Introduction
There are demanding health and safety issues to be addressed for projects involving organisms with unnatural combinations of genetic material since these newly created life-forms lack a history of safe use. To protect both people and the environment from such organisms these projects are tightly controlled by specific Regulations, in addition to other general health and safety legislation such as Management of Health and Safety at Work Regulations. These specific Regulations address risks to people and the environment caused by the genetic modification of an organism. They do not address the risks to humans caused by other aspects of the project such as the presence of adventitious viruses in cell lines or the use of hazardous substances such as plasmid DNA encoding oncogenes.

Abbreviations and Web Addresses

Abbreviations

ACGM: Advisory Committee on Genetic Modification
BSA: Biological Safety Adviser
COSHH: Control of Substances Hazardous to Health
GMM: Genetically Modified Micro-organism
GMO: Genetically Modified Organism

HoD/HoS; Head of Division/Head of School

HSE: Health and Safety Executive

PI: Principal Investigator

UBSA: University Biological Safety Adviser

Web addresses


The Advisory Committee on Genetic Modification Compendium of Guidance is available at [http://www.hse.gov.uk/biosafety/gmo/acgm/acgmcomp](http://www.hse.gov.uk/biosafety/gmo/acgm/acgmcomp)

Quick Guide

a. Biological Safety Advisers (BSA) should discuss research projects with Principal Investigators (PI’s).

b. They should decide if projects involve the contained use of a GMO or GMM. Refer to definitions of GMO, GMM, and contained use given below.

c. BSA’s should advise PI’s to plan projects such that they form a connected programme of work to avoid having to make several risk assessments. A connected programme of work consists of projects (and foreseeable aspects of the projects) that form a coherent and integrated programme addressing a specific research goal. Refer to definitions below for advice.

d. BSA’s should advise PI’s to carry out a risk assessment on each activity comprising the connected programme of work in respect of human health and safety, and environmental protection. The forms listed below are designed to assist in carrying out a suitable and sufficient risk assessment:

(i) USO/Genetically Modified Micro-organisms for connected programmes of work involving GMM;

(ii) USO/Genetically Modified Plants for connected programmes of work involving genetically modified plants;

(iii) USO/Genetically Modified Animals for connected programmes of work involving genetically modified animals (vertebrates and non-vertebrates).

Contact UBSA for advice on which form(s) to complete in cases of uncertainty.
The connected programme of work must include:

(i) GMO obtained from external sources (e.g., a transgenic animal obtained from a collaborator, or a commercial supplier);

(ii) the breeding on of a GMO;

(iii) the crossing of a GMO with non-modified organism, unless tests reveal beyond reasonable doubt that no genetically modified material has been passed to progeny.

e. A Principal Investigator (PI) should complete as many risk assessments as they wish, the key consideration is that all risks to the people and the environment are identified and minimised to lowest reasonably practicable level. As a guide a risk assessment should be completed for each research goal.

f. A risk assessment must provide justification for the connected programme of work to be undertaken at the stated Containment Level: the logic of the argument should be clear, some claims may need to be supported by references, and sufficient detail must be provided to allow review by competent people.

g. PI's should send a copy of the risk assessment to the UBSA who will arrange for it to be reviewed by appropriate members of the Genetic Modification Safety Committee (usually Convener and other BSA). Work can commence as soon as these members give approval.

h. For moderate risk work (Class 2) the Health and Safety Executive (HSE) must be notified and a fee paid before the work commences, and for high risk work (Class 3 & 4) they must give consent. Notification to the HSE will be co-ordinated by the UBSA. Note that all the information submitted to the HSE is potentially disclosable to anyone on request unless a claim for confidentiality is accepted by the HSE and Scottish Ministers. Furthermore, some items of information will appear on a public register available on the Internet.

i. PI's should review risk assessments whenever new work is undertaken or new information becomes available. In addition risk assessments must be reviewed bi-annually. Minor changes do not require review by the Genetic Modification Safety Committee, but significant changes that potentially affect the risk will require review such as: change of scale; change in control measures; change of waste disposal, availability of new information. Unless the risk assessment requires review by the Genetic Modification Safety Committee do not send a revised version to the UBSA.

Regulations Concerning Genetically Modified Organisms
Genetically Modified Organisms (Contained Use) Regulations 2000

These are concerned with protecting human health and the environment from risks associated with genetically modified micro-organisms (GMM). In addition they cover the human health risks associated with genetically modified organisms (GMO) that are not GMM such as plants and animals.

Environmental Protection Act 1990 Part VI

Section 108(1)(a) of this Act covers the environmental risks associated with work involving GMO that are not GMM. It requires that anybody creating such a GMO which is not an approved product (under the regulations in paragraph 1.3), or obtaining one from elsewhere should carry out an assessment of environmental risks.

Genetically Modified Organisms (Risk Assessment) (Records and Exemptions) Regulations 1996


These require that records of environmental risk assessment for GMO, like those for GMM, should be kept for 10 years.

They also deal with the marketing and deliberate release of GMO into the environment. They require that anyone intending to release or market a GMO must obtain consent from the Secretary of State.

Deliberate release of a GMO is not covered by this Guidance Note. Contact the University Biological Safety Adviser (UBSA) for advice on regulations covering the deliberate release/marketing of a GMO.

Animal and plant licences

The following types of projects may require a licence from the appropriate agency before they can commence:

- working with animal pathogens, or material that may carry such a pathogen. The Importation of Animals Pathogens Order 1980 prohibits the importation into Great Britain from outside the European Community of a pathogen, or any potentially infected material,
that may cause disease in agricultural animals or birds unless a licence has been issued by the Secretary of State. The Specified Animal Pathogens Order 1998 prohibits research involving specified pathogens of agricultural livestock unless a licence has been issued by the Secretary of State. The Order covers intact pathogens, attenuated and genetically modified pathogens, nucleic acid that could produce a pathogen, and any material that is known to contain a pathogen eg blood, animal tissue. A list of pathogens that require a licence under this Order are given in Appendix 1.

- fish pathogens
- working with plant pests, including plant viruses;
- working with GMO that contain sequences derived from animal or plant pathogens;
- working with genetically modified animals and Octopus vulgaris, or animals infected with GMM.

Contact the UBSA for further advice if your project is of this type.

**Control of Substances Hazardous to Health Regulations 2002**

These regulations cover only GMM that create a hazard to human health. Risk assessment and notification requirements covered by the Genetically Modified Organisms (Contained Use) Regulations 2000 comply with the relevant Control of Substances Hazardous to Health (COSHH) Regulations, and in most cases need not be repeated. Other Regulations not covered by GMO Regulations, such as health surveillance and keeping records of exposure to Hazard Group 3 and 4 micro-organisms, must be fulfilled.

**Definitions and Guidance From The Contained Use Regulations**

**Organism and micro-organism**

An organism means a biological entity capable of replication or of transferring genetic material and includes a micro-organism but not humans or human embryos.

A micro-organism means a microbiological entity, cellular or non-cellular, capable of replication or of transferring genetic material. This includes bacteria, fungi, protozoa, viruses and viroids, prions, cell and tissue cultures from humans, animals and plants, and full length copies of viral genomes that are known to be infectious even when they are not encapsulated or enveloped.
Genetic Modification

Genetic modification is defined as the alteration of genetic material of an organism in a way that does not occur naturally by mating and/or natural recombination.

Examples of techniques constituting genetic modification:

- recombinant nucleic acid techniques involving the formation of new combinations of genetic material by the insertion of nucleic acid molecules, produced by whatever means outside an organism, into any virus, bacterial plasmid or other vector system and their incorporation into a host organism in which they do not occur naturally but in which they are capable of continued propagation;
- techniques involving the direct introduction into an organism of heritable genetic material prepared outside the organism including micro-injection, macro-injection and micro-encapsulation;
- cell fusion or hybridization techniques where live cells with new combinations of heritable genetic material are formed through the fusion of two or more cells by means of methods that do not occur naturally.

Techniques which are not considered to result in genetic modification:

- *in vitro* fertilisation
- conjugation, transduction, transformation or any other natural process
- polyploidy induction

Techniques to which the Regulations (except Regulation 17) do not apply:

- mutagenesis
- cell fusion (including protoplast fusion) of prokaryotic species which can exchange genetic material through homologous recombination
- cell fusion (including protoplast fusion) of cells of any eukaryotic species including production of hybridomas and plant cell fusions
- self-cloning, where the resulting organism is unlikely to cause disease to humans, animals or plants. Self-cloning means the removal of nucleic acid sequences from a cell of an organism which may or may not be followed by re-insertion of all or part of that nucleic acid
(or a synthetic equivalent), whether or not altered by enzymic or mechanical processes, into cells of the same species or into cells of phylogenetically closely related species which can exchange genetic material by homologous recombination. Self-cloning may include the use of recombinant vectors, with an extended history of safe use in the particular organism, to manipulate and reinsert the nucleic acid sequences, but the vectors shall not consist of any genetic elements other than those designed for vector structure, vector replication, vector maintenance or marker genes.

**Contained Use**

Contained Use is defined as any activity in which organisms are genetically modified or in which GMO are cultured, stored, used, transported, destroyed or disposed of and where barriers are used to limit contact of the GMO with humans and with the environment. This limitation in contact can be achieved through control measures which include physical, biological or chemical barriers, or any combination of these. Note that physical barriers need not always be present, but in these cases it must be clear that the biological/chemical barriers are sufficient for the level of risk. A high level of safety for people and the environment must be provided.

Projects that involve contained use of GMO within the University include:

- laboratory operations
- housing and/or breeding of modified animals in animal houses
- use of glass houses or other plant growth facility
- large-scale fermentors

**Connected programme of work**

There are two types of connected programme: first, a single activity carried out at different notified premises by the same person; second, more than one activity at the same notified premises carried out by the same person. For multiple activities at the same site to be a connected programme they must form a coherent and integrated programme of work addressing a specific research goal that could form the basis of a single, standard research grant application. A programme may include any combination of activities that are notifiable to the HSE, plus activities that do not require notification.
Activity

Activity is defined as any operation involving the contained use of a GMO. This includes using, culturing, storing, transporting and disposal of a GMO.
Specific Requirements For Work with GMM

Risk Assessment

An assessment of risks to human health and of damage to the environment must be carried out by completing Form USO/Genetically Modified Micro-organisms or an equivalent before starting the work. The risk assessment must identify the containment measures required to eliminate or to reduce exposure of humans and the environment to the GMM, to the lowest reasonable practicable level. Examples of frequently used containment measures are given in Appendix 1. The level of detail required in the risk assessment will vary depending upon the nature of the hazards and the level of uncertainty. For example, projects involving routine cloning in disabled hosts such as *E.coli* K12 will require only a brief assessment; whereas projects using reagents without a history of safe use will require an in depth assessment of risks. Examples of risk assessments can be found in the Advisory Committee on Genetic Modification (ACGM) Compendium of Guidance.

The final aspect of the risk assessment is to classify the each activity comprising the connected programme of work into one of four classes (Appendix 2). Classification is based on the containment measures required to control the risk and not on the actual measures used. Frequently a higher level of containment is used than is strictly necessary to control the risk. It is important to carry out a classification based on risk to avoid unnecessary notification. For example, a person using a class 2 microbiological safety cabinet is genetically modifying a well characterised animal cell line known to be free from human pathogens. The microbiological safety cabinet is being used to protect the work and not the person and hence should not be taken into account when classifying this project.

Normally, a risk assessment carried out to comply with GMO (Contained Use) Regulations 2000 (GMO Regulations) considering the hazards posed by recipient and donor micro-organism, the inserted DNA, the vector, and the resulting GMM also will satisfy the COSHH Regulations. However, when working with cell lines this is not the case because the GMO Regulations do not consider the possible presence of a human pathogen present in the cell line, whereas the COSHH Regulations do. For this reason two risk assessments must be carried out: one should focus on the hazards associated with the cells and their genetic modification; whilst the other should consider the possible presence of human pathogens. The work must be carried out at the highest level of containment identified by either of these risk assessments. However, for notification purposes only the risk assessment under GMO Regulations should be taken into consideration. For example, the GMO risk assessment of work involving liposome mediated transfection of a
harmless reporter gene into a primary human cell line would identify that the containment required for this project is Level 1, and hence this project would be Class1. However, the COSHH risk assessment would identify that the containment required for this project is Level 2, and the work should be carried out at this level.

In addition to containment measures identified in the risk assessment, the principles of good microbiological practice and good occupational safety and hygiene must be applied (see ACGM Compendium of Guidance Part3, paragraph 25).

The risk assessments must be reviewed whenever new work is undertaken or new information becomes available. In addition Class 1 activities must be reviewed annually, and Class 2 and 3 at six monthly intervals. Minor changes do not require review by the Genetic Modification Safety Committee, but significant changes that potentially affect the risk will require review such as: change of scale; change in control measures; change of waste disposal, and the advent of new information.

Safety Services will retain a copy of risk assessments for at least ten years from the date of cessation of the project.

**Requirement to notify the HSE**

Class 1 activity

HSE do not require notification.

Class 2 activity

HSE require notification. The UBSA will supply the necessary form for completion by the PI and arrange for a Genetic Modification Safety Committee to appraise the completed form. Following approval by a Genetic Modification Safety Committee the UBSA shall submit the form and the fee to the HSE. The fee will be recovered from the School. The activity may commence as soon as acknowledgement of the submission from the HSE is received, normally within ten working days. Alternatively, it is possible to request formal authorisation from the HSE to commence the activity but this will be subject to a 45 day notification period. The HSE must be notified when the activity ceases.
Class 3 and 4 activities

HSE require notification. The UBSA will supply the necessary form for completion by the PI and arrange for a Genetic Modification Safety Committee to appraise the completed form. Following approval by a Genetic Modification Safety Committee the UBSA shall submit the form and the fee to the HSE. The fee will be recovered from the Department/School. The activity cannot commence until the HSE has given written consent. The decision on whether or not to issue consent will be given within 45 days but not less than 30 days after the date on which the acknowledgement of submission was sent by the HSE to Safety Services. The HSE must be notified when the activity ceases.

Record of an individual’s work with a Hazard Group 3 or 4 micro-organism

Records must be kept when working with Hazard Group 3 and 4 micro-organisms. The records must include the following:

- names of employees and when they began and finished the work;
- name of the micro-organism;
- details of work;
- details of accidents and incidents.

Normally these records should be kept for 10 years but if there is a possibility of delayed onset of ill health records must be kept for 40 years.

Contact UBSA for further advice.

Accidents and emergency plans

The HSE has to be notified (via Safety Services) if an accident occurs. An accident is defined in the Regulations as “any incident involving a significant and unintentional release of GMM which represents a hazard, immediate or delayed, to either human health and safety or the environment”.

A large scale spillage of some Class 1 GMM and spillages of Class 2, 3 or 4 GMM are likely to present a hazard and should be reported.

An emergency plan must be prepared when as a result of a reasonably foreseeable accident the health and safety of people outside the premises is liable to be affected seriously or there is a risk of serious damage to the environment. There are many reasonably foreseeable accidents that could lead to a loss of containment (eg fire) so the key issues to consider are:
• the potential of the GMM to cause harm to humans, animals or plants;
• the possible level of exposure to the GMM, ie scale of the activity is important;
• the likelihood of spread to humans, or to the environment.

The Advisory Committee on Genetic Modification provide guidelines on the whether an emergency plan is required or not (Appendix 4).

**Disclosure of information and confidentiality**

All the information submitted to the HSE as part of a notification may be disclosed to the public unless justification for withholding items of information is given. Some items of information will be placed on a public register accessible on the Internet. It is possible to request confidentiality for the information provided on various grounds including: information relating to commercial confidentiality; intellectual property rights; personal details. A full and detailed justification must be provided to support a claim for confidentiality at the time of notification. Contact the UBSA for further information.
Specific Requirements For Work With GMO That Are Not GMM

**Risk Assessment**

An assessment of risks to human health and of damage to the environment must be carried out by completing Form USO/Genetically Modified Plants, USO/Genetically Modified Animals or an equivalent. The design of these forms recognises that for these projects the greatest risk is likely to be damage to the environment, although the possibility of harm to humans (e.g. allergenicity, toxicity) should not be ignored. If risks to human health and safety or the environment are identified then containment measures must be used to eliminate or to reduce exposure to the lowest reasonably practicable level. There is no legislation stating the containment measures that must be used for varying levels of risk but the ACGM gives guidance on containment measures to work with plants and animals that are unlikely to cause environmental harm (Containment A, ACGM Compendium of Guidance Part 3B and 3D respectively) and on measures for work with plants and animals that could damage the environment (Containment B, ACGM Compendium of Guidance Part 3B and 3D, respectively). These measures **must** be used as a minimum, unless after reviewing the risk assessment the Genetic Modification Safety Committee has given permission for other, equally effective measures to be used.

Fortunately, for most projects involving GMO there is little risk of harm to people or the environment and the most important factor is to ensure that the GMO (including seeds and pollen of genetically modified plants) does not escape into the environment. This would breach the contained use regulations and constitute an unauthorised deliberate release. To prevent such an occurrence a minimum of Containment A (ACGM Compendium of Guidance Part 3B and 3D) should be used for projects involving GMO.

The final aspect of a risk assessment is to classify all activities into one of two classes (notifiable or non-notifiable) based on whether or not the genetically modified organism is potentially more harmful to human health than the non-modified organism.

The risk assessments must be reviewed regularly, at least annually. Minor changes do not require review by the Genetic Modification Safety Committee, but significant changes that potentially affect the risk will require review such as: change of scale; change in control measures; change of waste disposal, and the advent of new information.
Safety Services will retain a copy of risk assessments for at least ten years.

**Requirement to notify the HSE**

1. As safe as non-modified organism

   HSE do not require notification

2. Not as safe as non-modified organism

   HSE require notification. The UBSA will supply the necessary form for completion by the Principal Investigator and arrange for the GMSC to appraise the completed form. Following approval by the GMSC the UBSA shall submit the form and the fee to the HSE. The fee will be recovered from the Department/School. The HSE will acknowledge receipt within 10 working days. The activity may commence 45 days after the date on which the acknowledgement of submission was sent to you by the HSE, unless approval is given earlier. The HSE must be notified when the activity ceases.

**Accidents and emergency plans**

The HSE has to be notified (via Safety Services) if an accident occurs. An accident is defined in the Regulations as “any incident involving a **significant** and unintentional release of GMOs which represents a hazard, immediate or delayed, to either human health.”

An emergency plan must be prepared when as a result of a reasonably foreseeable accident the health and safety of people outside the premises is liable to be seriously affected.

**Disclosure of information and confidentiality**

All the information submitted to the HSE as part of a notification is potentially disclosable on request to anyone who asks to see it. Some items of information will be placed on a public register accessible on the Internet. It is possible to request confidentiality for the information provided on various grounds including information relating to commercial confidentiality, intellectual property rights and personal details. A full and detailed justification must be provided to support a claim for confidentiality.
General Requirements For Work with GMO

**Genetic Modification Safety Committee**

Genetic Modification Safety Committees have been formed at the City Campus and Ninewells Hospital and Medical School that have the knowledge and experience to address the validity:

- of the assessment of risks to humans and the environment of projects involving GMO
- of the containment measures to control these risks
- of the classification of the project

The Conveners of these committees are responsible for the effective running of the committee, such that all members’ views are heard and that decisions made by the committee reflect the views of committee and not a single member.

**Notification of premises**

The Health and Safety Executive (HSE) has to be notified of the first-use of the premises to be used for work GMO. The University has made two notifications which cover the City Campus and Ninewells Hospital and Medical School respectively. The City Campus and Ninewells Hospital and Medical School have notified use of Class 1, 2 and 3 activities, and GMO that are not GMM.

**Health Surveillance**

Generally this is not required since the working procedures are designed to prevent exposure. However, for some individuals (eg immuno-compromised) or in some unusual situations where exposure cannot be adequately controlled, or where an infection may not lead to obvious symptoms then health surveillance may be required.

Health surveillance is appropriate when there is a:

- reasonable likelihood of exposure to a GMO capable of causing ill health
- technique to detect exposure or the onset of ill health
- benefit to the employee

Since most GMO present no identifiable risk to human health, surveillance is not required. However, surveillance may be appropriate when working with:
- GMM derived from hazard group 2, 3 or 4 micro-organisms with altered tissue tropism, decreased susceptibility to therapeutic agents, or altered recognition by immune system
- oncogenic or tumorigenic sequences, mutant tumour suppressor genes or anti-sense constructs for tumour suppressor genes
- modified prion protein genes
- GMO expressing biologically active molecules that pose a risk to health
- cloned human genes that may lead to auto-immune disease
- materials that may cause respiratory sensitisation, especially large scale culture of GMO

Contact the Occupational Health Service for advice on whether health surveillance may be required. Records of health surveillance must be kept for 40 years.

**Training**

Before starting work with a GMO, research staff and students must have:

- instruction in local rules;
- training in good microbiological practice.

In addition, on the job training to a level where constant supervision is not required must be provided for:

- required techniques;
- use of microbiological safety cabinet;
- safe transport of GMO;
- safe storage of GMO;
- waste disposal procedures;
- spillage procedures including use of disinfectant;
- accident reporting including spillage of GMM and escape of GMO.

Written records of training should be kept for every member of staff and student.
Supervision

All members of staff and students must be continually supervised until a satisfactory level of competence has been demonstrated.
Appendix 1: Pathogens requiring a licence under the Specified Animal Pathogens Order 1998 for possession or introduction into an animal

African horse sickness virus

African Swine fever virus

Aujeszky’s disease virus

Avian influenza viruses which are:

(a) uncharacterised; or

(b) pathogenic

Babesia bovis, B. bigemina, B. caballi and B. equi

Bacillus anthracis

Bluetongue virus

Bovine leukosis virus

Brucella abortus

Brucella melitensis

Brucella ovis

Brucella suis

Burkholdaria (Pseudomonas) mallei

Classical swine fever virus

Cochliomyia hominivorax

Cowdria ruminatum

Eastern and Western equine encephalomyelitis viruses

Echinococcus multilocularis and E. granulosis

Equine infectious anaemia virus

Equine morbillivirus

Foot and mouth disease virus

Histoplasma farcinosum

Japanese encephalitis virus

Lumpy skin disease virus
Mycoplasma agalactiae
Mycoplasma capricolum sub species capripneumoniae
Mycoplasma mycoides sub species mycoides SC and mycoides LC variants
Mycoplasma mycoides var capri
Newcastle disease virus (avian paramyxovirus type 1) viruses which are:
(a) Uncharacterised
(b) Pathogenic
Peste de petits ruminants virus
Rabies virus and all viruses of the genus Lyssavirus
Rift Valley Fever virus
Rinderpest virus
Sheep and goat pox virus
Swine vesicular disease
Teschen disease virus
Theileria annulata
Theileria parva
Trichinella spirallis
Trypanosome brucei, T. Congolense, T. equiperdum, T. evansi, T. simiae and T. vivax
Venezuelan equine encephalomyelitis virus
Vesicular stomatitis virus
Live viral haemorrhagic disease of rabbits
Appendix 2: Containment Measures used In Laboratories

- microbiological safety cabinet
- laboratory coat
- protective clothing in addition to standard laboratory coat
- gloves
- access restricted to authorised personnel
- sharps prohibited unless essential
- centrifuges with sealed buckets or rotors
- isolated laboratory suite
- laboratory sealable for fumigation
- entry to lab via airlock
- negative pressure relative to the pressure of the immediate surroundings
- HEPA filtered extract and input air
- shower
- laboratory to contain its own equipment
- an observation window or alternative so that occupants can be seen
- control of disease vectors (e.g., rodents, insects) which could disseminate GMM
- autoclave required in laboratory
## Appendix 3

<table>
<thead>
<tr>
<th>Class</th>
<th>Description</th>
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<tbody>
<tr>
<td>1</td>
<td>Activities of no or negligible risk, for which Containment Level 1 is appropriate to protect human health and the environment</td>
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<tr>
<td>2</td>
<td>Activities of low risk, for which Containment Level 2 is appropriate to protect human health and the environment</td>
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<td>3</td>
<td>Activities of moderate risk, for which Containment Level 3 is appropriate to protect human health and the environment</td>
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<tr>
<td>4</td>
<td>Activities of high risk, for which Containment Level 4 is appropriate to protect human health and the environment</td>
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## Appendix 4: Classification Of Projects Involving Genetically Modified Micro-organisms

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<tr>
<th>Containment Level necessary to control risk</th>
<th>Classification</th>
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<tbody>
<tr>
<td>Level 1 (or less)</td>
<td>Class 1</td>
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<tr>
<td>Level 1 plus additional measure(s) from Level 2 or Level 2 (without additional measures)</td>
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<td>Level 2 plus additional measure(s) from Level 3 or Level 3 (without additional measures)</td>
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</tr>
<tr>
<td>Level 3 plus additional measure(s) from Level 4 or Level 4 (with or without additional measures)</td>
<td>Class 4</td>
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<td>Class of activity</td>
<td>Scale</td>
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