in Section 3) or with insects containing genetically engineered pathogens (Category A(iii) in Section 3) may warrant the use of insectaries with additional containment features and operating procedures higher than those of BSL2 (see Appendix 16). Each project will be considered on an individual basis, and in many cases additional operating procedures to be used with a GI-BSL2 facility rather than a GI-BSL3 may be recommended. The following requirements are recommended for institutions which may be planning to build insectaries providing containment greater than GI-BSL2.

The notes in this Appendix are provided so that IBCs can identify some of the requirements which need to be incorporated into the design of GI-BSL3 containment facilities.

The GM-BSL3 standard insectary and operating procedures shall meet all of the requirements in the BSL2 standard as well as those listed below.

Construction

1. The outermost door of the insectary shall be fitted with a fire-escape lock accessible from the outside only by using a key but freely accessible from the inside.
2. The insectary shall be provided with an access room and anteroom located in series. The access room shall be finished with dark coloured walls and have no direct source of natural or artificial lighting. Directional entry and exit signs inside the access room should preferably be in luminous paint. Both the anteroom and access room should be fitted with insect traps of the high voltage electrical type or chemical spray type. Access room doors should be sealed to be insect-proof and preferably be electrically interlocked so that only one door is open at a time. The anteroom shall be provided with a wash-basin and vacuum system to enable staff to remove any insects, eggs or larvae from their person before leaving the facility.
3. The joins between any structural components of the insectary shall be sealed. Transparent sections, e.g. windows, shall be made of an impact-resistant material. Windows shall be permanently sealed.
4. Air supply and exhaust ducts shall be fitted with fine screens (thirty-gauge 30/32 mesh wire gauze) and designed so as to preclude insect escape.
5. The insectary shall be provided with contained cabinets for handling/transfer of insects.

Operating procedures

6. The insectary shall only be accessible to those people directly involved in laboratory work. Works are to be carried out by personnel having specific training in handling insects and are directed by competent scientists.
7. Personnel shall decontaminate their hands by washing with soap and warm water in the wash-basin provided on entering and leaving the insectary. When entering, personnel shall put on overshoes and covering clothes (boiler suit style) and hat in the anteroom. Before personnel leave the insectary, stray insects shall be removed from these garments with the vacuum device provided, and the garments removed and kept in the anteroom between uses. Prior to washing (or disposal), garments shall be sealed in bags and autoclaved.
8. Materials taken into and out of the insectary shall be treated with a technique demonstrated to be effective in destroying or removing all stages of the life-cycle of insects and their pathogens. This requirement applies to soil substitutes and soil. Soil substitutes which can be readily decontaminated shall be used in preference to soil.

APPENDIX 18: PROCEDURES FOR EXPERIMENTS INVOLVING FISH AND OTHER AQUATIC ORGANISMS

Genetic manipulation work involving the use of fish and other aquatic organisms includes:

- production or use of transgenic aquatic organisms;
- use of genetically modified microorganisms to infect aquatic organisms.

The primary objective in designing containment facilities and procedures for genetic manipulation work involving aquatic organisms is to prevent escape of transgenic aquatic organisms or recombinant infectious agents into natural waterways.

Proposals for such work will be examined by IBC on a case-by-case basis. Investigators submitting proposals for research involving transgenic aquatic organisms shall describe in the proposal the containment facilities to be used and procedures proposed for treatment of waste water from the facility.

Adherence to the biosafety guidelines does not exempt researchers from practising responsible laboratory animal care and maintain basic welfare standards (useful references: Guide for the Care and Use of Laboratory Animals, National Research Council, 1996 and Guide to the Care and Use of Experimental Animals, Canadian Council on Animal Care). Researchers should also be aware that they are subject to Singapore laws that legislate against cruelty to animals. This is contained in Part IV of the Animals and Birds Act (Cap. 7).

The following general guidelines are provided regarding the basic requirements for genetic manipulation work involving aquatic organisms.

General

- The rearing area shall be confined in a secured building and be restricted to authorized personnel only.
- All water shall leave the plant through a common drain.
- All effluent water shall be passed through at least two screens. The size of the screening shall be set to retain the smallest life history stage of the organisms in use. The screens shall be cleared regularly to prevent blockage and overflow.
- Effluent water shall not discharge into a major system containing related fish species.
- The building shall be structurally sound and of sufficient elevation to preclude flooding or unintentional escape of these transgenic organisms.

Work with transgenic aquatic organisms

- To prevent escape of adult aquatic organisms into the sewerage system, a grill or mesh, with an appropriate grid size to prevent passage of adults of the species being used, shall be fitted to outlets used for disposal of tank water.
- Water from tanks containing only adult transgenic aquatic organisms, and not involving use of recombinant infectious agents, may be discarded untreated down the sink, provided that a filtering mechanism to retain adult aquatic organisms is in place.
- Tank water that has any potential to contain embryos, sperm, eggs or larvae of transgenic aquatic organisms shall be treated to ensure inactivation of viable

transgenic material before disposal. The proposed treatment procedures and evidence for their efficacy shall be provided to AVA for case-by-case assessment.

- Since many fish species have sticky eggs which attach firmly to substrates, nets and other equipment used in the tank during spawning shall be sterilised after use. If fish are induced to spawn on the sides of tanks, the tanks shall be decontaminated after use by a procedure of demonstrable efficacy in sterilising eggs and sperm for the species used.

Work with infectious recombinant microorganisms in aquatic organisms

- General practices shall be as required for GM-BSL2 or GM-BSL3 laboratory work depending on the microorganism.
- To prevent escape of adult aquatic organisms into the sewerage system, a grill or mesh, with an appropriate grid size to prevent passage of adults of the species being used, shall be fitted to outlets used for disposal of tank water.
- Tank water used for work with infectious recombinant microorganisms, or tank water that has any potential to contain embryos, sperm, eggs or larvae of infected aquatic organisms, shall be treated to ensure inactivation of viable material before disposal. The proposed treatment procedures shall be provided to AVA for case-by-case assessment.

APPENDIX 19: REGULATED ORGANISMS

Please note that all organisms under CDC Risk Group 4 are strictly prohibited. Organisms under CDC Risk Group 3 (as listed below) requires special permission from the relevant authorities.

BACTERIA, CHLAMYDIA, RICKETTSIAE AND MYCOPLASMA

Bacillus anthracis
Brucella spp
Franciscella tularensis
Mycoplasma agalactiae
Mycoplasma mycoides var *mycoides* (contagious bovine pleuropneumonia)
Pseudomonas mallei (Glanders)
Rickettsia ruminantium (Heart water)

PARASITES

Babesia equi (Equine piroplasmiasis)
Babesia caballi (Equine piroplasmiasis)
Chrysomya bezziana (Screw-worm fly)
Ehrlichia sp (Potomac fever)
Psoroptes ovis (Sheep scab)
Theileria parva sp (East coast fever)
Trichinella spiralis (Trichinosis)
Trypanosoma evansi (Surra)
Trypanosoma equiperdum (Dourine)

VIRUSES

Family and genus

Arteriviridae

Regulated species

Equine viral arteritis
 Porcine reproductive respiratory syndrome

Bunyaviridae

Bunyavirus
 Nairobi virus
 Phlebovirus

Cache Valley
 Nairobi sheep disease
 Rift Valley fever

Caliciviridae

Calicivirus

Vesicular exanthema

Circoviridae

Circovirus

Chicken anaemia

Coronaviridae

Coronavirus

Transmissible gastro -enteritis

* This list is not exhaustive. Importation of other animal disease organisms may be prohibited. An additional list of prohibited organisms from the Bio-Security Assurance Arrangement (published by AVA) and the Notifiable Diseases list of the Animal and Birds Act are included in this Appendix. The Agri-food and Veterinary Authority should be consulted for updates to the following lists of prohibited organisms from the Bio-Security Assurance Arrangement Guidelines of the Agri-food and Veterinary Authority and the Notifiable Diseases list of the Animal and Birds Act.

VIRUSES (cont'd)**Family and genus***Flaviviridae*

Flavivirus

Pestivirus

Herpesviridae

Alphaherpesvirinae

Orthomyxoviridae

Influenza A and B

Paramyxoviridae

Paramyxovirus

Morbillivirus

Picornaviridae

Aphthovirus

Enterovirus

Poxviridae

Capripoxvirus

Reoviridae

Orbiviruses

Retroviridae

Lentivirus

Rhabdoviridae

Lyssavirus

Vesiculovirus

Regulated species

Japanese encephalitis

St. Louis encephalitis

Wesselsbron disease

Hog cholera (Classic swine fever)

Duck plague

Malignant catarrhal fever

Pseudo rabies (Aujeszky's disease)

Avian influenza

Equine influenza

Swine influenza

Newcastle disease (exotic)

Rinderpest

Pest des petites ruminant

Foot-and mouth disease

Swine vesicular disease

Duck viral hepatitis

Goat pox

Sheep pox

Lumpy skin disease

African horse sickness

Bluetongue (exotic)

Equine encephalosis

Jembrana disease

Maedi/visna

Rabies

Rabies related: Duvenhage, Fin,

Kotonkan, Lagos bat, Mokola,

Obodhiang

Chandipura, Piry, Porton S, Vesicular

stomatitis - New Jersey, Indiana,

Indiana 2 (Cocal), Indiana 3 (Alagoas),

Indiana 4 (Maraba)

VIRUSES (con't)**Family and genus***Togaviridae*

Alphavirus

Regulated species

Eastern equine encephalitis
 Western equine encephalitis
 Venezuelan equine encephalitis

Not Classified

African swine fever

Scrapie agent (prion)

Scrapie
 Bovine spongiform encephalopathy
 Spongiform encephalopathies of other animals

REFERENCE

Geering, W A and Forman, A J, *Exotic Animal Diseases: A Field Manual for Australian Veterinarians* (1995), Australian Government Publishing Service, Canberra.

PESTS**BACTERIA***Corynebacterium flaccumfaciens**C. nebraskense**C. sepedonicum***MAIN HOST**

Soybean

Maize

Potato

COMMON NAME

Wilt soya

Leaf freckles and wilt

Bacteria ring rot

*Pseudomonas garcae**P. syringae*

Coffee

Maize

Bacterial leaf spot

Spot, leaf blight, top rot

*Xanthomonas ampelina**Xanthomonas campestris* pv. *cassavae**X. phaseoli*

Grape

Cassava

Mung bean

Blight

Leaf spot

Common blight

FUNGI*Aecidium cantensis**Angiosorus solani**(Thecophora solani)*

Potato

Potato

Deforming rust

Thecophora smut

*Ascochyta gossypii**(A. phaseolorum)*

Cotton

Ascochyta blight

*Cercospora elaeidis**Claviceps gigantea**Cochliobolus carbonum**(Drechslera zeicola)*

Oil palm

Maize

Maize

Freckle

Ergot, Horse's tooth

Charred ear mould

*Colletotrichum coffeanum**Crinipellis perniciosus**(Marasmius perniciosus)*

Coffee

Cocoa

Coffee berry disease

Witches broom

*Cryptosporella eugeniae**Deuterophoma tracheiphila**(Phoma tracheiphila)*

Clove

Citrus

Dieback

Mal secco

PESTS (cont'd)		
FUNGI	MAIN HOST	COMMON NAME
<i>Diaporthe phaseolorum</i> var. <i>caulivora</i>	Soybean	Stem canker
<i>Erysiphe polygoni</i>	Mango	Powdery mildew
<i>Fusarium oxysporum</i> f.sp. <i>elaeidis</i>	Oil Palm	Fusarium wilt
<i>F. xylarioides</i> (<i>Gibberella xylarioides</i>)	Coffee	Tracheomyces
<i>Hemileia coffeicola</i>	Coffee	Powdery rust, grey leaf rust
<i>Marasmiellus cocophilus</i>	Coconut	Lethal bole
<i>Microcyclus ulei</i>	Rubber	South American Leaf Blight
<i>Moniliophthora roreri</i> (<i>Monilia roreri</i>)	Cocoa	Pod rot, watery pod rot
<i>Mycena citricolor</i> (<i>Omphalia flavida</i>)	Coffee	American leaf spot
<i>Mycosphaerella fijiensis</i> var. <i>difformis</i>	Banana	Black sigatoka
<i>Peronospora tabacina</i>	Tobacco	Blue mould
<i>Phaeolus manihotis</i>	Cassava	Root rot
<i>Phoma exigua</i> var. <i>fourata</i> (<i>P. exigua</i> var. <i>exigua</i>)	Potato	Gangrene
<i>Phiomopsis theae</i>	Tea	Stem canker
<i>Phyrenotrichopsis omnivorum</i>	Cotton, Groundnut	Texas root rot
<i>Polyscytalium pustulans</i> (<i>Oospora pustulans</i>)	Potato	Skin spot
<i>Puccinia pittieriana</i> <i>P. psidii</i>	Potato Guava	Common rust Guava rust
<i>Sphaceloma arachidis</i> <i>S. manihoticola</i>	Groundnut Cassava	Scab Super elongation
<i>Synchytrium endobioticum</i>	Potato	Black wart, Black scab
<i>Trachysphaera fructigena</i>	Coffee, Cocoa	Trachysphaera pod rot
<i>Verticillium albo-atrum</i>	Groundnut	Verticillium wilt
<i>V. dahliae</i>	Groundnut	Verticillium wilt
INSECTS		
<i>Acanthosellides obtectus</i>	Mung Bean	Bean bruchid
<i>Anastrepha obliqua</i>	Citrus	West Indian fruit fly
<i>A. fraterculus</i>	Citrus	South American fruit fly
<i>A. ludens</i>	Citrus	Mexican fruit fly
<i>A. spp.</i>	Citrus	Fruit fly
<i>Antestiopsis</i> spp.	Coffee	Antestia bug
<i>Antliomomus vestitus</i>	Cotton	Peruvian cotton boll weevil

PESTS (cont'd)**INSECTS**

	MAIN HOST	COMMON NAME
<i>A. grandis</i>	Cotton	Mexican cotton boll weevil
<i>Aonidomytilus albus</i>	Cassava	Cassava scale
<i>Bathycoella thalassina</i>	Cocoa	Cocoa bug
<i>Bruchus pisorum</i>	Mung Bean	Pea pod weevil
<i>Caliotlirips masculinus</i>	Cassava	Thrips
<i>Ceratitis rosa</i>	Citrus	Natal fruit fly
<i>C. capitata</i>	Citrus	Mediterranean fruit fly
<i>Chaetanaphotrips orchidii</i>	Banana	Banana rust thrip
<i>Chrysomplialus aonidium</i>	Citrus	Florida red scale
<i>Coclaenomenodera elaeidis</i>	Coconut	Leaf miner
<i>C. elaeidis</i>	Oil Palm	Leaf miner
<i>Dacus tryoni</i>	Citrus	Queensland fruit fly
<i>Diatrea abbreviatus</i>	Sugarcane	Sugarcane root stalk borer
<i>Distantiella theobroma</i>	Cocoa	Cocoa Capsid
<i>Epilaelina varivestis</i>	Mung Bean, Soybean	Mexican bean beetle
<i>Eugcepes poslfasciatus</i>	Sweet potato	West Indian sweet potato Weevil
<i>Helopeltis bergrothi</i>	Cocoa	Helopeltis bug
<i>Hercinotlirip bicinctus</i>	Banana	Banana thrip
<i>Rynchophorus phoenicis</i>	Oil palm	African palm weevil
<i>Leguminivora glycinivorella</i>	Soybean	Soybean pod borer
<i>Leptinotarsa decemilineata</i>	Potato	Colorado potato beetle
<i>Leptopharsa heveae</i>	Rubber	Lace bug
<i>L. gibbicarina</i>	Oil Palm	
<i>Leucoptera coffeella</i>	Coffee	Coffee leaf miner
<i>Lissorhoptrus oryzepilus</i>	Rice	Rice water weevil
<i>Melittomma insulare</i>	Coconut	Wood borer
<i>Menalonium sp.</i>	Cocoa	Mirid bug
<i>Noorda albizonalis</i>	Mango	
<i>Oryctes boas (=O. monoceros)</i>	Coconut	Rhinoceros beetle
<i>Pachymerus lacerdae</i>	Oil palm	Kernel borer
<i>Pachymerus nucleorum</i>	Oil palm	Kernel borer
<i>P. nucleorum</i>	Coconut	Coconut borer
<i>Pimelephila ghesquierii</i>	Oil palm	Palm moth
<i>Planococcus kenyae</i>	Coffee	Kenya mealy bug
<i>Prostephanus truncatus</i>	Maize	Large grain borer
<i>Pseudothraupis wayi</i>	Coconut	Coreid bug
<i>Quadraspidiotus perniciosus</i>	Citrus	San jose scale
<i>Rynchophorus palniaruni</i>	Coconut	South American palm Weevil
<i>Sacododes pyralis</i>	Cotton	False pink boll worm
<i>Sahlbergella singularis</i>	Cocoa	Cocoa Capsid
<i>Sesamia cretica</i>	Maize	Durra/sorghum stalk borer
<i>Sophronica ventralis</i>	Coffee	Berry borer
<i>Stenoma decora</i>	Cocoa	Cocoa shoot

PESTS (cont'd)**INSECTS**

Trogoderma granarium
Xyleborus ferrugineus

MAIN HOST

Rice
 Cocoa

COMMON NAME

Khapra beetle
 Black twig borer

MITES

Aceria guerreronis
 (= *Eryophyes guerreronis*)

Coconut

Coconut mite

Monochellus tanajoa
 (= *Ononychelie tanajoe*)

Cassava

Oligonychus peruvianus
 (= *Homonychus peruvianus*)

Cassava

MYCOPLASMA/MYCOPLASMA LIKE ORGANISMS

Mycoplasma - like organism
 (MLO)

Apple

Flat limb

(Mycoplasma - like organism)

Banana

Cameroon marbling
 disease

Coconut

Lethal yellowing

Grape

Flavescence doree

Grape

Pierce's disease

Oil palm

Leaf mottle

Phytomonas staheli

Oil palm

Sudden wjijer

Phytomonas sp.

Corn

--

Spiroplasma citri

Citrus

Stubborn disease

S. kunkehi

Corn

Corn stunt

Sugarcane

Grassy root

NEMATODES

Anguina agrostis

Bent grass,
 Rye grass

Seed gall nematode

A. graminis

Bent grass

Seed gall nematode

A. tritici

Rye, Wheat

Seed gall nematode

Aphasmatylenchus straturatus

Shea butter trees,
 Soybean

-

Aphelenchoides arachidis

Groundnut

Testa, nematode

A. blastophorus

Ornamental, Rose

Stern and bulb nematode

A. fragariac

Ferns, Strawberry

Bud & leaf spring dwarf

A. liliurn

Lily

Bud nematode

Bursaphelenchus lignicolus

Pine

Pine wilt nematode

Ditylenchus destructor

Carrot, Dahlia,
 Irish, Potato, Tulips

Potato rot nematode

D. destructor

Mushroom

Potato rot

D. myceliophagus

Mushroom

Mushroom nematode

Globodera pallida

Potato

Cyst nematode

PESTS (cont'd)**NEMATODES***Hemicycliophora arenaria***MAIN HOST****COMMON NAME**Chilly, Citrus
Cucumber, Grape

Sheath nematode

Heterodera avenae

Grasses, Oat, Rye, Oat cyst nematode

Wheat

H. cacti

Cactus

Cactus cyst nematode

H. cajani

Cashew

Cashew cyst nematode

H. carotae

Carrot

Cyst carrot

H. cruciferae

Crucifer

Crucifer cyst

H. cyperi

Carrot

Cyst nematode

H. fici

Ficus cari

Fig cyst nematode

H. geottingiana

Field bean,

Pea cyst nematode

Soybean,

Sweet pea, vetches

H. longicaudata

Grasses, Wheat

Cyst nematode

H. oryzicola

Rice

Rice cyst nematode

H. sacchari

Sugarcane

Sugarcane cyst nematode

H. schactii

Cabbage, Mustard,

Sugarbeet cyst

Sugarbeet

H. sorghi

Sorghum

Sorghum cyst nematode

H. vignae

Pea

Pea cyst nematode

H. zaeae

Maize

Corn cyst nematode

Hirschmanniella miticausa

Taro

Taro nematode

H. spinicaudata

Rice, Rose

Rice root tip nematode

Hoplolaimus colombus

Grasses, Maize,

Lance nematode

Sorghuni,

H. colombus lance

Soybean

Lance nematode

H. indicus

Banana, Brassica,

Lance nematode

Cabbage, Chilly, Citrus,

Mango, Millet, Peach,

Peas, Rice, Sorghum,

Spinach, Sweet pea,

Sugarcane

H. indicus lance

Guava, Rice,

Lance nematode

Wheat

H. pararobustus

Banana, Coffee,

Lance nematode

Mango, Oil palm, Guava,

Papaya, Sugarcane, Tea

H. pararobustus

Rice

Lance nematode

Longidorus attenuatus

Cabbage, Carrot,

Needle nematode

Clove, Grape,

Lucerne, Pumpkin,

Rye grass, Strawberry,

Sugarbeet, Wheat

Macroposthonia xenoplex

Bonsai, Carnations, Ring nematode

Grape

PESTS (cont'd)**NEMATODES**

	MAIN HOST	COMMON NAME
<i>Meloidogyne africana</i>	Coffee	Root knot nematode
<i>M. baurensis</i>	Soybean	Root knot nematode
<i>M. brevicauda</i>	Tea	Root knot nematode
<i>M. chitwoodi</i>	Grasses	Root knot nematode
<i>M. coffeicola</i>	Coffee	Root knot nematode
<i>M. decalineata</i>	Coffee	Root knot nematode
<i>M. exigua</i>	Chilly, Citrus, Coffee, Pepper, Tea, Watermelon	Root knot nematode
<i>M. graminis</i>	Grasses	Root knot nematode
<i>M. indica</i>	Citrus	Root knot nematode
<i>M. inornata</i>	Soybean, Tobacco	Root knot nematode --
<i>M. mali</i>	Apple, Grape Prune, Rose	Root knot nematode
<i>M. megadora</i>	Coffee	Root knot nematode
<i>M. naasi</i>	Grasses, Onion, Rye, Sugarbeet	Root knot nematode
<i>M. oteifae</i>	Coffee	Root knot nematode
<i>Merlinius brevidens</i>	Alfaifa, Banana, Brassica, Carrot, Cress, Cucumber, Cumin, Garlic, Grape, Hop, Linseed, Maize, Oats, Olive, Onion, Peas, Rose, Rye, Sugarcane, Sweet pea, Wheat	----
<i>Nacobbus aberrans</i>	Cabbage, Cactus, Carrot, Cucumber, Lettuce, Radish, Sugarbeet, Sweet pea, Turnip	False root knot
<i>Pratylenchus fallax</i>	Cherry, Chrysanthemum, Ornamental, Rose, Strawberry	Lesion nematode
<i>P. neglectus</i>	Crucifer, Peppermint, Strawberry	Lesion nematode
<i>P. .thornei</i>	Apple, Cherry, Grape, Grasses, Maize, Onion, Ornamental, Pear, Plum, Strawberry, Sugarbeet, Sugarcane, Wheat	Lesion nematode
<i>P. zeae</i>	Barley, Rye	Lesion nematode

PESTS (cont'd) NEMATODES	MAIN HOST	COMMON NAME
<i>Punctodera punctata</i>	Grasses, Oats, Sweet pea, Wheat	Cyst nematode
<i>Rhadinaphelenchus cocophilus</i>	Bent grass, Coconut, Oil palm	Red ring nematode
<i>Scutellonema bradys</i>	Banana, Cassava, Maize, Oil palm, Papaya, Pineapple, Rubber	Yam rot nematode
<i>Trichodorus viruliferus</i>	Grape, Sugarbeet, Sweet pea, Wheat,	Stubby root nematode
<i>Xiphinema index</i>	Citrus, Fig, Grape, Walnut, Prune	Dagger nematode

VIRUSES	MAIN HOST
African cassava mosaic virus	Cassava
<i>Axithocyanosis</i>	Cotton
Arabis mosaic virus	Grape
Artichoke Italian latent virus	Grape
Blister spot virus	Coffee
Bunchy top virus	Papaya
Cassava brown streak virus	Papaya
Cassava witches boom virus	Cassava
Corky bark virus	Grape
Corn stunt virus	Maize
Dwarf virus	Rice
Dwarf virus	Sugarcane
Dwarf virus	Sweet potato
Fan leaf virus	Grape
Hoja blanca virus	Rice
Hungarian chrome mosaic virus	Grape
Internal cork virus	Sweet potato
Leaf crumple virus	Cotton
Leaf curl virus	Cotton
Leaf mosaic virus	Cotton
Leaf mottle virus	Cotton
Leaf roll virus	Grape
Leaf virus	Grape
Marginal chlorosis virus	Groundnut
Mosaic virus	Maize
Mosaic virus	Papaya
Mosaic virus	Rubber
Mosaic virus	Sweet potato
Peach rosette mosaic grape	Grape
Peanut stunt virus	Maize
Pliloem necrosis virus	Tea
Rayado fino virus	Tea
Red mottle virus	Cocoa

PESTS (cont'd)**VIRUSES**

Rice transitory yellowing virus	Rice
Rice yellow mottle virus	Rice
Stem pitting virus	Grape
Stenosis, small leaf	Cotton
Streak virus	Maize
Terminal stunt	Cotton
Tobacco ringspot virus	Soybean
Waialua disease	Papaya
Wrinkled stunt and witches brown	Rice virus
Yellow spot virus	Pineapple
Yellow vein banding virus	Cocoa

DISEASE OF UNKNOWN ETIOLOGY

Awka	Coconut
Bristle tip	Coconut
Coconut wilt	Coconut
Frog's skin	Cassava
Head droop	Coconut
Kerala wilt	Coconut
Leaf mottle	Coconut
Leaf scorch	Coconut
Little leaf	Coconut
Mango malformation	Mango
Thatipaka wilt	Coconut

PARASITES

AGENT	DISEASE
<i>Babesia bigemina</i>	Bovine babesiosis
<i>Babesia bovis</i>	Bovine babesiosis
<i>Babesia caballi</i>	Equine piroplasmiasis
<i>Babesia equi</i>	Equine piroplasmiasis
<i>Chorioptes species</i>	Horse mange
<i>Chrysomya bezziana</i>	Old World screwworm
<i>Cochliomyia hominivorax</i>	New World screwworm
<i>Cowdria ruminantium</i>	Heartwater
<i>Echinococcus granulosus</i>	Echinococcosis/hydatidosis
<i>Leishmania species</i>	Leishmaniasis
<i>Taenia metacestodes</i>	Cysticercosis of bovine and porcine origin
<i>Theileria species</i>	Theileriosis
<i>Toxoplasma gondii</i>	Toxoplasmosis
<i>Trichinella species</i>	Trichinellosis
<i>Trichomonas species</i>	Trichomonosis
<i>Trypanosoma equiperdum</i>	Dourine
<i>Trypanosoma evansi</i>	Surra
<i>Trypanosoma species</i>	Trypanosomiasis

BACTERIA, RICKETTSIAE, CHLAMYDIA & MYCOPLASMAS

AGENT	DISEASE
<i>Anaplasma centrale</i>	Bovine anaplasmosis
<i>Anaplasma marginale</i>	Bovine anaplasmosis
<i>Bacillus anthracis</i>	Anthrax
<i>Borrelia burgdorferi</i>	Lyme disease
<i>Brucella abortus</i>	Bovine brucellosis
<i>Brucella abortus</i>	Porcine brucellosis
<i>Brucella melitensis</i>	Caprine/ovine brucellosis
<i>Burkholderia mallei</i>	Glanders (Farcy)
<i>Burkholderia pseudomallei</i>	Melioidosis
<i>Campylobacter fetus</i> subspecies <i>veneraelis</i>	Bovine genital campylobacteriosis
<i>Chlamydia psittaci</i>	Psittacosis (ornithosis)
<i>Clostridium chauvoei</i>	Black quarter (blackleg)
<i>Corynebacterium</i> <i>pseudotuberculosis</i>	Ulcerative lymphangitis
<i>Coxiella burnetii</i>	Q fever
<i>Dermatophilus congolensis</i>	Dermatophilosis
<i>Erysipelothrix rhusiopathiae</i>	Swine erysipelas
<i>Escherichia coli</i> O157	<i>Escherichia coli</i> O157
<i>Francisella tularensis</i>	Tularaemia
<i>Histoplasma farciminosum</i>	Epizootic lymphangitis
<i>Leptospira interrogans</i>	Leptospirosis
<i>Listeria monocytogenes</i>	Listeriosis
<i>Mycobacterium avium</i> subsp. <i>paratuberculosis</i>	Paratuberculosis
<i>Mycobacterium avium</i> subspecies <i>avium</i>	Avian tuberculosis
<i>Mycobacterium bovis</i>	Bovine tuberculosis
<i>Mycoplasma agalactiae</i>	Contagious agalactia
<i>Mycoplasma capricolum</i> subsp. <i>capripneumoniae</i>	Contagious caprine pleuropneumonia
<i>Mycoplasma gallisepticum</i>	Avian mycoplasmosis
<i>Mycoplasma mycoides</i> subsp. <i>mycoides</i>	Contagious bovine pleuropneumonia
<i>Mycoplasma synoviae</i>	Avian mycoplasmosis
<i>Pasteurella hemolytica</i>	Ulcerative lymphangitis
<i>Pasteurella multocida</i>	Fowl cholera and Haemorrhagic septicaemia
<i>Salmonella abortusovis</i>	Salmonellosis
<i>Salmonella enteritidis</i>	Salmonellosis
<i>Salmonella gallinarum</i>	Fowl typhoid
<i>Salmonella pullorum</i>	Pullorum disease
<i>Streptococcus equi</i> subsp. <i>equi</i>	Strangles
<i>Taylorella equigenitalis</i>	Contagious equine metritis

VIRUSES AND PRIONS

FAMILY	GENUS	SPECIES	DISEASE
AFS-like virus			African swine fever
Arenaviridae	Unclassified	LC virus	Lymphocytic choriomeningitis
Birnaviridae	Unclassified	IBD virus	Infectious bursal disease (Gumboro disease)
Bunyaviridae	Hantavirus	6 species	Hanta virus disease
Bunyaviridae	Nairovirus	NSD virus	Nairobi sheep disease
Bunyaviridae	Bunyavirus	RVF virus	Rift Valley fever
Caliciviridae	Unclassified	RHD virus	Rabbit haemorrhagic disease
Coronaviridae	Coronavirus	IBV	Avian infectious bronchitis
Filoviridae	Unclassified	Ebola virus	Ebola disease
Filovirus	Unclassified	Marburg virus	Marburg disease
Flaviviridae	Flavivirus	JE virus	Japanese B encephalitis
Flaviviridae	Flavivirus	MVE virus	Murray Valley Encephalitis
Flaviviridae	Pestivirus	SFV (or HCV)	Swine fever
Flaviviridae		YF virus	Yellow Fever
Herpesviridae (alpha)	Porcine herpesvirus 1	ADV	Aujeszky's disease (Pseudorabies)
Herpesviridae (alpha)	Avian herpesvirus 1		Avian infectious laryngotracheitis
Herpesviridae (alpha)	Duck herpesvirus 1	DE virus	Duck virus enteritis (duck plague)
Herpesviridae (alpha)	Equine herpesvirus types 1 & 4	EHV-1 and EHV-4	Equine rhinopneumonitis
Herpesviridae (alpha)	Bovine herpesvirus 1	IBR virus	Infectious bovine rhinotracheitis
Herpesviridae (alpha)	Avian herpesvirus 2	MDV serotype 1	Marek's disease
Herpesviridae (alpha)	Cercopithecine herpesvirus 1	Simian B Herpes virus, or "B virus"	Simian B Herpes virus
Orthomyxoviridae	Influenzavirus A	EI virus	Equine influenza
Orthomyxoviridae	Influenzavirus A	AI virus	Fowl plague (avian influenza)
Ovine herpesvirus-2			Bovine malignant catarrh
Paramyxoviridae		Menangle virus	Menangle virus disease
Paramyxoviridae	Paramyxovirus	NDV PMV type 1	Newcastle disease
Paramyxoviridae	Unclassified	Nipah virus	Nipah virus disease
Paramyxoviridae	Morbillivirus		Peste des petits ruminants
Paramyxoviridae	Morbillivirus	Rinderpest virus	Rinderpest
Paramyxoviridae	Parainfluenza virus 1	Sendai virus	Sendai virus infection
Paramyxovirus	Morbillivirus	Hendra virus	Hendra virus disease
Picornaviridae	Enterovirus	DH virus	Duck virus hepatitis
Picornaviridae	Enterovirus	SVD virus	Swine vesicular disease
Picornavirus	Aphthovirus	FMD virus	Foot-and-mouth disease
Poxviridae	Avipoxvirus	Fowlpox virus	Fowl pox
Poxviridae		Uasin Gishnu virus	Horse pox
Poxviridae	Leporipoxvirus	Myxoma virus	Myxomatosis
Poxviridae	Capripoxvirus	SP virus / GP virus	Sheep pox/goat pox
Poxviridae	Capripoxvirus	LSD virus	Lumpy skin disease

FAMILY	GENUS	SPECIES	DISEASE
Reoviridae	Orbivirus	AHS virus	African horse sickness
Reoviridae	Orbivirus	Bluetongue virus	Bluetongue
Reoviridae	Orbivirus	Eq encephalosis virus	Equine encephalosis
Retroviridae	Lentivirus	CAE virus	Caprine arthritis/encephalitis
Retroviridae	Unclassified	Bovine leukemia virus	Enzootic bovine leucosis
Retroviridae	Lentivirus	MD virus	Maedi-visna
Retroviridae (temp classification)			Equine infectious anaemia
Retrovirus	unclassified		Ovine pulmonary adenomatosis
Rhabdoviridae	Lyssavirus	Rabies virus	Rabies
Rhabdovirus	Lyssavirus	Several species	Lyssa encephalitis
Rhabdovirus	Vesiculovirus	VSV	Vesicular stomatitis
Togaviridae	Alphavirus	VEE, WEE, EEE	Equine encephalomyelitis
Togaviridae	Pestivirus	EA virus	Equine viral arteritis
Togaviridae	Alphavirus	Getah virus	Getah virus disease
Unknown		BSE agent	Bovine spongiform encephalopathy
Unknown		TSE agent	Transmissible spongiform encephalopathies
Unknown		Scrapie agent	Scrapie

APPENDIX 20: GLOSSARY

Note: Words are defined in this Glossary according to the use they have in these Guidelines

<i>Agrobacterium tumefaciens</i>	A bacterium which infects plants and contains a plasmid (<i>q.v.</i>) that can be used to introduce foreign DNA into plant cells.
amphotropic retrovirus	A retrovirus (<i>q.v.</i>) that will grow in the cells from which it was isolated and also in cells from a wide range of other species.
amplify	To increase the number of copies of a gene or DNA sequence
autoclave	A device in which materials are sterilised using steam under high pressure.
AVA	Agri-food and Veterinary Authority of Singapore.
bacterium	A single-celled prokaryotic (<i>q.v.</i>) organism.
bacteriophage	A virus that infects bacteria; also called phage .
baculovirus	A group of viruses that infect insects and can be used as vectors (<i>q.v.</i>) to produce foreign proteins in insect cells.
biological safety cabinet/biosafety cabinet	Specially constructed cabinets which are designed to protect workers and the environment from dangerous agents, especially bacteria and viruses.
cell	The smallest structural unit of living organisms that is able to grow and reproduce independently.
characterised DNA	DNA which has been sequenced and for which there is an understanding of the gene products.
chromosome	A structure in the cell, consisting of DNA and proteins, that carries the organism's genes.
clone	As a noun: a group of genes, cells or organism derived from a common ancestor and genetically identical. As a verb: to generate replicas of DNA sequences or whole cells using genetic manipulation techniques.
conjugative plasmid	A plasmid (<i>q.v.</i>) which codes for its own transfer between bacterial cells by the process of conjugation ('mating').
construct	As a noun: genetically manipulated DNA.

containment	Prevention of the spread of genetically manipulated organisms outside the laboratory. Physical containment is accomplished by the use of special procedures and facilities. Biological containment is accomplished by the use of particular strains of the organism which have a reduced ability to survive or reproduce in the open environment.
containment level	The degree of physical containment provided by a laboratory or facility, which depends on the design of the facility, the equipment installed, and the procedures used. GMAC physical containment levels are numbered from 2 to 4, 4 being the highest level.
defective virus	A virus that is unable to reproduce in its host without the presence of another ('helper') virus.
deliberate release	Intentional release of a genetically modified organism into the open environment.
DNA	Deoxyribonucleic acid, the molecule which carries the genetic information for most organisms; consists of four bases and a sugar-phosphate backbone.
donor	The organism or cell from which DNA is derived for insertion into another organism (the host).
<i>Drosophila</i>	A genus of flies whose genetics has been extensively studied.
embryo-rescue	The process in plant breeding whereby tissue from young embryo plants is excised and propagated <i>in vitro</i> for subsequent growth as differentiated plants.
<i>Escherichia coli</i> (<i>E. coli</i>)	A bacterium that inhabits the intestinal tract of humans (and other animals).
<i>Escherichia coli</i> K12	A strain of <i>E. coli</i> that has been maintained in culture in laboratories for many years. It has lost the ability to colonise the intestinal tract of humans and animals, is well-characterised genetically, and is often used for molecular cloning work.
<i>Escherichia coli</i> B	Another well-characterised laboratory strain of <i>E. coli</i> .
eukaryotic	Belonging to the group of organisms whose cells contain a true nucleus. Eukaryotic organisms include animals, plants and fungi.
expression	Manifestation of a characteristic that is specified by a gene; often used to mean the production of a protein by a gene that has been inserted into a host organism.
fungi	Non-photosynthetic eukaryotic organisms, including moulds, that feed on organic matter.

fusion	Joining of the cell membranes of two cells to create a daughter cell that contains the genetic material from both parent cells.
gamete	A reproductive (egg or sperm) cell.
gene	A hereditary unit of nucleic acid which specifies the structure of a protein or RNA molecule.
gene therapy	The replacement of a defective gene in a person or other animal suffering from a genetic disease.
genetic engineering	See genetic manipulation .
genetic manipulation	A technology used to alter the genetic material of living cells or organisms in order to make them capable of producing new substances or performing new functions.
genome	The total genetic complement of a given organism.
genotype	The genetic make-up of an organism, as distinguished from its physical appearance (the phenotype).
germline cells	Gametes and the cells from which they are derived. The genetic material of germline cells, unlike that of somatic cells (<i>q.v.</i>), can be passed to succeeding generations.
GA-BSL	Biosafety Level for genetic modification of animal
GI-BSL	Biosafety Level for genetic modification of insects
GM-BSL	Biosafety Level for general genetic modification work
GP-BSL	Biosafety Level for genetic modification of plants
GMAC	Genetic Modification Advisory Committee.
GMO	Genetically Modified Organism.
growth factor	A protein that stimulates cell division when it binds to its specific cell-surface receptor.
helper virus	A virus which, when used to infect cells already infected by a defective virus (<i>q.v.</i>), enables the latter to multiply by supplying something the defective virus lacks.
HEPA filter	High efficiency particulate air filter.
HIV	Human immunodeficiency virus (a retrovirus).
host	A cell or organism into which foreign DNA is introduced to enable production of proteins or further quantities of the DNA.

host range	For a virus, the range of species that can be infected by that virus.
host-vector system	Combination of host (<i>q.v.</i>) and the vector (<i>q.v.</i>) used for introducing foreign DNA into the host.
hybridoma	A hybrid cell, used in production of monoclonal antibodies (<i>q.v.</i>), which is produced by fusing an antibody-producing cell (a B lymphocyte) with a tumour cell.
IBC	Institutional Biosafety Committee.
<i>in vitro</i>	Literally 'in glass'; performed in a test tube or other laboratory apparatus.
<i>in vivo</i>	In a living organism.
knockout mouse	A mouse that has been genetically modified by deletion or inactivation of a specific gene.
LD50	The dose of a toxin or infectious agent which will kill half of a population of organisms.
microorganism	An organism that can be seen only with the aid of a microscope.
MOH	Ministry of Health
MOM	Ministry of Manpower
monoclonal antibody	An antibody that is derived from a single clone (<i>q.v.</i>) of hybridoma (<i>q.v.</i>) cells and recognises only one antigen.
NEA	National Environment Agency
oncogene	An activated (modified) cellular gene which causes normal cells to become cancerous.
oocyte	A cell that divides to form the female reproductive cell.
packaging	In the process of virus replication, the assembly of the components of the virus to form the complete virus particle.
pathogen	An organism that causes disease.
PCR	See polymerase chain reaction .
phage	See bacteriophage .
plasmid	A small, self-replicating molecule of DNA which contains a specific origin of replication. Plasmids are often used as cloning vectors (<i>q.v.</i>).

polymerase chain reaction	A technique for generating, <i>in vitro</i> , an increased quantity of a target segment of DNA.
prion	An infectious agent of unknown etiology which causes spongiform encephalopathies of humans and animals.
prokaryotic	Belonging to the group of microorganisms whose DNA is not enclosed within a nuclear membrane.
promoter	A DNA sequence, located in front of a gene, that controls expression of the gene. It is the sequence to which RNA polymerase binds to initiate transcription.
protein	A molecule composed of amino acids.
protoplast	A plant or bacterial cell which has had the outer cell wall removed.
receptor	Cell-surface protein to which molecules such as hormones and growth factors bind to exert their effects on the cell, or to which viruses bind to gain entry to the cell.
recombinant	Organisms, cells, viruses etc. which contain recombinant DNA (<i>q.v.</i>).
recombinant DNA	DNA formed by joining, <i>in vitro</i> , segments of DNA from different organisms.
recombination	The occurrence or production of progeny with combinations of genes other than those that occurred in the parents.
replication	Reproduction.
retroviral vector	A retrovirus (<i>q.v.</i>) which is used to introduce foreign DNA into animal cells, usually by replacing part of the viral genome with the foreign DNA of interest.
retrovirus	A virus that uses the enzyme reverse transcriptase to copy its RNA genome into DNA, which then integrates into the host cell genome.
RNA	Ribonucleic acid, a molecule similar to DNA, whose functions include decoding the instructions for protein synthesis that are carried by the genes; comprises the genetic material of some viruses.
sharps	Sharp laboratory items such as syringe needles, scalpel and razor blades, and broken glass.
shot-gun cloning	The production of a large random collection of cloned fragments of the DNA of an organism, from which genes of interest can later be selected.

somatic cell	Any cell of a multicellular organism other than germline cells (<i>q.v.</i>).
Ti plasmid	A large plasmid of the bacterium <i>Agrobacterium tumefaciens</i> (<i>q.v.</i>) which carries genes for tumour induction in some plants. A disarmed form of the plasmid which lacks the tumour-inducing genes is often used as a vector to introduce foreign DNA into plant cells.
tissue culture	<i>In vitro</i> growth of tissue cells in nutrient medium.
toxin	A poisonous substance, produced mainly by microorganisms, but also by some fungi, plants and animals.
transgenic (organism)	An organism whose cells, including the germline cells, contain foreign DNA; transgenic animals are produced by the insertion of the foreign DNA into the newly fertilised egg or embryo.
tumour suppressor gene	A type of gene in which inactivating mutations contribute (or anti-oncogene) to tumour development.
vector	A self-replicating agent (e.g. plasmid or virus) used to transfer foreign DNA into a host cell.
viroid	A disease-causing agent of plants, which is smaller than a virus and consists of a naked RNA molecule.
virulence	Ability of an organism to cause disease.
virus	A submicroscopic infectious particle, containing genetic material (DNA or RNA) and protein, which can replicate only within the cell of an organism (plant, animal or bacteria).
zygote	The cell produced by the union of the male and female gametes.