The Biological Agents and Genetically Modified Organisms (Contained Use) Regulations 2010

Biosafety Guidelines

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Section 1

Introduction

Following the investigations into the outbreak of foot and mouth disease in Surrey in 2007, a review of the regulatory framework for handling animal pathogens was commissioned. The final report provided a number of recommendations which were accepted in full by the Government with expectations that resulting changes would strengthen the regulation of deliberate work in this area. A key element of this report was the recommendation to develop a Single Regulatory Framework (SRF) to govern all work with human and animal pathogens including genetically modified organisms (GMOs).

Deliberate handling of human pathogens, listed animal pathogens and GMOs was previously governed by three separate sets of regulations (see Table 1), all providing similar requirements for working safely with hazardous pathogens at different levels of containment.

Table 1: Principal legislation for handling microorganisms in Great Britain prior to the Contained Use Regulations 2010

♦ Control of Substances Hazardous to Health Regulations 2002
♦ Genetically Modified Organisms (Contained Use) Regulations 2000
♦ Specified Animal Pathogens Order 2008/ Specified Animal Pathogens (Wales) Order 2008/ Specified Animal Pathogens (Scotland) Order 2009

Although the risks posed to animal or human health vary according to the nature of the different pathogens, the Callaghan review considered it unhelpful to have in place separate regulatory systems, each dealing with aspects of what is essentially the same thing i.e. the need to contain the pathogen and prevent its release such that it can cause harm. The review therefore recommended the implementation of an SRF that would govern work with wild-type and genetically modified human and animal pathogens, targeted towards the greatest risks and with a clear understanding of the necessary requirements to achieve adequate control. This new framework also provides for the Health and Safety Executive (HSE) as the single independent regulator with all the necessary legal powers to carry out its function effectively.

The main components for effective implementation of these new regulations include:

- The formulation of a common set of hazard group definitions and containment measures applicable to both animal and human pathogens that can be understood by dutyholders and enforced by regulators.

- The development of a single, integrated notification system to be incorporated within the new regulatory framework as a 'one-stop' shop to cover all notifiable work.

- The development of a cost recovery regime in accordance with Government and HSE policy.

This new regulatory approach provides the foundation for successful compliance and emphasises that primary responsibility for safe working rests with dutyholders i.e. those who carry out contained use. All reasonably practicable measures must be taken to protect humans and the environment and others from harm and dutyholders will be required to demonstrate this by a thorough risk based assessment of their activities, with identified measures to obtain adequate control.

The sections of the previous regulations (see Table 1) that dealt with the contained use of wild-type biological agents and genetically modified organisms have now been revoked and have been replaced by the **Biological Agents and Genetically Modified Organisms (Contained Use) Regulations 2010** (hereafter referred to as CU 2010) which came into force on xx April 2010. The range of pathogens covered by CU 2010 can be found in the revised Approved List 2010 ***(include link)*** which lists all the pathogens now falling within the scope of these regulations. In addition to the wild type biological agents listed in the Approved List 2010, CU 2010 also covers other elements previously covered by the Genetically Modified Organisms (Contained Use) Regulations 2000.

In summary, CU 2010 will apply in Great Britain and covers everything that was previously covered in the:

- Genetically Modified Organisms (Contained Use) Regulations 2000;
- Deliberate work with wild-type microorganisms previously covered by Schedule 3 of the Control of Substances Hazardous to Health Regulations 2002 (COSHH); and
- Parts of the Specified Animal Pathogens Order 2008 (SAPO) (including Scotland and Wales SAPO) that cover contained use of specified animal pathogens.

The Importation of Animal Pathogens Order (IAPO) and the application for IAPO licences, remains under separate legislation for which Defra retains responsibility and is subsequently not included in CU 2010.

Introduction of CU 2010 has necessitated changes to COSHH. As already mentioned, COSHH will no longer cover the duties of those carrying out contained use of wild-type biological agents. However, incidental exposure and other work with wild-type biological agents remains within the scope of amended COSHH which retains requirements to prevent or adequately control exposure to microorganisms from workplace activities where incidental exposure presents risk e.g. farmers or sewage plant workers. This guidance document is only concerned with containment and control measures for

people carrying out contained use of wild-type biological agents and genetically modified organisms..

Contained use, as defined in the regulations, covers activities in which:

(i) organisms are genetically modified; or

(ii) genetically modified organisms or wild-type biological agents are cultured, stored, transported, destroyed, disposed of or used in any other way;

and for which physical, chemical or biological barriers are used to provide a high level of protection for, humans, susceptible animals or the environment.

This guidance is intended to cover contained use in all types of facilities. This includes research, teaching, clinical, forensic, veterinary and environmental laboratories. It covers deliberate use of biological agents in production facilities and also with experimental animals and work with infected patients in human and animal healthcare settings.

Further guidance as to what constitutes 'contained use' can also be found in the 'Guide to the Biological Agents & Genetically Modified Organisms (Contained Use) Regulations 2010' (provide link).

Purpose of the guidance

The purpose of this publication is to provide guidance to dutyholders under the new regulations and is aimed at facilities where there is a deliberate intention to manipulate human or animal pathogens including GMOs. CU 2010 describes the minimum containment requirements necessary for those who carry out contained use of wild-type biological agents and genetically modified organisms. These requirements are written to incorporate the minimum standards required by the European Directives on the protection of workers from risks related to exposure to biological agents at work (Directive 2000/54/EC), the contained use of genetically modified microorganisms (Directive 98/81/EC) and the community measures for the control of foot-and-mouth disease (Directive 2005/83/EC). These directives were previously implemented in the UK via COSHH, the Genetically Modified Organisms (Contained Use) Regulations 2000 and SAPO (including Scotland and Wales SAPO).

As was the case in previous GM legislation, CU 2010 also covers work with genetically modified organisms ie (transgenic) animals and plants. For additional guidance on working with genetically modified plants (including plant-associated genetically modified microorganisms) or genetically modified animals please refer to the Scientific Advisory Committee on Genetic Modification (SACGM) Compendium of Guidance Part 4 and Part 5 respectively. Work that involves the use of genetically modified microorganisms (GMMs) in a clinical setting is also covered and specific guidance can be found in the SACGM Compendium of guidance Part 6.

This guidance is primarily aimed at those organisations and individuals who are responsible for the management and operation of containment facilities deliberately handling pathogens. One of the key aims of this guidance is to emphasise that it remains the dutyholders' responsibility to manage the risks created from the work undertaken at their premises. It describes in some detail the minimum containment measures as laid out in the new regulations.

The guidance should be used to ensure that current containment and control measures are suitable and sufficient to meet the minimum requirements. Additionally, the guidance should be consulted prior to any changes in function, upgrading or building of facilities to be used for the type of work previously described.

- **Section 2** covers the legislation and includes relevant regulations governing laboratory work with microorganisms and genetically modified plants and animals.

- **Section 3** covers general health and safety issues, such as health and safety management that are applicable to all relevant workplaces.

- **Section 4** gives specific guidance on the risk assessment based approach for activity classification and the notification requirements

- **Section 5** covers the principles for design and operation of containment facilities and explains the rationale for the various containment and control measures.

The effective implementation of a biosafety programme requires a combination of containment measures and working practices, supplemented by management controls, to prevent the inadvertent exposure of susceptible species to biological agents and their distribution in the wider environment. In practice, this requires a comprehensive system of both physical and procedural controls to minimise potential release of a pathogen along with suitable arrangements to minimise its subsequent spread.

The principal consideration in respect of safe handling of wild-type biological agents and genetically modified organisms is that of 'containment' i.e. the way in which they are managed in a laboratory, plant growth facility, animal unit or other type of facility e.g. large-scale to minimise/prevent release and consequent exposure to workers, other people, animals and the wider environment.

Section 2

Health and Safety legislation

The overarching legislation governing CU 2010 is the Health and Safety at Work etc Act 1974. The Act, places general duties on employers and others and these have been summarised in Table 2.

As the 'Health and Safety at Work etc. Act 1974' did not allow for the making of regulations in relation to animal health, Section (1) has been amended by means of a Legislative Reform Order to extend authority for the specific purpose of regulating contained use of animal pathogens. Making this amendment provides the vires to make new regulations for animal pathogens under HSWA. This however, will not extend into use of animal pathogens outside containment or regulation of general animal welfare or animal disease control.

Table 2: Summary of general duties required under the Health and Safety at Work etc Act 1974

- To ensure, so far as is reasonably practicable, the health, safety and welfare at work of employees.
- To conduct their undertakings in such a way as to ensure, so far as is reasonably practicable, that other persons who may be affected by the work are not exposed to risks to their health and safety. Non-employees include students and visitors. Students who are involved in contained use activities are treated as if they were employees of the university or college, etc, where they are studying.
- Self-employed people have general duties to conduct their undertakings in such a way as to ensure, so far as is reasonably practicable, that they and other persons are not exposed to risks to their health and safety from the work. In relation to genetically modified micro-organisms only this duty is extended beyond employers to any person carrying out contained use.
- Employees have a general duty to take reasonable care for the health and safety of themselves and of other persons who may be affected by their work, and to co-operate with their employer or any other person to enable them to comply with any health and safety duties.

The Act is further qualified in regulations such as the Management of Health and Safety at Work Regulations 1999.

HSE, in collaboration with others, has published many different guidance documents on specific areas of work with biological agents e.g. SACGM Compendium of Guidance and the Advisory Committee on Dangerous Pathogens (ACDP) Management, Design and Operation of Microbiological Containment Laboratories. Guidance documents are aimed at providing an interpretation of the regulations and clear examples of ways in which

dutyholders can comply with the regulations. Guidance documents will often describe what would be considered as best practice in order to comply with current health and safety legislation.

The guidance that existed prior to the introduction of CU 2010 will often refer to COSHH or the Genetically Modified Organisms (Contained Use) Regulations 2000. The regulations referred to in these documents no longer exist (or have been amended). However, such guidance should still be considered relevant, unless already superseded, or until such a time as they have been updated.

Where links are provided from this document to specific parts of other guidance that existed prior to implementation of the new regulations, please consider the guidance as current but ignore references to old legislation. If links are provided to other guidance, we have endeavoured to ensure that the information provided in those sections is consistent with what is required under the CU 2010.

Other relevant legislation

Accidents involving human or zoonotic pathogens

The Reporting of Injuries, Diseases and Dangerous Occurrences Regulations (RIDDOR) 1995 are designed to provide a national record of certain types of injury, diseases and dangerous occurrences that might jeopardise the health and safety of workers and therefore covers wild-type human pathogens, zoonotic pathogens and genetically modified versions of the aforementioned. There is a requirement in RIDDOR for employers to report 'acute illness which requires medical treatment where there is reason to believe that this resulted from an exposure to a biological agent or its toxins'.

Employers must also report ‘any infection reliably attributable to the performance of particular work’, specified as being 'work with micro-organisms; work with live or dead human beings in the course of providing any treatment or service or in conducting any investigation involving exposure to blood or body fluids; work with animals or any potentially infected material derived from any of the above’. There is also a duty to report any ‘accident or incident which resulted or could have resulted in the release or escape of a biological agent likely to cause severe human infection or illness’.

Further information on RIDDOR can be found in accident and incident reporting later in this guidance.

The reporting of incidents and accidents involving specified animal pathogens and the additional requirements for reporting accidents involving GMMs can be found in accident and incident reporting.

Laboratory biosecurity legislation

Some materials will require safe storage under Part 7 of the Anti-Terrorism, Crime and Security Act 2001 (ATCSA). Laboratories have a duty to ensure that the storage and use of dangerous pathogens and toxins listed within Schedule 5 of the Act are as secure as reasonably practicable. Notes to this schedule include GM derivatives of listed pathogens and toxins, and relevant sequences derived from such organisms. In broad terms ATCSA requires laboratories to:

- Register with the Home Office their holdings of Schedule 5 substances.
- Inform the police of the security measures in place and the personnel who have access to the Schedule 5 substances.
- Ensure that Schedule 5 substances and the premises in which they are kept, stored, worked on and disposed of are secure.
- Ensure that access to said substances is authorised and controlled.

Further information is available by contacting the local counter terrorism security advisor or national counter terrorism security office pathogens@homeoffice.gsi.gov.uk.

Environmental Protection Legislation

From the perspective of environmental protection, aspects relating to the contained use of genetically modified plants and animals are, in addition to CU 2010, also covered by the Environmental Protection Act 1990 (EPA). Briefly, the requirements of the EPA can be covered by ensuring that your risk assessment for the GM activities covers details of what environmental damage would be caused by an accidental release into the environment of the GM animal/ plant and what control measures are in place to minimise this risk. Where GMOs are intentionally released from containment into the environment e.g. field trials for transgenic crops, such activities are regulated by The Genetically Modified Organisms (Deliberate Release) Regulations 2002 in England and Wales or the Scottish equivalent and not CU 2010.

Animal Legislation

It should be noted that there is other legislation that must be complied with in relation to animal welfare. Further details on legislation relevant to working with animals are available in the SACGM Compendium of Guidance Part 5.

Medicines legislation

Those wishing to undertake any form of clinical research studies should seek advice from the Medicines and Healthcare Products Regulatory Agency. Further details on legislation and regulatory approval for clinical trials can be found in the SACGM Compendium of Guidance Part 6.

Good Manufacturing Practice (GMP) **Legislation**

Section 3

Management of Biosafety

The legal responsibility for health and safety rests primarily with the employer and in view of the potential risks associated with work with biological agents, especially at higher risk levels, it is essential that there is a clear and effective health and safety policy in place for the organisation to follow. It is essential that the policy not only covers duties to protect the health and safety of employees but also includes the need to protect both susceptible animals and the wider environment. Acceptance of, and commitment to, the management of health and safety by senior managers is key in achieving effective management of health and safety.

Under the Health and Safety at Work etc Act 1974 (HSWA), employers must prepare a statement of their health and safety policy. There is a similar provision in the Management of Health and Safety at Work Regulations 1999 and where there are five or more employees, health and safety arrangements must be recorded and the health and safety policy brought to the notice of all employees. Details of the management structure, individual responsibilities and employee involvement and responsibilities should be included.

In practice, to ensure that adequate biosafety precautions are in place, the responsibility is often delegated down the line management chain. In some occupational settings a formal line management structure may not be obvious. However, if an individual is responsible for directing, controlling or supervising the work of others, e.g. researchers, scientists and ancillary staff, etc, then they should be regarded as 'managers' for the purposes of identifying who is responsible for health and safety management. For instance, a head of department for a laboratory will have a key role in health and safety management, however, they may designate a laboratory supervisor to assist, oversee and implement health and safety arrangements.

The concept of employer is defined very widely in the regulations and includes educational establishments and the self-employed. The regulations further provide that where there is no employer in relation to the contained use work the regulations apply to any person carrying out that work. In practice there will nearly always be someone who meets the definition of an employer.

Employees have a duty to report defects and deficiencies in management arrangements and to co-operate with their employer, e.g. by applying agreed local rules and procedures.

If people working under the control and direction of others are treated as self-employed for tax and national insurance purposes they are nevertheless treated as their employees for health and safety purposes. It may therefore be necessary to take appropriate action to protect them. If any doubt exists about who is responsible for the health and safety of a worker this must be clarified and should be included in the terms of a contract or other document. However, a legal duty under section 3 of HSWA cannot be passed on by means of a contract and there will still be duties towards others. If such

workers are to be employed on the basis that they are responsible for their own health and safety, legal advice should be sought before doing so.

For further details on biosafety management in containment level (CL) 4 facilities please refer to Part 2 of the Principles, Design and Operation of Containment Level 4 Facilities.

The position of Biological Safety Adviser (BSA)

Regulation 7 of the Management of Health and Safety at Work Regulations 1999 requires every employer to appoint one or more competent persons to assist them in undertaking the measures required to comply with the relevant statutory duties. Further advice on the role of the BSA can be found in the SACGM Compendium of Guidance Part 1. It is essential that the safety adviser has sufficient relevant training, experience and knowledge of the type of work being conducted in that facility in order to properly assist management in meeting statutory provisions.

The role and composition of genetic modification and biological safety committees

CU 2010 places a statutory obligation on anyone carrying out a risk assessment for GMMs or GMOs to establish a genetic modification safety committee. Further guidance can be found in the Guide that accompanies the CU2010 Regulations (include link). Additionally, anyone carrying out a risk assessment for class 3 or 4 activities with wild-type microorganisms must also establish a biological safety committee. Although the statutory purpose is solely to advise the management on the adequacy of any risk assessment, the committee can also provide a beneficial influence on ensuring good practice if there is full discussion with all those concerned, on safety, training and laboratory discipline. Members' local knowledge and expertise can be particularly important. Safety committees are often involved in the formation of local rules and in the consideration of accidents and incidents. HSE attach great importance to the safety committee, which often plays a key role in the organisation of safety procedures.

Depending on the nature of the work being undertaken it may be necessary to have a range of representatives from various technical disciplines, representing both management and employees (e.g. Union reps), health and safety advisor(s) such as a biological safety officer and, if necessary, input from clinicians/ veterinary surgeon.

While it is important to have the correct representation on the safety committees, centres should avoid having unnecessarily large and unwieldy committees. The composition can be tailored for different studies ie GM/ non-GM and animal pathogens studies and outside expertise can be drafted-in where necessary. As the committee is responsible for a wide range of topics under CU 2010, it may be more appropriate to have more than one committee depending on areas of expertise.

Particular emphasis should be placed on the value of having a balanced committee representing both management and employees and the need for the committee to be run in such a way that all members' views are heard.

Safety policies and local codes of practice

Local health and safety policies provide important general information about how managers intend to develop and maintain a safe working environment. Such documents should also make reference to every day safe working practices within the laboratory and how this will be supervised and managed.

Most of this information will usually be found in local codes of practice which provide important information to staff and make a valuable contribution to the process of safe working. Local managers should make arrangements for codes to be drawn up and made accessible to all staff to help as a checklist for identifying areas which staff should understand before being judged as competent. All staff, including newcomers, contractors and temporary workers, must be made aware of them. A guide to the main areas that should be covered is provided in Table 3.

Another route for conveying health and safety information to employees is through the use of standard operating procedures as many procedures within the laboratory will be carried out using them. They are often used to meet external (and internal) quality standards but by integrating the health and safety arrangements into the standard operating procedures, employers can ensure that they also meet acceptable standards of health and safety. The standard operating procedure should be developed in consultation with staff to ensure commitment to the safe working procedures.

Employers need to make arrangements for supervising work and checking that health and safety measures remain effective. Supervision is necessary because even after safe working practices are put in place, people can still deviate from established practices and ill health, injuries or damage to the wider environment may then result. The level of supervision will depend on the risk associated with the job or task and the competence of the person being supervised. Even fully competent individuals will require some level of periodic monitoring to ensure that standards are being met consistently.

Employers also have a duty to consult employees on health and safety matters. The Safety Representatives and Safety Committees Regulations 1977 and the Health and Safety (Consultation with Employees) Regulations 1996 require employers to consult trade union safety representatives, other employee representatives, or employees where there are no representatives, about health and safety matters. This includes changes to the work that may affect their health and safety at work.

Table 3: Main areas to be covered in local codes of practice

- **Introduction**- this should state the reasons for having such a code and refer to other relevant health and safety documents. Staff should be made aware of the nature and range of agents to which they or the environment might be exposed, the possible source of infection and the containment (physical and procedural) measures to be used. Staff should be made aware of the training and supervision arrangements for working in the laboratory. If the laboratory is a shared facility, staff should be made aware of all the risks to which they might be exposed.

- **General procedures**- these should specify which staff (or grade of staff) are authorised to carry out particular procedures. There should also be appropriate guidance for maintenance staff, contractors and visitors etc.

- **Operation of unit**- this should detail start-up procedures, etc, how the ventilation system works and its controls, operation of safety cabinet(s), procedures for operating equipment, e.g. centrifuges, and use of personal/respiratory protective equipment and cleaning procedures.

- **Local rules**- these should cover such issues as entry/exit procedures for the laboratory, maximum numbers allowed in laboratory or other local rules as required depending on the nature of the work conducted. It may be a suitable place to include details on quarantine periods for staff working with animal pathogens to minimise the risk posed to susceptible species if applicable.

- **Waste**- this should detail the waste disposal and disinfection policy (both routine and emergency, i.e. spills and fumigation).

- **Staff health**- this should include the immunisation policy and arrangements for reporting injuries/ infections and post exposure prophylaxis.

- **Testing and maintenance**- this should cover the maintenance and testing procedures for engineering controls such as microbiological safety cabinets, autoclaves etc.

- **Emergency procedures**- this should cover procedures for dealing with accidents involving wild-type biological agents and genetically modified organisms including the name of the person to whom incidents should be reported.

Emergency procedures

Employers are required to draw up plans for dealing with accidents involving wild-type biological agents and genetically modified microorganisms. Staff should be aware of and familiar with the procedures to follow in the event of a significant accident or incident. Clear instructions should be available, kept up to date and distributed to all relevant staff. It is important that suitable account is taken of senior staff availability, for example during period of leave and that appropriate cover is provided to ensure adequate management of any accident or incident. It may be useful, where possible, to carry out incident simulations to ensure staff are fully aware of how to respond to particular

circumstances. Guidance on the action to take in the event of a spillage can be found in Appendix 3 of The Management, Design and Operation of Microbiological Containment Laboratories. For information on room fumigation please refer to Appendix 2 of The Management, Design and Operation of Microbiological Containment Laboratories or Part 3 of the SACGM Compendium of Guidance.

CU 2010 and the Management of Health and Safety at Work Regulations 1999 require procedures to be in place for responding to serious and imminent danger, e.g. fire or flooding. A suitable risk assessment should be in place to identify all the foreseeable incidents to be covered by the emergency procedures. The Management of Health and Safety at Work Regulations 1999 also require that the emergency services have sufficient knowledge of the hazards within the containment facility should they have to enter the premises to respond to an emergency situation. For CL4, further information on emergency planning is provided in Part 5 of the Principles, Design and Operation of Containment Level 4 Facilities.

Accident & Incident reporting

The requirement to notify accidents and incidents varies, depending on the nature of the microorganisms involved. There are three routes by which you may need to notify accidents or incidents involving microorganisms:

1. For all incidents/ accidents with microorganisms which have (or could have) resulted in human infection you may need to notify accidents and dangerous occurrences that could cause serious human infection through RIDDOR. Further information on RIDDOR can be found in Appendix 2.

2. If an accident occurs whilst working with GMMs you may have to notify the Competent Authority of any accidents which are defined as 'a significant and unintended release of GMMs in the course of their contained use which could present an immediate or delayed hazard to human health or the environment'. The Competent Authority must be notified of such accidents by reporting them to HSE using form CU3 which can be downloaded from the HSE website at the following link: https://www.hse.gov.uk/forms/genetic/index.htm. Following receipt of an accident notification, HSE is obliged to investigate the accident and send a report to the European Commission. It should be noted, regardless of whether the incident qualifies as an accident as defined above for GMMs, that such incidents may still require notification under RIDDOR.

3. If an accident occurs whilst deliberately working with specified animal pathogens there is a requirement to notify the Competent Authority as soon as possible. An accident in this context is defined as an incident which has or may have resulted in the release of a specified animal pathogen which could cause serious disease in susceptible animals. Details of the information required following an accident can be found

in the guide that accompanies the CU 2010 regulations. In the event of an infection in the field due to release, the Regional Veterinary Office, Animal Health Section, Defra should be contacted.

Training

Training of staff is an employer's responsibility under the HSWA, the Management of Health and Safety at Work Regulations 1999 and also of the CU 2010 regulations. Employees must have a clear understanding of any identifiable risks to their health arising from work and the actions to be taken in dealing with situations in which exposure may occur. Examples of different types of training which you may wish to consider are provided in Table 4. The level of training provided should be appropriate to the level of risk or the complexity of the procedures being undertaken. At CL3 and above, a more formal approach to training is required, with written records of training kept., as required by CU 2010 Regulations.

Table 4: Examples of training programmes

- Induction training following recruitment, for example, training in good microbiological practice and familiarisation with the local rules before beginning practical work.
- Ongoing training commensurate with the tasks required of staff to ensure they are competent to perform their duties.
- Training when a significant change to work, equipment, work environment, work activity or responsibilities takes place, especially where increased or new risks may be involved.
- Refresher training (where appropriate) to maintain standards.
- Training in risk assessment procedures will often be useful (although not specifically required by the legislation).

Supervision & monitoring of standards

Regulation 5 of the Management of Health and Safety at Work Regulations 1999 covers the supervision of workers and the monitoring of standards. This states that arrangements must be made for the effective planning, organisation, control and monitoring of preventive and protective measures.

Monitoring of health and safety standards by locally organised inspections is recommended. The level of monitoring will depend on the risks associated with the work and the competence of the workers. Fully competent individuals will still require some level of monitoring to ensure that standards are being met. The safe working practices should themselves be reviewed to ensure that they are effective and still relevant to the work being carried out.

Human health surveillance

Health surveillance is about putting in place procedures to detect adverse reactions or ill health among employees that are exposed to health risks as a result of their work. This is so that action can be taken to prevent further harm to those workers or others who may be exposed.

Health surveillance is required by the CU 2010 (and the Management of Health and Safety at Work Regulations 1999) if all of the following criteria are true:

- The work could result in harm to health in some way.
- There are safe and practical ways of detecting diseases or conditions associated with exposure.
- Damage to health may occur under particular conditions at work.
- Surveillance will benefit the employee or workforce.

The benefits of health surveillance are that it can:

- Provide information so you can detect harmful health effects at an early stage, so protecting employees and confirming whether they are still fit to do their jobs.
- Provide data, by means of health records, to detect and evaluate health risks.
- Provide an opportunity to train and instruct employees further in safe and healthy working practices (e.g. how to use personal protective equipment properly).
- Give employees the chance to raise any concerns about the effect of their work on their health.
- Alert employers of any changes to the health status of their employees that may affect work with pathogens

Health surveillance is critical where the agent causes serious disease that may have an insidious onset, and where there is an effective treatment available. However, in the case of work with GMOs and GMMs, the risks may be less well defined compared to the organism from which they were derived, or arise as a direct result of the modification. Users should consider whether the organism being modified, or the modification itself, gives rise to a significant risk to health and consequently, whether surveillance is required.

Employees should be familiar with the clinical manifestations resulting from infection with the organisms being worked with, e.g. vaccinia virus lesions, and the correct procedures for reporting instances of disease/ ill health to their employer.

The occupational health provider should be alert to unusual patterns of disease or ill health within the workforce, irrespective of the control/ containment measures being used. It may be possible to check the immune status of workers to see if they have protection against a potential infectious agent they could be exposed to in the course of their work. This could be

carried out as part of pre-employment screening, or else by making checks on immunity following a course of vaccination.
Any health surveillance programme that is undertaken should include keeping a health record for each individual. The health record is different from a clinical record. The health record should be about the individual's fitness for work or any specific precautions that should be taken. It should not include any confidential clinical data. The elements of a health record include:

- Personal details of the individual.
- An historical exposure record (it may be sensible to combine this with any list of workers' exposure to a hazard group (HG) 3 or 4 microorganisms (see section on exposure records)) and a record of any immunisations and the conclusions of any checks on immunity.
- The health record and any list of exposed workers needs to be accessible by the employer in order to monitor control measures that are in place and to ensure that employees are not at risk. Records which include medical information arising from clinical examination are held in confidence by the doctor or nurse and can only be released with the written consent of the individual.

Immunisation

If the risk assessment shows there to be a risk of exposure to biological agents or microorganisms for which effective vaccines exist, these should be offered if the employee is not already immune. The advantages and disadvantages of immunisation versus non-immunisation should be fully explained when making the offer.

HSWA requires that protective measures such as immunisation be provided to workers free of charge. Employees may not wish to take up the offer of immunisation, or else do not respond to a vaccine. If so, employers should carry out a local assessment to determine the likelihood of that particular individual being exposed and acquiring an infection. If existing controls are deemed to be inadequate, then controls should be implemented to allow them to work safely. This might include the provision of extra PPE.

Immunisation should only be seen as a useful supplement to control measures required to prevent exposure and should never be relied upon for worker protection.

Records of exposure

An exposure record is not the same as a health record required for the purposes of health surveillance under the Management of Health and Safety at Work Regulations 1999. However, exposure records must be available to any individual appointed for health surveillance, e.g. the local occupational health physician. It must also be available to any employee specifically responsible for health and safety (such as a safety manager).

Each employee must have access to the information that relates to him or her personally. If records are kept (computerised or manual) about individuals in connection with health and safety legislation, the requirements of the Data Protection Act 1998 may apply. These requirements include informing people that certain information is held about them and granting them access to that information, should they request it.

In practice the exposure record might best be kept with other transferable confidential information, e.g. information accessible only by authorised individuals, in the employee's occupational health record. Exposure in this context means working with the agent, not accidental exposure/ loss of containment. Records of exposure should be kept for work with certain microorganisms. These include all microorganisms classified in hazard groups 3 and 4 that could cause disease in humans, for which records should be kept for 40 years after work ceases.

Retaining exposure records of individuals who have worked with oncogenes would be of value. However, the nature of 'infection' with such material does not lend itself to traditional formal health surveillance. Any such records should be stored securely. Upon termination of a contract, a copy of the records should be given to the worker so that they may be given to the next employer. This may be particularly important for researchers undertaking a number of short-term contracts.

Section 4

Risk assessment and Notification

A fundamental principle associated with the former Genetically Modified Organisms (Contained Use) Regulations 2000 was the classification of an activity and this has been a familiar model to those working with GMMs and GMOs. CU 2010 extends this approach to cover contained use of all biological agents and genetically modified organisms . Activity classification may therefore be a new concept for those working with non-GM pathogens. However, this model will provide for a proportionate risk based approach to selection of control measures from one of four containment levels (1-4). The containment level is determined by carrying out a suitable and sufficient risk assessment, taking into account the initial hazard group of the agent (if applicable), any modifications to virulence and the type and scale of work performed. The risk assessment should indicate which control measures are necessary to minimise risks to humans, and additionally in the case of animal pathogens, susceptible animals and in the case of genetically modified micro-organisms the environment from the conduct of the work. This will consequently allow a final classification to be assigned to the activity they are carrying out based on the highest containment level from which a control measure is required.

This process of a risk based classification is described in this section but it must be understood that final classification not only takes into account the initial hazard group of an organism but also the consequences of attenuation or modifications and whether any of the procedures require additional containment or control measures to minimise risks to humans, animals or the environment as appropriate to the contained use. For a flow chart representation of the process of assigning an activity classification refer to Figure 1.

Detailed advice on carrying out risk assessments can be found in other HSE publications e.g. the Management, Design and Operation of Microbiological Containment Laboratories, the Principles, Design and Operation of Containment Level 4 Facilities or Part 2 of the SACGM Compendium of Guidance. Additionally, the guidance that accompanies CU 2010 details the factors that should be considered when carrying out a risk assessment.

Categorisation of pathogens according to hazard group

Categorisation of biological agents into one of four hazard groups has been the traditional method of separating out biological agents based on a range of characteristics including; pathogenicity; mode of transmission; minimum infectious dose; host range; availability of preventative measures and effective prophylaxis or treatment.

The categorisation of wild-type biological agents in this guidance is taken from the Approved List 2010 (include link) made under Section 15 of HSWA. CU 2010, by making reference to this list, impose requirements which are legally

binding. . The list also implements the Community Classification of biological agents set out in European Community Directive 2000/54/EC.1. The Approved List 2010 combines human, animal and zoonotic biological agents into one document, recognising the traditional 4 hazard groups which have been redefined in CU 2010 to take account of the SRF now in place for governing deliberate work with wild-type biological agents and GMOs.

Table 5: Hazard group definitions

(1) When provisionally categorising a biological agent the biological agent should be assigned to one of the following Groups according to its level of risk of infection to humans and according to it's level of risk to susceptible animals. Where the pathogen meets the definition in more than one group, the higher group should be assigned.

(a) Group 1—

) is unlikely to cause human disease; **and**

) in relation to susceptible animals is unlikely to produce disease or is enzootic and does not produce notifiable animal disease;

(b) Group 2—

) can cause human disease and may be a hazard to employees; it is unlikely to spread to the community and there is usually effective prophylaxis or treatment available; **or**

) in relation to susceptible animals is exotic, novel or produces notifiable diseases; and it has both of the following characteristics —

(aa) is of low clinical significance; and

(bb) has low likelihood of spread.

(c) Group 3—

) can cause severe human disease and may be a serious hazard to employees; it may spread to the community, but there is usually effective prophylaxis or treatment available; **or**

) in relation to susceptible animals is exotic, novel or produces notifiable disease and it has one or both of the following characteristics—

(aa) moderate clinical significance;

(bb) moderate likelihood of spread.

(d) Group 4—

) causes severe human disease and is a serious hazard to employees; it is likely to spread to the community and there is usually no effective prophylaxis or treatment available; **or**

) in relation to susceptible animals is exotic, novel or produces notifiable disease; and it has one or both of the following characteristics—

(aa) the disease has serious clinical significance;

(bb) has a high likelihood of spread.

(2) Susceptible animals are any kind of mammal except man, any kind of four-footed beast which is not a mammal and any species of bird likely to be affected by the biological agent.

(3) Novel means a new strain of biological agent not previously seen.

(4) Spread means the passing of the biological agent from one susceptible animal to another and ssumes any necessary enzootic vector is present.

Risk assessment approach

The Approved List 2010 assigns hazard groups to all wild-type human and animal biological agents within the scope of the CU 2010 regulations except new and emerging biological agents. For new and emerging wild-type biological agents an initial hazard grouping must be determined by the dutyholder by applying the most appropriate definition for hazard groups according to the definitions from the CU 2010 and reproduced in this guidance. For animal/ plant microorganisms that are going to be genetically modified, an initial classification should be assigned to the microorganism based on the containment level from which measures are required to protect animals or the environment according to the risk assessment.

The risk assessment should identify what changes will be made to the microorganism or biological agent i.e. is it wild-type, attenuated through natural means or genetically modified. The variety of work conducted means that a wide range of procedures will also be employed. Consideration of the risks posed by carrying out these procedures helps determine the final activity classification.

In cases where no modifications will be performed e.g. in a research laboratory where the biological agent is a wild-type, a risk assessment should be completed to identify the containment and control measures required for safeguarding risks to human health and the environment. In many scenarios involving wild-type biological agents, it is likely that the final activity classification would be identical to the initial hazard grouping i.e. HG2= class 2 activity. However, it should be noted that because the activity classification is determined by a risk based approach, the risk assessment may indicate a higher activity classification compared to the initial hazard grouping. For example, a risk assessment for research with *Neisseria meningitidis* (HG2) may indicate that one of the procedures involves culturing the organism in volumes that could pose a risk to human health if a spillage occurred. In this case, the risk assessment may indicate that the laboratory where *N. meningitidis* is being manipulated needs to be sealable to permit fumigation in case of a large spillage. As laboratory sealability is a CL3 requirement, the final activity classification would therefore be 3. For further details on how an activity classification is determined please refer to the activity classification section.

In some cases the final classification for a wild-type biological agent may be lower than the initial hazard grouping where a pathogen has been attenuated through natural means such that it no longer presents the same level of risk to humans or the environment. It may therefore be possible to dispense with all of the control measures from the containment level equivalent to the initial hazard grouping. For example, *Bacillus anthracis* is a HG3 agent. However, the Sterne strain of *B. anthracis* has been sufficiently attenuated such that it is of a reduced hazard to humans and the environment. Due to this reduction in the inherent hazard associated with the Sterne strain of *B. anthracis*, none of the containment or control measures may be required from CL3. It is

therefore possible to have a final activity classification of 2 for this particular strain of *B. anthracis*. However, this is not an automatic reclassification as the risk assessment may indicate that one or more of the containment and control measures from containment level 3 is required because of the procedures i.e. activities being carried out e.g. a laboratory may be culturing large volumes where a spillage may still pose a risk to humans or the environment and the laboratory therefore needs to be sealable to permit fumigation and may need to have extract air passing through a high efficiency particulate air (HEPA) filter.

For work involving genetic manipulation of microorganisms, the final classification may vary from the initial hazard grouping more often, either increasing or decreasing depending on the nature of the modifications and the procedures to be carried out. The risk assessment process for a genetically modified microorganism should consider the impact of the modifications e.g. addition/ deletion of virulence genes, changes in tropism or host range or changes in routes of transmission. Please refer to the SACGM Compendium of Guidance Part 2 for a comprehensive overview of the factors to be considered when carrying out a GM risk assessment. Again, the risk assessment will determine the control measures necessary to minimise risk to humans and the environment from the activities being conducted and therefore determine the final classification. It may be necessary to take into account other local factors when carrying out a risk assessment. For example, the risk posed by a genetically modified crop microorganism or transgenic plant may represent a significantly higher risk in a rural environment compared to the centre of a large urban area.

Activity classification

The activity classification is determined by taking into account the findings of the risk assessment and should indicate whether:

(i) The activities being conducted will involve procedures that do not increase the risk to humans or the environment in which case the final activity classification would be the same as the initial hazard grouping;

(ii) The activities being conducted may increase the risk to humans or the environment and may therefore require additional containment and control measures from a containment level greater than the initial hazard grouping indicated or;

(iii) The activities being conducted mean that particular control measures are not required so the final classification may be lower than the initial hazard grouping indicated.

Table 6: Classes of contained use activity

Class	Description
1	Activities of no or no negligible risk, for which containment level 1 is

	appropriate to protect human health, specified animal health and the environment
2	Activities of low risk, for which containment level 2 is appropriate to protect human health specified animal health and the environment.
3	Activities of moderate risk, for which containment level 3 is appropriate to protect human health, specified animal health and the environment.
4	Activities of high risk for which containment level 4 is appropriate to protect human health, specified animal health and the environment.

The tables for laboratory containment, plant growth facility containment, animal unit containment and other containment facilities e.g. closed systems not covered by laboratory, plant growth or animal facilities provide a list of containment and control measures for containment levels 1 to 4. If any measure is identified as being required from a particular containment level then the final classification will be equal to the containment level listing of that requirement e.g. if measures are required from CL3 that are not required at CL2 then the activity classification will be 3 i.e. class 3. To avoid over-classification, it should be noted that the activity classification is determined by the measures deemed necessary to protect humans or the environment. It does not mean that particular control measures used for product protection or convenience etc. would determine the final classification. For example, if a microbiological safety cabinet is used and gloves worn solely to protect product sterility it does not mean the final activity is class 2 unless other CL2 measures are required to protect humans or the environment.

Derogations

Due to the all encompassing nature of the SRF it is difficult to describe containment levels where all the control measures are necessary to protect humans or the environment. The containment and control measures necessary will vary depending on numerous factors such as the transmission route of a microorganism or the host range. For this reason, it is possible to apply for specific derogations from specified containment and control measures that may be granted by the Competent Authority subject to a suitable and sufficient justification as to why. For example, if a pathogen is not known to be infectious via the aerosol route e.g. hepatitis B (HG3) the risk assessment may indicate that it is not necessary to have an air pressure that is negative relative to the surroundings. However, it would be appropriate to have other control measures from CL3 e.g. a requirement for the facility to be separated from other areas in the same building. In this example, the final classification would be 3 but derogations could be requested for the measures not deemed necessary.

Derogations can be requested for work with any GMMs and specified animal pathogens but only certain wild-type human pathogens, due to the constraints of the European Directive (2000/54/EEC) If the activity involves the use of non-genetically modified microorganisms from the Approved List capable of human infection, it is imperative to check whether derogations can be requested. For a list of wild-type microorganisms that can be derogated please refer to Annex 1 of the Approved List 2010 (include link when

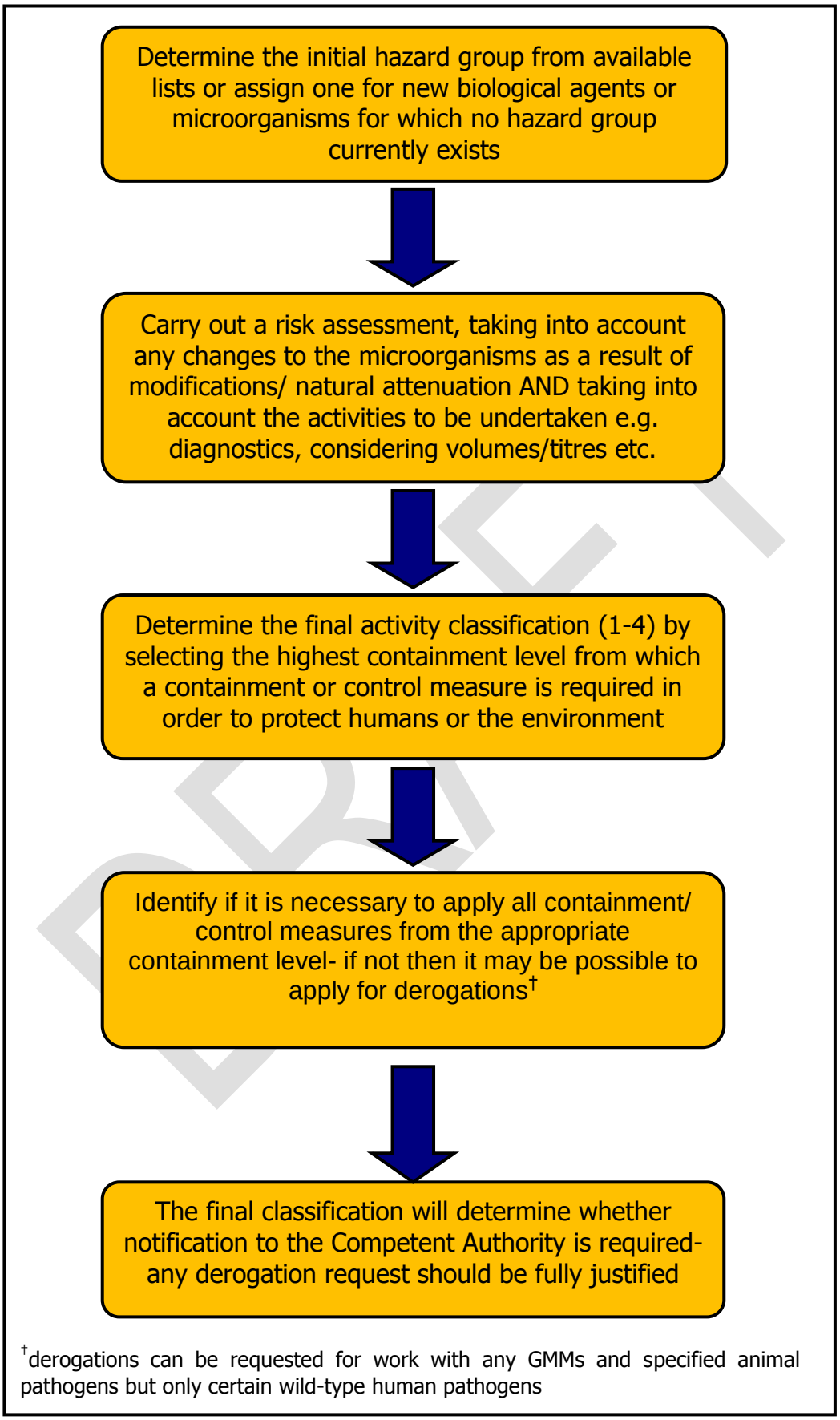
available). For work involving any GMMs or specified animal pathogens, there are no constraints on which derogations may be requested. However, the final decision on whether to grant a derogation request will remain with the Competent Authority.

Due to the nature of the SRF it is envisaged that the risk assessments for some activities, particularly class 3 and 4 activities involving non-zoonotic animal pathogens, will indicate that a number of containment measures from that class are not required. This is to be expected and all derogation requests should be fully justified.

Notification

Following determination of an activity classification, it may be necessary to submit a notification to the UK Competent Authority. Full details of when notification is required and what information should be included can be found in the guidance that accompanies CU 2010. (Include link)

Figure 1: Procedure for carrying out activity classification



Section 5

Principal requirements of containment

This guidance is intended to offer advice with respect to how to achieve the appropriate standards described in the containment tables in CU 2010 and reproduced in this guidance. Some of the listed control measures will not be required at the lower containment levels and, in some cases, the guidance will simply reflect this. The guidance may also highlight other measures that are considered good practice or approaches that can be implemented to achieve the standards required by the legislation. These approaches are illustrative and users may adopt other methods so long as the standards set by the legislation are met.

The tables describe containment for the use of microorganisms in laboratories, animal houses, plant growth facilities and for closed systems e.g. industrial research and production facilities. There are some settings for which these tables are not particularly appropriate, for example, a clinic. Users in such settings must execute containment and control, although it is acknowledged that application and interpretation of the tables may be difficult and users in these situations should contact HSE for further guidance. Specific guidance for the use of genetically modified microorganisms in a clinical setting can be found in the SACGM Compendium of Guidance Part 6.

Definitions

Containment tables

The following containment tables have been copied from CU 2010 and represent the minimum containment measures to be implemented.

Table 7: Containment measures applicable to contained use of wild-type biological agents and genetically modified microorganisms in **laboratories**

Table 8: Containment measures for work involving genetic modification of microorganisms in **Plant Growth Facilities** (to be read with Table 7)

Table 9: Containment measures applicable to contained use of wild-type biological agents and genetically modified microorganisms in **animal units** (to be read with Table 7)

Table 10: Containment measures for contained use of wild-type biological agents and genetically modified microorganisms in **Premises other than those referred to in Tables 6, 7 and 8 e.g. closed systems**

Table 7: Containment measures applicable to contained use of wild-type biological agents and genetically modified microorganisms in laboratories

Containment measures		***Containment levels***			
		1	**2**	**3**	**4**
1	The laboratory suite **(Note 1)** is to be separated from other areas in the same building or is in a separate building.	Not required	Not required	Required	Required
2	Input and extract air from the laboratory to be filtered using HEPA or equivalent.	Not required	Not required	Required on extract air	Required on input air, double on extract air **(Note 2)**
3	Access to be restricted to authorised persons only.	Not required	Required	Required	Required via airlock (**Note 3)**
4	The laboratory is sealable to permit fumigation	Not required	Not required	Required	Required
5	Specified disinfection procedure	Required where and to extent the risk assessment shows it is required	Required	Required	Required
6	The laboratory **(Note 4)** to be maintained at an air pressure that is negative relative to the immediate surroundings	Not required	Not required	Required	Required
7	Efficient vector control e.g. for rodents and insects	Required where and to extent the risk assessment shows it is required	Required for GM and animal pathogens, otherwise required where and to extent the risk assessment shows it is required	Required	Required
8	Surfaces impervious to water, easy to clean and resistant to acids, alkalis, solvents, disinfectants and decontamination agents used for decontamination	Required for bench (GM only)	Required for bench	Required for bench and floor	Required for bench, floor, walls and ceiling
9	Safe storage of biological agents	Required where and to extent the risk assessment shows it is required	Required	Required	Safe and secure storage required
10	An observation window or alternative is to be present, so that occupants can be seen	Required where and to extent the risk assessment shows it is required	Required where and to extent the risk assessment shows it is required	Required	Required
11	A laboratory is to contain its own equipment	Not required	Not required	Required where and to extent the risk	Required

Containment measures		***Containment levels***			
		1	**2**	**3**	**4**
				assessment shows it is required	
12	Infected material to be handled in a safety cabinet or isolator or other suitable physical containment	Not required	Required where and to extent the risk assessment shows it is required	Required; safety cabinet or enclosure required for GM	Required; safety cabinet or enclosure required for GM
13	Specific measures to control aerosol dissemination	Not required	Required so as to minimise	Required so as to prevent	Required so as to prevent
14	Shower prior to leaving the contained area **(Note 4)**	Not required	Not required	Required where and to extent the risk assessment shows it is required	Required
15	Protective clothing	Suitable protective clothing required	Suitable protective clothing required	Suitable protective clothing required; footwear required where and to extent the risk assessment shows it is required	Complete change of clothing and footwear required before entry and exit to the contained area
16	Gloves	Not required	Required where and to extent the risk assessment shows it is required	Required	Required
17	Inactivation of biological agents in effluent from hand-washing sinks and showers and similar effluents	Not required	Not required	Required where and to extent the risk assessment shows it is required	Required
18	Inactivation of biological agents in contaminated material and waste	Required where and to the extent the risk assessment shows it is required	Required by a validated means	Required by a validated means, with waste inactivated in the laboratory suite	Required by a validated means, with waste inactivated in the laboratory
19	Entry to the contained area **(Note 4)** via airlock **(Note 3)**	Not required	Not required	Required where and to the extent the risk assessment shows it is required	Required
20	Autoclave	Required on the premises, for GMMs only	Required in the building	Required in the laboratory suite **(Note 5)**	Double ended autoclave required in the laboratory

Containment measures		***Containment levels***			
		1	**2**	**3**	**4**
21	Use of biohazard sign	Required where and to extent the risk assessment shows it is required	Required	Required	Required

Note 1 - Laboratory suite means one or more laboratories, together with the supporting infrastructure, equipment and services including ancillary rooms such as airlocks, changing rooms, storage rooms and rooms for the inactivation or disposal of biological agents or micro-organisms.

Note 2 – Where viruses are not retained by the HEPA filters, extra requirements will be necessary for extract air.

Note 3 - Airlock – entry must be through an airlock which is a chamber isolated from the laboratory. The clean side of the airlock must be separated from the restricted side by changing or showering facilities and preferably by interlocking doors.

Note 4 – Contained area means the laboratory except for wild-type animal pathogens that don't pose a risk to human health when it means the laboratory suite.

Note 5 - With validated procedures allowing the safe transfer of material into an autoclave outside the laboratory and providing an equivalent level of protection

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Table 8: Containment measures for work involving genetic modification of microorganisms in Plant Growth Facilities (to be read with Table 7)

Containment measures		***Containment levels***			
		1	**2**	**3**	**4**
1	Permanent structure **(Note 6)**	Required where and to the extent the risk assessment shows it is required	Required	Required	Required
2	Entry via a separated room with two interlocking doors	Not required	Required where and to the extent the risk assessment shows it is required	Required where and to the extent the risk assessment shows it is required	Required
3	Control of contaminated run-off water	Required where and to the extent the risk assessment shows it is required	Required so as to minimise run-off	Required so as to prevent run-off	Required so as to prevent run-off
4	Effective control of disease vectors such as insects, rodents and arthropods which could disseminate GMMs	Required	Required	Required	Required
5	Effective control of pollen, seeds and other plant material which could disseminate GMMs	Required where and to the extent the risk assessment shows it is required	Required so as to minimise dissemination	Required so as to prevent dissemination	Required so as to prevent dissemination
6	Procedures for transfer of living material between the plant growth facilities, protective structure and laboratory shall control dissemination of GMMs	Required so as to minimise dissemination	Required so as to minimise dissemination	Required so as to prevent dissemination	Required so as to prevent dissemination

Note 6 – A permanent structure refers to a fixed structure with walls, a roof and a floor. Where the permanent structure is a green house, that structure shall have a continuous waterproof covering and self-closing lockable outer doors, and be located on a site designed to prevent the entry of surface run-off water.

Table 9: Containment measures applicable to contained use of wild-type biological agents and genetically modified microorganisms in animal units (to be read Table 7)

Containment measures		***Containment levels***			
		1	**2**	**3**	**4**
1	Isolation of animal unit **(Note 7)**	Required where and to the extent the risk assessment shows it is required	Required	Required	Required
2	Animal facilities **(Note 8)** separated by lockable doors	Required where and to the extent the risk assessment shows it is required	Required	Required	Required
3	Animal facilities designed to facilitate decontamination (waterproof and easily washable material (cages etc.))	Required where and to the extent the risk assessment shows it is required	Required where and to the extent the risk assessment shows it is required	Required	Required
4	Floor, walls and ceilings easily washable	Required where and to the extent the risk assessment shows it is required	Required for floor	Required for floor, walls and ceilings	Required for floor, walls and ceilings
5	Incinerator for the disposal animal carcasses	Required to be accessible (for GM only)	Required to be accessible	Required to be accessible	Required to be on site
6	Appropriate barriers at the room exit and at drains or ventilation duct work	Required where and to the extent the risk assessment shows it is required	Required	Required	Required
7	Animals kept in appropriate containment facilities, such as cages, pens tanks etc..	Required where and to the extent the risk assessment shows it is required	Required where and to the extent the risk assessment shows it is required	Required where and to the extent the risk assessment shows it is required	Required where and to the extent the risk assessment shows it is required
8	Animals kept in isolators or isolated rooms	Required where and to the extent the risk assessment shows it is required	Required where and to the extent the risk assessment shows it is required	Required, where infection is by airborne route	Required
9	Appropriate filters on isolators **(Note 9)** or isolated rooms	Not required	Required where and to the extent the risk assessment shows it is required	Required	Required

Note 7 – Animal unit: a building, or separate area within a building containing facilities and other areas such as changing rooms, showers, autoclaves, food storage areas etc...

Note 8 – Animal facility: a facility normally used to house stock, breeding or experimental animals or one which is used for the performance of minor surgical procedures

Note 9 – Isolators: transparent boxes where small animals are contained within or outside a cage; for large animals, isolated rooms may be more appropriate

Table 10: Containment measures for contained use of genetically modified microorganisms and wild-type biological agents in Premises other than those referred to in Tables 7, 8 and 9 e.g. closed systems

Containment measures		***Containment levels***			
		1	**2**	**3**	**4**
1	Viable microorganisms and biological agents should be contained in a system which physically separates the process from the environment (closed system)	Required where and to the extent the risk assessment shows it is required (for GM only)	Required	Required	Required
2	Control of exhaust gases from the closed system	Not required	Required so as to minimise dissemination	Required so as to prevent dissemination	Required so as to prevent dissemination
3	Control of aerosols during sample collection, addition of materials to the closed system or transfer of material to another closed system	Required where and to the extent the risk assessment shows it is required (for GM only)	Required so as to minimise release	Required so as to prevent release	Required so as to prevent release
4	Inactivation of culture fluids as a bulk before removal from the closed system	Required where and to the extent the risk assessment shows it is required (for GM only)	Required by validated means	Required by validated means	Required by validated means
5	Seals should be designed so as to minimise or prevent release	Not required	Required so as to minimise release	Required so as to prevent release	Required so as to prevent release
6	The controlled area should be designed to contain spillage of the entire contents of the closed system	Required where and to the extent the risk assessment shows it is required (for GM only)	Required where and to the extent the risk assessment shows it is required	Required	Required
7	Controlled area sealable to permit fumigation	Not required	Required where and to the extent the risk assessment shows it is required (for GM only)	Required where and to the extent the risk assessment shows it is required	Required
8	Biohazard signs posted	Required where and to the extent the risk assessment shows it is required	Required	Required	Required
9	Entry via airlock	Not required	Not required	Required where and to the extent the risk assessment shows it is required	Required

Containment measures		***Containment levels***			
		1	**2**	**3**	**4**
10	Specific measures to adequately ventilate the controlled areas to minimise air contamination	Required where and to the extent the risk assessment shows it is required (for GM only)	Required where and to the extent the risk assessment shows it is required	Required where and to the extent the risk assessment shows it is required	Required
11	Controlled area maintained at an air pressure that is negative to the immediate surroundings	Not required	Not required	Required where and to the extent the risk assessment shows it is required	Required
12	Input and extract air to the controlled area should be HEPA filtered	Not required	Not required	Required for extract air, required for input air where and to the extent the risk assessment shows it is required	Required for input and extract air
13	Access restricted to authorised personnel only	Not required	Required	Required	Required via airlock
14	Decontamination and washing facilities provided for personnel	Required	Required	Required	Required
15	Personnel should shower before leaving the controlled area	Not required	Not required	Required where and to the extent the risk assessment shows it is required	Required
16	Personnel shall wear personal protective clothing	Required (work clothing)	Required (work clothing)	Required	Required, complete change
17	Inactivation of biological agents and GMMs in effluent from handwashing sinks and showers or similar effluents	Not required	Not required	Required where and to the extent the risk assessment shows it is required	Required
18	Inactivation of biological agents and GMMs in contaminated material and waste including those in process effluent before final discharge	Required where and to the extent the risk assessment shows it is required	Required by validated means	Required by validated means	Required by validated means

Laboratory containment measures (Table 7)

The mechanism for determining the containment measures is underpinned by the requirements that the risk through exposure of humans and the environment, as a result of activities involving microorganisms, should be reduced to the lowest level that is reasonably practicable. In addition to the containment measures set out in CU 2010, the principles of *good microbiological practice* and *good occupational safety and hygiene* must be applied, to the extent to which they are appropriate. The application of the general principles of *good microbiological practice* and of *good occupational safety and hygiene* are required for *all activities* in *any setting*.

It is important that users consider measures other than those set out in the tables. Some control measures deemed necessary by the risk assessment may not be specifically mentioned. For example, the use of sealed centrifuge rotor buckets or respiratory protective equipment might be required in certain circumstances to protect the user against aerosols. The risk assessment should be used to identify particular elements of containment that are lacking and the measures implemented accordingly to afford protection for human health and the environment.

The laboratory suite is to be separated from other areas in the same building or is in a separate building

The laboratory suite is to be separated from other areas in the same building or is in a separate building	Not required	Not required	Required	Required

At CL3 and CL4, this requirement reflects the intrinsically greater hazards associated with the work. Separation can be achieved by locating the laboratory suite away from busy (or in the case of some CL3 laboratory suites, public) thoroughfares of the building. Separation helps to reinforce the demarcation between the different working practices and management arrangements required at CL3 and CL4 compared with CL1 and CL2.

Input and extract air from the laboratory to be filtered using HEPA or equivalent

Containment measure	CL1	CL2	CL3	CL4
Input and extract air from the laboratory to be filtered using HEPA or equivalent	Not required	Not required	Required on extract	Required on input air, double on extract

HEPA filters on the extract system are required at CL3 and CL4 to maintain containment of the facility in the event of an uncontrolled release of microorganisms. For CL4 facilities, the requirement for HEPA filtration on the supply and double HEPA filtration on the extract system reflects the greater hazards associated with a release outside of the laboratory. Two HEPA filters are used on the extract system as a contingency to maintain secondary containment in the event of a failure in one of the filters and or seals. Here, HEPA filters should be arranged in series and be able to be accessed safely for testing and changing. The requirement for HEPA filtration on the supply air system to CL4 provides an additional layer of safety that protects against the loss of secondary containment through the laboratory becoming positively pressurised. It may be possible to use equally effective alternatives to a HEPA filter on the supply air system e.g. the use of gas tight dampers which automatically close in the event of a failure in the extract system fan(s) i.e. the dampers are interlocked to the extract fan(s).

HEPA filters should meet the performance criteria of a class H14 filter as defined in BS EN 1822-1: 1998, for viruses. For larger organisms, lower H13 or H12 filters should be appropriate.

Access to be restricted to authorised persons only

Containment measure	CL1	CL2	CL3	CL4
Access to be restricted to authorised persons only	Not required	Required	Required	Required Via airlock

Restriction of access to CL2, CL3 and CL4 laboratories is required to prevent inadvertent or deliberate access to the facility by people who are unaware of the risks posed in such facilities, or have not been appropriately trained in order to conduct themselves safely.

The means by which access is restricted will vary between facilities and will depend heavily on the containment level. At CL2, it would be acceptable to restrict access using management controls i.e. monitoring who is entering the laboratory during periods when the doors are unlocked. Include reference to overarching security legislation i.e. ATCSA 2001, to keep certain pathogens secure.

At CL3 it is more important to restrict who enters the laboratory or animal facility so it may be necessary to install mechanical restriction. One possible solution could be to install a lock and key or swipe/ proximity card system. Digital locks that operate by pressing a sequence of buttons on the lock may be acceptable but it is important that the sequence code is changed if staff members change or the code becomes known by unauthorised individuals.

At CL4 it is recommended that at least two methods to restrict entry are used simultaneously e.g., proximity card and personal identification number. It may be beneficial to contact your local counter terrorism security advisor or national counter terrorism security office when deciding upon a system for restricted access at CL4.

The laboratory is sealable to permit fumigation

Containment measure	CL1	CL2	CL3	CL4
The laboratory is sealable to permit fumigation	Not required	Not required	Required	Required

At CL3 and CL4 the laboratory must be sealable to permit fumigation. This reflects the greater hazards associated with HG3 and HG4 microorganisms. In the event of an uncontrolled release it is of critical importance that the laboratory is properly decontaminated in order that work may recommence safely. Given the serious consequences of exposure to HG3 or HG4 agents capable of causing human infection following a release within the laboratory, and the often low infectious doses of such organisms, the most effective means of disinfecting a whole room is the use of a gaseous/ vaporised disinfectant since this will contact all surfaces.

The purpose of the requirement for laboratory sealability is to ensure that the fumigant is retained within the laboratory in order to effectively decontaminate the surfaces. It should also be noted that the escape of fumigant from the room during the fumigation process is also undesirable due to harmful effects on human health that could result from exposure to the fumigant. Currently, the most common means of disinfecting CL3 and CL4 facilities is to fumigate using formaldehyde vapour, which, upon exposure, is known to cause serious adverse health effects.

The requirement for room sealability will remain if alternatives to formaldehyde are used unless it can be demonstrated that the fumigant is harmless to human health. HSE has published guidance on methods available to assess laboratory sealability and the frequency of such assessments. Part 3 of the SACGM Compendium of Guidance provides further details on fumigation of rooms and microbiological safety cabinets. It also provides an overview of the various types of fumigants available.

Specified disinfection procedure

Containment measure	CL1	CL2	CL3	CL4
Specified disinfection procedure	Required where and to extent the risk assessment shows it is required	Required	Required	Required

At CL2, CL3 and CL4 specified disinfection procedures must be in place and in some instances they may be needed at CL1. It is important that disinfection protocols are in place for both routine use and for use following an unintended release of microorganisms and that their efficacy has been assessed under in-use conditions. Efficacy can be assessed in a number of ways and may involve a combination of: examining manufacturers' literature; examining relevant peer-reviewed literature; and use of in-house testing.

Disinfection procedures should detail the type of disinfection to be used, the working concentration of the disinfectant and contact times that give effective disinfection for the microorganisms used in the facility. Other factors that should be considered should include the volume of spilled material and the location of the spill e.g., outside of a micro-biological safety cabinet (MSC). Clearly, disinfection procedures will be influenced by the particular hazards posed by the microorganisms used. For example, it is likely that an unintended release of HG3 agents outside of the confines of a MSC will result in fumigation of the room unless the risk assessment indicates otherwise.

Further advice on disinfection procedures at CL2 and CL3 can be found in the HSE publication the Management, Design and Operation of Microbiological Containment Laboratories and in Biological agents: Managing the risks in laboratories and healthcare premises. When considering disinfectants for use with specified animal pathogens, you should refer to the Department for Environment, Food and Rural Affairs (Defra) approved list of disinfectants.

The laboratory to be maintained at an air pressure that is negative relative to the immediate surroundings

Containment measure	CL1	CL2	CL3	CL4
The laboratory to be maintained at an air pressure that is negative relative to the immediate surroundings	Not required	Not required	Required	Required

At CL3 and CL4 maintenance of a negative air pressure ensures that there is a net inward airflow and is a means of ensuring the secondary containment of the facility i.e. protection of people and the environment outside of the facility in the event of an uncontrolled release of category 3 or 4 biological agents/microorganisms within the laboratory.

There are no legal specified pressure differentials for CL3 and CL4 but typical values for CL3 should range between -30 to -50 Pa. At CL4 a negative pressure cascade should exist between the exterior environment and the laboratory as you move through airlocks and showering/ changing rooms etc. Where practical, a fall of approximately -30 Pa for each layer of the cascade is recommended. It may not always be possible to achieve this, e.g. facilities with numerous rooms, but you should ensure that the pressure differentials are sufficient to maintain containment, notably an inward movement of air into the containment area.

For CL3 facilities negative pressure can be achieved by a variety of means. Depending on the size of the room, some facilities are able to generate sufficient inward airflow by means of a MSC ducting exhaust air to atmosphere using passive make-up air through vents in walls or doors. For other CL3 facilities, independent mechanical ventilation may be used to provide the necessary negative pressure, or there may be a combination of both. At CL4 independent mechanical ventilation should be used.

At both CL3 and CL4, where independent mechanical ventilation provide the inward airflow, it must be capable of safe isolation e.g. by means of dampers to ensure that the room can be sealed to allow fumigation. The supply and extract fans must also be interlocked to prevent the possibility of the room becoming positively pressurised in the event of extract fan failure.

Efficient vector control, e.g. for rodents and insects

Containment measure	CL1	CL2	CL3	CL4
Efficient vector control, e.g. for rodents and insects	Required where and to the extent the risk assessment shows it is required	Required for GM and animal pathogens otherwise required where and to the extent the risk assessment shows it is required	Required	Required

At CL1, this control measure must be applied where the risk assessment shows that it is necessary to have an efficient system for the control of disease vectors that could disseminate the microorganism. The precise

control method will depend upon the nature of the vector e.g. rodents or insects. At CL2 there is a requirement to control vectors when working with GMMs or animal pathogens and for wild-type human pathogens where the risk assessment indicates that it is necessary. At CL3 and CL4 this measure is required for all microorganisms covered by CU 2010.

This measure will be especially important when working with microorganisms that can infect rodents or be transmitted by insects but consideration should also be given to pathogens that could be mechanically transferred to susceptible species by vectors.

Surfaces impervious to water, easy to clean and resistant to acids, alkalis, solvents, disinfectants and decontamination agents used for decontamination

Containment measure	CL1	CL2	CL3	CL4
Surfaces impervious to water, easy to clean and resistant to acids, alkalis, solvents, disinfectants and decontamination agents used for decontamination	Required for bench (GM only)	Required for bench	Required for bench and floor	Required for bench, floor, walls and ceiling

There is a regulatory requirement for the laboratory bench surfaces to be easily cleaned, be impervious to water and resistant to acids, alkalis, solvents, disinfectants and other decontamination agents that may be in use. The rationale for this requirement is due to the need to be able to adequately decontaminate benches, floors etc. in the event of a spillage of microorganisms.

If surfaces have been damaged due to the use of acids, disinfectants etc., then a spillage could result in the microorganisms penetrating the material used for benching, flooring etc. making it difficult to decontaminate. At CL1, for work with GMMs, this control measure is required for benches only. For all types of microorganisms it is required for benches at CL2, benches and floors at CL3 and benches floors, walls and ceilings at CL4. This is particularly important where *in vivo* work is conducted which could result in widespread contamination of all surfaces depending on the microorganisms being studied.

Safe storage of biological agents

Containment measure	CL1	CL2	CL3	CL4
Safe storage of biological agents	Required where and to extent the risk assessment shows it is required	Required	Required	Safe and secure storage required

There may be a regulatory requirement to have a system for the safe storage of microorganisms at CL1 if the risk assessment indicates that it is necessary and to what extent Generally, cultures should be stored in appropriate vessels, be clearly labelled and be, so far as is reasonably practical, stored within the laboratory or nearby. The same would apply at CL2 with storage being within the laboratory or laboratory suite.

Ideally, viable materials requiring level 3 containment should only be stored and handled within the CL3 laboratory itself. Fridges and freezers used for storage outside of the laboratory should be kept locked. At CL4, all viable material must only be stored and handled within the containment level 4 suite. Fridges, freezers and storage containers should be kept locked when not in use. For work with pathogens (and toxins) listed in Schedule 5, Part 7, Anti-Terrorism, Crime and Security Act 2001, it is likely there will be a requirement for safe storage for biosecurity purposes. The increase in stringency with increasing containment levels is a simple reflection of the potential damage that could be caused to humans and the environment if unauthorised access was gained to viable material either accidentally or intentionally.

An observation window or alternative is to be present so that occupants can be seen

Containment measure	CL1	CL2	CL3	CL4
An observation window or alternative is to be present so that occupants can be seen	Required where and to extent the risk assessment shows it is required	Required where and to extent the risk assessment shows it is required	Required	Required

This requirement is in place to facilitate rapid identification of problems which could occur within a laboratory. For example, if an occupant were to lose consciousness and were working alone they rely on others being able to see into the laboratory and take appropriate action or to respond to a spillage of biological agents capable of infecting humans which may require immediate assistance from persons outside of the laboratory. In addition, a method

visualising the occupants' means that people from outside can see what work is being done and choose an appropriate time to enter the laboratory.

At CL1 and CL2, an observation window or alternative method of visualizing the laboratory occupants might be required where the risk assessment indicates that it is necessary. It is unlikely that such a system will be required for safety reasons at these levels, although it may offer additional protection for lone workers. At CL3 and CL4, this measure is required and often a glass panel in the laboratory door/ wall will be adequate. Where the view into a laboratory is restricted it may be possible to solve the problem by installing a convex mirror in the laboratory.

Alternatives are sometimes used, particularly at CL4 where laboratory suites are often stand-alone buildings where, for security reasons, there may not be windows or glass panels in doors. In such cases, it may be necessary to install a closed circuit television system, or equivalent, in order to be able to observe occupants in the laboratory. However, where possible at CL4, it should be noted that a second competent person should be present in the laboratory suite when it is occupied. It is also worth consulting the Anti Terrorism, Crime and Security Act 2001 before choosing the method of observing laboratory occupants if working with Schedule 5 agents.

For work with non-zoonotic specified animal pathogens it may be possible to derogate this control measure subject to approval from the Competent Authority.

A laboratory is to contain its own equipment

Containment measure	CL1	CL2	CL3	CL4
A laboratory is to contain its own equipment	Not required	Not required	Required where and to extent the risk assessment shows it is required	Required

At CL1 and CL2 there is no requirement to have equipment solely dedicated for use in those laboratories. However, equipment should be cleaned and thoroughly decontaminated before removing from the laboratory for repair or servicing.

At CL3 there is a requirement for the laboratory to contain its own dedicated equipment, where the risk assessment indicates that it is necessary. For example, you may wish to use of a specialised piece of equipment located at CL2 which is used almost exclusively lower hazard work e.g. flow cytometer. In this example, it may not be reasonably practicable to have a duplicate piece of equipment at CL3 due to expense and the amount of time it will be required for class 3 activities. It would also be undesirable to have untrained/ unauthorised persons entering the CL3 to use the equipment for lower hazard

work as this may create additional risks. If equipment, located in other laboratories is required, material should be transported and stored without spillage in properly labelled robust containers that are opened only in an appropriate laboratory.

At CL4, no equipment may be removed from the laboratory without disinfection. A secondary ventilated airlock that can be fumigated may be required to pass equipment into, and out of, the laboratory unit. Equipment should only be removed from the secondary airlock by responsible or competent persons and in accordance with defined local codes of practice.

Infected material to be handled in a safety cabinet or isolator or other suitable containment

Containment measure	CL1	CL2	CL3	CL4
Infected material to be handled in a safety cabinet or isolator or other suitable containment	Not required	Required where and to extent the risk assessment shows it is required	Required safety cabinet or enclosure required for GM	Required; safety cabinet or enclosure required for GM

At CL1 there is no requirement for the use of microbiological safety cabinets or other similar equipment for worker protection. However, procedures should be in place to limit the production and dissemination of aerosols. Containment equipment such as a microbiological safety cabinet might be used to prevent contamination of the work or products being handled at CL1 but are not required to protect humans and the environment.

At CL2, if the microorganisms can be disseminated by aerosol and are capable of causing human disease, procedures that are likely to generate aerosols, e.g. pipetting, vigorous shaking or sonication, should take place within a microbiological safety cabinet or similar containment equipment. Class I or II cabinets may be used depending on which is deemed the most appropriate. Extract air from microbiological safety cabinets should always be HEPA filtered.

At CL3 all work with infectious material that can be disseminated by aerosol and are capable of causing human disease must take place in a microbiological safety cabinet or similar containment equipment. Normally a Class I or Class II microbiological safety cabinet will be used, but a class III cabinet may be required for work with organisms with an airborne route of transmission that are capable of causing human disease. Where re-circulating Class II cabinets are used, exhaust air should be passed through two HEPA filters in series and consideration given to heat and humidity build up and fumigation procedures. Where microorganisms are not capable of causing human disease it would be feasible to apply for derogation from using this specific measure at CL3.

At CL4 it is a regulatory requirement that a Class III microbiological safety cabinet or equivalent be present and that all procedures with infectious material must take place within such containment equipment. Exhaust air should be passed through two HEPA filters in series before it is vented to outside air or re-circulated. An open-fronted (class I or class II) cabinet may be used with agreement from the Competent Authority. An open-fronted cabinet may be used in agreement with the operator if there is no risk to the operator.

For laboratories which are considering using suits as a measure to protect the operator should refer to Part 4 of the Principles, Design and Operation of Containment Level 4 Facilities for further information.

Specific measures to control aerosol dissemination

Containment measure	CL1	CL2	CL3	CL4
Specific measures to control aerosol dissemination	Not required	Required so as to minimise	Required so as to prevent	Required so as to prevent

Procedures to minimise aerosol dissemination are required at CL2. Some work may be conducted on the open bench but procedures that may result in aerosol production, e.g. shaking sonication or centrifugation, should be contained within suitable equipment e.g. a MSC or, for centrifugation, sealed centrifuge buckets. Sealed buckets should be tested in accordance with BS EN 61010-2-20:1995.

At CL3 measures to prevent aerosol dissemination are required. All work at CL3 involving infectious material must take place within a microbiological safety cabinet, isolator or similar (see previous containment requirement). Centrifugation should take place within sealed containers that have been tested in accordance with BS EN 61010-2-20:1995.

Measures to prevent aerosol dissemination are required and all work at containment level 4 material must take place within a Class III MSC, isolator or similar unless the risks are solely environmental (see previous containment requirement).

Shower prior to leaving the contained area

Containment measure	CL1	CL2	CL3	CL4
Shower prior to leaving the contained area	Not required	Not required	Required where and to extent the risk assessment shows it is required	Required

At CL1 and CL2 there is no requirement for a showering facility to be present and workers are not required to shower when leaving the facility. However, hands should be washed immediately if contamination with microorganisms is suspected, after handling viable microorganisms or before leaving the laboratory. The same applies at CL3 unless the risk assessment indicates that it is necessary to shower before leaving the facility. At CL4 a shower must be installed and all personnel must shower before leaving the facility.

If a shower is required, careful consideration should be given to its location i.e. it must be located before leaving the contained area. For biological agents capable of causing human disease, the shower should be located before leaving the laboratory suite. For biological agents/microorganisms which only present a risk to susceptible animals or the environment, the shower should be located at the exit of the contained envelope of the facility. Any additional information for employees, e.g. minimum time it is necessary to spend in the shower, should be included in the local code of practice.

For showers used for the decontamination of suits (if used), please refer to part 4 of the Principles, Design and Operation of Containment Level 4 Facilities for further information.

Protective clothing

Containment measure	CL1	CL2	CL3	CL4
Protective clothing	Suitable protective clothing required	Suitable protective clothing required	Suitable protective clothing required; footwear required where and to extent the risk assessment shows it is required	Complete change of clothing and footwear required before entry and exit to the contained area.

At all containment levels there is a requirement for suitable protective clothing to be worn. At CL1 and CL2 this would normally comprise laboratory coats or gowns that are worn when in the laboratory and removed upon exit. Eye protection might also be required if airborne contamination is possible and there is a risk to the operator.

At CL3, suitable protective clothing normally comprises laboratory coats or gowns (side- or back-fastening) that are worn when in the laboratory and removed prior to hand washing upon exit. Laboratory gowns should be changed on a regular basis and immediately if they become contaminated. Gowns must be autoclaved before laundering. Where the risk assessment shows it to be required, protective footwear, e.g. disposable overshoes, must

also be worn. Eye protection might also be required if aerosols or airborne contamination is possible and there is a risk to the operator.

At CL4 there should be a complete change of clothing and footwear. After work, clothing should be removed on the containment side of the airlock and placed in a container for autoclaving. For specific CL4 guidance on the use of suits as a method of operator protection please refer to the Principles, Design and Operation of Containment Level 4 Facilities.

Obviously the specific requirements for protective clothing will vary depending on the actives that are being carried out and whether the risk is to the operator or the environment. For example, some animal studies may require additional protective clothing e.g. waterproof clothing or, if there is a risk of transmission to the operator, the use of masks/ respirators for certain activities may be required. The risk assessment should identify all protective clothing required above and beyond the legal minimum in this guidance.

Gloves

Containment measure	CL1	CL2	CL3	CL4
Gloves	Not required	Required where and to extent the risk assessment shows it is required	Required	Required

At CL1 there is no regulatory requirement for gloves to be worn. However, it is acknowledged that gloves may be used to prevent contamination of the work or to protect workers against other chemical or biological contaminants and wearing gloves for these reasons would not constitute a class 2 activity. At CL2 it is necessary to wear gloves where the risk assessment indicates that they are necessary to protect the operator and perhaps only for certain tasks.

If gloves are necessary they should be removed for handling items that will be touched by others who may not be wearing gloves (e.g. telephone handsets, door-handles). At CL3 and CL4 there is a requirement for disposable protective gloves to be worn for all work involving infectious material. This measure is in place to protect the operator and there may be some activities with non-zoonotic animal pathogens that do not require the use of gloves. If this is the case derogation should be requested from the Competent Authority.

Inactivation of biological agents in effluent from hand-washing sinks and showers and similar effluents

Containment measure	CL1	CL2	CL3	CL4
Inactivation of biological agents and GMMs in effluent from hand-washing sinks and showers and similar effluents	Not required	Not required	Required where and to extent the risk assessment shows it is required	Required

There is no requirement for this at CL1 and CL2. At CL3, inactivation of biological agents and GMMs in effluent from hand washing sinks and showers will be required prior to release if shown to be necessary by the risk assessment. Generally, this will not be required, as gloves should be worn. Effluent should only need to be collected if a gross contamination of hands is suspected, or the risk assessment shows that showering is required to protect humans or the environment.

At CL4, inactivation of microorganisms in effluent from hand washing sinks and showers will be required prior to discharge. It is essential that the method of choice for inactivation of agents is sufficient to completely inactivate the microorganisms in the effluent. The preferred method, and accepted method at CL4, is heat inactivation as it is the most reliable and reproducible method although it is still necessary to demonstrate that the parameters of use are sufficient for complete inactivation of the microorganisms. If a suited CL4 laboratory is being used please refer to part 4 of the Principles, Design and Operation of Containment Level 4 Facilities for further information on decontamination of suits.

It may be possible to use chemical inactivation at CL3 although this would require a comprehensive validation programme to demonstrate that complete inactivation was achieved. It is also imperative that effluent is safely and securely transported to the area where it will be inactivated. If this is via pipework it, and any holding tanks, should be periodically examined to ensure that they are intact and not likely to present a risk to humans or the environment through leakage.

Inactivation of biological agents in contaminated material and waste

Containment measure	CL1	CL2	CL3	CL4
Inactivation of biological agents and GMMs in contaminated material and waste	Required where and to extent the risk assessment shows it is required	Required by a validated means	Required by a validated means with waste inactivated in the laboratory suite	Required by a validated means with waste inactivated in the laboratory

At CL1, the risk assessment will indicate whether it is necessary to inactivate biological agents in contaminated material and waste. If it is necessary to inactivate material or waste according to the risk assessment it should be done using a method known to be efficacious against the microorganisms present. At all other containment levels, waste material containing viable microorganisms, including spent culture fluid and other media, are required to be inactivated by validated means prior to disposal. Contaminated laboratory glassware and other materials awaiting disinfection should be stored in a safe manner and pipettes should be totally immersed in disinfectant, where necessary. Materials that require inactivation and disposal at a secondary facility, either within the building or off-site (for CL1 and CL2 waste only), should be transported in leak-proof containers to prevent spillage.

Inactivation methods should be monitored to ensure that they are working correctly under all working conditions e.g. the effectiveness of some disinfectants can be impaired by the presence of large amounts of organic matter or the use of buffered culture media. At CL3 all waste material containing viable microorganisms must be inactivated within the laboratory suite prior to removal. Reliance on methods such as chemical inactivation may not be appropriate for some CL3 work. Physical methods, such as autoclaving, rather than chemical methods of inactivation should therefore be used in preference. Chemically inactivated material should preferably be autoclaved prior to discharge, unless it can be demonstrated that complete inactivation has been achieved (note that chlorine-based disinfectants have the potential to cause damage to the autoclave).

At CL4, all material and waste must be inactivated and made safe by validated means within the laboratory prior to removal. Materials that cannot be autoclaved must be decontaminated by disinfection before removal. A double-ended dunk-tank with an effective disinfectant or an equivalent system may be required for this purpose. If fumigation of the facility is required, the dunk-tank should be sealable if the disinfectant is incompatible with the fumigant used. At CL4, chemical inactivation should not be used as the sole inactivation method, but may be used in conjunction with autoclaving. Inactivation methods should be monitored to ensure that they are working correctly. The performance of the autoclave should be regularly tested using an independent thermocouple placed at the centre of the load and waste should only be discharged if the cycle was completed successfully. Waste

should only be removed or handled by responsible or competent persons in accordance with defined local codes of practice.

In large animal facilities at CL4 (and possibly CL3), it is likely that heat inactivation will be used as a method for inactivation of agents in bedding and manure.

Entry to the contained area via airlock

Containment measure	CL1	CL2	CL3	CL4
Entry to the contained area via airlock	Not required	Not required	Required where and to extent the risk assessment shows it is required	Required

There is no requirement for an airlock at CL1 and CL2. At CL4 and where the risk assessment indicates a need at CL3, entry to the laboratory must be via an airlock or lobby, i.e. a chamber isolated from the laboratory, except in relation to animal pathogen that don't pose a risk to human health where the airlock can be located at the entrance to the laboratory suite.. An airlock may be a single chamber but the changing/ showering facilities often act as the airlock. In either case there should be a net inward airflow from the clean side of the air lock towards the contained side. Ideally, the entrance and exit to the airlock should be fitted with interlocking doors. In practice, a lobby area rather than a mechanically ventilated airlock is sufficient at CL3 and it is unusual to have a dedicated showering facility.

Autoclave

Containment measure	CL1	CL2	CL3	CL4
Autoclave	Required on the premises (GM only)	Required in the building	Required in the laboratory suite	Double ended autoclave required in the laboratory

At CL1 an autoclave is required to be available on the premises, but not necessarily in the same building for GM only. At this level of containment disinfection will usually be a satisfactory means of waste treatment and if no autoclave is available derogation may be sought provided that a validated means of microorganism inactivation is in place. Alternative methods, including waste removal by contractors, may also be acceptable provided that the disposal method, e.g. heat treatment, is validated and that waste is stored and transported in a way that does not increase risk to humans and the environment.

At CL2 an autoclave is required to be available within the same building as the laboratory. At CL2, disinfection will often be a satisfactory means of waste treatment and, if no autoclave is available, derogation may be sought from the Competent Authority provided that a validated means of inactivation is in place. Again, alternative methods, including waste removal by contractors, may also be acceptable provided that the disposal method is validated and that waste is stored and transported in a way that does not increase risk.

At CL3 an autoclave is required to be available within the laboratory suite. Where the autoclave is outside the laboratory but within the laboratory suite, validated procedures for the safe transfer of material into that autoclave are required that provide a level of protection equivalent to having an autoclave in the laboratory. Although it is permissible for waste materials to be inactivated by chemical means prior to disposal, it is considered good practice to autoclave waste at CL3. Where chemical disinfection is used, the disinfection procedures must be validated under working conditions.

At CL4 a double-ended autoclave is required to be installed within the laboratory. The equipment should have interlocking doors, be loaded within the laboratory with inactivated waste removal in a outside of the contained area.

Use of a biohazard sign

Containment measure	CL1	CL2	CL3	CL4
Use of a biohazard sign	Required where and to extent the risk assessment shows it is required	Required	Required	Required

At CL1 a biohazard sign should be displayed if the risk assessment shows that this is required. At CL2, CL3 and CL4 a biohazard sign must be clearly displayed at the entrance to the facility to inform people of the risks from microorganisms. Other legislation, in particular ATCSA 2001, may indicate an increased security risk by displaying biohazard signs where work is being undertaken with agents listed in ATCSA 2001, Schedule 5. In such cases, this legislation would apply over and above the Directive requirements and display of biohazard signs would therefore not be required. In this case, derogation should be sought from the Competent Authority from applying this containment, with full justification for the request.

Plant growth facility containment measures (see table 8)

This section is intended to give guidance to help users determine the appropriate standards of containment and control that should be applied to work involving microorganisms in conjunction with plants, for example within a plant growth facility. For activities with plants that involve handling microorganisms, the relevant containment measures for *laboratory activities* must be applied and therefore users should read laboratory containment measures in conjunction with this guidance. Where microorganisms and GM plants are both being handled, users should read Part 4 of the SACGM Compendium of Guidance, which covers activities involving the genetic modification of plants.

It should be noted that there are currently no CL4 facilities in the UK for work involving GMMs in association with plants. For this reason, the following guidance does not describe the requirements for this level of containment. If such work is proposed, or the construction of such a facility is planned then you should discuss the details of containment requirements, management control and design of the facility etc. in advance with the Competent Authority.

Permanent structure

Containment measure	CL1	CL2	CL3	CL4
Permanent structure	Required where and to the extent the risk assessment shows it is required	Required	Required	Required

At CL1 it is permissible to use a non-permanent structure. Facilities such as basic polytunnels may be appropriate, although the structure should be of suitable design and construction and be appropriately maintained so as to withstand normal climactic conditions over the period of the activity. Where the facility is a glasshouse it shall have a continuous waterproof covering. Permanent structures must have self-closing, lockable outer doors. It is recognised that most facilities of this type have doors that are not self-closing. Provided doors are not left open when the facility is not in use, users may consider this requirement to be met.

At CL2 there is a regulatory requirement that the facility is a permanent fixed structure with walls, a roof and a floor. Where the facility is a glasshouse (DN wording in directive is Greenhouse), it shall have a continuous waterproof covering. The facility must have self-closing, lockable outer doors. It is recognised that most facilities of this type have doors that are not self-closing. Provided doors are not left open when the facility is not in use, users may consider this requirement to be met. It is likely that the majority of such facilities will be a standard research glasshouse, although recent

technological advances in alternatives to glass may mean other structures are suitable. Facilities should be designed to withstand the local weather conditions and the potential for breakage through other activities, e.g. vandalism. The structure at CL2, 3 and 4 must be located on a site designed to prevent the entry of surface run-off water.

At CL3 there is a regulatory requirement that the facility is a permanent fixed structure with walls, a roof and a floor. It is likely that a CL3 plant growth facility will comprise either a highly engineered glasshouse or, more likely, growth rooms or cabinets within a controlled environment suite. Where a glasshouse or similar structure is used, an increased level of containment is expected when compared to an equivalent CL2 facility. For example, all joints, overlapping panes etc should be effectively caulked and, at the highest level, break-resistant glazing/polycarbonate sheeting should be used. The facility must have self-closing, lockable outer doors.

Entry via a separated room with two interlocking doors

Containment measure	CL1	CL2	CL3	CL4
Entry via a separated room with two interlocking doors	Not required	Required where and to the extent the risk assessment shows it is required	Required where and to the extent the risk assessment shows it is required	Required

At CL2, where the risk assessment shows that entry to the facility should be via a separated room with two interlocking doors, this can be achieved by either having a dedicated entrance lobby/vestibule (for example to a stand-alone glasshouse facility) or by using a shared header house area within a larger facility. Where access is via a lobby/vestibule, at its simplest containment can be achieved by staff being trained not to have the two doors open at the same time. It is good practice to lock the facility when unattended to prevent unauthorized access.

It is expected that a CL 3 plant growth facility handling moderately hazardous GMMs in association with plants will be entered via a lobby/vestibule with self closing doors. Entry via an airlock with a separate chamber with showering and changing facilities is not required. Consideration should be given to a system (e.g. audio/visual alarm or electronic interlock) that ensures that the two doors are not open at the same time. Within the lobby area, there should be space to store laboratory coats dedicated to the facility and hand washing facilities should be provided with taps that can be operated without being touched by hand.

Control of contaminated run-off water

Containment measure	CL1	CL2	CL3	CL4
Control of contaminated run-off water	Required where and to the extent the risk assessment shows it is required	Required so as to minimise run-off	Required so as to prevent run-off	Required so as to prevent run-off

At CL1 where the risk assessment identifies that a GMM could be disseminated via the drainage system, control measures must be used to control run-off water. No plants should be planted directly into the ground. All higher plants should be grown in pots, trays or similar containers. All lower plants should be grown in physical containers such as flasks, tanks or fermenters. This could be supplemented with appropriate filters/ mesh covers to limit the amount of soil, plant material and water entering the drains. The facility is not required to have a dedicated drainage system and therefore soakaways may be sufficient.

At CL2 control measures must be taken to minimise the dissemination of GMM material via run-off water (i.e. the drainage route). It is recognised that the benching used may not be impervious to water and saucers or trays should be used, supplemented with appropriate hygiene measures to limit the amount of soil, plant material and water entering the drains. For example, hand-watering systems are likely to be in place as opposed to automatic systems and appropriate filters/ mesh covers could be fitted to the floor drains.

At CL3 there is a regulatory requirement to control run-off water within a CL3 facility so as to prevent the dissemination of GMM material. In addition to placing all pots on impervious trays or lining all benches with impervious plastic sheeting, the floor of the facility should be impervious to water. Where practicable, the facility should have no drainage or the drains should be blocked throughout the course of the activity with an appropriate system in place to collect and treat any large volumes of water. Where the facility remains connected to the drains throughout the course of the activity, it should be connected to an appropriate “kill tank” for the validated inactivation of any potential GMM material that may enter the system.

Effective control of disease vectors such as insects, rodents and arthropods which could disseminate GMMs

Containment measure	CL1	CL2	CL3	CL4
Effective control of disease vectors eg insects, rodents, arthropods which could disseminate GMMs	Required	Required	Required	Required

At CL1 there is a regulatory requirement for effective control of vectors that could disseminate the GMM material. For a CL1 facility, there should be effective screening against e.g. rodents and birds. For example, a polytunnel is unlikely to offer appropriate protection against invertebrate or fungal vectors. Where the risk assessment shows that these should be controlled, a permanent structure, such as a glasshouse, might be more appropriate.

At CL2 there is a regulatory requirement to control potential disease vectors that could disseminate the GM plant pathogens from the facility. This should include invertebrates. Vents should have a mesh screen appropriate to the invertebrate species to be excluded. Caulking materials should be used to seal any gaps, such as those between glass panes and service pipes, and brushes or pneumatic strips should be fitted around the edges of doors. In addition an efficient control regime should be used involving monitoring traps (such as sticky traps) and where necessary appropriate chemical control. Where biological control agents are to be introduced into the facility, the risk assessment should consider the possibility of these agents themselves disseminating the GMM. If the risk assessment has identified soil-borne organisms (such as nematodes and fungi) as vectors for the GMM, the control of these should be achieved using similar measures to those described for run-off water.

In addition to the control measures for CL2, it is expected that a CL3 glasshouse would not have openable vents, with temperature regimes instead being maintained by air-conditioning or air-handling arrangements. Soil-borne vectors should be controlled using the arrangements described above to prevent dissemination by run-off water. It is likely that CL3 facilities will be the only ones in which the deliberate, experimental transmission of GMM material using invertebrate vectors are permitted. However, the use of specialist insectary facility containing growth cabinets in which plants can be grown is encouraged. Within such a facility temperature and light gradients can be used to provide additional barriers to control the movement of invertebrates. The experiments should involve the minimum number of plants, should be short term and ideally should be undertaken when the environmental conditions outside of the facility are less likely to permit the survival of the vector.

Effective control of pollen, seeds and other plant material which could disseminate GMMs

Containment measure	CL1	CL2	CL3	CL4
Effective control of pollen, seeds and other plant material which could disseminate GMMs	Required where and to the extent the risk assessment shows it is required	Required so as to minimise dissemination	Required so as to prevent dissemination	Required so as to prevent dissemination

At CL1, where the risk assessment shows that it is required, the dissemination of GMMs in plant pollen, seeds and other plant material must be effectively controlled. For example, a polytunnel may not provide a suitable level of assurance that this can be successfully achieved and therefore, a more permanent structure (e.g. a glasshouse) may be more appropriate. The use of a certain degree of biological containment is inherent to all facilities. GMMs within the facility may be unable to infect plants in the receiving environment, either because there are no suitable host species or because the environmental conditions are unfavourable. The facility should be dedicated to experimental plants only and the growing of ornamental plants for decorative purposes should not take place.

At CL2, the dissemination of GMMs in plant pollen, seeds and other plant material must be minimised. In addition, the dissemination of GMM in other plant material (including plant sap) should be minimised and suitable measures employed to prevent spread of mechanically transmitted GM pathogens. Since class 2 GMMs have been identified as being able to infect species in the environment, the growth of plants in the immediate vicinity of the facility should be restricted in order to control against potential GMM hosts and compatible relatives of the GM plants. This can be reasonably achieved by employing a paving or gravel barrier around the facility, in conjunction with herbicide treatment regimes. There should be different compartments within the facility for GM and non-GM work. Where the sharing of compartments between different activities is unavoidable, the risk assessment should clearly outline the likelihood of contamination, taking into account susceptibility of plants to infection with the GMM and sexual compatibility.

Where the risk assessment shows that it is required, the dissemination of GMMs in plant pollen and seeds must be prevented. As well as pollen and seeds, there remains the regulatory requirement to prevent the dissemination of GMMs in other plant material (including plant sap). This should be prevented and suitable measures employed to prevent spread of mechanically transmitted GM pathogens. The most appropriate measures for controlling such dissemination are based on ensuring good levels of hygiene. Appropriate protective clothing must be worn and dedicated protective footwear, sticky floor mats or a footbath containing an appropriate validated chemical disinfectant could be used to control the dissemination of the GMM

on the feet of staff. GMMs that have been identified as being able to infect species in the environment, the growth of plants in the immediate vicinity of the facility should be restricted in order to control against potential GMM hosts and compatible relatives of the GM plants. This can be achieved as described for CL2 above.

Procedures for transfer of living material between the plant growth facilities, protective structures and laboratory shall control dissemination of GMMs

Containment measure	CL1	CL2	CL3	CL4
Procedures for transfer of living material between the plant growth facilities, protective structures and laboratory shall control dissemination of GMMs	Required so as to minimise dissemination	Required so as to minimise dissemination	Required so as to prevent dissemination	Required so as to prevent dissemination

At CL1 and CL2, when transferring GM material between different facilities on site, there is a regulatory requirement that the dissemination of GMMs be minimised. Secondary containment (e.g. a bag or box) should be used in conjunction with a transfer container, such as a wheelie bin.

At CL3 and CL4 the dissemination of the GMM needs to be prevented during transfer, secondary containment (e.g. a bag or box) should be used in conjunction with a robust, leak-proof secondary container that should contain the GMM in the event of an accident.

Animal unit containment measures (see table 9)

This section is intended to give guidance to help users determine the appropriate standards of containment and control that should be applied to work involving microorganisms in conjunction with animals, for example within an animal facility. For activities with animals that involve handling microorganisms, the relevant containment measures for *laboratory activities* must be applied and therefore users should read laboratory containment measures in conjunction with this guidance. Where microorganisms and GM animals are both being handled, users should read Part 5 of the SACGM Compendium of Guidance, which covers activities involving the genetic modification of animals.

The Regulations set out certain specific requirements for activities being undertaken in animal units. In some cases the specifications *modify* those for laboratory containment; in others they impose *additional* requirements. The guidance in this section outlines the additional animal house requirements. Some control measures deemed necessary by the risk assessment may not be listed in the containment tables. The activity class is determined solely by those measures actually listed. The risk assessment must always take precedence and **all** measures identified as necessary must be applied (there is a general requirement for the exposure of humans and the environment to microorganisms to be as low as reasonably practicable and the principles of good microbiological practice and of good occupational safety and hygiene must also be applied).

The containment measures indicated by the risk assessment may consist of a mixture of measures from two different containment levels. In these cases, the higher level of containment will determine the activity class and must be applied. A request can be made to the Competent Authority at the time of notification for permission to derogate the need for certain measures from the higher containment level. Unless you have received permission for such derogation, you must apply all of the containment and control measures from the higher level.

Animal containment facility to be separated from other areas in the same building, or be in a separate building

Containment measure	CL1	CL2	CL3	CL4
Isolation of animal Unit	Required where and to the extent the risk assessment shows it is required	Required	Required	Required

At CL1, the Regulations require that the animal unit be isolated from areas used for other activities, if the risk assessment shows that it is required. At

CL2, CL3 and CL4 the animal unit must be isolated from areas used for other activities. This means separation of the animal unit from other areas in the same building (or situated in a separate building) and away from offices, communal areas and sections frequented by non-technical or non-authorised staff.

This requirement is the same as the laboratory containment measure for the workplace to be separated from other areas in the same building except that the requirement for separation is extended to CL2 for animal units.

Animal facilities separated by lockable doors

Containment measure	CL1	CL2	CL3	CL4
Animal facilities separated by lockable doors	Required where and to the extent the risk assessment shows it is required	Required	Required	Required

At CL1, animal facilities are required to be separated from other areas by lockable doors, where the risk assessment shows that this is required. Despite this measure only being necessary where the risk assessment indicates so, it is good practice to limit access to authorised persons only. At CL2, CL3 and CL4 this measure must be in place.

Animal facilities designed to facilitate decontamination (waterproof and easily washable material (cages etc.))

Containment measure	CL1	CL2	CL3	CL4
Animal facilities designed to facilitate decontamination (waterproof and easily washable material (cages etc.))	Required where and to the extent the risk assessment shows it is required	Required where and to the extent the risk assessment shows it is required	Required	Required

At CL1 and CL2, animal cages and other enclosure facilities must be designed to facilitate decontamination where the risk assessment shows this to be necessary. At CL3 and CL4 this measure must be used. Good hygiene should be maintained at all times and the use of waterproof and easily washable materials will aid this.

It is vitally import to be able to effectively decontaminate cages etc in order to minimise risks to humans and the environment. The method of choice for decontamination will vary depending on the agents involved. At higher containment levels it is common for cages to be fumigated and autoclaved so it is essential that suitable materials are used for them. Where it is not possible to autoclave cages etc. a suitable efficacious disinfectant should be used to decontaminate them following an experiment.

If facilities are unable to meet this requirement it may be feasible to use disposable cages which would require incineration after use.

Floor, walls and ceiling easily washable

Containment measure	CL1	CL2	CL3	CL4
Floor, walls and ceiling easily washable	Required where and to the extent the risk assessment shows it is required	Required for floor	Required for floor and walls and ceiling	Required for floor, walls and ceiling

At certain containment levels there is a regulatory requirement for the bench surfaces to be easy to clean and to be impervious to water and resistant to those acids, alkalis, solvents, disinfectants and other decontamination agents that may be expected in normal use. Furthermore, in animal containment facilities, at CL1, the floors, walls and ceilings of the facilities must be easily washable where the risk assessment shows that it is required and to what extent.

At CL2, CL3 and CL4 the floors of animal containment facilities must be easily washable. At CL3 and CL4 the walls of animal containment facilities must also be easily washable. At CL4 this requirement is extended to the ceiling.

This requirement is in place to ensure that all surfaces that can potentially be contaminated are composed of material that will facilitate ease of washing. This is particularly important in large animal containment facilities where contamination could be widely disseminated within the room.

Appropriate filters on isolators or isolated rooms

Containment measure	CL1	CL2	CL3	CL4
Appropriate filters on isolators or isolated rooms	Not required	Required where and to the extent the risk assessment shows it is required	Required	Required

At CL1, where the room itself is acting as an isolator, ventilated air must be HEPA filtered, if the risk assessment shows it is necessary (see animals kept in isolators). If the room is not being used as the isolator then there is no requirement at CL1. However, the need for appropriate filters on isolators and isolated rooms is determined by the risk assessment at CL2 and is required for CL3 and CL4.

It is worth noting that an isolator/ cabinet may be required to prepare the microorganisms for inoculation into the animal, although this is often done in a separate laboratory. If using an isolator, air extracted from the animal room itself must be HEPA filtered in addition to the air from the enclosure/ isolator.

Incinerator for the disposal of animal carcasses

Containment measure	CL1	CL2	CL3	CL4
Incinerator for the disposal of animal carcasses	Required to be accessible (GM only)	Required to be accessible	Required to be accessible	Required to be on site

At CL1, waste containing viable microorganisms, including animal waste and carcasses, must be inactivated by validated means before final disposal. At CL1, for carcasses containing viable GMMs, an incinerator must be accessible for the disposal of animal carcasses. Waste removal by contractors may also be acceptable, provided that the final disposal method e.g. incineration is validated and that waste is stored and transported in a way that does not increase risk. Agreement for the disposal of waste by a third party must be obtained from the Competent Authority.

At CL2 and CL3 the legislation requires that an incinerator is accessible for the disposal of animal carcasses but this can be off-site. Waste removal by contractors may also be acceptable, provided that the final disposal method e.g. incineration is validated and that waste is stored and transported in a way that does not increase risk. Agreement for the disposal of waste by a third party must be obtained from the competent authority

At CL4 an incinerator must be located on-site for the disposal of animal carcasses.

Appropriate barriers at the room exit and at drains or ventilation duct work

Containment measure	CL1	CL2	CL3	CL4
Appropriate barriers at the room exit and at drains or ventilation duct work	Required where and to the extent the risk assessment shows it is required	Required	Required	Required

This measure is designed to guard against escape or entry of animals which could act as vectors for the microorganisms. At CL1 and CL2, where the risk assessment shows it is required and at CL3 and CL4 there is a regulatory requirement for appropriate barriers to be placed at the exits and major penetration points (ventilation ducts and drains) within the facility. This may consist of a rodent barrier to be placed at the entrance/ exit to the facility to prevent small mammals that are at housed within the facility from escaping or mammals entering from the environment. In order to contain larger animals, it may be necessary to have a two-door entry system separated by a small chamber or change area. Mesh barriers should be placed on ventilation ducts and drains and be sufficient to contain those species that are being handled within the facility. Note that drains are not appropriate at CL4 unless they are connected to a system for validated inactivation of the waste.

Animals kept in appropriate containment facilities such as cages, pens, tanks etc.

Containment measure	CL1	CL2	CL3	CL4
Animals kept in appropriate containment facilities such as cages, pens, tanks etc.	Required where and to the extent the risk assessment shows it is required	Required where and to the extent the risk assessment shows it is required	Required where and to the extent the risk assessment shows it is required	Required where and to the extent the risk assessment shows it is required

Where the risk assessment shows that it is required, animals must be kept in appropriate confinement equipment, such as cages, pens or tanks.

Animals kept in isolators or isolated rooms

Containment measure	CL1	CL2	CL3	CL4
Animals kept in isolators or isolated rooms	Required where and to the extent the risk assessment shows it is required	Required where and to the extent the risk assessment shows it is required	Required where infection is by airborne route	Required

At CL1 and CL2, where the risk assessment shows that it is required, animals must be kept in isolators. HSE has published guidance on the use, testing and maintenance of laboratory and animal isolators for the containment of biological agents. Isolators might be needed for work with microorganisms that could pose a hazard to humans, other animals in the facility or the wider environment. Independently ventilated cages are not considered to be isolators and their use needs to be carefully assessed to determine if they can offer an equivalent level of protection to humans and the environment under specific conditions of use.

At CL3 and CL4 the use of specialised air-fed isolators will be required. However, it is not necessary to use isolators for all class 3 and 4 activities. For example, using air-fed suits for workers in conjunction with cages, pens & tanks for working with animals too large for isolators may be appropriate, although derogation should be sought from the Competent Authority, providing an explanation as to why isolators are not practicable and providing details on the effectiveness of the alternative method of animal containment. In addition the infection of large animals with SAPO agents which are not zoonotic is unlikely to take place in an isolator as such but the room may act as the isolation unit.

Containment measures for premises other than laboratories, plant growth facilities and animal facilities e.g. large-scale (see table 10)

The section is intended to give guidance to help users determine the appropriate standards of containment and control that should be applied to work involving microorganisms in closed systems e.g. for large-scale activities. The prime consideration has to be the nature of the containment and control measures appropriate to the activity. It will normally be obvious which guidance (both text and tables) users should follow for their particular activity. Highly engineered, closed systems involving the use of seals, pipe-work, measures to control exhaust gases and *in situ* probes are all factors found more normally in large-scale activities. The use of small bench-top chemostats and fermenters are likely to constitute laboratory scale activities. Pilot plant facilities may be more suited to large-scale control measures. Once the scale has been decided users should follow the appropriate guidance, although it may be necessary to consider both sets of guidance for operations of an intermediate nature.

Many closed systems will be required to operate in accordance with good manufacturing practice (GMP). The control measures required in order for the facility to comply with GMP are put in place to ensure the product quality, rather than to offer protection to the operator or environment. Thus, there is a potential conflict between the measures designed to offer protection to the operator/ environment and those designed to protect the product. However, in most cases, it will be possible to assign equivalent biosafety measures while permitting the maintenance of GMP. For example, some facilities may require that specified activities take place in a positively pressurised clean environment to protect the product from contamination. Thus, a microbiological safety cabinet could be used to protect the operator and the wider environment without the need for the entire facility to be under negative pressure. Furthermore, many of the measures required for manufacturing purposes will also offer operator/ environmental protection. However, biosafety will need to take precedence where there is a conflict with the requirements of GMP.

The risk assessment must be used to determine the appropriate control measures that are needed to afford protection to both human health and the environment. Users should compare the measures warranted by the risk assessment with the table of containment measures to determine the final activity class. The activity class, in turn, determines the minimum containment-level required for the activity.

Some control measures deemed necessary by the risk assessment may not be listed in the containment tables. Although the activity class is determined solely by those measures actually listed, the risk assessment must always take precedence and **all** measures identified as necessary must be applied

Users might find it helpful to refer to the ACDP publication “The large-scale contained use of biological agents”, ISBN 0-7176-1544-8 (available from HSE Books).

Viable microorganisms should be contained in a system which physically separates the process from the workplace and the wider environment (closed system)

Containment measure	CL1	CL2	CL3	CL4
Viable biological agents and GMMs should be contained in a system which physically separates the process from the environment (closed system)	Required where and to the extent the risk assessment shows it is required (GM only)	Required	Required	Required

At CL1, where the risk assessment shows that it is required, there is a regulatory requirement for viable biological agents and GMMs to be contained in a closed system. The need for a closed system will depend upon the risk assessment, but for most activities at CL1 such a system will not be needed and fermentation processes may use GMMs in open vessels. The building itself will likely provide suitable limitation of contact with people and the wider environment and normal equipment used in the industry will probably be suitable e.g. ventilated flasks, open top fermenters, open mixing vessels, baking tins and trays, moulds etc.

At CL2, CL3 and CL4 it is a regulatory requirement for viable microorganisms to be contained in a closed system and be physically separated from workers and the environment. The nature of the closed system will depend upon the hazards and be determined by the risk assessment, but for most activities a stainless-steel fermenter or chemostat with welded pipework will be suitable. At these containment levels microorganisms must be physically contained such that release is prevented.

Disposable single-use bioreactors or “cellbags” are being increasingly used in the biopharmaceutical industry as closed systems. Their use in association with microorganisms needs to be carefully considered to ensure that they offer an equivalent level of containment as traditional systems. If they are used they will need to meet the requirements listed in the regulations. In reality, it is unlikely that these types of systems will be used for high risk bulk cultures.

Control of exhaust gases from the closed system

Containment measure	CL1	CL2	CL3	CL4
Control of exhaust gases from the closed system	Not required	Required so as to minimise dissemination	Required so as to prevent dissemination	Required so as to prevent dissemination

At CL1 there is no requirement to control exhaust gases. At CL2 exhaust gases must be treated to minimise dissemination of microorganisms. Exhaust gases can be controlled using a variety of methods, either individually or in combination. This includes filtration, impingement filtration, cyclone separation, spraying gases with hypochlorite in spray-towers or off-gassing through chemical disinfectants. This list of examples is not exhaustive and other techniques may be used, provided they are sufficient to control the risks. It is important to keep filters dry in order to maintain their efficiency and they should be easy to remove safely for maintenance purposes.

At CL3 and CL4, exhaust gases must be treated to prevent dissemination of microorganisms. Exhaust gases should be controlled using filtration through fit-for-purpose HEPA filters (preferably two filters in series). It is important to keep filters dry to maintain their efficiency and pre-filters may be necessary to prevent clogging and wetting. Filters should sterilised before removal for maintenance or discard. Impingement filtration, cyclone separation, spraying gasses with hypochlorite in spray-towers or off-gassing through chemical disinfectants is not recommended at CL3 and strongly discouraged at CL4.

Control of aerosols during sample collection, addition of material to a closed system or transfer of material to another closed system

Containment measure	CL1	CL2	CL3	CL4
Control of aerosols during sample collection, addition of material to a closed system or transfer of material to another closed system	Required where and to the extent the risk assessment shows it is required (for GM only)	Required so as to minimise release	Required so as to prevent release	Required so as to prevent release

At CL1, where the risk assessment shows that it is necessary, measures to control aerosols during addition of material to a closed system, transfer of material to another closed system or sample collection will be required for GMMs. The release of microorganisms into the workplace and wider environment should be minimised in any case. The stringency of these measures should be determined by the risk assessment. Where there is little risk of harm, elaborate methods for controlling escape will probably not be necessary.

At CL2, measures to minimise release of aerosols during addition of material to a closed system, transfer of material to another closed system or sample collection are required. Inoculation of seed vessels can be by direct injection using a sterile needle/ septum technique or by using a transfer vessel that is part of the closed system. Where needles are used, procedures should be applied that minimise the likelihood of a needle-stick injury. All potentially

contaminated liquids should be transferred in closed piping and all pipework and valves should be leak-tight. Samples should be taken using aseptic techniques into a vessel designed to minimise aerosol generation and release. Running a mid-stream sample directly to drain is not acceptable; all material collected must be inactivated and the sampling valve/ connection may need to be sterilised

At CL3 and CL4, measures to prevent release of aerosols during addition of material to a closed system, transfer of material to another closed system or sample collection are required. Inoculation of seed vessels should be done using a transfer vessel that is part of the closed system although direct injection using a sterile needle/ septum technique may be adequate if well controlled for activities at CL3 but would not be acceptable at CL4. Again, where needles are used, procedures should be applied that minimise the likelihood of needle-stick injury. All potentially contaminated liquids should be transferred in closed piping which is leak-tight. Sampling should take place using a closed aseptic technique. All material collected must be inactivated within the contained area and the sampling valve/ connection may need to be sterilised.

Inactivation of culture fluids as a bulk before removal from the closed system

Containment measure	CL1	CL2	CL3	CL4
Inactivation of culture fluids as a bulk before removal from the closed system	Required where and to the extent the risk assessment shows it is required (for GM only)	Required by validated means	Required by validated means	Required by validated means

The purpose of this requirement is to avoid the release of bulk culture fluids to effluent prior to inactivation. If there is a need to remove the product from the closed system for further processing, e.g. for the production of live vaccines, it is likely that the product will have been purified from the remaining bulk culture which requires inactivation.

At CL1, bulk culture fluids that are removed from a closed system e.g. for a further processing step may require inactivation where the risk assessment shows that it will be necessary for GMMs. Inactivation will not always be required before removal from the closed system but the requirement to inactivate all waste before final disposal remains.

At CL2, CL3 and CL4 the regulations require that viable microorganisms in bulk culture fluids be inactivated using a known efficacious method prior to removal from the closed system. Chemical or physical methods are acceptable, but must be appropriate to the organism and level of risk. At CL4,

physical methods (such as heat treatment or autoclaving) are recommended as, generally, chemical methods vary in their efficiency and are less easy to validate. All waste must be inactivated by validated means prior to final disposal.

Seals should be designed so as to minimise or prevent release

Containment measure	CL1	CL2	CL3	CL4
Seals should be designed so as to minimise or prevent release	Not required	Required so as to minimise release	Required so as to prevent release	Required so as to prevent release

There is no requirement for seals (where they are present) to be specifically designed to minimise/ prevent release of the microorganisms at CL1. However, it is considered good practice to do so in order to limit the possibility of contamination.

At CL2 there is a requirement that all seals be designed to minimise release of microorganisms. This includes static seals on equipment. Examples of typical types of seals appropriate for most CL2 work include single "O" ring seals, flat gaskets, sealed couplings, single or double faced mechanical seals and sanitary couplings with gaskets. Where necessary, seals can be enclosed in HEPA (or equivalent) filtered housings (these examples are not exhaustive and alternatives may be used provided they are appropriate to control the risks). Where the equipment is connected to utility services, backflow should be prevented using a pressure differential, steam locks or "double block and bleed" systems (non-return valves may be unreliable from a microbiological point of view and their use should be considered very carefully). It will be necessary to assess the operating pressure and the risk of the microorganisms being released through seal failure. Pressure-relief systems may be used, but the design needs to be considered carefully to prevent microorganism release during venting. Fixed or retractable sensors can be used.

At CL3 there is a requirement that all seals are designed to prevent release of microorganisms. Pipework should be welded wherever possible or practical and mechanical seals should be double faced with condensate fed to the interspaces (ideally with the condensate temperature being monitored and alarmed). If necessary, seals can be enclosed in HEPA (or equivalent) filtered housings. Where the equipment is connected to utility services, backflow should be prevented using a pressure differential, steam locks or "double block and bleed" systems. Retractable sensors should not be used since duplicate sensors are safer for high-risk activities.

At CL4, pipework should be welded and seals should be enclosed in HEPA (or equivalent) filtered housings wherever possible. The equipment should not be connected to utility services and retractable sensors should not be used since duplicate sensors are safer for high-risk activities.

For further information on types of seals and valves used in closed systems please refer to the ACDP publication "The large-scale contained use of biological agents", ISBN 0-7176-1544-8 (available from HSE Books).

The controlled area designed to contain spillage of the entire contents of the closed system

Containment measure	CL1	CL2	CL3	CL4
The controlled area designed to contain spillage of the entire contents of the closed system	Required where and to the extent the risk assessment shows it is required (GM only)	Required where and to the extent the risk assessment shows it is required	Required	Required

At CL1 (GM only) and CL2, where the risk assessment indicates that there is risk of harm to humans or the environment arising from a catastrophic loss of primary containment, and at CL3 and CL4, the controlled area must be designed to contain a spillage of the entire contents of the closed system. Possible approaches include bunding at the periphery or the use of enlarged drainage channels. The containment method employed should allow for inactivation of the spillage and this could be achieved by direct drainage into an effluent tank. Use of open drainage channels is not recommended at CL3 and would not be acceptable at CL4.

The entire contents of a closed system could be extremely large if there are a number of vessels arranged in series. However, the risk assessment should indicate the approximate volume which may be lost due to a foreseeable failure in a valve, seal etc. The findings from this should allow for a sensible approach to deciding exactly what volume of spillage the controlled area should be capable of containing and the volume of disinfectant required.

Controlled area sealable to permit fumigation

Containment measure	CL1	CL2	CL3	CL4
Controlled area sealable to permit fumigation	Not required	Required where and to the extent the risk assessment shows it is required (GM only)	Required where and to the extent the risk assessment shows it is required	Required

At CL2 (for GM only) and CL3, controlled areas must be sealable for the purposes of fumigation where the risk assessment shows that it is required. Where necessary, validated fumigation procedures must be used in the event of a major spillage or prior to maintenance. Air handling and externally ducted safety cabinets should be controllable from outside the laboratory so that fumigant can be vented safely without the need to re-enter the room unless purging of the fumigant is achieved by another method.

At CL4 the controlled areas must be sealable for the purposes of fumigation. Validated fumigation procedures must be in place and used in the event of a major spillage or prior to maintenance. Laboratory ventilation and externally ducted secondary containment devices should be controllable from outside the laboratory to permit the safe venting of fumigant without the need to re-enter the room.

Biohazard signs posted

Containment measure	CL1	CL2	CL3	CL4
Biohazard signs posted	Required where and to the extent the risk assessment shows it is required	Required	Required	Required

At CL1 a biohazard sign should be displayed if the risk assessment indicates that it is necessary to inform people of the risks from biological agents. At CL2, CL3 and CL4 a biohazard sign must be clearly displayed at the entrance to the controlled areas. Other legislation, in particular ATCSA 2001 may indicate an increased security risk by displaying biohazard signs where work is being undertaken with agents listed in ATCSA 2001, Schedule 5. In such cases, this legislation would apply over and above the Directive requirements and display of biohazard signs would therefore not be required. In this case, derogation should be sought from the Competent Authority from applying this containment, with full justification for the request.

Entry via airlock

Containment measure	CL1	CL2	CL3	CL4
Entry via airlock	Not required	Not required	Required where and to the extent the risk assessment shows it is required	Required

There is no requirement for an airlock at CL1 and CL2. At CL3, it is required where the risk assessment indicates it is necessary and entry to the controlled area must be via an airlock or lobby, i.e. a chamber isolated from the controlled area.

Access to controlled areas operating at CL4 must be via an airlock or a separate chamber. This must be maintained at a pressure negative to the surroundings (for example -15 to -25 Pa relative to the outer area would be acceptable) but positive with respect to the controlled area itself.

Specific measures to adequately ventilate the controlled areas in order to minimise air contamination

Containment measure	CL1	CL2	CL3	CL4
Specific measures to adequately ventilate the controlled areas in order to minimise air contamination	Required where and to the extent the risk assessment shows it is required (GM only)	Required where and to the extent the risk assessment shows it is required	Required where and to the extent the risk assessment shows it is required	Required

Where the risk assessment shows it to be necessary, there is a requirement for adequate ventilation of the controlled area in order to minimise air contamination at CL1 (for GM) and for all work involving microorganisms at CL2 and CL3. Mechanical ventilation is not normally needed for activities requiring CL1, CL2 or CL3 although the work place should be a safe and comfortable environment and good ventilation may be needed for the removal of heat from process operations and worker comfort. Adequate ventilation of the controlled area to minimise air contamination is required at CL4.

Controlled area maintained at an air pressure that is negative to the immediate surroundings

Containment measure	CL1	CL2	CL3	CL4
Controlled area maintained at an air pressure that is negative to the immediate surroundings	Not required	Not required	Required where and to the extent the risk assessment shows it is required	Required

There is no requirement to maintain negative air pressure to contain airborne microorganisms at CL1 and CL2 although some processes might necessitate

positive air pressure to maintain product integrity. This is acceptable provided that it does not conflict with the need to contain airborne microorganisms in the event of an accident. The use of containment equipment such as a microbiological safety cabinet, or a bespoke isolator, could be considered to provide both product and operator protection.

It is necessary to maintain controlled areas at a negative pressure with respect to the immediate surroundings at CL3. In terms of regulatory requirements "immediate surroundings" can be interpreted as being outside the building or in adjacent parts of the building. Typically, the controlled area should be maintained at least -30 Pa via a continuous inflow of air whilst work is in progress. If an airlock is used, this should be maintained at negative pressure which should be an intermediate value, e.g. -15 to -25 Pa, to maintain the laboratory pressure differential with the surroundings. Negative pressure is often achieved via the implementation of a controlled supply and extract of air by mechanical ventilation systems. The supply and extract airflow should be interlocked to prevent positive pressurisation of the room in the event of failure of the extract fan. Some processes might necessitate positive air pressure to maintain product integrity. This is acceptable provided that it does not conflict with the need to contain airborne microorganisms in the event of an accident. The use of containment equipment such as a microbiological safety cabinet could be considered to provide both product and operator protection provided it is validated for use *in situ*.

Typically, at CL4, the controlled area should be maintained at an air pressure of at least -30 Pa via a continuous inflow of and extraction of air whilst work is in progress. The airlock should also be at negative pressure but this should be an intermediate value to maintain the laboratory pressure differential with the surroundings. Negative pressure is often achieved via the implementation of a controlled supply and extract of air by mechanical ventilation systems. The supply and extract airflow should be interlocked to prevent positive pressurisation of the room in the event of failure of the extract fan. The ventilation system should be alarmed, connected to an emergency power supply and incorporate a system to prevent reverse air flows.

Input and extract air from the controlled area should be HEPA filtered

Containment measure	CL1	CL2	CL3	CL4
Input and extract air from the controlled area should be HEPA filtered	Not required	Not required	Required for extract air, required for input air where and to the extent the risk assessment shows it is required	Required for input and extract air

This is not a requirement at CL1 and CL2. However, there may be a need for supply air to be HEPA filtered for GMP purposes. HEPA filters on the extract system are required at CL3 and input air may need to be HEPA filtered on the supply system if the risk assessment indicates it is necessary. At CL4 HEPA filters are required on input and extract systems to maintain secondary containment of the facility in the event of an uncontrolled release of biological agents.

At CL3, supply air can be optionally HEPA filtered to ensure that contaminated air cannot be inadvertently expelled through supply vents during a transient positive-pressurisation event. Easy and safe removal of HEPA filters should be possible for standard replacement and maintenance purposes.

For CL4 facilities, the requirement for double HEPA filtration on the extract system reflects the greater potential hazard associated with a release outside of the facility. Two HEPA filters are used as a contingency to maintain secondary containment in the event of a failure in one of the filters. Here, HEPA filters should be arranged in series and be able to be accessed safely for testing and changing. The requirement for HEPA filtration on the supply air to CL4 facilities provides an additional layer of safety that protects against the loss of secondary containment through the facility becoming positively pressurised.

Access restricted to authorised personnel only

Containment measure	CL1	CL2	CL3	CL4
Access restricted to nominated personnel only	Not required	Required	Required	Required via airlock

Restriction of access to CL2, CL3 and CL4 laboratories is required to prevent inadvertent or deliberate access to the facility by people who are unaware of the risks posed in such facilities, or have not been appropriately trained in order to conduct themselves safely.

The means by which access is restricted will vary between facilities and will depend heavily on the containment level. At CL2, it would be acceptable to restrict access using management controls i.e. monitoring who is entering the laboratory during periods when the doors are unlocked.

At CL3 it is more important to restrict who enters the facility so it may be necessary to install mechanical restriction. One possible solution could be to install a lock and key or swipe/ proximity card system. Digital locks that operate by pressing a sequence of buttons on the lock may be acceptable but it is important that the sequence code is changed if staff members change or the code becomes known by unauthorised individuals.

At CL4 it is recommended that at least two methods to restrict entry are used simultaneously e.g., proximity card and personal identification number. It may

be beneficial to contact your local counter terrorism security advisor or national counter terrorism security office when deciding upon a system for restricted access at CL4. As already mentioned previously, entry to CL4 facilities should be via an airlock.

Decontamination and washing facilities provided for personnel

Containment measure	CL1	CL2	CL3	CL4
Decontamination and washing facilities provided for personnel	Required	Required	Required	Required

The provision of washing and decontamination facilities is required for all activities involving viable microorganisms in these facilities. The washing facilities will probably consist of hand washing facilities with taps that can be operated without being touched by hand and a supply of disinfectant soap. Hands should be washed immediately if contamination with microorganisms is suspected, after handling viable microorganisms or before leaving controlled areas.

Personnel should shower before leaving the controlled area

Containment measure	CL1	CL2	CL3	CL4
Personnel should shower before leaving the controlled area	Not required	Not required	Required where and to the extent the risk assessment shows it is required	Required

At CL1 and CL2 there is no requirement for a showering facility to be present and workers are not required to shower when leaving the facility. However, hands should be washed immediately if contamination with microorganisms is suspected, after handling viable microorganisms or before leaving the laboratory. The same applies at CL3 unless the risk assessment indicates that it is necessary to shower before leaving the facility. At CL4 a shower must be installed and all personnel must shower before leaving the facility.

If a shower is required, careful consideration should be given to its location i.e. it must be located before leaving the contained area. For microorganisms capable of causing human disease, the shower should be located before leaving the laboratory suite. For microorganisms which only present a risk to the environment, the shower should be located at the exit of the contained envelope of the facility. Any additional information for employees, e.g.

minimum time it is necessary to spend in the shower, should be included in the local code of practice.

Personnel shall wear personal protective clothing

Containment measure	CL1	CL2	CL3	CL4
Personnel shall wear personal protective clothing	Required (work clothing)	Required (work clothing)	Required	Required, complete change

At CL1, CL2 and CL3 there is a regulatory requirement for suitable protective clothing to be worn. This will normally comprise disposable coveralls or gowns that are worn when in controlled areas and removed prior to hand washing upon exit. Clothing should ideally be kept in a dedicated locker and decontaminated prior to laundering where the risk assessment shows it to be necessary. The wearing of dedicated work wear will often be enforced to protect the purity of the product in containment facilities and this will often supersede the need for specific protective clothing. For containment levels 1 to 3, the risk assessment will indicate the degree of personal protective clothing which is required.

Suitable protective clothing must be worn and a complete change is required before entering and exiting controlled areas in CL4 facilities. Personal protective clothing should be stored in the change facility in dedicated lockers. Protective work-wear should be decontaminated by autoclaving prior to laundering. Contaminated clothing that is being transported to an autoclave for decontamination should be safely enclosed in secondary containment during transfer.

Inactivation of biological agents in effluent from hand washing sinks and showers or similar effluents

Containment measure	CL1	CL2	CL3	CL4
Inactivation of biological agents in effluent from hand washing sinks and showers or similar effluents	Not required	Not required	Required where and to the extent the risk assessment shows it is required	Required

There is no requirement for this at CL1 and CL2. At CL3, inactivation of microorganisms in effluent from hand washing sinks and showers will be required prior to release if shown to be necessary by the risk assessment. In reality, it is likely that effluent will only need to be collected if the risk assessment shows that showering is required to protect humans or the environment.

In CL4 facilities, inactivation of microorganisms in effluent from hand washing sinks and showers will be required prior to discharge from the contaminated area. It is essential that the method of choice for inactivation of agents is efficacious against the microorganisms in the effluent. The preferred method at CL3, and only acceptable method at CL4, is heat inactivation as it is generally the most reliable and reproducible method although it is still necessary to demonstrate that the parameters of use are sufficient for complete inactivation of the microorganisms.

It is imperative that effluent is safely and securely transported to the area where it will be inactivated. If this is via pipework it, and any holding tanks, should be periodically examined to ensure that they are intact and not likely to present a risk to humans or the environment through leakage.

Inactivation of biological agents in contaminated material and waste including those in process effluent before final discharge

Containment measure	CL1	CL2	CL3	CL4
Inactivation of biological agents in contaminated material and waste including those in process effluent before final discharge	Required where and to the extent the risk assessment shows it is required	Required by validated means	Required by validated means	Required by validated means

At CL1 where the risk assessment shows it is required and at CL2, CL3 and CL4, there is a regulatory requirement that contaminated material and waste (including culture fluids and other media) is inactivated before final discharge or disposal.

Heat inactivation is generally considered more appropriate for large-scale discharge of waste as chemical disinfectants may be environmentally damaging (waste discharge must comply with relevant environmental legislation). If chemical inactivation is to be used, sufficient contact time should be given to afford adequate kill to minimise release of viable microorganisms. The inactivation method chosen must be appropriate to the risk and its efficacy must be validated against the organism being used. The potential damage to stainless steel process equipment by chlorine-based products should be considered when selecting disinfectants.

At CL3 and CL4, physical methods such as heat inactivation are considered more appropriate for large-scale discharge of waste as chemical disinfectants vary in efficiency.

Appendix 1: Abbreviations

ACDP	Advisory Committee on Dangerous Pathogens
ATCSA	Anti-terrorism, Crime and Security Act 2001
CL	Containment Level
COSHH	Control of Substances Hazardous to Health Regulations 2002
DEFRA	Department for Environment, Food and Rural Affairs
EPA	Environmental Protection Act 1990
GM	Genetically Modified
GMMs	Genetically Modified Microorganisms
GMOs	Genetically Modified Organisms
GMP	Good Manufacturing Practice
HEPA	High Efficiency Particulate Air
HG	Hazard Group
HSE	Health and Safety Executive
HSWA	Health and Safety at Work etc Act 1974
MSC	Micro-biological Safety Cabinet
RIDDOR	Reporting of Injuries, Diseases and Dangerous Occurrences Regulations 1995
SAPO	Specified Animal Pathogens Order
SRF	Single Regulatory Framework

Appendix 2: Guidance on reporting of accidents or incidents

RIDDOR reporting

RIDDOR requires the reporting of any infection reliably attributable to work with live or dead humans or animals, exposure to blood or body fluids or any potentially infected material derived from any of the above. There is also the separate need to report any accident or incident which resulted or could have resulted in the release or escape of biological agent which is likely to cause severe human disease (hazard group 3 or 4 biological agents or Class 3 or 4 GMMs - where the classification is based on hazard to human health).

In order to help those responsible for safety to monitor and review the effectiveness of safety precautions within the containment facility it is recommended that a local record is made of all accidents and occurrences (including near misses) involving microorganisms. This record should cover a range of incidents wider than would be covered by the statutory schemes such as the RIDDOR.

Under RIDDOR you must report all work-related accidents, disease and dangerous occurrences. The following are reportable if they arise 'out of or in connection with work':

- Accidents which result in an employee or self-employed person dying, suffering a major injury, or being absent from work or being unable to do their normal work for more than three days;
- Accidents which result in a person not at work suffering an injury and being taken to hospital (if the accident happens at hospital, it must still be reported);
- An employee or self-employed person suffering one of the specified work-related diseases; and
- One of the specified 'dangerous occurrences'. These do not necessarily result in injury but have the potential to do significant harm.

The duty to notify and report rests with the 'responsible person'. This may be the employer of an injured person, a self-employed person or someone who is in control of the premises where the work is carried out.

Reporting human infections

In terms of reportable incidents that might arise as a result of work with pathogens, you must report certain infections as well as any other infection that is reliably attributable to work with biological agents or materials that may contain them, e.g. blood and other body fluids or animals.

Infections must be reported only when you have been notified by a doctor, in writing, that one of your employees is suffering from one of the infections listed in RIDDOR which is linked to the corresponding activity described in the guidance accompanying the regulations.

Infections that could have been acquired equally easily in the community as at work are not reportable. Many infections such as those causing diarrhoea and colds are common in the community and everyone is exposed to them. These minor illnesses cannot generally be attributed to infection contracted at work and they are not generally reportable. However, where there is reasonable circumstantial evidence, e.g. known contact with the infectious agent in laboratory work, then a report should be made.

For the purpose of RIDDOR an infection is the entry and multiplication of an infectious microorganism in the body, causing a damaging reaction in the tissue. The infection and the damage caused may give clinical signs and symptoms of disease or may not be evident (asymptomatic/ sub-clinical).

Colonisation, i.e. the presence and multiplication of infectious microorganisms, such as *Staphylococcus aureus*, on or in the body without a damaging reaction in the tissue, is not the same as infection and is not reportable as a disease.

Info box A- Examples of reportable and non-reportable infections

Reportable:

- A nurse catches tuberculosis after nursing a patient with tuberculosis;
- A diagnostic laboratory worker catches typhoid after processing specimens containing *Salmonella typhi*;
- A veterinary surgeon catches *Streptococcus suis* after examining a herd of pigs suffering from meningitis;
- A laboratory worker becomes hepatitis B positive following a percutaneous injury whilst working with infected cells.

Non-reportable:

- A nurse is found to be MRSA positive (but free from disease) during routine screening after having nursed patients infected with MRSA;
- A cleaner in a hospital catches chicken pox. Patients in the area where they work have chicken pox but so does their child.

Reporting of Dangerous occurrences

Under RIDDOR, you must also report any accident or incident which results in, or could have resulted in, the release of a biological agent that could cause severe human disease. This is known as a dangerous occurrence. This would include diseases caused by HG3 and HG4 agents as well as certain HG2 agents, e.g. *Neisseria meningitidis*, which are capable of causing severe human disease.

Info box B: Examples of reportable and non-reportable dangerous occurrences

Reportable:

- A nurse suffers a needlestick injury from a needle and syringe known to contain hepatitis B-positive blood;
- A university research worker drops and breaks a flask containing a culture of *Mycobacterium tuberculosis*.

Not reportable:

- A university researcher drops and breaks a tissue culture flask containing cells infected with measles virus;
- A doctor suffers a needlestick injury and is exposed to a patient's blood. The patient is not known to be suffering from any infection.

How to report

You should report all qualifying incidents to the Incident Contact Centre: Incident Contact Centre, Caerphilly Business Park, Caerphilly, CF83 3 GG, tel: 0845 300 99 23, e-mail: riddor@natbrit.com, website: www.riddor.gov.uk. You can report incidents in a variety of ways, by telephone, fax, via the internet, or by post.

Appendix 3: References (To be drafted)

Annex 1: Approved List 2010 (To be inserted)

Annex 2 ACDP Containment Working Group members Acknowledgements (To be inserted)