Centre for Biological Engineering (CBE)

CODE OF PRACTICE FOR WORK WITH BIOLOGICAL AGENTS AND GENETICALLY MODIFIED ORGANISMS

The primary purpose of the CBE Containment Level 2 Laboratory Unit is translational research aimed at the generation of new medical therapies, healthcare technologies and associated enabling technologies with a particular focus on manufacturing and bio-processing. Much of the work in the Unit involves biological material. The Unit has therefore been designed as a controlled environment and operates under a Quality Management System to both be compliant to the necessary regulations, to ensure research quality and relevance and to protect research materials.

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SECTION 1 INTRODUCTION

The Centre for Biological Engineering (CBE) facility includes a self-contained, Containment Level 2 Laboratory Unit comprising 6 laboratories with ancillary rooms such as changing rooms, store rooms and an autoclave room (*see information box below*). The CBE Laboratory Unit is a shared multi-user facility. The primary purpose of the Unit is translational research aimed at the generation of new medical therapies, healthcare technologies and associated enabling technologies with a particular focus on manufacturing and bio-processing. Much of the work in the Unit involves biological material. The Unit has therefore been designed as a controlled environment and operates under a Quality Management System to both be compliant to the necessary regulations, to ensure research quality and relevance and to protect research materials.

1.1. PURPOSE OF THE CODE OF PRACTICE

This Code of Practice (CoP) sets out the arrangements of the Centre for Biological Engineering (CBE) Containment Level 2 Laboratory Unit[1] in order to comply with the University's Biological Safety Policy. The purpose of this local Code of Practice is to ensure that all work involving the use of hazardous or potentially hazardous biological material is subject to the standards of control necessary to prevent, or where this is not possible to minimise, risks to human health and the wider environment.

The Centre for Biological Engineering (CBE) comprises:

1. A CBE Laboratory Suite consisting of:

A. CBE Laboratory Unit (Room Numbers/ Names)

H32 - CBE Containment Level 2 Laboratory Unit Entrance
H33 - Cleaners Store Room
H18 – General Store Room [add 'Access to General Cold Store Room']
H17 – General Cold Store Room
H31 – Autoclave Room
H20* - Automated Cell Culture Suite (Room numbers H21 and H22)
H23 - Analytical Laboratory
H24* - Animal Cell Culture Laboratory (Room number H25)
H26* - Microbial Cell Culture Laboratory (Room number H27)
H28** - Biophotonics Laboratory (Room Number H29)
H30 - Plasma Diagnostics Laboratory

Key: **change room number; **Lobby room number.*

B. CBE Unclassified Laboratory (Room Numbers/ Names)

H34 - Cold Atmospheric Plasma (CAP) Laboratory

[1] For the purposes of this COP – a laboratory unit is a separate building or self contained suite within a building containing one or more laboratories and with ancillary rooms such as changing rooms, autoclave rooms etc. The CBE Laboratory Unit is a shared, multi-user facility consisting of multiple laboratories at Containment Level 2, This COP also covers work practices in the CL2 CBE Tissue Engineering Laboratory located in the Wolfson School of Manufacturing & Mechanical Engineering, Loughborough University.

1.2. BIOLOGICAL HAZARDS AND THE LEGISLATION

Enacted under the Health and Safety at Work Act, the Control of Substances Hazardous to Health (COSHH) Regulations are designed to protect persons against risks to their health arising from exposure to hazardous substances, including biological hazards (biohazards), associated with their work. Work with Biological Agents (BAs) is subject to controls under the 2002 COSHH Regulations. If the agent is genetically modified then the Genetically Modified Organisms (Contained Use) Regulations 2000, as amended 2005, also apply and impose additional requirements in terms of protection against harm to the environment. The requirements of other pieces of legislation, such as various plant health and animal pathogen orders administered by the Department of the Environment, Food and Rural Affairs (DEFRA) must also be taken into account for work with some Biological Agents.

Legislation covering activities involving both BAs and GMOs applies directly to work within the CBE Laboratory Unit. This Code of Practice, which details how particular general duties and additional provisions apply in relation to work with BAs and GMOs within the CBE Laboratory Unit, together with extensive guidance, is intended to support these regulations. This CoP is designed to bring together the legislative requirements and guidance from the various published sources to provide a single point of reference on biosafety for CBE personnel. Workers in the CBE must refer to and follow the guidance relevant to their work.

1.3. SCOPE OF THE CODE OF PRACTICE

This Code of Practice (CoP) aims to:

1. Set down the health, safety and environmental standards for how BAs and GMOs should be handled, stored, transported and disposed of in the Containment Level 2 CBE Laboratory Unit.
2. Give information and guidance on identifying levels of risk to health and of harm to the environment from exposure to or unplanned release of BAs or GMOs.
3. Provide practical advice on the assessment of risk to health and of harm to the environment.
4. Provide linking information to assist investigators to complete any internal or external notifications.

This Code of Practice is relevant to all activities involving the use of BAs and/or GMOs in the CBE Laboratory Unit.

Adoption of the standards outlined in this document will ensure the CBE facility fulfils its requirements and responsibilities under the Control of Substances Hazardous to Health Regulations 2002 and the Genetically Modified Organisms (Contained Use) Regulations 2000. It is not intended to provide a comprehensive overview of the Regulations and it does not include the more general requirements of the COSHH Regulations which also apply. This CoP should be read in conjunction with the main Approved Code of Practice (ACOP) and guidelines detailed in the in these regulations (see Section 8).Workers in the CBE should also refer to University Biological Safety Policy with which they must also comply.

In addition the storage of certain material may be subject to additional requirements under the Human Tissue Act (HTA), which are not covered in this Code of Practice. Workers should refer to the guidance available at http://www.hta.gov.uk/guidance.cfm and advice should be sought from the University Biological Hazards & Genetic Modification Safety Committee (BHGMSC) via the local BGMSA or the University Biological Safety Officer (BSO) to confirm whether the material and work activity falls under the terms of the act.

This local Code of Practice applies to deliberate work involving non-GM Hazard Group 1 and 2 Biological Agents and to activities involving Class 1 Genetically Modified Organisms (which are GMMs) according to the definitions given under the COSHH regulations and the GMO (CU) Regulations respectively.

Activities in the CBE Laboratory Unit include projects assessed at more than one containment level (Containment Level 1 or 2), such that all lower level work must be carried out under the management standards imposed by the higher level (Containment level 2). This applies under circumstances in which the project may be divided into several phases, or where more than one project may be under way in the CBE Laboratory Unit simultaneously, or where the laboratory unit might be in use for non-GM projects requiring higher containment i.e. involving Hazard Group 2 biological agents. Projects involving the use of Hazard Group 1 BAs or Class 1 GMMs (see below for definitions) that require Containment Level 1 are carried out at Containment Level 2 for reasons other than the safety issues; this includes the need to ensure product protection (e.g. the use of a class II safety cabinet and controlled environment maintained at positive pressure) and to impose a quality assurance discipline

Where guidance is given, this is considered to be best practice for Containment Level 2; however the use of containment and control of measures should be determined by risk assessment. As well as specific containment requirements, additional control measures under the provisions of COSHH and the GMO (CU) regulations are also described. In this local Code of Practice, **'must'** indicates a mandatory requirement (as defined in legislation) whereas **'should'** reflects a strong recommendation. Statements using **should** relate to the required standard and any modification must be justified through the process of a suitable and sufficient risk assessment.

1.4. WORK NOT PERMITTED IN THIS FACILITY TYPE

At the time of writing, the following work must not be conducted in the CBE Laboratory Unit:

1. activities with any BA that requires a physical containment level higher than Level 2;
2. activities with any GMM that is classified above activity class 1
3. activities involving GMOs which are not micro-organisms (e.g. GM plants or animals)
4. the housing/keeping/rearing of any animals, arthropods, or aquatic organisms;
5. the growing of any plants (except those in tissue culture, or contained in a plant growth cabinet or other containment device).

1.5. GLOSSARY OF TERMS AND ACRONYMS

Certain terms are defined in the Regulations. The following are of particular note for biological work. Biological agents are included within the definitions of a "substance hazardous to health".

1.5.1. Acronyms

The following abbreviations are used throughout the document.

ACDP: Advisory Committee on Dangerous Pathogens
ACGM: Advisory Committee on Genetic Modification
COSHH: Control of Substances Hazardous to Health Regulation 2002
GMO [CU]: Genetically Modified Organisms [Contained Use] Regulations 2000
GM: Genetic modification / Genetically modified
GMM: Genetically modified micro-organism

GMO: Genetically modified organism (includes GMMs)
DEFRA: Department for the Environment and Rural Affairs
HSE: Health & Safety Executive
BSC: Biological Safety Cabinet
BA: Biological Agent
BSO: University Biological Safety Officer
BHGMSC: University Biological Hazards & Genetic Modification Safety Committee
BGMSA: Local (CBE) Biological & Genetic Modification Safety Advisor
DSO: Department Safety Officer
OHU: University Occupational Health Unit
HS&E: University Health, Safety and Environment Department

1.5.2. Biological agents, GMOs, micro-organisms and cell cultures

Under the COSHH regulations:

The selection of containment and control measures for BAs is prescribed according to their risk to human health. Biological agent means a micro-organism, cell culture, or human endoparasite, **whether or not genetically modified** (although not all GMMs are BAs), which may cause infection, allergy, and toxicity or otherwise create a hazard to human health;

(i) micro-organism means a microbiological entity, cellular or non-cellular, which is capable of replication or of transferring genetic material;

(ii) cell culture means the in-vitro growth of cells derived from multicellular organisms;

NOTE: *Nucleic acid is not a biological agent, however, it can still be a substance hazardous to health falling within the description of those substances which "because of its chemical or toxicological properties and the way it is used or is present in the workplace creates a risk to health". An example would be an oncogenic DNA sequence.*

Under the Genetically Modified Organism (Contained Use) Regulations:

The selection of containment and control measures for GMMs is prescribed according to their risk to human health **and the environment**.[2] 'Contained use' covers any activity involving genetically modified organisms (GMOs – which include GMM) under the conditions of containment laid down by the Regulations. **All the work in the CBE Laboratory Unit falls under this heading.**

Activities covered also include the actual process of genetic modification as well as using GMOs once constructed.

(i) Contained use means an activity in which organisms are genetically modified or in which genetically modified organisms are cultured, stored, transported, destroyed, disposed of or used in any other way and for which physical, chemical or biological barriers, or any combination of such barriers, are used to limit their contact with, and to provide a high level of protection for, humans and the environment.

(ii) Genetic modification in relation to an organisms means the altering of the genetic material in that organism in a way that does not occur naturally by mating or natural recombination or both and within the terms of the definition in Parts I and II of Schedule 2 *i.e. for GM to have occurred there must have been a change to an organism's genetic material and the method used to achieve that change was not based on natural mating or recombination..*

[2] For activities involving GMOs which are not micro-organisms (e.g. GM plants or animals) the regulations apply to risks to human health only.

(iii) Micro-organism means a microbiological entity, cellular or non-cellular, capable of replication or of transferring genetic material, and includes bacteria, fungi, viruses, viroids, cell cultures and tissue cultures, including those from animals, plants and humans.

(iv) Organism means a biological entity capable of replication or of transferring genetic material and covers, in addition to micro-organisms, all multi-cellular organisms not defined as micro-organisms, including plants and animals, but not including humans or human embryos. covers

1.5.3. Classification

For Biological Agents, the choice of control measures is largely based on the Hazard Group of the BA that is being used (or may be present). Biological agents are classified into one of the four Hazard Groups to which that agent is assigned according to its level of risk of infection to healthy adults, based on (i) pathogenicity - ability to produce disease; (ii) infectivity - ability to spread from person to person; (iii) invasiveness - ability to spread within the host; and (iv) virulence - properties of an organism that affect the severity of the disease:

Hazard Group 1 - unlikely to cause human disease;

Hazard 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;

Hazard 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;

Hazard 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.

The classification (for Hazard Groups 2-4) is set out in the Approved List of Biological Agents. The Health and Safety Commission publishes the categorisations of a list of well recognised pathogens in the form of an "Approved List" made under Section 15 of the Health and Safety at Work etc Act 1974. The COSHH Regulations impose legally binding requirements by reference to this list; available on the HSE website at http://www.hse.gov.uk/pubns/misc208.pdf.

While COSHH covers the risks to human health, additional controls may be required under GMO (CU) regulations to control the risks to the environment.

Genetically Modified Micro-organisms[3] are classified into one of four risk classes:

Class 1: Activities of no or negligible risk, for which containment level 1 is appropriate to protect human health and the environment.

Class 2: Activities of low risk, for which containment level 2 is appropriate to protect human health and the environment.

Class 3: Activities of moderate risk, for which containment level 3 is appropriate to protect human health and the environment.

[3] For activities involving organisms other than micro-organisms e.g. GM plants or animals, a risk class is not used.

Class 4: Activities of high risk, for which containment level 4 is appropriate to protect human health and the environment.

1.5.4. Laboratory Containment Levels

Containment Levels 2, 3 and 4 are specified in the COSHH Regulations as a combination of containment measures to control the exposure of workers to biological agents in the different Hazard Groups. These are set out in Schedule 3 Part II of the Regulations and can be found at http://www.legislation.hmso.gov.uk/si/si2002/20022677.htm#sch3. Guidance on control measures for Containment Level 2 activities is given in Section 2.

Under the GMO (CU) Regulations, assessors are required to classify the activity as either Class 1, 2, 3 or 4. This classification is directly related to the containment level required for the conduct of the work: (i) Containment Level 1 = Class 1; (ii) Containment Level 2 = Class 2; Containment Level 3 = Class 3; Containment Level 4 = Class 4. Guidance on control measures for Class 1 GMM activities is given in Section 4.

1.6. ADMINISTRATIVE PROCEDURES FOR SAFE USE OF BIOLOGICAL MATERIALS

The University has determined the policy to be adopted for implementing the legislation on the use of hazardous substances, including biohazards, at work. The responsibility derives from the Health and Safety at Work etc. Act, 1974. It is the duty of all Heads of Group to ensure that all aspects of the University Biological Safety Policy are complied with within their area of responsibility.

Decisions on how best to work safely with biohazards stem from risk assessments. It is illegal to carry out a work activity involving biohazardous materials without first making such an assessment, which in almost all cases will require to be recorded in writing, and made available for inspection by interested parties such as Health and Safety Executive Inspectors, the University's insurers or members of the University Health, Safety and Environment (HS&E) Department.

1.6.1. Advisory Appointments

The University has appointed a Biological Safety Officer (BSO), within the University HS&E Department, to provide specialist professional guidance and advice on matters relating to the containment of biological hazards and the safety of staff, to ensure compliance with relevant legislation, the University Biological Safety Policy, and current best practice. All contact and liaison with the enforcing authorities (primarily the Health and Safety Executive's Biological Agents Unit) on matters relating to biological safety should be via, or in consultation with, the University BSO (See the University Biological Safety Policy for further details).

1.6.2. Biological Hazards and Genetic Modification Safety Committee (BHGMSC)

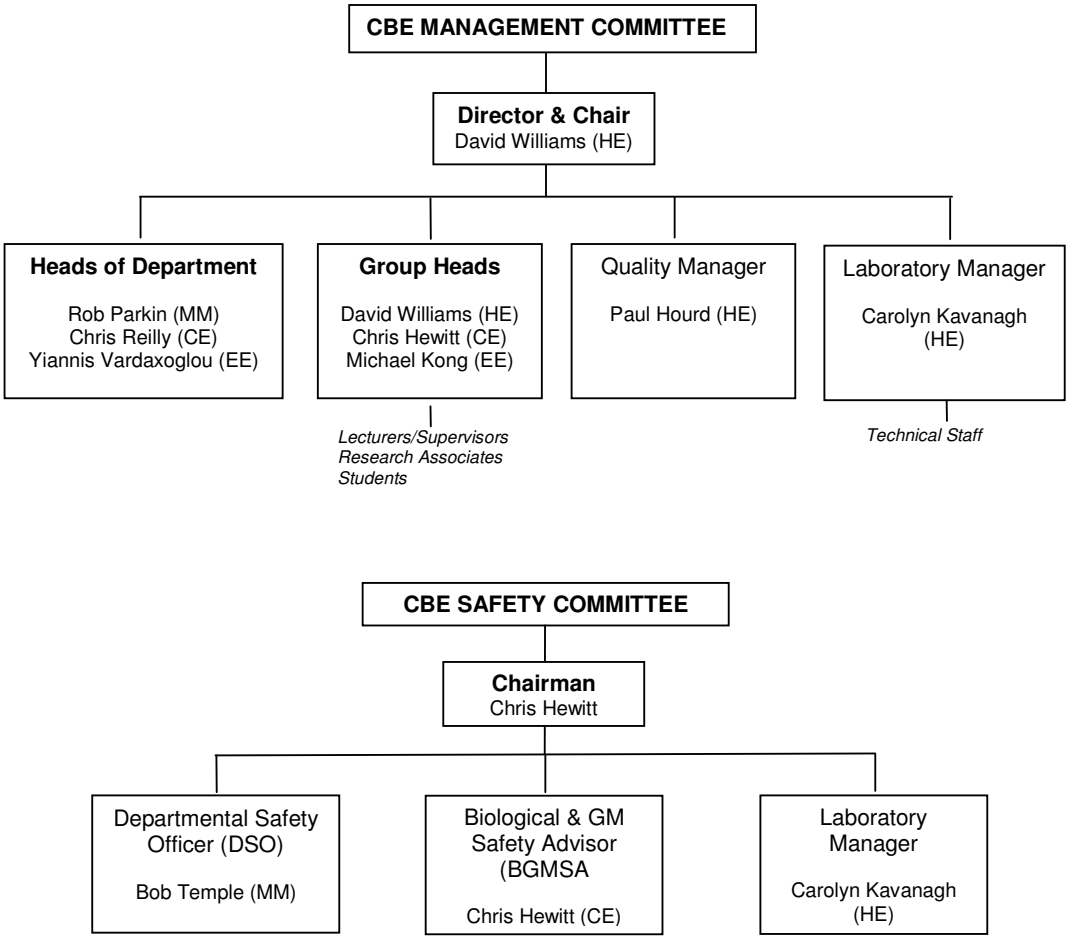
The University BHGMSC is the means by which the risk assessments for work involving Genetically Modified Organisms or infectious material in Hazard Group 2 or above are scrutinised. The role of the BHGMSC is to ensure consistency in approach and outcome of risk assessments and to help ensure that risk assessments are peer reviewed within a sensible time frame, before work is due to commence. Guidance on the remit and membership of the GM Safety Committee is provided in the University Biological Safety Policy.

1.7. RESPONSIBILITIES OF DUTY HOLDERS

This CoP describes the local rules and arrangements made within the CBE Laboratory Unit to comply with the University Biological Safety Policy. These arrangements identify the duty holders and specify the responsibilities placed on each named duty holder.

The responsibilities of duty holders within the CBE are indicated in the flow diagram below:

Figure 1: The CBE Organisational Management Structure - The CBE Management Committee reports to the Loughborough University Dean of Engineering; the CBE Safety Committee reports to the Loughborough University Safety Committee. (*KEY: HE = Healthcare Engineering Group; MM = Wolfson School of Mechanical and Manufacturing Engineering; CE = Chemical Engineering Department; EE = Electronic and Electrical Engineering Department*).



1.7.1. Head of Group (HoG)

(i) Hazard Awareness

1. It is the duty of all HoG to ensure that all aspects of the University's Biological Safety Policy are complied with within their area of responsibility.
2. Each HoG must take appropriate measures to ensure that all relevant persons are made aware of any hazards associated with the biological materials encountered during the course of their work and of the requirements to adopt working procedures designed to keep the risks to their health, and to the health of other persons who might be affected thereby, as low as reasonably achievable.
3. In addition, each HoG must ensure the University Biological Safety Policy is supplemented by local rules relating to specific activities of the CBE Laboratory Unit, so that, when read in conjunction with the Policy, the documents form an effective means of securing the safe use of biological materials, as well as potentially hazardous equipment and hazardous processes.
4. Each HoG is required to appoint a local Safety Advisor to cover areas where genetic modification work is undertaken and for those areas where biological work is undertaken but this does not include genetically modified organisms. For the purpose of this CoP, this person is referred to as the local Biological and Genetic Modification Safety Advisor (BGMSA).
5. Each HoG is responsible for ensuring risk assessments are carried out **in advance** of work commencing, communicated to relevant workers and reviewed whenever there are significant changes to the work and at least annually.
6. Each HoG is responsible for ensuring that work with biological materials is undertaken only in CBE facilities suitable for the purpose and using appropriate working practices.

(ii) Notifications

7. Each HoG must ensure an up-to-date inventory is maintained of BAs and GMOs on their premises. A copy of this information is to be provided to the University BSO who should be advised of any amendments as they occur. An annual declaration should be made in writing to inform the University BSO of work with biological material in Hazard Groups 1-4 that has not been notified previously.
8. Each HoG must ensure that all work involving infectious material at a classification of Hazard Group 2 (or above) is subject to peer review by the members of the BHGMSC **before** they are acquired and the work commences.
9. Each HoG must ensure that the University BSO is informed of holdings on their premises of any micro-organism or material controlled under anti-terrorism legislation, or in advance of any intentions to acquire such micro-organisms or materials.
10. Each HoG must ensure that all work involving genetically modified organisms is subject to peer review by the members of the BHGMSC **before they are acquired and** the work commences.
11. Each HoG must ensure that all work involving plant pathogens that require a DEFRA licence is subject to peer review by members of the BHGMSC **before** they are acquired and the work commences.
12. Each HoG must ensure that all staff working in the CBE Laboratory Unit are made aware of the requirement to notify certain work to the enforcing authority and to pay the accompanying fee where appropriate (*see Appendix 1 of the Biological Safety Policy*).

13. Each HoG must ensure that no work with agents in Hazard Group 3 or 4 (including work with GM material that could become more hazardous following its modification) is carried out.

(iii) Facility Management

14. The HoG should allocate day to day responsibility for housekeeping in the shared, multi-user CBE facilities to a named member of staff i.e. the Laboratory Manager to ensure satisfactory standards are maintained.
15. Each HoG is responsible for ensuring CBE laboratories or other facilities where biohazardous micro-organisms or materials are present are labelled at the point of entry with appropriate signs to prevent unauthorised access.
16. Each HoG is responsible for ensuring appropriate systems are in place to provide safe and suitable procedures for fumigation or decontamination in the CBE biological laboratories. In conjunction they must ensure adequate and appropriate instruction, training and supervision are provided for workers undertaking fumigation procedures.
17. Each HoG is responsible for ensuring appropriate systems are in place to provide safe and suitable procedures for use of liquid nitrogen in the CBE biological laboratories and associated facilities. In addition, they must ensure adequate and appropriate instruction, training and supervision is provided for workers using liquid nitrogen.
18. Each HoG is responsible for ensuring appropriate systems are in place to provide safe and suitable equipment for use in the CBE biological laboratories and associated facilities. In addition, they must ensure adequate and appropriate instruction, training and supervision is provided for workers using the equipment.
19. Each HoG must ensure all autoclaves and other pressure vessels (such as gas cylinders) owned by the CBE are notified to the University's Engineering Insurance Surveyor, who will inspect each item at the statutorily required interval. Notification of such items should be made through the HS&E. Notification of newly acquired equipment is required before it is brought into use, to ensure compliance with the Pressure Systems Regulations.
20. Each HoG must ensure there is a clear documented disinfection policy indicating suitable concentrations, contact times and applications for all disinfection requirements within the CBE Laboratory Unit.
21. Each HoG is responsible for the management of waste arising in areas under their control. They must ensure all infectious or potentially infectious biological waste produced within the CBE Laboratory Unit is autoclaved or treated with another validated waste treatment method prior to disposal.
22. Each HoG is responsible for ensuring that all hazardous biological material is stored safely and securely and that a register or inventory is kept of material in storage.

(iv) Health and Safety

23. Each HoG must ensure that persons working with biological material are competent to do so, including scrutiny of professional qualifications, experience, completion of induction training and authorisation made in writing.
24. Each HoG must identify the training needs of anyone with duties under the University Biological Safety Policy and ensure that systems are in place to provide instruction, information, training and supervision where appropriate, so that risks to the health and safety of all persons involved are controlled. They should also ensure that suitable arrangements in place to monitor and review the levels of supervision and training received in practice.

25. Each HoG should ensure that training and authorisation are retained for anyone working with biological material at Containment Level 2.
26. Each HoG must ensure that all persons undertaking any role in the transport chain are properly trained and have a detailed understanding of the relevant Regulations to ensure they are able to undertake their responsibilities to the required standards. The level of training should be commensurate with those responsibilities.
27. Each HoG should ensure any work is prohibited which entails a risk of serious personal injury or fire by persons working alone in the evenings or at weekends, irrespective of the status and experience of the worker.
28. Each HoG is responsible for ensuring the health and safety of all persons on their premises and must make appropriate arrangements to minimise the likelihood of accidents, incidents or instances of occupational ill health occurring. Needle stick and sharps injuries are particularly serious and each HoG must ensure all workers handling needles and sharps receive instruction and training on safe procedures.
29. Each HoG must ensure that records of all assessments, training, testing of equipment, accidents and near misses involving potentially hazardous biological material (HG2 and any GMO) are retained and maintained centrally within the CBE facility.
30. Each HoG must ensure that copies of accident and near misses records involving potentially hazardous biological material (HG2 and any GMO) are forwarded immediately to the University BSO.
31. Each HoG must ensure arrangements are made to deal with emergencies and other untoward events that may arise in areas where biological work is carried out, particularly puncture wounds, spillage and airborne release. All workers must be made aware of what action they need to take in the event of an emergency and those with specific roles must receive training in order for them to carry out their responsibilities effectively.
32. Each HoG is responsible for ensuring the requirement for any health surveillance be considered and determined as part of the risk assessment process.
33. Each HoG is responsible for ensuring the requirement for any immunisations be considered and determined as part of the risk assessment process.
34. Each HoG is responsible for ensuring the health and safety of all persons on their premises and must have appropriate systems in place to control access to biological laboratories. They should also ensure that suitable arrangements are in place to monitor and review access controls and how they work in practice.
35. Each HoG has a responsibility to ensure all arrangements for ensuring the health and safety of workers and others who may be affected by work activities are suitable and effective, and are appropriate for the particular work activities carried out.
36. Each HoG is responsible for ensuring CBE personnel carry out regular and systematic local health and safety inspections and audits to scrutinise health and safety standards and the effectiveness of the health and safety management systems in place.
37. Each HoG is responsible for ensuring regular reviews are undertaken of the health and safety arrangements (local policies, procedures etc) in the areas for which they are responsible to confirm they are appropriate and are working effectively. Where it is identified that any improvements to arrangements should be made then these must be implemented. Serious consideration should also be given to any other changes that could result in improved or better standards of health and safety management and standards.

1.7.2. Laboratory Manager/Quality Manager

1. Ensure that risk assessments are carried out in advance of acquisition of biological material and work commencing. Details of any proposals to acquire material in Hazard Group 2 (or above) or any GMO must be forwarded to the University's BSO as quickly as possible.
2. Ensure that risk assessments are reviewed whenever there are significant changes to the work and at least annually to ensure that they remain suitable and sufficient.
3. Ensure that persons working with biological material are competent to do so; professional qualifications are scrutinised, induction training completed and authorisation made in writing.
4. Ensure the training needs of anyone working in the CBE facility are provided with the instruction, information and training where appropriate.
5. Ensure that records of training and authorisation are retained for anyone working with material at Containment Level 2.
6. Ensure that appropriate measures are provided to eliminate or, where this is not reasonably practicable, reduce risks arising from work with biological material.
7. Ensure that equipment and facilities are maintained and tested.
8. Ensure that biohazard signs are maintained and security arrangements are implemented to prevent unauthorised access in areas identified by biohazard signs.
9. Ensure that all hazardous biological material is stored safely and securely and a register is maintained of all hazardous biological material kept in storage.
10. Ensure that all infectious biological material is autoclaved or treated by another validated waste treatment method prior to its disposal.
11. Ensure that records of all assessments, training, testing of equipment and accidents or near misses involving potentially hazardous biological material (Hazard Group 2 or any GMO) are maintained and copies of accident and near misses records involving potentially hazardous biological material forwarded immediately to the University BSO.
12. Ensure the names of all individuals working with human biological material or hepatitis B viruses are notified to the Occupational Health Advisor to arrange for vaccination against hepatitis B, if deemed necessary.

1.7.3. Duties and Responsibilities of Research Group Leaders/ Supervisors/ Managers

The Research Group Leader/Supervisor of a given research group or research personnel, or the supervisor/manager of a unit or work area, are required to:

1. Report all accidents and incidents, particularly those involving a release or, or exposure to, a biological agent.
2. Take ownership of the risk assessments for all work activities carried out by themselves and those persons under their supervision. Ensure that the work under their supervision has been assessed and approved by the appropriate group as specified in this document **before** work commences.
3. Ensure genetic modification work is undertaken only if a valid risk assessment approved by the BHGMSC is in place to cover the work.
4. Give careful attention to the health and safety of those under their supervision. Ensure all workers they are responsible for supervising receive the appropriate safety information and training and that this is suitably documented. Provide appropriate supervision and monitor compliance with this policy and local rules. Assess the competence of persons under their control to work safely and where appropriate arrange for the necessary training. An

assessment of competence should be carried out on all persons new to the CBE and new to a type of work or risk category.

5. Maintain the training record for each person for whom they have responsibility. Supervisors should clearly identify training needs as part of induction procedures and work should be carried out under close supervision until it has been confirmed that individuals are competent to carry out their work safely.
6. Ensure that research workers do not carry out practical laboratory work in the evening or at weekends unless a risk assessment has been approved and explicit permission is given.
7. In the event of an accident or incident occurring, the individual(s) involved must inform the manager/person who has responsibility for the particular area and if this is not their immediate supervisor they must also inform them. The individual and manager/supervisor all have a responsibility to ensure an accident and incident, or occupational ill health, report is completed. All accidents and instances of occupational ill health (illness reliably attributed to a work activity) must be reported to the HS&E Department as soon as possible after the incident has occurred.
8. All persons with supervisory or managerial roles, and those appointed to safety related roles such as the local BGMSA should routinely monitor working practices and have a responsibility to identify any instances where the required safety standards are not met and ensure that appropriate corrective action is taken to improve the situation. If they are aware of any safety-related problem in an area for which they themselves are not responsible then they must bring this to the attention of the person whose responsibility it is or to a more senior member of staff.

1.7.4. Duties and Responsibilities of Individuals

1. It is the duty of all employees and students to observe those parts of the University Health and Safety Policy that are relevant to their own work as well as observing any additional local rules and Regulations on health and safety published at CBE level.
2. Individual workers should ensure they are aware of the content of risk assessments relevant to the work they carry out and have a duty to follow all necessary control measures detailed therein.
3. It is the responsibility of the individual user to determine whether or not any micro-organism or material they wish to use is required to have a licence from DEFRA, and to apply to the appropriate government department.
4. It is the responsibility of the individual user to determine whether or not any micro-organism or material they wish to use is controlled under anti-terrorism legislation, and to inform the University BSO that they either have, or intend to acquire, such micro-organisms or materials.
5. All workers must be aware of the various routes of infection and the control measures necessary to block these and more specifically of the particular route(s) of infection of any BA (or BAs present within any biological material) with which they work. Sharps injuries are a significant concern and all workers in biological laboratories must receive instruction and training on safe working practices.
6. Individual workers must have access to and adhere to local rules. Adopt safe practices (standard operating procedures) in activities involving biological material, in particular to carry out work in designated areas, wear appropriate personal protective equipment.
7. Individual workers must always closely follow instructions provided for use of equipment, use it only for the purpose it was intended and never tamper with or over-ride any safety related devices.

8. Workers must follow the local disinfection policy and new disinfectants should not be introduced without first consulting the Laboratory Manager.
9. Workers must follow the local rules and procedures for disposal of waste. Each worker in the CBE has a duty of care, imposed under the Environmental Protection Act, to ensure that waste is managed properly and disposed of safely and in accordance with legal requirements.
10. All workers in the CBE must ensure Regulations applicable to the transport of biological materials are complied with for each particular consignment and not carry, consign, package or play any other role in the transport chain if they are not competent to do so.
11. Report any incident, accident or defect in equipment relating to the handling of biological materials. The Occupational Health Unit should be informed immediately in the event of any accident where exposure to a pathogen, genetically modified micro-organism or potentially infectious material may have occurred.
12. In the event of an accident or incident occurring, the individual(s) involved must inform the manager/person who has responsibility for the particular area and if this is not their immediate supervisor they must also inform them. The individual and manager/supervisor all have a responsibility to ensure an accident and incident, or occupational ill health, report is completed.
13. All accidents and incidents that do occur should subsequently be reviewed by the individual(s) involved in conjunction with their immediate supervisor.
14. If individuals have concerns about the effect of any work activity on their health they should seek advice from the Occupational Health Unit or, if they prefer, from their own General Practitioner.
15. All workers in the CBE are directed to take notice of what is going on around them and report to their supervisor, or to a more senior member of staff, any instances where University Health and Safety Policy is not being followed or any other safety-related concern they may have.

SECTION 2	BIOSAFETY REQUIREMENTS FOR WORK WITH BIOLOGICAL AGENTS IN THE CL2 CBE LABORATORY UNIT
PART 1	PROCEDURES TO BE ADOPTED BEFORE STARTING WORK: ADMINISTRATION AND EXPOSURE CONTROLS

2.1. ASSESSMENT OF RISK

The risk to human health and the environment should be assessed to determine the level of containment and the control measures required to undertake activities involving Biological Agents (BAs) and Genetically Modified Organisms (GMOs). The COSHH Regulations and the GMO (Contained Use) Regulations set out various criteria that must be considered as part of the risk assessment process.

This section provides specific guidance for the risk assessment of activities involving the BAs under the COSHH Regulations. Where a risk assessment is made under the GMO (Contained Use) Regulations, specific guidance is provided in Section 4 of this CoP. Other guidance on risk assessment is given in "Biological Agents: Managing the risks in laboratories and healthcare premises" and Part 2 of "SACGM Compendium of Guidance" (see Section 8).

A risk assessment comprises 5 steps:

1. Hazard identification;
2. Deciding who is at risk from the hazard and how harm could arise;
3. Assessing how likely it is that harm will arise and whether existing precautions are adequate;
4. Making a record of findings, including the control measures selected and any action identified as necessary to reduce the risk of exposure further; and
5. Reviewing and revising the assessment as necessary especially if the nature of the work changes or if something else suggests that it may no longer be valid, e.g. as a result of an incident.

2.1.1. Hazard Identification

Hazards can be categorised into three main groups: physical hazards, chemical hazards, and biological hazards. A risk assessment plan should consider all these hazards in relation to the proposed work. This assessment should not be limited only to the laboratory and laboratory personnel, but should also cover risks to people in the entire CBE Laboratory Unit, people in the external environment and to the environment itself.

NOTE: *Risks to the environment are generally due to poor waste disposal, leading to contamination of water, air or soil, or the escape from containment of hazardous materials. The environment can also be contaminated by release of biological material due to accidents, including transport accidents, and systems should be put in place to prevent or minimise the potential for such damage.*

(i) Physical hazards

The laboratories within the CBE Containment Level 2 Laboratory Unit do not pose any specific physical hazards. However, laboratories and workspaces should always be kept clean and tidy, and free of material stored on the floor or anywhere where it can cause risk to other people. Any equipment or apparatus used should meet national safety guidelines. Equipment such as autoclaves, fume hoods or biological safety cabinets should have a programme of maintenance for safe use. The correct operation of equipment should also be regularly checked. Procedures should

be in place for ensuring the safest possible use of equipment connected with ultra-violet light, liquid nitrogen and pressurised gases.

(ii) Chemical hazards

The laboratories within the CBE Containment Level 2 Laboratory Unit are not a particularly dangerous place to work with regard to chemical hazards. However, some chemicals have ill defined or unknown biological effects, so general safety standards should always be maintained to protect workers against these uncertain hazards. Material Safety Data Sheets for all chemicals used in the laboratory unit should be requested from the suppliers. For any substances that are potentially hazardous to health (for example, mutagens, cryoprotectants, labelling dyes), these data should form the basis of a risk assessment for the use of this chemical, as the level of risk will vary, depending on, for example, the quantities being used and the techniques being employed. Approved waste disposal procedures should always be followed.

NOTE: *Some useful advice on general laboratory hazards and on the specific problems that arise when handling chemical substances can be found in Annex 3; this guidance should be consulted wherever it might be relevant to the work of the biological laboratory. Likewise, the relevant University guidelines should be consulted where ionising, non-ionising or laser radiations are in use.*

(iii) Biological hazards

The starting point for any risk assessment for work with biological materials is to consider which biological agents are being handled (or may be present) and their respective hazard group classification. A wide range of biological materials are handled within the CBE Laboratory Unit and there is substantial variation in the types of hazards associated not only with the different types of materials but in some cases the differing sources of the materials.

Hazard Group classification, in relation to a biological agent, means one of the four Hazard Groups to which that agent is assigned according to its level of risk of infection. This forms the basis of the risk assessment and determines the level of containment under which the work must be undertaken. Additional control measures may then need to be assigned depending on the route of infection of the particular BA and the nature of the work.

Classifying Biological Agents into Hazard Groups

The biological agents being handled, or those that might be present in the biological material, should be identified and each allocated to one of four Hazard Groups. BAs are classified into one of the four hazard groups (HG 1-4) using the following criteria:

(i) is the organism pathogenic for man?
(ii) is it a hazard to workers?
(iii) is it transmissible to the community?; and
(iv) is effective prophylaxis or treatment available?

The classification gives an indication of the inherent hazard of the BA's listed, but does not consider how the agent is used, the amount, titre used or procedures undertaken. The classification is based on the infective hazard to healthy workers and does not allow for any additional risk for example caused by pre-existing disease, the effects of medication, compromised immunity, pregnancy or breastfeeding and the possible effects on the environment, e.g., on animal or plant life. Additional risks to such workers must be addressed in risk assessments before commencing work with these agents.

Since the classification is based only on disease caused by infection, other hazards associated with the BA or its products, such as it allergenic or toxic properties must also be considered. Some BAs for example are not infectious at all but the infectious criteria are the only ones used for classification purposes, even though a BA may have toxic, allergenic or other harmful properties. While a non-infectious BA may be classified as Hazard Group 1, substantial control measures may still be needed; for example if it has toxic properties, then COSHH would apply.

Biological agents in Hazard Groups 2, 3 and 4 are referred to as pathogens. Whilst it is unlikely that organisms in Hazard Group 1 will cause disease, many have the potential to cause opportunistic infections and this should always be borne in mind. Although not usually dangerous to the user, cells and tissues for example, have the potential to permit the replication of viruses potentially pathogenic to humans, and should therefore be routinely treated as if they are a potential health risk. The biological agents are classified in the four hazard groups are defined as below:

Hazard Group (HG)	Pathogenicity for Humans	Hazard to Workers	Spread to Community	Effective Prophylaxis or Treatment
1	**Unlikely to cause human disease.** *E.g. Tissues & cell lines of non-primate/non human origin. Human/primate cell lines that are well characterised, authenticated, long established and have long history of safe use [e.g.MRC5, HeLa cells]. Disabled/attenuated/non-pathogenic strains of some bacteria and virus.*			
2	**Can cause human disease** *E.g. tissues and primary cell lines of human/primate origin. Adenovirus, clostridium, most strains of E coli*	May be	Unlikely	Usually available
3	**Can cause severe human disease.** Eg *HIV, Hepatitis B, E coli 0157, salmonella typhi.*	May be serious	May spread	Usually available
4	**Causes severe human disease** *E.g. Rabies, Ebola Virus but it is highly unlikely that any such agents would be permitted in the University*	Serious	Likely	Usually none

NOTE: *Biological agents may also be classified as genetically modified micro-organisms (GMMs), although not all GMMs are BAs. While COSHH covers the risks to human health, additional controls may be required under the Genetically Modified Organisms (Contained Use) Regulations 2000 to control the risk to the environment.* ***Hence a BA that is classified as Hazard Group 1 under COSHH may also be classified as a GMM under the GMO (CU) Regulations. The standards described under the Contained Use Regulations are broadly equivalent to those of COSHH, but where there is a difference, the more stringent requirements should be followed.***

Many biological agents in Groups 2-4 are listed in a classification list approved by the Health and Safety Commission (referred to as the Approved List of biological agents) so reference should be made to this list when classifying. The Approved List is available on the HSE website at http://www.hse.gov.uk/pubns/misc208.pdf.

If a biological agent is not on the approved classification list this does not automatically infer it is in Hazard Group 1 and classification should be made taking account of available evidence of human pathogenicity, using the definitions given in Schedule 3 of the COSHH Regulations. If there is any uncertainty on classification then the higher of the two possible groups should be chosen.

NOTE: *Amendments may be made to the list from time to time, and the Approved List on HSE's website should be consulted to ensure that the most up-to-date version is used.*

In some cases, such as for attenuated vaccine strains, it is acceptable to reclassify an agent as though it is different to the named agent on the Approved List. This should only be done in consultation and agreement with the Health and Safety Executive (HSE) unless the HSE have issued specific guidance indicating what to do in specific circumstances.

2.1.2. Evaluate who is at risk from the hazard and how harm could arise

Assessing risk involves examining the extent of the likelihood of a material causing harm in the actual circumstances of the work. The risk assessment should include consideration as to whether any particular groups of employees may be at increased risk. These include students, trainees, young workers, new and expectant mothers and employees who may be more susceptible to certain illnesses because of their individual health profile. They may also include those who may not be directly involved with the activity but who may still be affected by the process

(i) Who will do the work and where is it proposed they do it?

At an early stage of carrying out the risk assessment, consideration must be given to who will actually do the work. This assessment is made by considering the competence of the staff, taking into account relevant factors that may affect safe working. This may relate to physical features such as size and strength; or pregnancy; or a member of staff possessing a particular disability. All these factors may affect the risk assessment, the overall objective being to ensure that competent staff are able to do the work in a safe manner.

Consideration of the basic facilities required for the work must be done at a very early stage. At the extreme, work may be proposed when there is simply no possibility of providing the proper facility. Examples may include work with a Hazard Group 3 organism when there is no prospect of providing a proper laboratory, or work with volatile toxic substances when total enclosure is not practicable and no fume cupboard is available.

(ii) Routes of Infection and Exposure Limits

In the natural environment micro-organisms use several different routes of infection to gain access although these are often characteristic of, and specific to, the micro-organisms and the diseases they cause. For example, gastrointestinal diseases usually result from ingestion of contaminated food or drink whereas respiratory diseases usually result from inhalation of an infectious aerosol. In the laboratory setting, primary consideration must always be given to a pathogen's normal route of infection but it should also be remembered that laboratory manipulations might potentially give rise to exposures that would not normally be encountered in everyday life. For example, a high concentration of a respiratory pathogen could be injected directly into the body as a result of a needle stick injury and whilst this may not deliver the pathogen to its primary site of infection the potential for it to cause disease would still be significant.

Micro-organisms can gain access to the body by ingestion (mouth), instillation (eyes), inhalation (respiratory tract) or via the percutaneous route (skin). Whilst many chemicals can be absorbed through intact skin, micro-organisms cannot and only enter the body through skin that is damaged (cuts and grazes or puncture wounds) or the mucous membranes. Working practices and control measures are based on blocking these routes of infection by the use of well established and standardised precautions.

All workers must be aware in general of the various routes of infection and the control measures necessary to block these and more specifically of the particular route(s) of infection of any micro-organism (or the micro-organisms that may be contained within any biological material) with which they work. There is generally no dose-response relationship and with many micro-organisms able to infect at very small doses there are no exposure limits. Therefore exposure to micro-organisms should be controlled to as low as reasonably practicable taking account of the risk. Working practices when handling biological materials should always follow the precautionary approach of routinely blocking routes of infection. The following summarises the routes of infection that may occur within the CBE Laboratory Unit and the principal means of blocking them:

- **Ingestion route** - never ever put anything in the mouth whilst in the laboratory and avoid subsequent transfer to items such as food by always washing hands before leaving.
- **Percutaneous route** - avoid the likelihood of puncture wounds by careful handling procedures and always keep any breaks in the skin covered whilst in the laboratory. Care should be taken to ensure working practices do not contaminate mucous membranes by, for example, splashing or transfer. Sharps injuries are a significant concern and all workers in biological laboratories must receive instruction and training on safe working practices.
- **Inhalation route** - care must be taken to minimise the production of aerosols and where infectious aerosols may be generated the work should be carried out in a biological safety cabinet.
- **Instillation route** - care should be taken to ensure working practices do not contaminate eyes by splashing or transfer. If these may be likely then the wearing of suitable eye protection is paramount.

Further guidance on blocking routes of infection is given in the guidance on good microbiological practice and containment in Section 2, Part 4. Further information on what to do in the event of an accident or incident involving biological materials is given in Section 6.

2.1.3. Evaluate how likely that harm will arise and whether existing precautions are adequate

This is the process of estimating the likelihood of an event occurring, such as exposure to a micro-organism, plus identifying the likely consequence of exposure. The major consideration of the assessment is likely to be the risks to human health. However, risks to the environment, including to animal, fish and plant life, must be included. The evaluation of the risk to human health may include: the possibilities of acquiring a progressive infection, becoming sensitised to an allergen or coming in contact with a toxin. The threat to the environment is likely to be via unintentional release, either through a breakdown in containment or through uncontrolled disposal or discharge of waste.

The risks (low / medium / high) to which individuals might be exposed should be evaluated. This will be a subjective evaluation but should be used to give an indication of the priority with which the risk needs to be addressed. Where risks are already controlled, the effectiveness of the control should be monitored to decide whether they are sufficient. Where the risk to individuals is thought to be medium or high, additional control measures must be considered

(i) Hazard and Risk

Hazard, in relation to a substance, means the intrinsic property of that substance which has the potential to cause harm to the health of a person, and hazardous should be construed accordingly.

Risk, in relation to the exposure of an employee to a substance hazardous to health, means the likelihood that the potential for harm to the health of a person will be attained under the conditions of use and exposure and also the extent of that harm. The risk takes account of both likelihood and consequence as detailed in the risk matrix below:

CONSEQUENCE OF HAZARD	LIKELIHOOD OF HAZARD			
	High	Medium	Low	Negligible
Severe	High	High	Medium	Effectively zero
Medium	High	Medium	Medium/Low	Effectively zero
Low	Medium/Low	Low	Low	Effectively zero
Negligible	Effectively zero	Effectively zero	Effectively zero	Effectively zero

(ii) Risk Control

Although much of the biological work in the CBE Laboratory Unit does not involve materials known to be infectious, it is important to note that many biological materials may contain pathogens, that laboratory procedures may support the growth of pathogenic contaminants and that many micro-organisms whilst not generally regarded as human pathogens may, in certain circumstances, cause infections. Health and safety precautions are therefore essential for all forms of biological work being carried out in the CBE Laboratory Unit because of the ever present possibility that laboratory workers, students and other personnel who access the Unit might be affected by accidental infections or allergic reactions. The approach used is known as working in, or under, containment and is described in more detail below. This precautionary approach is well tried, tested and established having been successfully used for many years across multidisciplinary work areas. It also forms the basis of the regulatory frameworks in the COSHH and GM (Contained Use) Regulations.

Workers must decide what controls are necessary to reduce the risk to individuals and to comply with any relevant statutory requirements (compliance with statutory requirements is a minimum level of control). Assistance should also be sought from relevant Health and Safety Executive (HSE) guidance or accepted industry guidance. All precautions or measures that are reasonably practicable to eliminate, minimise or control exposure to risk must be taken. The term 'reasonably practicable' incorporates consideration of cost against benefit, but there is an order, or 'hierarchy', which should be followed reflecting the fact that eliminating and controlling risk by using physical engineering controls and safeguards is more dependable than relying solely on systems of work:

- **eliminating risks**: e.g. by avoiding the hazard - can the hazard be avoided or altered to reduce the likelihood or risk? By substituting a hazardous biological agent with something less/non-hazardous, e.g. using a non-toxigenic strain of a biological agent when carrying out laboratory quality control (QC) tests; Procedural controls – can the procedure be altered to avoid or reduce the risk? Can the individual be removed / distanced from the risk? Can the activity be carried out at a time that would have a lesser impact on others?
- **controlling risks at source:** by using engineering controls and giving collective protective measures priority, e.g. using containment equipment such as a biological safety cabinet when work could create an infectious aerosol, or using needle safety devices to prevent and control needle stick injuries; and
- **minimising risks by designing suitable systems of working**: e.g. having an effective hand hygiene policy in place in the laboratory, the use of personal protective clothing and equipment (PPE), the use of biological safety cabinets. In addition, the principles of good microbiological practice, e.g. the use of good aseptic techniques should underpin the physical control

measures. Emergency procedures – set procedures to follow in the event of things going wrong e.g., an accident or incident.

In addition to the these general controls, the COSHH and Contained Use Regulations also sets out a number of specific measures which must be used to control exposure to or release of BAs and GMOs respectively, as indicated by the risk assessment. These are specified as the **minimum** containment measures under the COSHH and Contained Use Regulations

(iii) Control Exposure

Wherever possible, exposure should be prevented but where this is not reasonably practicable then exposure must be adequately controlled. Special control measures are described in Schedule 3 of COSHH Regulations for certain types of work or activities where the appropriate containment level is derived from the hazard classification of the agent or what is suspected about the possible presence of an agent.

The number of the hazard group of a particular BA indicates the minimum level of containment under which it must be handled. In matching hazard group with containment level the pathogenic potential, host susceptibility, epidemiological consequence and availability of effective treatment have all been taken into account. The need for additional precautions should also be considered as part of the risk assessment taking account not only of the pertinent features of the BA and its route of transmission but also the type of work being carried out and the likelihood of infection occurring during normal work and in the event of an accident.

Details of the control measures that should be considered, and applied where indicated by the risk, are given in Parts II and III of Schedule 3 of COSHH. These specifications include the more general control measures, good practice measures and the current minimum statutory requirements and are therefore reproduced in Tables 1 and 2. These Tables show the minimum containment requirements of the COSHH Regulations for work in Containment Level 2 laboratories. Containment Level 2 is suitable for a broad range of clinical, diagnostic and research (i.e. deliberate) work with biological agents which, although capable of causing disease, only present a low-to-moderate risk to employees in the CBE and are unlikely to spread to the community, with effective treatment or prophylaxis being available.

Similarly, where the work involves genetically modified organisms the ACGM containment measures should be applied (these are reproduced in Section 4; Tables 3 and 4). It is important to note that where the work involves animal or plant pathogens the DEFRA containment measures should be applied. Where the work involves the use of more than one of these hazards then a combination of the standards for all relevant containment levels are to be met.

For example:

- African horse sickness virus is classified as a hazard group 3 animal pathogen but because it does not infect humans is only assigned to ACDP hazard group 1. Whilst ACDP Containment Level 1 is all that is required to protect human health and health safety, DEFRA Containment Level 3 precautions are required to prevent escape to the environment and protect animals.
- Rabies virus is assigned to hazard group 3 on the basis of risks to human health and safety (ACDP classification) and hazard group 4 on the basis of animal pathogenicity (DEFRA classification). Work with rabies virus must therefore be carried out in a facility that meets both ACDP Containment Level 3 and DEFRA Containment Level 4 standards.
- If either of these viruses were to be genetically modified, the ACGM level of containment determined in the risk assessment would need to also be applied.
- In both cases, the viruses are controlled under the Specified Animal Pathogens Order and a licence would be required in advance of the work starting.

The COSHH Regulations not only require general prevention or control of exposure to BAs but also require minimum containment measures for laboratories handling particular groups of BAs. The minimum containment levels required for different types of work are-

- Containment Level 2 for activities which involve working with a Hazard Group 2 BAs;
- Containment Level 3 for activities which involve working with a Hazard Group 3 BA (except there are certain circumstances when not all measures normally required at Containment Level 3 need be applied when working with the Hazard Group 3 agents specified in Annex 1 of the Approved List provided specialist guidance for work with these agents is followed - see the Approved List for further details);
- Containment Level 4 for activities which involve working with a Hazard Group 4 BA;
- Containment Level 2 for laboratories which do not intentionally propagate, concentrate or otherwise increase the risk of exposure to a biological agent but work with materials in respect of which it is unlikely that a Hazard Group 3 or Hazard Group 4 BA is present;
- Containment Level 3 or 4, where appropriate, for laboratories which do not intentionally propagate, concentrate or otherwise increase the risk of exposure to a Hazard Group 3 or Hazard Group 4 BA but where the employer knows, or it is likely, that such a containment level is necessary; and
- Containment Level 3 for activities where it has not been possible to carry out a conclusive assessment but where there is concern that the activity might involve a serious health risk for employees.

This works well wherever the identity and thus the pathogenicity of the agent are known. Containment requirements in those situations where the identity or presence of a biological agent is not known are now included within the law. Amongst the requirements is the following:

Where uncertainty exists over the presence of pathogenic biological agents	Minimum of Containment Level 2
Where the presence of a pathogenic biological agent is known or suspected	Minimum of Containment Level appropriate to the agent
Where the assessment is inconclusive but where the activity might involve serious risk	Minimum of Containment Level 3

Depending on the nature of the BA or the particular activity, additional control measures may also be necessary in some cases whereas in others there are provisions for derogations and less stringent control measures may be applied. The need for additional precautions to those specified as the minimum should be determined on a case by case basis by risk assessment.

Table 1: Containment Measures for Work with Biological Agents in Laboratories

[Source: reproduced from Schedule 3 of the 2002 COSHH Regulations]

Containment measures		Containment levels		
		2	3	4
1	The workplace is to be separated from any other activities in the same building	No	Yes	Yes
2	Input air and extract air to the workplace are to be filtered using HEPA or equivalent	No	Yes, on extract air	Yes, on input and double on extract air
3	Access is to be restricted to authorised persons only	Yes	Yes	Yes, via air-lock key procedure
4	The workplace is to be sealable to permit disinfection	No	Yes	Yes
5	Specified disinfection procedure	Yes	Yes	Yes
6	The workplace is to be maintained at an air pressure negative to atmosphere.	No	Yes	Yes
7	Efficient vector control eg rodents and insects	Yes, for animal containment	Yes, for animal containment	Yes
8	Surfaces impervious to water and easy to clean	Yes, for bench	Yes, for bench and floor (and walls for animal containment)	Yes, for bench, floor, walls and ceiling
9	Surfaces resistant to acids, alkalis, solvents, disinfectants	Yes, for bench	Yes, for bench and floor (and walls for animal containment)	Yes, for bench, floor, walls adn ceiling
10	Safe storage of biological agents	Yes	Yes	Yes, secure storage
11	An observation window, or alternative, is to be present, so that occupants can be seen	No	Yes	Yes
12	A laboratory is to contain its own equipment	No	Yes, so far as is reasonably practicable	Yes
13	Infected material, including any animal, is to be handled in a safety cabinet or isolator or other suitable containment	Yes, where aerosol produced	Yes, where aerosol produced	Yes
14	Incinerator for disposal of animal carcases	Accessible	Accessible	Yes, on site

Table 2: Containment Measures for Industrial Processes using Biological Agents

[Source: reproduced from Schedule 3 of the 2002 COSHH Regulations]

Containment measures		Containment levels		
		2	3	4
1	Viable micro-organisms should be contained in a system which physically separates the process from the environment (closed system)	Yes	Yes	Yes
2	Exhaust gases from the closed system should be treated so as to -	Minimise release	Prevent release	Prevent release
3	Sample collection, addition of materials to a closed system and transfer of viable micro-organisms to another closed system, should be performed so as to -	Minimise release	Prevent release	Prevent release
4	Bulk culture fluids should not be removed from the closed system unless the viable micro-organisms have been -	Inactivated by validated means	Inactivated by validated chemical or physical means	Inactivated by validated chemical or physical means
5	Seals should be designed so as to -	Minimise release	Prevent release	Prevent release
6	Closed systems should be located within a controlled area -	Optional	Optional	Yes, and purpose-built
7	(a) biohazard signs should be posted;	Optional	Yes	Yes
8	(b) access should be restricted to nominated personnel only;	Optional	Yes	Yes, via air-lock
9	(c) personnel should wear protective clothing;	Yes, work clothing	Yes,	Yes, a complete change
10	(d) decontamination and washing facilities should be provided for personnel;	Yes	Yes	Yes
11	(e) personnel should shower before leaving the controlled area;	No	Optional	Yes
12	(f) effluent from sinks and showers should be collected and inactivated before release;	No	Optional	Yes
13	(g) the controlled area should be adequately ventilated to minimise air contamination;	Optional	Optional	Yes
14	(h) the controlled area should be maintained at an air pressure negative to atmosphere;	No	Optional	Yes
15	(i) input and extract air to the controlled area should be HEPA filtered;	No	Optional	Yes
16	(j) the controlled area should be designed to contain spillage of the entire contents of closed system;	Optional	Yes	Yes
17	(k) the controlled area should be sealable to permit fumigation.	No	Optional	Yes
18	Effluent treatment before final discharge.	Inactivated by validated means	Inactivated by validated chemical or physical means	Inactivated by validated physical means

2.1.4. Submission of Risk Assessment Proposals for Hazardous Materials

The Research Group Leader of a given research group, or the supervisor/manager of research personnel or a unit or work area, is required to take ownership of the risk assessments for all work activities carried out by themselves and those persons under their supervision. Whilst this does not necessarily mean that such individuals are required to actually formulate each risk assessment personally, they would be required to scrutinise, verify and countersign. In order to effectively discharge this responsibility, those with supervisory or managerial roles must themselves be competent in safety related matters and, where necessary, should seek additional training (or refresher training) as appropriate.

The person who carries out the risk assessment must be competent to do so. This does not necessarily mean particular qualifications are required. However, the person should

- have adequate knowledge, training and expertise in understanding hazard and risk;
- know how the work activity uses or produces substances hazardous to health;
- have the ability and authority to collate all the necessary, relevant information;
- and have the knowledge, skills and experience to make the right decisions about the risks and the precautions that are needed.

The risk assessment relating to a particular work activity should be produced so that it can be easily understood by persons who need to refer to it. All persons undertaking a work activity must be made aware of the content of the risk assessment in order that they are aware of the risks associated with the work and the control measures necessary for them to carry out their work safely. Individual workers should ensure they are aware of the content of risk assessments relevant to the work they carry out and have a duty to follow all necessary control measures detailed therein. Signatures should be obtained from all relevant personnel to show that workers have read, understood and agree to adhere to the documented risk assessments.

A risk assessment will be considered to be suitable and sufficient if the details and expertise with which it is carried out are in accord with the nature and degree of risk arising from the work and the complexity of the work concerned.

NOTE: Frequently observed shortcomings in submitted risk assessments include:

- *Poor or no justification of the control measures. It is common for information to be simply copied from the data sheet, with no consideration of the task being carried out.*
- *Few assessments highlight the consequences of exposure. This is important as it helps you to decide what is 'reasonably practicable' when justifying control measures.*
- *Poor identification of exactly who might be exposed as a result of the work task, and how long they could be exposed for. E.g. Often the immediate operator was considered, but not other operators working in the same area or visitors who may be exposed.*
- *No clear identification of the different routes of exposure, which might include: inhalation, ingestion, and skin absorption.*
- *Poor links to supporting documents. The COSHH assessment should act as a 'map' to point to the supporting evidence of the justification it provides.*

A risk assessment form should be completed **before** acquiring the material and must be completed and approved **before** commencing the work. This risk assessment form should be completed for **all** work activities and should be filed in the laboratory along with any supporting documentation e.g. a written protocol. Although the risk assessment process may be delegated, the person managing the work area or activities remains responsible for the findings and for ensuring that the conclusions

relating to any remedial action are implemented. The assessment form requires that the responsible person to confirm their acceptance of any delegated assessments.

In analysing the risks arising from any particular activity each of the hazards involved needs to be considered separately against the precautions, which are already provided. These may or may not be satisfactory. Where the precautions are dealt with by other documents (such as local rules and procedures (e.g. Standard Operating Procedures) for working with hazardous substances, the use and maintenance of specialist items of equipment etc) then it is only necessary to refer to these documents and conclude whether the detailed contained therein is sufficient to control the hazards.

Risk assessments required by the GM (Contained Use) Regulations must always be recorded, must be considered and approved by a competent GM Safety Committee in advance of the work starting, be regularly reviewed and, for higher risk activities, be forwarded as part of a notification to the Health and Safety Executive. These risk assessments must also incorporate consideration of the potential impact upon the environment of any deliberate, or accidental, release of genetically modified material likely to result from the work activity - **a requirement of the Environmental Protection Act that is repeatedly highlighted by HSE Inspectors**. Further details on how to complete risk assessment for activities involving GMOs are provided in Section 4.

Blank templates of the Risk Assessment Forms for the following work activities are available on the CBE website or from the Laboratory Manager. These model forms serve to keep information in a consistent manner and assist the CBE to comply with the detailed requirements for risk assessment and classification as set out in the COSHH and GM (Contained Use) Regulations.

A. Proposals for Work with Biological Materials

The University BHGMSC will consider and approve work with non-genetically modified biological material. All work with non-GM Hazard Group 2 biological material should be submitted for examination on the first occasion of its use in the CBE Laboratory Unit. Proposals must be submitted to the University BSO on the **'Risk Assessment for Work with Biological Agents'** form and approved by the BHGMSC for HG2 work or by the local BGMSA for HG1 work **prior** to commencement of work. This form is to be used when working with any biological agent (or material that may contain them) in procedures that may be carried out for both Hazard Group 1 and 2 BAs. Approved risk assessments should be reviewed annually.

NOTE: *Unscreened/untreated blood should be classed as a Hazard Group 2 biohazard.*

B. Proposals for Work with Genetically Modified Organisms (Refer to Section 4)

The University BHGMSC will consider and approve work with genetically modified organisms. All work involving GM material will be examined by the committee. Unless there is significant alteration in the way in which the GM material is used or significant alteration in the environment of the workplace in which it is used there is no need to submit details for subsequent examination of projects. Proposals must be submitted to the University BSO[4] on the **'Risk Assessment for Work with Genetically Modified Organisms'** form and approved by the BHGMSC **prior** to commencement of work. Approved risk assessments should be reviewed annually but may be more frequent dependent on the risk. Guidance for completing the risk assessment, based on the ACGM Compendium of Guidance, is provided in Section 4 of this CoP.

[4] The University BSO shall send copies of the GM risk assessment form to two independent members of the BHGMSC for comment. Should comments conflict then a third member of the committee shall receive the risk assessment for a decision to be made on whether to permit the project to go ahead as planned or whether risk controls need to be improved.

C. Hazardous Work Activity Associated with Physical Agents (e.g. Equipment, Processes), Chemical or Biochemical Reagents

Proposals must be submitted on the relevant Risk Assessment form and approved by the local Department Safety Officer (DSO) **prior** to commencement of work. If the **work activity is new or associated with new physical agents or hazardous chemical reagents (COSHH forms)** and the risk assessment has not yet been made, **an application for approval must be made prior to the commencement of the activity.** Guidelines on making health risk assessments under the COSHH Regulations 2002 are available at http://www.lboro.ac.uk/admin/hse/policies/download/Guidance%20on%20COSHH%20Procedures.pdf. Additional guidance is available at http://www.coshh-essentials.org.uk/.

2.1.5. Management and Review

A good management system that provides for regular appropriate monitoring coupled with a review of risk assessments is essential to make risk assessments 'live', accurately reflecting and, where appropriate, modifying current work practices. Thus, monitoring the work for compliance with set procedures also enables judgements to be made on the procedures themselves, which may in turn lead to modifications being made. Regular review of risk assessments will identify any changes made within the review period, which again in turn may lead to changes in the assessments themselves.

Records of risk assessments should be maintained locally where the work takes place and should be reviewed, on a frequency determined by the risk (i.e. at least annually), to ensure that each is still relevant for the work activity concerned. All risk assessments should be reviewed at least annually, or following significant change in the work. Each Head of Group is responsible for ensuring risk assessments are carried out, communicated to relevant workers and regularly reviewed. Risk assessments must be available for inspection by relevant parties, both from within and outside the University.

(i) Maintain, examine and test control measures

In order to ensure that systems and equipment provided to control exposure perform as intended there are requirements for regular visual checks, inspection, testing, preventative servicing and remedial work. Control measures subject to thorough examination and test include engineering controls, local exhaust ventilation (LEV) plant and respiratory protective equipment (RPE). Examples of such systems and equipment in the CBE Laboratory Unit include the laboratory air handling systems, biological safety cabinets and autoclaves. Records should be kept for at least 5 years from the date of test. Where equipment has been contaminated with biological agents, it is important to ensure these are appropriately decontaminated prior to servicing and test etc.

- Personal protective equipment (PPE) used to protect workers against biological agents should be stored, checked and cleaned in such ways as to prevent the equipment being a means by which biological agents are transmitted.
- Biological Safety Cabinets must be serviced & tested in accordance with the requirements of BS EN 12469 2000. They should also be subject to routine maintenance checks at regular intervals. For more detail on the correct use of BSC's, see Annex 4.
- Autoclaves must be subject to routine maintenance checks and to regular validation and pressure vessel inspections. For more detail on the correct use of autoclaves, see Annex 5.
- Centrifuges and their rotors/buckets must be subject to routine cleaning and inspection of seals. Regular service by a competent engineer is recommended for all centrifuges. Servicing and maintenance requirements must be determined following local risk assessment. This should consider the size, operating speed and level of use and the potential damage that could be incurred in the event of a major centrifuge accident, such as rotor disruption. As a rule high

speed and ultra centrifuges should be annually maintained and serviced by a competent engineer. Similarly rotors used in large, high speed and ultra centrifuges must be inspected annually by a competent person and records maintained.

- If the risk assessment deems it appropriate monitoring for BAs/GMOs outside of the primary containment may be required. Such methods might include swab testing of surfaces or the use of settle plates.

(ii) Monitor Exposure

Standard air sampling and personal sampling techniques are not normally appropriate to biological agents and there is no requirement under the Regulations to monitor exposures as such in the CBE Laboratory Unit. However, there may be cases, particularly for industrial applications, that testing for the presence of a biological agent outside the primary physical confinement may need to be carried out using, wherever possible, a harmless indicator organism.

(iii) Inspection, Audit and Review

There should be procedures in place to confirm that the arrangements for biological work activities within the CBE Laboratory Unit are effective and remain valid. There are various means by which this should be achieved and the following are expected to be in place.

a. Monitoring

All persons with supervisory or managerial roles, and those appointed to safety or quality related roles, should routinely monitor working practices and have a responsibility to identify any instances where the required safety or quality standards are not met and ensure that appropriate corrective action is taken to improve the situation. If they are aware of any safety or quality related issues in an area for which they themselves are not responsible then they must bring this to the attention of the person whose responsibility it is or to a more senior member of staff.

All workers within the CBE Laboratory Unit are directed to take notice of what is going on around them and report to their supervisor, or to a more senior member of staff, any instances where University Biological Policy, local CoP or SOPs are not being followed or any other safety or quality related concern they may have.

b. Inspection and Audit

Each Head of Group is responsible for ensuring CBE personnel carry out regular and systematic local health and safety inspections and audits to scrutinise health and safety standards and the effectiveness of the health and safety management systems in place. The purpose of inspections and audits is to identify any unsafe or unhealthy conditions or work practices that may already be occurring and to prevent any arising in the future. The findings of audits and/or inspections should be recorded and these should be retained with a record of corrective and preventative actions taken to address any recommendations. Procedures should be in place to follow up and ensure any recommendations made are carried out. A checklist which may be used for annual inspections of the CBE Containment Level 2 Laboratory Unit is available on the CBE website.

Central auditing programmes carried out by or in conjunction with the University HS&E Department, will also contribute a higher level view. Interested parties, such as Health and Safety Executive Inspectors, the University's insurers or members of the HS&E Department, may wish to see these documents and they should be made available on request.

c. Review

In order to ensure that health and safety arrangements remain valid, each Head of Group is responsible for ensuring that periodic reviews are undertaken that take account of any changes in work activities, any new information on risks or technological advances in particular work areas, management and organisational changes, the results of inspections and audits, and any changes in relevant legislation and best practice recommendations. Where it is identified that any improvements to arrangements should be made then these must be implemented. Serious consideration should also be given to any other changes that could result in improved or better standards of health and safety management and standards.

The University BSO is responsible for monitoring changes in legislation and expert guidance relevant to biological work and, where necessary, updating Biological Safety Policy and associated University guidance. Information on any changes shall be disseminated within the University to ensure any amendments required to local arrangements within the CBE Laboratory Unit are identified.

2.2. PROVISION OF INFORMATION, INSTRUCTION AND TRAINING

Employees must be provided with the appropriate information, instruction and training for them to be able to carry out their work safely. The information and instruction provided should include local rules, the procedures to be taken in the event of accidents and incidents and details of the risk assessment explaining both the nature of the hazards and the use of control measures. The requirement to provide information and instruction also extends to other persons such as contractors (e.g. maintenance engineers) and visitors. The amount of information provided should be proportionate to the risk. Details of the requirements are provided in Section 3.

2.3. PROVIDE HEALTH SURVEILLANCE

There are no hard and fast rules about the features of a health surveillance programme and precise details should be identified by risk assessment **before** commencing work.

Health surveillance should be used to detect at as early a stage as possible any adverse changes in health status which may be attributable to exposure to substances hazardous to health. Details of what is considered suitable health surveillance, where it is appropriate and the type of records that should be kept are detailed in the Approved Code of Practice in the COSHH and Contained Use Regulations. As a practical guide, the type of health surveillance relevant for biological workers in the CBE includes (i) pre-employment screening (i.e. questionnaire to check immune status and identify those who may be more susceptible to infection because of a pre-existing medical condition such as eczema), and (ii) immunisation - if the risk assessment shows that there is a risk of exposure to biological agents for which effective vaccines exists, such vaccines should be offered unless an employee is already immune. Other testing or taking of samples is not generally regarded as necessary except in the event of an accident or if there is an indication that infection may have occurred. Further details can be found in HSE guidance “Health Surveillance under COSHH”.

NOTE: *Work with BAs or GMOs should not preclude staff making blood donations to National Blood Service (NBS). However, if they work with organisms classified as Hazard Group 2 or above they should inform the NBS staff, at the time of donation, of the nature of work they are involved in.*

2.3.1. Vaccination

The University is required by law to offer immunisations to individuals who may be exposed to pathogens at work, where an effective vaccine is available. Each Head of Group is responsible for ensuring the requirement for any immunisations be considered and determined as part of the risk

assessment process. The ACDP Approved List of Biological Agents identifies pathogens for which vaccination is available.

Staff who may as a result of their work be exposed to human biological material such as tissues or primary human cell lines should receive vaccination against Hepatitis B before starting the work. It is the responsibility of the Head of Group to ensure that potential exposure is identified to OHU prior to employment or the work commencing.

NOTE: *A full course of hepatitis B vaccine consists of 3 injections at intervals of 0, 1 and 6 months. A single booster is required if at continued risk after 5 years. The vaccine is effective in around 90% of people; a blood test is required 2 months after the third dose of vaccine to ensure good immunity has been achieved.*

If any member of the CBE chooses to reject advice to receive an immunisation, a signed declaration should be obtained to this effect. Immunisation should always be regarded as a back up rather than a control measure, and must never be regarded as a substitute for safe working practices.

2.4. PREGNANCY

The ACGM Compendium of Guidance states that for most GM work there are no additional hazards in respect of new or expectant mothers. There are however some biological agents that, if infection were to occur, might have more serious consequences during pregnancy or breast-feeding. Certain BA's within Hazard Groups 2, 3 and 4 can affect the unborn child if the mother is infected during pregnancy. These may be transmitted across the placenta while the child is in the womb or during or after birth e.g. if the child is breast-fed. Examples of agents that might affect the child in this way are hepatitis B & C, HIV, Herpes, TB, syphilis, chickenpox, brucella and typhoid.

If there is a known or suspected risk of exposure to a highly infectious agent, then it is appropriate for the pregnant worker to avoid exposure altogether. Rubella (German measles) and toxoplasmosis can harm the unborn child, as can some other biological agents e.g. cytomegalovirus. Exposure to these biological agents should be avoided except where the pregnant woman is protected by her state of immunity. If a worker expects to conceive or believes herself to be pregnant, she may wish to discuss this with the Occupational Health Advisor.

2.5. MAKE ARRANGEMENTS TO DEAL WITH ACCIDENTS AND INCIDENTS

There should be emergency procedures in place to deal with any accident, incident or emergency situation that could cause or threaten any employee to be exposed to a hazardous substance well beyond that associated with normal day-to-day activities (see Section 6 for further details), or cause or threaten harm to the environment.

NOTE: *For work with biological agents, the requirements for specified emergency procedures is only likely to arise for work involving Hazard Group 4 biological agents or work with large volumes of Hazard Group 3 agents i.e. accidents or incidents which may have resulted in the release of a biological agent which could cause severe human disease.*

2.6. NOTIFICATIONS

Certain types of work involving Hazard Group 2 (and above) organisms (or where doubt exists concerning the classification) or GMOs may require notification to the HSE **prior to the commencement** of the work. The University HS&E Department must be informed of plans to work with Hazard Group 2 BAs (or where doubt exists concerning the classification) or GMOs.

NOTE: *The HS&E Department may keep a register of members of the CBE working with agents that are designated as significantly hazardous (**includes some HG2 agents** - see below).*

2.6.1. Notification for Storage and Use of Biological Agents

Under the COSHH regulations the HSE must be notified in writing using form **cba1** (see below) whenever biological agents in Hazard Group 2 are used:

1. **for the first time**
2. and, subsequently of the storage or use for the first time of any agent specified in Part V of Schedule 3. (Part V of Schedule 3 specifies all Hazard Group 3 and 4 agents, and the Hazard Group 2 agents Bordetella pertussis, Corynebacterium diphtheriae and Neisseria meningitidis. There are some instances, detailed in Schedule 3, where the notification requirements do not apply, for example where notification has previously been made under the Genetically Modified Organisms (Contained Use) Regulations 2000.

The HSE must be notified in writing at least 20 days in advance of the work commencing. **The University BSO must be advised of the intention to make a notification BEFORE the form is submitted.**

Further guidance on notification requirements can be found on the HSE website together with the **cba1** notification form (https://www.hse.gov.uk/forms/notification/cba1.pdf)

2.6.2. Notification for Storage and Use of GMOs

The vast majority of work with GMOs in contained use is inherently safe. This is because most work involves the insertion of genes into organisms that have been deliberately "crippled" with disabling mutations so that they will not grow outside of the controlled environment of a laboratory test tube. Safety is thus built into the experimental design. Only a small number of activities (if any) are likely to involve GMOs that are not disabled and still capable of growth outside of the laboratory.

The University BSO is a member of the University BHGM Safety Committee in the University and consequently will be aware of any activity notifications that need to be made, since risk assessments must be reviewed and approved by a BHGM Safety Committee in advance of the work starting. The Research Group Leader/Principal Investigator of a given research group, or the supervisor/manager of a unit or work area, is required to ensure genetic modification work is undertaken only if a valid risk assessment approved by the BHGM safety Committee is in place to cover the work. **Failure to notify a relevant project, or starting work on a GM project before approval or consent has been received, constitutes a criminal offence that is likely to lead to enforcement action against the University and/or individuals concerned.**

The risk assessment procedure will place the work with a GMO into a particular class of activity. The class will then determine both the notification period required before work can commence and whether written permission from HSE is required before work commences.

Under the GMO (CU) Regulations, assessors are required to classify the activity as either Class 1, 2 or 3. This classification is directly related to the containment level required for the conduct of the work.

- Containment Level 1 = Class 1
- Containment Level 2 = Class 2
- Containment Level 3 = Class 3

Regardless of class, HSE must be informed of all **first time activities**. The risk assessment and how waste material will be dealt with must be included with the first time risk assessment notification. For example, first-time Class 1 activities require notification to the HSE and work can start on receipt of HSE acknowledgement. First-time and subsequent Class 2 activities require notification to HSE and work may commence after the HSE has acknowledged receipt of the

notification. Where notification is made under GMO (CU), this will satisfy the notification requirements of COSHH. There are fees for these notifications, which must be met by the CBE.

Further details of the arrangements under the University Biological Safety Policy and the Genetically Modified Organisms (Contained Use) Regulations 2000 are described in Section 4 of this CoP.

2.6.3. Work with certain Animal or Plant Pathogens

Work with certain animal or plant pathogens, or pests, or any material that may be carrying such pathogens or pests, is strictly controlled by legislation enforced by the Department of the Environment, Food and Rural Affairs (DEFRA). Further information on the controls on animal and plants pathogens is provided in Annex 2. It is the responsibility of the individual user to determine whether or not any micro-organism or material they wish to use is required to have a licence from DEFRA, and to apply to the appropriate government department. Each Head of Group must ensure all relevant licences are obtained.

2.6.4. Work with Pathogens and Toxins listed in Schedule 5 of The Anti Terrorism Crime and Security Act 2001

Certain pathogens and toxins are controlled under the Anti-terrorism, Crime and Security Act 2001. The controlled agents are listed in Schedule 5 of this Act. It is the responsibility of the individual user to determine whether or not any micro-organism or material they wish to use is controlled under this legislation, and to inform the University BSO that they either have, or intend to acquire, such micro-organisms or materials. The holding, in storage or in use, of any micro-organism on Schedule 5 or genetic material from that micro-organism, is subject to notification to the Home Office. Each Head of Group must ensure the University BSO is informed of any holdings on their premises, or in advance of any intentions to acquire such micro-organism or materials, and the notification will be made to the Home Office by the HS&E Department. All enquiries the CBE receive from any sources about such materials must be referred to the HS&E Department before any information is provided.

2.7 REPORTING REQUIREMENTS

Where work with biological materials is undertaken, various duties and responsibilities are placed on Research Group Leaders/Principal Investigators/Supervisors/Managers under the University Biological Safety Policy.

2.7.1. Annual Survey of Hazardous Biological Material in the CBE Laboratory Unit

An inventory must be maintained of hazardous biological material (BAs/GMOs) held within the CBE Laboratory Unit. This should include both those in use and in storage. The information should be kept up-to-date as it may be requested at short notice by the enforcing authorities. The inventory should identify the proper name and hazard group categorisation of the biological material, whether it is subject to any controls under animal or plant health licensing Regulations or the Anti-terrorism, Crime and Security Act, where it is used or stored and the Research Leader/Principal Investigator/Supervisor under whose area of responsibility it belongs. A copy of this information is to be provided to the local BGMSA and the University BSO who should be advised/notified of any amendments as they occur. An annual survey may be undertaken by the University BSO to check the information held remains valid.

SECTION 2	BIOSAFETY REQUIREMENTS FOR WORK WITH BIOLOGICAL AGENTS IN THE CL2 CBE LABORATORY UNIT
PART 2	PRECAUTIONS AND MEASURES FOR CONTROLLING EXPOSURE TO BIOLOGICAL AGENTS: ENGINEERING CONTROLS

2.8. INTRODUCTION

The principles of containment are applied both in the basic design and facilities of the CBE Laboratory Unit and in the working practices of all the people in the laboratory. Containment describes the way in which biological agents are managed in the laboratory environment so as to prevent, or control the exposure to laboratory workers, other people and the outside environment. This can be achieved in a number of ways:

Primary containment – protection of worker and environment can be achieved through a combination of good microbiological practices or techniques and the use of containment devices or safety equipment e.g. biological safety cabinets.

Secondary containment – i.e. protection of people and the environment outside the laboratory can be achieved by a combination of laboratory design and operating procedures e.g. restriction of access, air handling and disposal of waste etc.

2.9. CBE LABORATORY UNIT: FIXTURE & FITTING CONDITIONS

The CBE Laboratory Unit is a dedicated facility constructed to meet the physical requirements for Containment Level 2. The physical attributes of the CBE Laboratory Unit must be maintained so that the following requirements continue to be met:

(i) The laboratory unit must be maintained so that it is a fully enclosable space bounded by walls, doors, windows, floors and ceilings.

(ii) Prior to any significant structural changes that could affect the containment of BAs/GMOs in the Laboratory Unit; the Heads of Group must inform the University BSO of any planned changes. For example, it may be possible to temporarily partition the facility to provide containment for BAs/GMOs in a designated part of the facility unaffected by the structural changes.

(iii) Before work activities can resume, the laboratory unit must be inspected by a person qualified to assess the facility's compliance with the conditions for the Containment Level 2 intended use.

(iv) The following surfaces in the laboratory unit must be maintained so they continue to be smooth, impermeable to water, cleanable, and resistant to damage by the cleaning agents and/or disinfectants that will be used in the facility:

- walls, floors, and benches;
- furniture, including seating; and
- any other surfaces, where contamination is likely to occur or where decontamination is required.

(v) The laboratory unit must be operated so that open spaces between and under benches, cabinets and equipment in the facility can be accessed for decontamination when required.

(vi) The laboratory unit must continue to contain either a wash basin fitted with taps of the hands-free operation type or some other means of decontaminating hands e.g. dispensers filled with decontaminant solutions are considered suitable.

(vii) Eyewash equipment (either plumbed eyewash equipment or single-use packs of sterile eye irrigation fluids) must be maintained within the laboratory unit.

(viii) Where work activities in CBE Laboratory Unit produce aerosols containing BAs/GMOs, then the unit must continue to contain a BSC, or other equipment that is designed to contain aerosols.

2.10. LABORATORY DECOMMISSIONING CHECKLIST

If any laboratory within the CBE Laboratory Unit is vacated, for example due to relocation or change of use, it is necessary to ensure that no hazardous materials are left behind and, where appropriate, the fixtures and fittings have been decontaminated and made safe for future use or removal. A checklist that can be used to record the laboratory has been suitably decommissioned is provided on the CBE website. On completion, the checklist should be left at the laboratory and the originator should retain a copy for their records. A completed decommissioning checklist precludes the need for maintenance staff and contractors to be issued with a Laboratory Permit to Work.

2.11. SECURITY AND ACCESS TO THE CBE LABORATORY UNIT

Each Head of Group is responsible for ensuring the health and safety of all persons on their premises and must have appropriate systems in place to control access to biological laboratories. They should also ensure that suitable arrangements are in place to monitor and review access controls and how they work in practice.

At Containment Level 2 and above it is a legal requirement that access be restricted only to authorised persons. Hence access to the CBE Laboratory Unit must be restricted to a list of authorised researchers and support personnel, which should be kept up to date. Refer to Section 3 for details on the requirements to gain authorised access.

2.12. ACCESS BY NON-LABORATORY PERSONNEL

2.12.1. Entry by Contractors and Maintenance Staff

Entry of maintenance staff and contractors into the CBE Laboratory Unit must be under a permit-to-work system unless in exceptional emergency situations* where this is not practicable.

All maintenance staff and contractors whose job involves them entering and working in laboratory areas should be provided with information and guidance on the measures they need to take to ensure the safety of themselves and others whilst they are in the laboratory. This is supported by the “Guidance for University Maintenance Staff and Contractors working in the CBE laboratories” provided in Annex 6. Provision of this information should be incorporated into the permit to work system. The CBE may use the same paperwork for outside contractors, maintenance and repair staff working in the laboratory unit. The model permit to work pro-forma and guidance for maintenance, repair staff and contractors can be accessed on the CBE website.

***Emergency call-out situations** - There may be exceptional (e.g. out of hours) emergency situations where the CBE Laboratory Unit has to be entered to conduct emergency repairs, or to make safe a part of a buildings structure, and when there is no competent laboratory staff immediately available to complete a permit-to-work. In all cases where there has been the need for emergency entry to the laboratory unit without a written permit-to-work being issued, for record purposes, a written permit-to-work should be completed subsequently and it should be indicated what verbal instructions had been given. If anyone has any doubts that it is safe to start or to continue to work then they should stop work until the problem is resolved.

2.12.2. Permit-to-work procedure

In the event of the failure of a piece of plant or equipment requiring the attendance of service maintenance/personnel the following procedure is intended to prevent exposure of maintenance operatives to hazardous processes and substances.

Prior to issuing a permit-to-work, it is the responsibility of laboratory staff to ensure areas are cleaned and disinfected to ensure that anyone entering the area will not come into contact with any infectious materials. Confirmation of this should be detailed on the permit-to-work along with any additional instructions or information that is necessary for maintenance staff or contractors. By following basic hygiene precautions and the simple rules in the permit-to-work, maintenance staff and contractors can carry out their work safely in the containment laboratories and avoid any exposure to infectious materials.

The principles are:

1. Entry of maintenance operatives into containment areas is prohibited without the permission of a responsible person for the area. Signage with contact details must be displayed at the entrance to the room, suite, or unit
2. The area must be safe from process hazards for the maintenance work to proceed. Adjacent surfaces and the equipment must be decontaminated according to appropriate procedures
3. Entry must be subject to a permit confirming either that the area is clear of process hazards or specifying the precautions to be followed to ensure safety. A signed authority/permit to enter must be obtained from the Laboratory Manager or authorised deputy. A risk assessment of the work area and the work proposed should be established to ensure that the work is carried out using the necessary safety precautions

2.12.3. Arrangements for Cleaning the CBE Laboratory Unit

Given the particular risks to cleaners within these areas, routine cleaning of the biological Containment Level 2 areas within the CBE Laboratory Unit is to be undertaken only by authorised users (i.e. authorised laboratory staff). However, arrangements may be made for cleaning staff to clean these areas during periods of temporary shutdown when the areas are to be made safe by the researchers prior to access being made available to cleaners under a permit-to-work system. This arrangement is considered satisfactory as long as appropriate control and supervision arrangements are in place to ensure the safety of the cleaning staff concerned.

2.12.4. New Staff and Visitors to the CBE Laboratory Unit

All new staff and visitors must have had a risk assessment for their work activities recorded by the named member of staff who will be responsible for them. The Laboratory Manager must also be informed so that the training and health surveillance requirements can be assessed as part of the risk assessment and authorisation process.

(i) Visitors

Only persons who have a valid, laboratory work related reason for entering a laboratory should be given access as a visitor. Casual access, for example by family, friends, office-based colleagues etc, should not be allowed.

- All visits should be by prior appointment whenever possible.
- All visitors including service engineers should be advised to first report to the reception area in the CBE.

- All laboratory visitors should be provided with a clean laboratory coat (and if necessary any other protective equipment) before entering the laboratory area.
- First-time visitors must be escorted whilst in the laboratories.

(ii) Animals and Pets

Dogs and other pets are not allowed in the CBE buildings, with the exception of assistance dogs. However, assistance dogs must be excluded from entering biological laboratories until risks have been assessed and specific control measures put in place to ensure the health and safety of the animal, and safety standards in the laboratory, are not compromised. The local BGMSA or the University BSO should be consulted for advice in such cases.

(iii) Children and young persons

Children (under 16 years of age) must be excluded from entering all laboratories where biological work is carried out. There may however be some occasions where access by children is required for a specific purpose, for example in the case of organised educational visits and open days. These would be regarded as exceptional cases and may proceed subject to agreement of the Head of Group and specific arrangements being put in place to ensure the health and safety of the children whilst visiting the laboratories. The areas should be rigorously cleaned and disinfected and all infectious and potentially infectious material moved or otherwise made inaccessible. The children must be accompanied and supervised at all times when they are in the biological laboratories.

2.12.5. Single/Lone Working and Out of Hours Working

Each Head of Group should ensure any work is prohibited which entails a risk of serious personal injury or fire by persons working alone in the evenings or at weekends, irrespective of the status and experience of the worker. Generally work with biological materials does not present an immediate risk of serious injury and there is no reason why work with high risk biological materials cannot be undertaken by lone workers or out of hours.

However, out-of-hours work should be restricted only to those activities that cannot be carried during normal working hours. Under this policy, there should not be a need to carry out certain activities, such as autoclaving waste, outside of normal working hours.

Researchers and academic staff will only be granted access to work out of normal hours if a risk assessment of the work to be carried out has been made and submitted to the local BGMSA and DSO. A template risk assessment form is available on the CBE website. In some cases the permission of the Head of Group will be required before access will be granted. Further guidance on lone and out of hours working is provided in Annex 7. Attention should be made to whether any further precautions need to be taken for work scheduled for 'Out of Hours'. Assessments, which should be made in writing, must be specific to the individual concerned and must specify the extent of the work permitted. Any work classified as being of high risk may only be conducted in the presence of or under the supervision of a suitably qualified member of academic or research staff. Wherever possible such work should only be conducted during normal hours.

Where single/lone working and out of hours working occurs, there must be appropriate monitoring to ensure standards of working practices are maintained when individual workers are on their own without any immediate supervision. **When working outside normal hours the worker must 'sign in' and 'sign out' of the CBE Laboratory Unit using the 'Out of Hours' log book.**

2.13. SIGNAGE

The COSHH Regulations require that suitable and sufficient warning signs be displayed. To be effective safety signs must be used judiciously. Signs must indicate current conditions and be regularly checked for validity. Each Head of Group is responsible for ensuring laboratories or other facilities where biological agents are present are labelled at the point of entry with the following signs:

(i) the international biohazard sign, which comprises a black biohazard symbol in a black triangle on a yellow background (a hazard warning sign),

(ii) the words Containment Level followed by the number of the level of containment at which the laboratory or facility is operating (this should be fixed immediately adjacent to the biohazard sign and also have markings/words in black on a yellow background), and

(iii) a prohibition sign restricting access to authorised persons only.

Other signs should also be considered and used as appropriate to reinforce local rules and procedures, for example:

(iv) at the point of exit - the mandatory sign indicating hands must be washed before leaving;

(v) in a prominent place - the mandatory sign indicating laboratory coats must be worn;

(vi) at a dedicated hand wash basin - the mandatory sign indicating this sink is to be used for hand washing only.

The signs (i-iii) must be placed on or next to each access door to the CBE Laboratory Unit so that persons entering the unit are able to clearly see they are entering a Containment Level 2 facility. The use of biohazard signs or labels within the CBE Laboratory Unit should not generally be required and should not be used unnecessarily. The displaying of a label on the point of entry as described above is usually sufficient. In exceptional circumstances, for example following an accident that requires a decontamination procedure, a biohazard sign (label or tape) may need to be displayed to indicate a significant hazard or one greater than would normally be expected. The labelling of fridges and freezers for example is unlikely to serve a useful purpose. However for segregated storage purposes it may be prudent depending on usage, especially for shared, mixed or for higher risk materials, to use the biohazard sign on particular items; for example on the outside of the secondary containment vessel.

2.14. CONTAINMENT EQUIPMENT

Primary barriers, such as Class II Biological Safety Cabinets (BSC) and Personal Protective Equipment (PPE), are required for aerosol generating or splashing manipulations of agents assigned to Containment Level 2. Personal protective equipment including laboratory clothing, gloves, respiratory protection, or goggles should be used as deemed appropriate for protection of employees. An autoclave must be available for sterilization of infectious waste.

Equipment must be maintained and, where necessary, tested to demonstrate it is working effectively. Where there is a British or European Standard specification for a particular type of equipment, only equipment meeting the relevant specification should be purchased unless an alternative is agreed by the Head of Group.

Documented operating instructions e.g. SOPs, Manuals, should be available for all pieces of equipment. For some items of equipment the manufacturer’s instructions will provide adequate systems of work whereas for others a local standard operating procedure should be drawn up applicable to the particular usage of the equipment. Individual workers must always closely follow instructions provided for use of equipment i.e. SOPs use it only for the purpose it was intended and never tamper with or over-ride any safety related devices.

2.14.1. Air Handling

The CBE Laboratory Unit is maintained at an air pressure positive to the atmosphere (Note that negative pressure relative to the pressure of the immediate surroundings is not a requirement for HG2 BAs at Containment Level 2 under the COSHH Regulations or for Class 1 GMOs under the Contained Use Regulations). Clean rooms within the CBE Laboratory Unit are maintained at positive pressure to ensure product protection. Procedures for the maintenance, examination and test of control measures, including local exhaust ventilation (e.g. BSC) and emergency measures must be in place.

2.14.2. Biological Safety Cabinets

Biological safety cabinets (BSC) constitute local exhaust ventilation (LEV) systems in that they offer protection to the worker (user) from airborne hazards. As such there is a requirement for regular maintenance, examination and test under the COSHH Regulations. Cabinets must be properly installed and commissioned and prior to use, the cabinet must pass the performance tests specified in the British Standard. This usually forms part of the service offered by the supplier or a similar competent contract service provider. As a minimum:

- Where any Class I or Class II BSC is installed and used for procedures with biological materials, it must be used and decontaminated in according to documented procedures.
- Where any Class I or Class II BSC is installed and used for procedures with biological materials, it must be inspected and tested. This testing is required at least every 12 months and additionally after relocation of a cabinet, after mechanical or electrical maintenance and after high efficiency particulate air (HEPA) filters are replaced. The inspection and testing of cabinets must be carried out by a qualified person. The cabinets must be tested for containment efficiency and a certificate, summarising the test results and the date of the next test, must be affixed to the cabinet. It is a requirement of the COSHH Regulations that a record be kept for 5 years of the examinations and tests and of repairs.
- Where testing has shown that the performance requirements for inward air velocity or HEPA filter integrity (Class I), or air barrier containment or exhaust HEPA filter integrity (Class II) are not met and the defect has not been corrected, the cabinet must be clearly marked to show that it is unsafe and must not be used for procedures that produce aerosols containing BAs/GMOs.

The requirement for a BSC, and where required the type, or class, of safety cabinet to be used for a particular work activity, should be determined as part of the risk assessment. Workers in the CBE Laboratory Unit should refer to the detailed guidance on BSCs provided in the ACDP “The Management, design and Operation of Microbiological Containment Laboratories”, which is summarised in Annex 4.

2.14.3. Autoclaves

Each Head of Group must ensure all autoclaves and other pressure vessels (such as gas cylinders) owned by the CBE are notified to the University's Engineering Insurance Surveyor, who will inspect each item at the statutorily required interval. Notification of such items should be made through the HS&E Department. Notification of newly acquired equipment is required before it is brought into use, to ensure compliance with the Pressure Systems Regulations.

Where an autoclave is used to decontaminate or make safe waste, the process must be validated at least annually and at any other times when the previous test may no longer be valid (such as part of re-commissioning after maintenance work). Records of validation should be kept for 5 years. The effectiveness of any heat-based equipment used to decontaminate BAs/GMOs must be validated by the use of:

- thermocouples or resistance thermometers, to ensure that the required temperature has been achieved; or
- chemical indicators which use a combination of moisture, heat and time and which progressively change colour with the time exposed at the specified temperature; or
- biological indicators such as spore strips; or
- enzyme indicators.

If any decontamination equipment is found to be defective and the defect has not been corrected, the equipment must be clearly marked to show that it is defective and must not be used for decontaminating BAs/GMOs, waste or equipment associated with dealings with BAs/GMOs until the defect has been corrected. Workers in the CBE Laboratory Unit should refer to the detailed guidance on the maintenance of autoclaves provided in Annex 5.

2.14.4. Liquid Nitrogen

Cryogenic storage of biological materials in liquid nitrogen is commonplace in the CBE Laboratory Unit and it is important that workers are aware of the potential hazards associated with the use of liquid nitrogen. These fall into three main areas:

- Temperature - the extremely cold temperature of -196°C means there is a very serious risk of cold burn on contact with the liquid. Items that have been in the liquid are cold and when touched may freeze to and stick to the skin. On evaporation, whilst unlikely to cause skin damage, the gas can cause damage to eyes and lungs.
- Explosion - if samples are stored in tubes in the liquid phase of the vessel, liquid nitrogen may seep into the tube. When the samples are removed and warmed, the liquid nitrogen changes to a gas rapidly expanding in volume and may cause the tube to explode. Certain materials when immersed in liquid nitrogen become brittle and may shatter unexpectedly.
- Asphyxiation - when liquid nitrogen evaporates and changes from a liquid to a gas there is a huge expansion of nearly 700 times in volume (1 litre of liquid gives 0.7m^3 of gas). A spillage of just a few litres of liquid in a poorly ventilated room would lower the oxygen concentration to such an extent that a person in or entering the room can lose consciousness and die.

Each Head of Group is responsible for ensuring appropriate systems are in place to provide safe and suitable procedures for use of liquid nitrogen in the CBE Laboratory Unit and associated facilities. In addition, they must ensure adequate and appropriate instruction, training and supervision is provided for workers using liquid nitrogen. When drawing up local rules and procedures note should be made of the following points:

- Eye protection, most appropriately in the form of a full face visor, thermal gloves and suitable footwear must always be worn when cryogenic liquids are being handled.
- Liquid nitrogen should be decanted into Dewar flasks which are designed for this purpose.
- Where significant volumes of liquid nitrogen are handled, additional low level, high volume ventilation will be required and the use of oxygen depletion monitors should be considered.

Workers in the CBE Laboratory Unit should refer to the guidance on the storage of samples in liquid nitrogen provided in Annex 8.

2.14.5. Personal Protective Equipment

Protective clothing must be worn in the Containment Level 2 CBE Laboratory Unit. All members of staff must wear properly fastened protective laboratory coat of an approved design at all times. They should be changed frequently and always immediately after any spill contamination.

Laboratory coats must not be worn outside the CBE Laboratory Unit. Other personal protective equipment (PPE) such as gloves must be worn and the wearing of two pairs should be considered if there is a risk of gloves being torn or punctured when high-risk samples are handled and where the loss of dexterity does not prejudice personal safety. A decision on the need for eye protection should be dependent upon the risk assessment, taking into account the possibility of splashing and the possible routes of transmission.

(i) Laboratory Coats:

- The laboratory coat should have a high neck and close fitting cuffs with either back or side fastenings e.g. Howie type.
- Within the CBE Laboratory Unit, laboratory coats should be changed before leaving segregated work activity containment areas e.g. moving from microbiology cell culture laboratories to human cell culture laboratories.
- Laboratory coats must never be worn, or otherwise taken, out of the CBE Laboratory Unit until they have been rendered safe (i.e. they must be autoclaved before sending for laundering).
- Procedures for the laundering of potentially contaminated laboratory coats or other protective clothing must be clearly laid down in a local safety policy or SOP.
- Coats must be changed on a regular basis or immediately contamination is suspected.
- When not in use coats must be hung on the hooks provided. There should be sufficient coat hooks to avoid 'double hanging' if practicable. Laboratory coats must not come into contact with outdoor clothes.

(ii) Gloves

- Gloves should be the correct size and disposable - except for heavy duty gloves provided for specific tasks (e.g. handling liquid nitrogen).
- Gloves (single pair is usually sufficient) must be worn at all times and removed before leaving segregated work activity containment areas e.g. moving from microbiology cell culture laboratories to human cell culture laboratories within the CBE Laboratory Unit. Gloves must be replaced immediately in the event of overt contamination with infectious material. Contaminated gloves must be disposed of in designated biohazard bins.
- Powdered latex (rubber) gloves must NOT be used because of the high risk of causing allergic reactions. If latex gloves are used they must be powder free and have a low level of extractable proteins (e.g. less than 50 mcg/g). Users must be made aware of the potential for developing allergy and measures should be in place for identifying others who have a pre-existing allergy. Nitrile gloves are often a good alternative to latex.
- All workers should wash their hands before and after wearing gloves and always before leaving. Designated hand washing facilities must be used with specified liquid soaps; these should contain a bacteriostatic agent to prevent the multiplication of any contamination. Alcohol-based hand rubs (minimum alcohol content 60%) may be used as an alternative to hand washing when hands are not visibly contaminated e.g. after removing gloves if hand-washing facilities are not available.

(iii) Eye Protection

- Glasses, goggles and masks should be available for working with biological material, chemicals or glassware. This rule applies in particular to the wearers of contact lenses. In most cases safety spectacles will suffice but full face visors should be available, if the work activity is sufficiently hazardous to warrant it.

- Safety glasses should be worn while working in the Containment Level 2 CBE Laboratory Unit if the risk assessment has identified that these are necessary. Safety glasses do not have to be worn while doing paperwork or when entering the laboratory solely to retrieve an item such as a document, provided that no manipulation of cultures is in progress
- Respiratory protective equipment in the form of disposable masks or respirators that give protection against nuisance odours, vapours, mist and dust should be available if the risk assessment calls for their use.

(iv) Footwear

- Shoes should be substantial with respect to splash-protection and safe movement throughout the laboratory. Where risk assessment identifies a requirement, disposable overshoes should be used.

SECTION 2	BIOSAFETY REQUIREMENTS FOR WORK WITH BIOLOGICAL AGENTS IN CL2 CBE LABORATORY UNIT
PART 3	ADDITIONAL MEASURES FOR CONTROLLING EXPOSURE TO BIOLOGICAL AGENTS: WORKING PRACTICES

2.15. GENERAL REQUIREMENTS FOR ALL WORK

For the purposes of this CoP, the following guidance and recommendations are given as minimum requirements pertaining to the Containment Level 2 CBE Laboratory Unit, directed at biological agents in Hazard Groups 1 and 2 and Class 1 GMOs. Although some of the precautions may appear to be unnecessary for some organisms in Hazard Group 1, they are desirable for training purposes to promote good laboratory practice, ensure product protection and impose a quality assurance discipline.

The CBE Laboratory Unit is a dedicated facility constructed to meet the physical requirements for Containment Level 2. According to the Regulations, this must be supplemented with requirements for good management and appropriate staff training, plus specific additional measures in relation to controlling exposure to biological agents and GMOs, including limiting access to the laboratories, displaying appropriate hazard warning signs (Section 2, Part 2), specifying disinfection procedures and systems for safe collection, storage and disposal of contaminated waste (Section 4 & 5) and specifying procedures for transporting biological material (Section 7).

The development of generic codes of practice and procedures for safe laboratory operations e.g. standard operating procedures is an important measure towards eliminating or at least minimising the risk of exposure to biological hazards and the risk of transporting potentially hazardous material outside the CBE Laboratory Unit. Individual workers must have access to and adhere to local rules. The Research Group Leader/Principal Investigator of a given research group, or the supervisor/manager of a unit or work area, is responsible for ensuring local rules are in place and are complied with. Risk assessments (Section 2, Part 1 & Section 4) should include cross-reference to the local rules and SOPs. This pre-empts any need to write out or duplicate the information within the risk assessment and ensures consistency in standards.

Information on the working practices and laboratory rules that are fundamental to containment, and the reason for these, are described in this section including guidance on good microbiological practice and aseptic technique. These should be used to tailor local conditions and activities.

2.16. STANDARD OPERATING PROCEDURES

On occasion there may be a need to be prescriptive in how specific work is to be done. The Quality/Laboratory Manager will be responsible for the introduction of Standard Operating Procedures (SOP). The decision to introduce a SOP should be based on either a need for absolute consistency, i.e. part of quality control, or through perceived high risk, or a combination of both. Divergence from the set procedure is likely to put the work or worker at risk. Access to specific SOPs for individual operations should be provided to all authorized workers and those responsible for local and University Health and Safety.

2.17. WORKING PRACTICES FOR CONTAINMENT

The principles of containment are applied in both the basic design and facilities in the laboratory and the working practices of all the people in the laboratory. The purpose of containment is not only to prevent the BAs/GMOs getting out of the laboratory but also to ensure that the workers are safe in the laboratory. The latter is achieved by blocking infection routes.

Working practices that are fundamental to containment include:

1. Access to the CBE Laboratory Unit is to be restricted to authorised persons.
2. Wear personal protective clothing and equipment.
3. Block routes of infection by the consistent application of simple precautions.
4. Specify disinfection procedures to prevent spread of any contamination.
5. Use waste disposal procedures that ensure that all contaminated materials are disposed of safely.
6. Record and report all accidents and incidents so that appropriate action can be taken to minimise the likelihood of illness.
7. Staff must be trained and proficient in safe working practices and techniques for the safety of themselves and other persons in the laboratory.

2.17.1. Access Control Procedures

1. Work may only be carried out in designated containment areas that have been formally approved by the University BSO. **Before** any experimental procedure can be undertaken a relevant risk assessments must be performed and acted upon.
2. A biohazard warning symbol and sign must be displayed on the doors of the rooms or CBE Laboratory Unit.
3. Only authorized persons are allowed to enter the CBE Laboratory Unit. The unit must be locked outside of normal working hours.
4. Except during the entry and exit of personnel, supplies, and/or equipment, doors of the CBE Laboratory Unit must be closed while procedures with BAs/GMOs are being conducted. Dedicated “emergency only” exits should not be used to enter the facility. Windows must remain closed while procedures with BAs/GMOs are being conducted.
5. Means of preventing cross-contamination, for example, non-GMO work by GMO dealings, animal work with human work etc, should include physical separation of the work, or separation by working at different times and ensuring any contaminated surfaces are decontaminated prior to commencing work. Where physical separation is not practicable, a risk assessment for the work activity should be used to identify any additional containment measures.
6. Servicing of equipment must only take place by authorised personnel and only when safe to do so, after appropriate decontamination measures have been taken and the area certified safe. Entry must be subject to a permit confirming either that the area is clear of process hazards or specifying the precautions to be followed to ensure safety. A signed authority/permit to enter must be obtained from the Laboratory Manager or authorised deputy.
7. Maintenance personnel (or visitors) must always obtain permission from a responsible member of staff in the area involved before entering a restricted area. Control of access for maintenance and service personnel (and visitors) should be through a permit to work system
8. Cleaners must not be allowed to enter the CBE Laboratory Unit. Cleaning must be done by authorised staff.
9. All items taken out of CBE Laboratory Unit must be suitably decontaminated first. Written documents that are expected to be removed from the laboratory must be protected from contamination while in the laboratory.
10. A certificate must be issued and signed for any equipment to be sent for repair.

2.17.2. Personal Protection Procedures

1. Before entering the CBE Laboratory Unit outdoor clothing must be removed. Outdoor clothing, personal belongings must not be brought into the laboratory. Personal food, drink, cosmetics and mobile phones must not be taken into the laboratory.
2. Laboratory coats must be worn at all times and properly fastened, even if the persons concerned are not actively engaged in experimental work. Laboratory coats should be stored the designated change rooms (on pegs). Re-usable cotton lab coats or disposable lab coats are permissible.
3. It is prohibited to wear protective laboratory clothing that has been used in the laboratory outside the CBE Laboratory Unit, e.g. offices, unclassified areas, Gas Pods. Personal protective clothing must be removed before leaving the laboratory unit. This does not apply if moving directly within the CBE Laboratory Unit.
4. Long hair must be tied back when working in the CBE Laboratory Unit.
5. Open-toed footwear must not be worn in CBE Laboratory Unit.
6. First aid equipment must be available in CBE Laboratory Unit and this must include eye wash bottles. Researchers must be aware of their locations.
7. Fire-fighting equipment must be readily available and its location known to researchers.
8. Routes of infection should be blocked by the consistent application of the following simple precautions:

   A. Ingestion route *- never ever put anything in the mouth:*

   i. Eating, chewing, drinking, smoking, storing of food or drink and applying cosmetics are prohibited in all laboratory or ancillary areas within the CBE Laboratory Unit.
   ii. Mouth pipetting, licking labels, chewing pens and finger nails, biting to cut or tear things instead of using scissors, holding things between the teeth, licking fingers or spitting to wet things, etc is prohibited in the CBE Laboratory Unit.
   iii. Hands must be disinfected or washed immediately when contamination is suspected, after handling infective materials and also before leaving the laboratory (contamination on hands commonly gets transferred to mouth by everyday activities).

   B. Percutaneous route - *avoid likelihood of puncture wounds and always keep breaks in skin covered:*

   i. Avoid using sharps wherever possible. If this is not feasible then handling procedures should be designed to minimise the likelihood of puncture wounds. Wherever possible glass items (including glass pipettes) should be replaced with plastic alternatives.
   ii. Used sharps should be placed directly into a sharps bin. Unless safe means have been introduced, needles should not be resheathed. Sharps bins should not be overfilled, used sharps protruding from bins are very dangerous for those who have to handle them.
   iii. The term sharp should be taken to refer to any item that is sharp and not be restricted to needles and scalpels. Commonly used items that could easily cause damage to the skin include all glass items (including microscope slides and cover slips), ampoules, pointed nose forceps, dissection instruments, scissors, wire loops that are not closed circles. This list is not exhaustive and all items should be assessed for sharp edges. Cracked and chipped glassware should always be discarded immediately.
   iv. All workers in the laboratory should cover cuts and abrasions with waterproof dressings.
   v. To prevent workers from spreading contamination that can be picked up from various sources by all staff in the CBE Laboratory Unit, good basic hygiene practices, including

regular hand washing, must be practised at all times; at the end of each working session (or day) benches and equipment should be routinely cleaned and disinfected.

vi. Appropriate gloves must be worn in the CBE Laboratory Unit at all times. After use, gloves should be removed aseptically. If the biological agent being handled has the potential to infect via the percutaneous route, it is recommended that two pairs of disposable gloves be worn when handling samples (minor damage to thin gloves often goes undetected until skin contamination is noticed).

vii. On completion of work, or if contamination is suspected, gloves should be removed and discarded. Personnel should wash their hands and replace gloves before leaving any of the designated laboratories (i.e. automated cell culture lab, animal, microbiological, cell culture labs, and analytical lab) within the CBE Laboratory Unit.

viii. Personnel must wash their hands before leaving the CBE Laboratory Unit. Using designated hand washing facility, the following is recommended:
- Use soap and running water (preferably warm water – hot water increases the risk of skin irritation)
- Wash all surfaces thoroughly including wrists, palms, back of hands and thumbs and under fingernails
- Rub hands together for at least 10-15 seconds
- Rinse and dry hands well (using paper towels or hand dryers – not on clothes!)

ix. Eye protection (goggles or safety glasses) and a plastic overall should be worn if splashing is likely to occur. Safety glasses, face shields (visors) or other protective devices must be worn when it is necessary to protect the eyes and face from splashes or if the risk assessment has identified that these are necessary. Safety glasses do not have to be worn while doing paperwork in the laboratory or when entering the laboratory solely to retrieve an item such as a document, provided that no manipulation of cultures is in progress. Forms for the purchase of prescription safety glasses can be obtained from the Departmental Safety Officer (DSO). It is strongly advised not to wear contact lenses in the laboratory as these can delay effective first aid

C. Inhalation route *- care must be taken to minimise the production of aerosols. Laboratory procedures that give rise to infectious aerosols must be conducted in a microbiological safety cabinet, isolator or be otherwise suitably contained:*

i. Good microbiological practice must be used to prevent aerosols being produced

ii. Ensure that manipulations likely to produce substantial aerosols e.g. shaking, homogenising, sonicating, etc., are carried out in the Class II BSC, except where the equipment itself is designed to contain the aerosol

iii. Any work with biological agents, which may produce small amounts of aerosol and require high sterility, should be carried out in a Class II BSC.

iv. Ensure that BAs/GMOs or material containing these, are adequately contained during transfer from safety cabinets or workstations to other areas of the laboratory, e.g. incubators/centrifuge, to prevent spillages within the laboratory.

2.17.3. Procedures to be carried out before leaving the laboratory

1. Housekeeping must be of a high standard. The work area should be left clean and tidy for the next person. Items such as cardboard boxes must not be stored in the cold room or under benches as these may become contaminated in the event of spillage.
2. All reagents should be returned to the appropriate fridge/freezer. Stocks of flammable reagents and solvents should be returned to their fire-resistant cupboards, cabinets or bins.
3. The area should be cleared of personal pens, calculators, notebooks etc (into designated drawers).

4. The sink should be clean and accessible (do not leave tips, pieces of tissues, disposable gloves).
5. Benches and the BSC should be cleaned with Virkon solution (1% w/v) followed by 70% IMS after work is completed.
6. The floor should be free from any unnecessary items.
7. Medium collection bottles should be emptied if full.
8. Gas, water and electricity supplies not in use should be turned off.
9. Bags containing wastes to be autoclaved should be removed to the Autoclave room.
10. If **any** equipment is left unattended, details of the equipment must be filled in on the yellow 'Unattended Form', providing details of emergency shut down procedures, hazards and contact name. **This is an individual responsibility** of anybody using the CBE laboratories. All experiments involving toxic and/or flammable substances must be checked and authorised by an experienced person prior to being left running overnight. It is recommended that the apparatus and/or experiment should be operated attended for at least one hour under the conditions it will run unattended overnight.
11. Laboratory coats and other PPE must be removed and hands must be washed before leaving the CBE Laboratory Unit

2.18. SPECIAL PRACTICES – CONTAMINATION CONTROL

Special practices required for work at Containment Level 2 include: decontamination of all contaminated waste prior to discharge and disposal, preparation of operational procedures which detail the hazards of the BA/GMO and procedures to eliminate risk, and implementation of an accident\incident policy which details exposure follow-up procedures and methods to clean up spills (these are detailed in other sections of this CoP).

2.18.1. Decontamination and Waste Handling Procedures

Under COSHH and the Contained Use Regulations fumigation of the laboratory under sealed conditions is not a routine requirement for work with BA or GMOs at Containment Level 2. However, for BSCs (and other Containment equipment such as the CompacT SelecT cabinet), where and to the extent the risk assessment shows it is required (this may also be for quality control reasons i.e. to eliminate potential cross-contamination in the CompacT for example) fumigation may be required. A hydrogen peroxide based system should be used. Whilst the chemicals used are less hazardous than formaldehyde, there are still risks associated with the procedures and appropriate control measures are required in order to carry out the work safely. If required this is should be contracted out to a specialist company e.g. Bioquell.

At Containment Level 2, specified disinfection procedures must be in place:

1. Disinfection procedures must be available for routine use i.e. decontamination of work benches, surfaces and equipment where procedures involving BAs/GMOs have taken place.
2. Disinfection procedures (displayed as notices if necessary) must be available for use in the event of spillage. Plans should be in place to deal with major spillage incidents
3. Disinfectants must be effective in rendering the BAs/GMO non-viable under in-use conditions.

Each Head of Group must ensure there is a clear documented disinfection policy or SOP indicating suitable concentrations, contact times and applications for all disinfection requirements within the CBE Laboratory Unit. Information on the working practices and local rules for the use of disinfectants in the CBE Laboratory Unit is provided in Section 5.

All waste from the Containment Level 2 CBE Laboratory Unit which contains biological material should be treated by a method validated as effective in rendering it non-infectious i.e. made safe, before it is removed from the unit. Methods for treatment and disposal of waste containing BAs and GMOs must be performed according to the relevant regulations. Where methods are not specified in these regulations, there is a requirement to assess and justify all proposed methods of waste disposal as part of the risk assessment. Methods must be in place before work with biological agents begins.

NOTE: *Similarly, appropriate methods for the disposal of hazardous chemicals must be identified as part of the risk assessment. Methods must be in place before work with chemical materials begins.*

Steam sterilization should be the preferred method of treatment for both health and safety and quality control reasons. An autoclave conforming to BS2646 1990-1993 and BS EN12347 should be readily accessible in the same building as the laboratory. There should be documented procedures incorporating risk assessment of the biological agents likely to be present in the wastes, the types and the quantities. Such procedures should identify each treatment option and operating parameters or conditions known to kill the agents that may be present under the laboratory conditions. Decontamination should take place in the CBE Laboratory Unit but can take place at another location, providing the waste is transported to the decontamination site in accordance with any transport guidelines.

Information on the working practices and local rules for the management of waste in the CBE Laboratory Unit is provided in Section 4 & 5.

2.18.2. Arrangements to deal with accidents, incidents and emergencies

There should be emergency procedures and control measures in place to deal with any accident or incident that may cause or threaten any CBE personnel to be exposed to a hazardous substance or may cause a serious risk to the environment.

There is a statutory requirement to report infections at work and dangerous occurrences which result, or could have resulted, in the release of a biological agent that could cause severe infection under RIDDOR. Where an accident or incident occurs involving a significant and unintended release (outside the primary containment) of GMOs which present a hazard, immediate or delayed, direct or indirect, to either human health or to the environment, immediate notification to competent authority (HSE) is required. In addition, a local record should be kept of all incidents (including near misses) involving infectious material or GMOs. This should be used to identify problem areas and allow checks to be made on the effectiveness of the control measures already in place.

Information relating to emergency procedures and actions to take in the event of spillage of BAs within the CBE Laboratory Unit is provided in Section 4 & 6.

2.18.3. Storage and Transport of BAs/GMOs

Under COSHH, Hazard Group 2 BAs (or material that contains these agents) must be stored safely at Containment Level 2. They must be located within a secure area and should not be stored outside of the Containment Level 2 CBE Laboratory Unit. This should also apply to all Class 1 GMMs stored in the CBE Laboratory Unit.

Safe storage of contaminated equipment and materials is required where appropriate. Appropriateness should be based on the assessment of risk. As part of any risk assessment equipment should be considered for its potential to act as a source of contamination for those using and maintaining it. Such equipment should have procedures in place to decontaminate it regularly, when it leaves the containment area or when it is serviced or maintained. The movement of

equipment between designated culture laboratories within the CBE Laboratory Unit should be avoided. If equipment needs to be moved it should be decontaminated first.

All biological material must be transported within the CBE Laboratory Unit according to the principles and rules described in Section 7. Biological material being transported out of the CBE Laboratory Unit, including transport to storage outside the facility, must be transported in accordance with the relevant legislation.

2.18.4. Good Housekeeping

Good housekeeping is important in all types of laboratories but it is especially so in laboratories handling biological materials. Cleanliness is fundamental to minimising any contamination and ensuring a safe working environment. In order to facilitate cleaning, the CBE Laboratory Unit should be tidy with no clutter or unnecessary items on benches and floors. It is also important that in the event of a spillage this does not seep into, onto or under items that need not be there.

Benches, floors and any items that may become contaminated should be easily cleanable. At the end of each working session or day, benches should be tidied and cleaned and, where appropriate, disinfected. Used culture plates and media for example should be disposed of as soon as they are no longer required to minimise growth of contaminants etc. Generally, items should not be stored in cardboard boxes, especially on floors, as these are impossible to clean. Cardboard boxes should never be used in the cold room because they tend to become damp, which encourages growth of moulds. Laboratory sinks should also be regularly cleaned and disinfected.

The Laboratory Manager should allocate day to day responsibility for housekeeping in the CBE Laboratory Unit to a named member of staff to ensure satisfactory standards are maintained. Cold rooms are areas where housekeeping is usually poor, often leading to mould contamination of walls and ceilings, equipment and experimental materials. This can result in unhealthy exposure to mould spores of workers entering the cold room. Attention should be paid to avoiding conditions where mould will result and any growth should be cleaned and disinfected as soon as it is observed.

As part of the housekeeping regime it should be ensured that hand wash sinks (including the taps) are regularly cleaned, and soap and paper towels are always available. If liquid soap is used this should be in a dispenser and, to prevent the multiplication of any contamination, dispensers should not be topped up from other bulk stocks. Single use paper towels are recommended for drying hands. Cloth towels must not be used.

NOTE: *Laboratories or similar facilities that are clean and tidy and have good standards of housekeeping are usually ones where there also is good management, organisation and working practices. Safety inspections often focus on housekeeping and workers should not underestimate its relevance to safety and should pay appropriate attention to this detail.*

SECTION 2	BIOSAFETY REQUIREMENTS FOR WORK WITH BIOLOGICAL AGENTS IN CL2 CBE LABORATORY UNIT
PART 4	ADDITIONAL PRECAUTIONS FOR TISSUE CULTURE WORK

2.19. ADDITIONAL PRECAUTIONS FOR WORK WITH BLOOD, BLOOD PRODUCTS AND OTHER HUMAN TISSUES OR RECOMBINANT DNA

Work with specific agents such as (i) recombinant DNA containing potentially oncogenic sequences, blood born viruses, transmissible spongiform encephalopathies or (ii) blood, blood products and other human tissue is not specifically covered in this CoP. Appropriate guidance should be sought for work with specific agents, see Annex 1.

2.20. ADDITIONAL PRECAUTIONS FOR TISSUE CULTURE WORK

In many cases tissue culture work will involve the use of genetically modified cell lines, in which case a risk assessment must be made in accordance with the requirements of the Genetically Modified Organisms (Contained Use) Regulations 2000 (see Section 4 for guidance). However, the following provides specific guidance for tissue work in general and should be applied in all cases even if genetic modification work is involved. The risks and control measures identified in the following are separate to those determined in the GM risk assessment. Any additional control measures are assigned under the requirements of the COSHH Regulations and do not affect the classification under the GM Regulations. Risks associated with genetic modifications are not considered further here (see Section 4).

Broadly, cell culture includes (1) primary cell cultures and early passage cultures - in vitro culture of harvested cells taken directly from freshly disaggregated tissue or body fluids (2) cell lines that comprise cells that are able to multiply for extended periods in vitro and can therefore be maintained by serial subculture – they can be subdivided into continuous cell lines, finite-life cell strains and stem cell lines. Cell culture is defined in COSHH as the 'in-vitro growth of cells derived from multicellular organisms'. It is included in the definition of a biological agent (BA) under the COSHH Regulations since they may be infected (deliberately or adventitiously) with BAs so they could present a risk of infection and could, in exceptional circumstances, proliferate if inoculated in vivo. Other risks such as allergy or toxicity should also be considered because of the production of biologically active substances.

Uncontaminated cell cultures do not appear to present a significant hazard as even direct dermal inoculation may result in only local inflammation. However, the long-term consequences of direct inoculation are uncertain. The main risk presented by cell cultures is as a result of their ability to sustain the survival and/or replication of a number of adventitious agents. The major agents of concern are viruses, but other agents, e.g. mycoplasma's such as *Mycoplasma pneumoniae,* should also be considered. In addition to these infection risks, other hazards that should also be assessed include (i) Components of the cell culture media – products of animal origin can act as a source of microbial contamination; and (ii) Cell products that could be biologically active.

Tissue culture involving non-human, non-primate animal cells or plant cells is generally regarded as low risk to human health and safety. For human and primate sourced materials there is a significant possibility there may be contaminating BAs that present a risk. However, once characterised and authenticated to be free from contaminating agents these too may present little risk.

2.20.1. Assessing the Risk

A risk assessment must be undertaken in advance of work starting. The following steps should be considered as part of the risk assessment when determining what agents, if any, might be present and the risk they pose:

1. Identify the Hazards

(i) Origin of cell line and source population from which cell line was derived

Agents infectious for humans are most likely to arise from cells of human or primate origin but other mammalian, avian and invertebrate cell lines may also present risks. The risk from any cell line should be considered in terms of the likelihood of contamination **and** the ability of the cell line to support growth (see below for further details).

(ii) Source of tissue

This will give an indication of potential contaminants and potential for expression/reactivation of latent viruses. Cells derived from peripheral blood and lymphoid cells present the greatest likelihood of contamination with serious human pathogens.

(iii) Type of cell line

Primary cell cultures should be regarded as higher risk. Continuous cell lines should not be regarded as low risk until they have been characterized and authenticated. Some cell lines are known to be persistently infected (e.g. B95-8 with EBV, MT4 with HTLV).

All of the above information should be available from the supplier (or the originator of the cell line, if not the same as the supplier), and/or peer-reviewed literature. Some cell lines may have undergone multiple passages in different laboratories and this may not have been recorded. The risk of infection associated with such cell lines would be difficult to assess, and it is better to obtain material from the originator of the cell line or a culture collection where the cell strains/lines will have been well characterised/authenticated, have a documented provenance and should have been screened for human pathogens.

2. Consider the nature of the risk

- Where the work will be carried out
- Whether the work could create aerosols or splashes
- Whether the work will require the use of sharps
- The level of production of any virus – this will depend on the culture conditions; any change in conditions requires a reassessment of risk
- Volume of culture and number of samples

3. Evaluate the risks and select the control measures

The following table provides guidance on selecting the appropriate containment measures for cell culture work. Any work that could give rise to infectious aerosols, such as with medium or high risk cells lines, must be carried out using suitable containment measures, e.g. a Class II BSC.

Hazard	Cell Type	Baseline containment
Low	Well characterised or authenticated finite or continuous cell lines of human or primate origin with a low risk of endogenous infection with a biological agent presenting no apparent harm to laboratory workers and which have been tested for the most serious pathogens.	CL1
Medium	Finite or continuous cell lines/strains of human or primate origin not fully characterised or authenticated, except where there is a high risk of endogenous biological agents, eg bloodborne viruses.	CL2
High	Cell lines with endogenous biological agents or cells that have been deliberately infected.	Containment appropriate to the agent

Source: Biological agents: Managing the risks in laboratories and healthcare premises

2.20.2. Supplementary Precautions to basic Containment Level 2 requirements

Particular attention should be given to the following precautions which should be applied when culturing permissive or mixed cells from sources not known, or not suspected, to be infected with human or simian retroviruses. These supplement the basic Containment Level 2 requirements and are to provide extra protection against percutaneous inoculation, and contamination of the skin, mucous membranes and working surfaces.

1. Protocols for the safe conduct of the work should be agreed and strictly adhered to. Local rules should be drawn up to ensure that working practices take into account the measures necessary to control exposure that may arise from the specific work activity. Laboratory rules, disinfection, waste disposal and emergency procedures must be specified.
2. Each procedure should be conducted in a designated area of the laboratory with sufficient space for working safely. Work should be conducted at a work station which is clearly identified. There should be sufficient room to work safely. There should be enough bench space to ensure the workstation is not cluttered and working practices are not compromised due to lack of space.
3. Procedures that may give rise to potentially infectious aerosols must be conducted in a BSC. Face protection (e.g., face mask) should be used if, when working outside the BSC, splashes or sprays are anticipated (i.e. if identified in the risk assessment).
4. Centrifugation must take place in sealed containers, ideally within sealed buckets/rotors.
5. The designated working area should be kept clear of any unnecessary equipment or apparatus before the work starts.
6. Access of unauthorised persons to the working area should be prevented to ensure that the person carrying out the work is free from the risk of disturbance or accidental physical contact with others.
7. Gloves and other personal protective items appropriate to the task (e.g. eye protection) should be worn throughout the work. If during use gloves become punctured or grossly contaminated they should be removed and disposed of, hands should be washed and clean gloves put on. After handling samples gloves should always be removed and discarded, and hands should be washed. Single use (disposable) gloves should not be re-used. Eye protection (goggles or safety glasses) and a plastic overall should be worn if splashing is likely to occur.
8. Lesions on exposed skin should be covered with visible waterproof dressings.

9. The use of glassware and sharps should be avoided (see Section 6).
10. The bench surface and any equipment used should be decontaminated immediately on completion of a session of work. Equipment must be fully decontaminated prior to maintenance work. A signed statement should be issued to this effect before maintenance work is allowed.
11. A satisfactory disinfection policy must be in operation. All surfaces should be disinfected immediately following any spillage, at the end of the working day and before any maintenance staff are permitted to work in the area. All contaminated waste must be disposed of safely. Local rules must specifically state laboratory procedures and arrangements for disposal of contaminated materials.
12. To prevent spillages within the laboratory, BAs/GMOs or material containing these, must be adequately contained during transfer from BSC and or workstations to other areas of the laboratory, e.g. incubators/orbital shakers.

2.20.3. Work with Primary Cultures

A major concern with primary cultures is the possibility that they may undergo spontaneous transformation. This tends to happen more frequently in rodent cells, but can occur with human and primate cells. If there is suspicion that a natural transformation of a primary culture has occurred or at any stage there is knowledge or suspicion that a cell culture contains a harmful biological agent, the work must be re-assessed and if necessary transferred to a higher level of containment. The following are signs that may indicate transformation or presence of virus particles:

- Changes to phenotype of cell, e.g. alteration of shape, size, and cell confluence, loss of contact inhibition
- Speed of cell division

Additional precautions for work with primary cultures include:

- Researchers must not use their own cells (or cells of anyone else who is working in the laboratory) for experimental purposes. This presents a particular hazard as any self-inoculation injury could have potentially serious consequences, as cells re-introduced back in the circulatory system of the host it will not be recognised as foreign by the immune system.
- Wherever practicable primary cells should be cultured for a short-term period. In the case of blood cultures this will normally be for a maximum of 48-72 hours. This will reduce the possibility of spontaneous transformation to virtually zero.
- Where possible tissues should be sourced only from screened sources and/or low risk sources.
- Records of primary cell cultures and the individuals from whom they were isolated should be kept.

2.20.4. Work with Genetically Modified Cell Lines

Where cell lines are to be infected/transfected with a GMO it will be necessary to consider the risks under both the GMO (CU) **and** COSHH regulations. The assessment under COSHH should consider the hazardous properties in relation to the safety of the worker. The GM risk assessment will be concerned with the properties of the cell line when modified by the GMO and will determine the containment and class for that GMO. It may be that when the risk assessments are completed the containment levels are different. In such cases the higher level of containment must be adopted.

For example, the COSHH assessment may require the cells to be handled at Containment Level 2, but the GM assessment identifies that the actual GMO can be assigned to Containment Level 1 since there is no additional hazard conferred. In this case the cells must be handled at Containment Level 2, but this will not necessitate notification of a Containment Level 2 activity under GMO (CU) Regulations. Further guidance is provided in Section 4.

2.20.5. Co-culture of Contaminating Viruses

Of particular concern (but not exclusively) is the presence in the material of blood-borne viruses (BBVs) such as hepatitis B and HIV and others including HTLV and hepatitis C. These present an associated risk of infection when handling the material. When the materials are cultured then the potential for inadvertent co-culture of the viruses must also be considered.

If the material is contaminated with any of the blood-borne hepatitis viruses, whilst residual infectivity may remain, there is no evidence to suggest that inadvertent co-culture of these viruses will occur. However, some cell culture systems incubated even for short periods may support the replication of any HIV or SIV that may be present in the starting material. Peripheral white blood cell cultures are of particular note, although all permissive cells (i.e. those carrying the CD4 receptor) should be regarded as HIV susceptible and able to support multiplication. It is also important to note that certain (permissive) continuous lines of cells of human or simian origin may be chronically infected with HIV or the virus may be inadvertently introduced during repeated passaging and use in the laboratory.

If it is intended to use continuous lines of permissive cells (of human or primate origin), the possibility that these may be latently infected with HIV or SIV must be considered as part of the risk assessment. If there is inadvertent co-cultivation of retrovirus the virus titre is unlikely to reach significant titres in 3-4 days incubation but this work would still be regarded as propagation of the virus and is therefore tightly controlled. With further incubation the risk increases significantly as virus titres increase.

Therefore, in order to contain work of this type safely:

i. the cultivation of cells from known or suspected cases of HIV infection or other primate (human or simian) retrovirus infection, must not be conducted in the Containment Level 2 CBE Laboratory Unit i.e. requires Containment Level 3;
ii. cultivation of permissive (CD4 +VE) or mixed cells from those not known, or not suspected, to be infected with human or simian retroviruses may be handled at Containment Level 2 with the additional precautions detailed below for work on potentially contaminated material provided that incubation of any cultures does not exceed 100 hours; and
iii. if incubation of permissive (CD4 +VE) or mixed cells from those not known, or not suspected, to be infected with human or simian retroviruses is to exceed 100 hours then this work MUST NOT be conducted in the Containment Level 2 CBE Laboratory Unit (i.e. requires Containment Level 3) unless a detailed risk assessment justifies that Containment Level 3 is not necessary.

The following outlines some of the key points that should be included within risk assessments for tissue culture of permissive or mixed cells in excess of 100 hours:

i. The overview of the work should make reference to the procedure involving tissue culture of material from human or primate origin in excess of 100 hours.
ii. The source(s) of material(s) should be identified and include details of the individual(s) or populations from which they were taken, the geographical locations of these, whether or not they include any known high risk groups of the population, whether donors have been screened, and the types of samples (blood, serum, tissues etc) being used.

iii. Identify the hazards associated with the use of these materials. The main concerns are possible contamination with pathogens such as hepatitis B and HIV and others including HTLV and hepatitis C. Provide an estimation of the incidence of the pathogens of concern in the donor population(s). Indicate that due to the particular activity of culturing the cell lines in vitro for in excess of 100 hours that retroviruses may multiply in the system. Assess the risks by taking account of whether the various tissue types to be cultured are permissive cell systems for multiplication of retroviruses, comment for example on the possibility that HIV can gain entry to non-permissive cells but if this happens only low titres of virus are produced so the risk is not significantly increased. Where appropriate, refer to stages in the procedure whereby any permissive cells may be removed (the problem of contaminating permissive macrophages and T lymphocytes should be specifically addressed) and if any steps are used to verify the culture of permissive cells is not occurring these should be identified.

iv. Consider whether alternative sources or systems can be used that do not have these hazards - could a lower risk source be used for the starting material, could donors be screened and only negatives be used, is culture for greater than 100 hours necessary, etc. The risk assessment must demonstrate that due consideration has been given to eliminating hazards wherever possible. However if this is not possible then control measures have to be implemented to reduce the risk to an acceptable level.

v. Assign control measures to minimise risks. If the particular system is such that retroviruses are unlikely to multiply then a minimum of Containment Level 2 with the additional control measures detailed below would be required and the working practices should be incorporated in to local rules or policy for this particular work. If retroviruses are likely to multiply in the system then the work must not be conducted in the Containment Level 2 CBE Laboratory Unit (i.e. assigned to Containment Level 3).

vi. Arrangements for regular checks on compliance with control measures should be given. Provision should be made for a high level of supervision and regular inspection of the facilities and working practices. A clear statement should be given on specific training requirements for this work. It should be noted that all workers will register with the Occupational Health Unit and will be offered vaccination against hepatitis B.

2.21. GOOD CELL CULTURE PRACTICE

2.21.1. Basic Techniques: The “Do’s and Don’ts” of Cell Culture

Given below are a few of the essential "do’s and don’ts" of cell culture. Some of these are mandatory e.g. use PPE. Many of them are common sense and apply to all laboratory areas within the CBE Laboratory Unit. However some of them are specific to cell culture activities.

1. The Do’s

i. Use PPE ie laboratory coat/gown, gloves at all times and eye protection as indicated by the assessment of risk. In addition, thermally insulated gloves, full-face visor and splash-proof apron should be worn when handling liquid nitrogen.

ii. Wear dedicated PPE for laboratories designated for tissue culture and keep separate from PPE worn in the general laboratory environment. The use of different coloured gowns or laboratory coats makes this easier to enforce.

iii. Keep all work surfaces free of clutter.

iv. Correctly label reagents including flasks, medium and ampoules with contents, date of preparation and name of researcher.

v. Only handle one cell line at a time. This will reduce the possibility of cross contamination by mislabelling etc. It will also reduce the spread of bacteria and mycoplasma by the generation of aerosols across numerous opened media bottles and flasks in the cabinet.

vi. Establish SOPs for routine isolation, handling and maintenance protocols for cells and tissues.

vii. Clean the work surfaces with a suitable disinfectant (e.g. 70% ethanol) between operations and allow a minimum of 15 minutes between handling different cell lines.

viii. Wherever possible maintain separate bottles of media for each cell line in cultivation.

ix. Examine cultures and media daily for evidence of gross bacterial or fungal contamination. This includes medium that has been purchased commercially.

x. Quality Control all media and reagents prior to use. Be aware that culture medium contains components [e.g. serum or antibiotics] that have sensitising properties and should be evaluated as part of the risk assessment.

xi. Keep cardboard packaging etc to a minimum in all cell culture areas.

xii. Ensure that incubators, BSCs, centrifuges and microscopes are cleaned and serviced at regular intervals.

xiii. Test cells for mycoplasma on a regular basis.

2. The Don'ts

i. Do not continuously use antibiotics in culture medium as this will inevitably lead to the appearance of antibiotic resistant strains and may render a cell line useless for commercial purposes.

ii. Don't allow waste to accumulate, particularly within the BSC or in the incubators.

iii. Don't have too many people in the laboratory at any one time.

iv. Don't handle cells from unauthenticated sources in the CBE Laboratory Unit. They should be handled in quarantine until quality control checks are complete.

v. Avoid keeping cell lines continually in culture without returning to frozen stock.

vi. Avoid cell culture becoming fully confluent. Always sub-culture at 70-80% confluency or as advised on the cell culture data sheet.

vii. Do not allow media to go out of date. Shelf life is only 6 weeks at +4ºC once glutamine and serum is added for example.

viii. Avoid water baths from becoming dirty by using Sigma Clean or equivalent

ix. Don't allow essential equipment to become out of calibration. Ensure BSCs are tested regularly.

2.22. ASEPTIC TECHNIQUE AND GOOD CELL CULTURE PRACTICE

1. Sanitize the BSC using 70% ethanol before commencing work.
2. Sanitize gloves by washing them in 70% ethanol and allowing to air dry for 30 seconds before commencing work.
3. Put all materials and equipment into the BSC prior to starting work after sanitizing the exterior surfaces with 70% ethanol.
4. Whilst working do not contaminate gloves by touching anything outside the BSC (especially face and hair). If gloves become contaminated re-sanitize with 70% ethanol before proceeding.
5. Discard gloves after handling contaminated cultures and at the end of all cell culture procedures.
6. Equipment in the BSC or that which will be taken into the BSC during cell culture procedures (media bottles, pipette tip boxes, pipette aids) should be wiped with tissue soaked with 70% ethanol prior to use.

7. Movement within and immediately outside the BSC must not be rapid. Slow movement will allow the air within the BSC to circulate properly.
8. Speech, sneezing and coughing must be directed away from the BSC so as not to disrupt the airflow.
9. After completing work disinfect all equipment and material before removing from the BSC. Spray the work surfaces inside the BSC with 70% ethanol and wipe dry with tissue. Dispose of tissue by autoclaving.

2.23. GOOD MICROBIOLOGICAL PRACTICE

The use of aseptic techniques and other good microbiological practices achieves two very important objectives:

(i) the prevention of contamination of the laboratory by the organisms being handled

(ii) the prevention of contamination of the work with organisms from the environment

The first is of prime importance for working safely. The second is critical to the quality of the research. The principles of good microbiological practice should be applied to all types of work in the CBE Laboratory Unit involving biological agents (including genetic modification work) irrespective of containment level. In addition aseptic technique is also invaluable for preventing contamination of tissue cultures.

Aseptic technique is based on creating a special (clean) micro-environment in which to grow and keep the organism of interest and prevent all contact with the outside world. This micro-environment is usually some sort of culture or holding vessel such as a flask, bottle (bijou, McCartney, universal etc) or petri dish and the organisms can either be on a solid agar medium or be suspended in a broth, diluents or other fluid medium.

The principles are:

i. Prior to use all components of the system (the inside of the vessel, the medium and any objects used in the manipulative processes) must be sterile; and
ii. In the inoculation, incubation and processing steps, particular care must be taken to avoid cross-contamination. This involves:
    - keeping the vessel closed except for the minimum time required to introduce or remove materials;
    - working with a bunsen burner and flaming the opening of the vessel (passing it quickly through the bunsen flame) whenever tops are removed. The upwards current of hot air created by the bunsen prevents contaminated air or particles dropping into the culture vessel when the lid is open.
    - using manipulation techniques that minimise any possibility of cross contamination e.g.: opening lids with the little finger so that tops are not put down on the benches; and
    - ensuring that all of the objects that may come into contact with the culture , such as loops and pipette tips, are sterile before use, are not contaminated by casual contact with the bench, fingers or the outside of the bottle etc during handling and are decontaminated or disposed of in a safe manner immediately after use.

In addition to aseptic technique, good microbiological practice encompasses a wide range of other working methods that minimise the bi-directional cross-contamination of work and workplace. These include for example:

1. Using manipulation techniques that minimise the possibility of producing aerosols:

- mix by gentle rolling and swirling rather than vigorous shaking (to avoid frothing);
- pipette by putting the tip into a liquid or onto a surface prior to gently ejecting the pipette contents (to avoid bubbling and splashing);
- have vessels in very close proximity when transferring liquids between them (to avoid falling drops splashing);
- use loops only after they have cooled down after flaming (to avoid sizzling);
- do not over-fill centrifuge pots (to avoid leakage into centrifuge); and
- always carry and store cultures etc (bottles and plates) in racks or other containers (to avoid accidental dropping and smashing).

2. Keeping the laboratory clean and tidy:

- only have on the bench those items necessary for the task in progress (to avoid unnecessary clutter which would increase the likelihood of things getting knocked over and also to minimise the problems of cleaning up in the event of a spill);
- plan and lay out work so that everything needed for an experiment is ready to hand (this should allow the worker to sit at the bench and work comfortably);
- at the end of each experiment tidy and clean the bench and always wash hands. In the event of spillage etc always clean it up immediately and wash hands;
- avoid putting anything on the floor (to avoid tripping hazards and minimise the problems of cleaning up in the event of a spill);
- regularly clean out water baths (to minimise microbial contamination in the water);
- regularly clean down open shelving, benching, window-sills etc and items on them (to prevent build up of dust and debris, store infrequently used items in cupboards and drawer);
- regularly clean floors (to prevent build up of dust and debris, particularly in areas that are difficult to get to);
- regularly sort through items stored in fridges and freezers, on shelves and benches etc and throw away unwanted items (to prevent clutter); and
- keep sinks clean (hand wash basins and taps should be cleaned daily).

3. Designating areas in the laboratory for storage of items at different stages in use cycles, and where appropriate, using visual systems (e.g. autoclave tape) for indicating status :

- for example: clean/clean awaiting sterilisation/clean and sterile ready for use/used not decontaminated/used being decontaminated/used and ready for wash up (these types of systems allow for compartmentalisation of work activities into clean and dirty areas);
- everyone in laboratory to be aware of the system to ensure no mix ups occur; and
- system should be logical and easy to follow in working practices (otherwise it won't work).

All micro-organisms and cultures should be handled as if they are pathogenic (even if they are working with Hazard Group 1 organisms) by routine use of aseptic techniques and other good microbiological practices. Whilst intending to grow a particular (non-pathogenic) organism, the possibility of unintentionally culturing a (pathogenic) contaminant should always be acknowledged. Furthermore whilst it is unlikely that organisms in Hazard Group 1 will cause disease, many have the potential to cause opportunistic infections and pathogenic potential may well be altered under laboratory growth conditions

Purity checks should be incorporated into experimental protocols or SOPs and undertaken at various stages of experiments as a matter of routine. This may involve, taking a sample of fluid from the vessel and plating (or streaking) it out for single colonies onto a non-selective solid nutrient medium; incubating at a suitable temperature (usually 30^{o}C as this will allow growth of contaminants originating from both the general environment and human sources); and examining the plates following incubation for evidence of any contamination (as indicated by colony types).

An indication of the purity of a liquid culture can also be obtained by microscopic examination. The advantage of this method is that the result is instant. A sample of the culture is placed on a microscope slide and this is then either examined wet (by phase contrast microscopy) or fixed and Gram stained. Contaminating organisms should be clearly visible. Purity checks are particularly useful in evaluating competence in good microbiological practice. Workers with poor aseptic techniques will suffer frequent contamination problems whereas skilled microbiologists will only occasionally have problems. It is important to recognise that poor practices resulting in cultures being contaminated probably also result in contamination from the work being spread in the laboratory and the Laboratory Unit.

SECTION 3 INFORMATION, TRAINING AND SUPERVISION

3.1. SAFETY TRAINING FOR WORK IN BIOLOGICAL LABORATORIES:

It is a legal requirement that all workers handling hazardous materials receive appropriate information, instruction and training in order to carry out their work safely. Workers must be trained and should be proficient in safe working practices and techniques to ensure the safety of themselves and other persons in the CBE Laboratory Unit. Training must specifically include all safety related matters in order that workers know how to effectively apply routine and emergency control measures. Records should be kept to demonstrate this has been carried out. Inspectors from the Health and Safety Executive (HSE) increasingly ask to see training records during routine or incident investigation visits.

Provision of information and instructions and attendance at training courses should not be regarded as all that is required. This should be supplemented by practical demonstration and assessment of competence in the laboratory. A suitable training programme should be drawn up locally taking into account the nature of the work concerned. On the job training is important and work practices should be monitored. Any shortfall in standards should be brought to the attention of the Laboratory Manager, or Research Group Leader/Principal Investigator, as appropriate, and be addressed immediately.

3.2. PROCEDURES FOR LABORATORY STAFF TRAINING AND INDUCTION

As part of the induction procedure when first arriving, all persons working in the CBE Laboratory Unit should be made aware of the University Health and Safety Policy and of any other local health and safety policies. The Research Group Leader/Principal Investigator of a given research group, or the supervisor/manager of a unit or work area, should ensure that all persons studying or working in the CBE biological laboratories receive information, training and supervision appropriate for the work undertaken, so that risks to the health and safety of all persons involved are controlled. This does not necessarily mean that they have to provide it themselves (it can be delegated or workers sent on courses etc) but they must assure themselves that it has been provided and understood and the worker is competent to work safely. In order to effectively discharge these responsibilities, those with supervisory or managerial roles must themselves be competent in safety related matters and, where necessary, should seek additional training (or refresher training) as appropriate.

In relation to work in the CBE Laboratory Unit, all persons handling biological materials must be able to recognise how exposure to biohazards can occur and how it can be prevented. Appropriate training programmes should be developed to provide information and instruction for working with biological material that may contain biological agents or GMOs. The programme should identify key competencies to be achieved and demonstrated, which must relate to the generic codes of practice and SOPs.

Before commencing work, staff must:

1. Complete the training pro-forma to ensure that they are familiar with the working environment and highlight any work activities that could require additional training or health monitoring to be initiated. These forms will be issued by the CBE administrator/Laboratory Manager.
2. Read the **written guidance** in the Codes of Practice
3. Read the **written local rules for working in the CBE Laboratory Unit**
4. Read relevant SOPs based on the risk assessment for the work activity. Standard Operating Procedures are used to meet internal quality standards but by integrating the Health and Safety

arrangements they should also be used to ensure acceptable local standards of Health & Safety.

5. Receive practical guidance and appropriate training in the safe handling of BAs and GMOs from one of the designated researchers in the CBE, to include as a minimum;
    i. waste disposal procedures;
    ii. disinfection procedures
    iii. the procedures to be taken in the event of accidents and incidents; including biological spillage and

6. Read details of the risk assessments for the work to be undertaken explaining both the nature of the hazards and the use of control measures. The risk assessments should include details of, or reference to documents containing the other bulleted points above.
7. Have demonstrated that they are competent. As an indication that training for work in a Containment Level 2 CBE Laboratory Unit has been received, the **safety documentation** should be **signed** and returned to the Laboratory Manager for a **written record of the training**.

The degree of training required should be proportionate to the risk. Where work involves handling of pathogens (or materials that may contain these) or genetically modified organisms, specific training should be given on how to work safely with these. The amount of training that needs to be provided will also depend on the experience of the person being trained but supervisors should not assume competence until it has been demonstrated.

Particular care must be taken in the training of students and in their supervision. Provision of adequate training and supervision applies not only to work on CBE premises but also work carried out elsewhere in the University.

NOTE: *It is likely that much of the training for work at Containment Level 2 can be given 'at the bench' under supervision. The level of supervision reduces as competence is acquired. Supervision appropriate to the degree of risk and the experience of the worker must be maintained.*

3.3. TRAINING AND SUPERVISION REQUIREMENTS

For all workers, specific laboratory training should as a minimum include familiarisation with local rules and working practices, use of personal protective equipment (lab coat, gloves, eye protection), use of biological safety cabinets, disinfection procedures, waste disposal procedures, accident and emergency procedures and discussion of relevant risk assessments.

(i). Research Associates/Fellows/Post-docs

A basic level of knowledge of Health & Safety issues and specific knowledge of COSHH, GM Regulations is expected, dependent on the level of experience and area of expertise. Deficiencies should be discussed with designated supervisors/senior staff and addressed by training as required. No work should commence until their supervisor or manager of a unit or work area is satisfied that they have read and understood the basic University Health and Safety Policy and of any other local procedures.

(ii) Students and inexperienced workers

The level of training and supervision required by inexperienced laboratory workers of any age will be greater than that required of more experienced workers. Supervisors should clearly identify training needs as part of induction procedures and work should be carried out under close supervision of trained personnel until they are able to receive training in relation to COSHH, GM Regulations, where applicable, and it has been confirmed that individuals are competent to carry out their work safely.

Undergraduates and inexperienced workers should not be allowed to carry out practical laboratory work out of normal working hours unless explicit permission is given on each occasion by their supervisor and adequate supervision is employed. If the supervisor is not a senior member of the academic staff then one who is must agree to the granting of the permission and only do so after they have satisfied themselves as to the individual's competency.

(iii) Visiting Staff

It is the responsibility of the person making the invitation to ascertain whether the visitor will require specific training and arrange it accordingly. For short visits formal training may be impractical and therefore arrangements should be made for close supervision and/or individualised training to be given.

3.4. TRAINING RECORDS

It is good practice to keep records of training for any staff working at Containment Level 2. A model training record proforma for workers in CBE Laboratory Unit is provided on the CBE website. Many of the basic procedures and control measures are common to all laboratories and the form can be tailored as appropriate for the different areas of work carried out. As such this proforma should be used as the basis of a training record for all workers at Containment Level 2 within the CBE Laboratory Unit, including work with blood and human tissues, pathogens and genetically modified micro-organisms. The model training record proforma should assist those with supervisory or managerial responsibilities to identify workers training needs. The Research Group Leader/Principal Investigator or the supervisor/manager is responsible for maintaining the training record for each person for whom they have responsibility.

SECTION 4 SAFE WORKING WITH GENETICALLY MODIFIED ORGANISMS

4.1. SCOPE

This section aims to:

1. Set health, safety and environmental standards for work with Genetically Modified Organisms (GMOs) in the CBE Laboratory Unit,
2. Give information on identifying levels of risk to health and of harm to the environment from exposure to or unplanned release of GMOs,
3. Provide practical advice on the assessment of risk to health and of harm to the environment,
4. Provide information to assist investigators to complete any external notifications required by the regulations.

4.2. APPLICATION

This section is relevant to all personnel who work with or intend to work with GMOs in the CBE Laboratory Unit. Work with GMOs forms an important part of the CBE's normal activity. The local rules and guidance detailed in this section provide a mechanism by which the CBE can take all reasonably practicable steps to control and manage the risks of working with GMOs, to keep records and to make such internal and external notifications as are necessary. As such it forms part of CBE's arrangements for safety under the University Biological Safety Policy in accordance with the Genetically Modified Organisms (Contained Use) Regulations 2000, as amended 2005 and the Control of Substances Hazardous to Health Regulations 2002 (COSHH), where applicable.

4.2.1. Definitions under the GMO (CU) Regulations 2000[5]

- **Genetic Modification (GM)** in relation to an organism means the altering of the genetic material in that organism in a way that does not occur naturally by mating or natural recombination or both in such a way as to preserve this change into successive generations.
- A **genetically-modified organism (GMO)** is one that has been altered in this way and can include GM micro-organisms, cultured cells and all organisms which are handled using similar techniques (**GMM**) or multicellular animals or plants (transgenics). NOTE: The

[5] Clarification of Class 1 following amendments to Genetically Modified Organisms (Contained Use) Regulations 2000, on the 21 December 2010 - Meaning of the term 'recipient or parental micro-organism'

The clarification of Class 1 genetically modified micro-organisms in full is:
"recognition that, in general, only activities involving genetically modified micro-organisms which show the following characteristics are appropriate for inclusion in class 1 as described in Schedule 1—

(i) the recipient or parental micro-organism is unlikely to cause disease to humans, animals or plants,
(ii) the nature of the vector and the insert is such that they do not endow the genetically modified micro-organism with a phenotype likely to cause disease to humans, animals or plants, or likely to cause deleterious effects on the environment, and
(iii) the genetically modified micro-organism is unlikely to cause disease to humans, animals or plants and is unlikely to have deleterious effects on the environment;".

The above clarification of the meaning of Class 1 refers to the 'recipient or parental micro-organism'. This description is taken directly from the Directive and is consistent with the description in the 2000 Regulations of information that should be notified to HSE. The terms 'recipient' and 'parental' micro-organisms are considered to be interchangeable, and refer to the organism into which 'donor DNA' or 'insert' is being cloned via a vector system. For the majority of work involving genetic modification it will be clear which organism is the donor and which is the recipient/parental organism.

definition of GM animals includes animals in which a significant proportion of cells have a foreign gene stably inserted (also known as “mosaics”).

- **Contained Use** is defined as any operation in which organisms are genetically modified **and/or** in which such GMOs are cultured, stored, used, transported, destroyed or disposed of, and for which any combination of physical, chemical or biological barriers are used to limit their contact with people and the environment. NOTE: This includes the handling of GMOs that have been constructed by another person and acquired by you and the storage of GMOs from a project temporarily in abeyance.
- **Hazard group:** A classification scheme devised by the ACDP for biological agents according to the severity of the damage that they can do to human health. Organisms are placed in four groups with those in HG1 causing no harm to health, through to HG4 whose organisms cause multiple fatalities and are readily spread in the community and against which there is no effective prophylaxis.
- **Containment level:** Descriptions of the four different design and management procedures suitable for laboratories in which agents of the four hazard groups will be handled.
- **Activity Class:** A classification of activities involving GMMs into one of four classes dependent on risk. This classification takes into account both the nature of the biohazard and of the laboratory manipulations which will be undertaken in a project. The four GM activity classes correspond closely with the ACDP system of classification of biological agents. It is a legal requirement to determine the Activity Class of all projects involving GMM.
- **Recipient (host) organism:** Any organism into which genetic material is inserted. This includes any vectors such as viruses used in the construction of the final product. The HG of the recipient organism is the starting point for the determination of the Activity Class of the project.
- **Donor organism:** The organism from which the genetic material is taken.
- **Insert:** The genetic material (DNA sequences, etc.) which has been introduced into the recipient. These may confer a phenotype on the recipient which affects the safety of people exposed to it or might cause harm to the environment if the GMO were to be released accidentally.
- **Vector:** May be a virus, bacterial plasmid, liposome or physical agent used to insert foreign genetic material into a recipient. NOTE: The vector will be one of the GMOs involved in the project if it is a microorganism.
- **A “connected programme of work”:** A series of integrated and coherent studies connected for the purpose of simplifying a statutory notification (i.e. to the HSE). Components of the work may be notified internally as separate projects yet form part of a continuing programme. If part of this programme involves activities classified as 2 or higher, these must be notified to the HSE. However, rather than having to notify several separate projects, these can be notified as a CPW. In making a judgement as to whether your work is a CPW you could ask yourself: “is (might) this work (be) covered by a single grant application?”

4.3. ASSESSMENT OF RISK TO HEALTH AND HARM TO THE ENVIRONMENT

The principles and practices described in this section of the CoP are aimed at mitigating the risk of damage to health and harm to the natural environment arising from exposure to genetically modified micro-organisms (GMMs)[6] accidentally released from CBE laboratory containment. This section provides practical advice on how to comply with the University Biological Safety Policy in

[6] For activities involving GMOs which are not micro-organisms (e.g. GM plants or animals) the regulations apply to risks to human health only.

accordance with the code of practice set out below. Where **text is highlighted, this is to indicate mandatory rules that must be followed in the CBE Laboratory Unit for work with GMOs.**

Before any work with genetically modified micro-organisms begins, an assessment must be made to assess: (1) the risk to human health **and** (2) the risk of harm to the environment.

This risk assessment must contain a judgement of the Activity Class of the project and describe the measures required to control risk to human health and harm to the environment. Guidance on completing the risk assessment is given in the following sub sections.

The requirements of the Genetically Modified Organisms (Contained Use) Regulations 2000, as amended 2005, are reflected in the University Biological Safety Policy which requires that risk assessment of all work with Genetically Modified Organisms must be carried out in advance of work commencing and, in addition, must be examined and approved by the University's BHGMSC. Work can only commence on approval of the risk assessment by the BHGMSC. Guidance on performing risk assessments is provided in the Compendium of Guidance from the ACGM. A simple outline of what is required from personnel working with GMOs in order to comply with the above legislation is provided below.

4.3.1. Is your work covered by the regulations?

If personnel are unsure whether their work is covered by The Genetically Modified Organisms (Contained Use) Regulations 2000 then they should refer to the relevant section of the regulations. The full text of these regulations is available on the HMSO website. The Scientific Advisory Committee on Genetic Modification (SACGM) has provided a Compendium of Guidance for help in preparing the GM Risk Assessment and identification of containment and control measures for different sorts of GMOs. If personnel are unsure in any way of the classification of the work they are doing or planning, they must consult the local GM Safety Advisor (BGMSA) and/or the University Biological Safety Officer (BSO) before undertaking or continuing with the work in question.

4.3.2. What do I do now?

Only GMO work which has had a risk assessment approved by the BHGMSC Committee can be undertaken. All GMOs must be registered with the BHGMSC Committee **prior** to acquisition or creation of a GMO. In order to obtain permission to work with GMOs you need:

1. To prepare a GM Risk Assessment
2. Ensure that laboratories, rooms etc. to be used have been inspected by the local BGMSA (unless already authorised for GM work).

4.3.3. The Proposer

The person undertaking activities involving GMOs must ensure that a suitable and sufficient risk assessment has been made. Under the regulations this does not necessarily mean that the person undertaking the activities needs to actually carry out the risk assessment. However, the proposer of the work activity should have overall responsibility for the work. It is recommended that this individual should be a permanent member of staff (i.e. not a postdoctoral researcher or postgraduate student). They should prepare the GM Risk Assessment and ensure that changes in information and personnel are reported to the University BHGM Safety Committee.

The local BGMSA, if necessary, will help in the preparation of the GM Risk Assessment, but ultimately it is the responsibility of the Proposer to ensure that the regulations are complied with. Additional assistance may also be sought from members of the BHGMSC, or colleagues with experience in preparing GM Risk Assessments.

4.3.4. Prepare a GM Risk Assessment:

The person carrying out the risk assessment must take into account the matters set out in Part I of, and include the steps set out in Part II of, Schedule 3 of the Genetically Modified Organisms (Contained Use) Regulations 2000, as amended 2005.

The risk assessment must take into account the matters in Part I of Schedule 3. These include; identification of any potentially harmful effects; characteristics of the proposed activity; the severity of any potentially harmful effects, and the likelihood of them occurring. **Part II of Schedule 3 sets out the steps which must be followed in making the risk assessment.** This includes the selection of the appropriate containment and control measures for the particular activity.

The initial risk assessment of an experiment should be based on what is expected to occur and what could reasonably be expected during the experiment. If a result occurs that is not expected then it will be necessary to review the risk assessment. Risk assessments should be written so that they are understandable by the reader, for example an HSE inspector, lab workers or local safety advisors. The GM Risk Assessment is probably one of the most important documents which personnel will produce. It is not possible to describe exactly what should go into an assessment as this must be decided on a case by-case basis. The University's GM Risk Assessment Form should be used for preliminary assessment of all GM proposals and for approval of Class 1 activities. This form contains a number of main sections, including:

- details of the Proposer, and an overview of the project including the characteristics donor, insert, vector, host and organisms involved,
- a list identifying the personnel and the rooms involved.
- an interim assignment of containment conditions to protect human health
- an assessment of the risk to the environment
- a monitor of containment and control methods and assignment of final activity Class

The subheadings within these sections should help with laying out the information, but guidance should be sought if unsure. The GM Risk Assessment should determine the containment measures required to control the identified risks. These containment levels decide the classification of the activity, and the classification determines the notification requirements.

NOTE: *In completing risk assessments it is important that any statement that is made is justified and a rationale provided. For example, a statement that a vector is disabled is not sufficient on its own. The statement should say why and how this is done. In the assessment of the risk to the environment, it is necessary to emphasise the containment measures that will prevent the risk being realised rather than just stating " no problem exists if X escapes" for example.*

NOTE: *Risk assessments will vary in the amount of detail necessary. Simple activities involving low hazard, well known and well understood micro-organisms may normally need less detailed consideration than complex activities involving hazardous and less familiar micro-organisms. For example, it would be permissible to undertake a generic risk assessment, covering specified activities, at a specific premises that involved a series of named E.coli K-12 strains, whose disablement is well characterised. Any future activities that fell within the boundaries set for this generic assessment would then be covered and would not require individual assessment.*

NOTE: *Frequently observed shortcomings in submitted risk assessments include:*

- *. one word answers;*
- *. Non-specific or general descriptions of sequences, vectors, hosts, such as "E. coli strains" and "sequences such as … ";*
- *. lack of justification (especially when accompanying an assertion that the risk level is low);*
- *. failure to describe adequately the nature and biological effects of the inserted sequences and how these could alter the nature and biology of the parental organism;*

- *. failure to consider the risk to the environment (i.e. land, air and water and any organisms that live in these habitats).*

4.3.5. Categorise the Laboratory Containment and Risk Activity for the Project

Work with GMOs must be carried out in containment laboratories whose design features and supervisory and management procedures are commensurate with the nature and severity of the assessed risk and in accordance with the control measures identified in the risk assessment. Good microbiological practice is a minimum standard for work at all levels.

Descriptions of laboratory containment levels 1-4 and the containment requirements for GM plants and animals are given in the ACGM/HSE Compendium of Guidance. Further guidance on laboratory design and management for microorganisms is given in the HSE publication "The management, design and operation of microbiological containment laboratories". The description of the microbiology containment levels parallels that given by the ACDP.

Where a project has been assessed at more than one containment level, all work carried out simultaneously in any laboratory must be carried out at the highest (or higher) level. Similarly, where a project at a lower classification is carried out in a laboratory simultaneously with other work at a higher classification, all the lower level work must be carried out under the management standards imposed by the higher level whether or not the higher level work involves a GMM.

There could be a variety of circumstances in which this would apply. The project may be divided into several phases, or more than one project may be under way in the same laboratory simultaneously, or the laboratory might be in use for a non-GM project requiring higher containment. Sometimes a higher level of containment may be chosen for reasons other than the safety issues belonging to the GM project. These might include the need to ensure product protection, or to impose a quality assurance discipline, or simply because no other (lower containment) laboratory is available for the work. This is most commonly found in Class 1 projects which are often carried out in laboratories designed to offer Containment Level 2 standards.

Certain GMMs may also be classified as BAs. Under COSHH, the selection of control measures for BAs is prescribed according to the risk to human health, while the Contained Use Regulations 2000 set out containment measures appropriate to both human health and environmental protection. Where there is a mismatch, the stricter requirements must be applied, for example, where a GM biological agent presents a low risk of disease in humans, but is environmentally harmful, the risk management measures to ensure environmental protection must be applied.

NOTE: *Since the Activity Class of a project is driven by the need to adopt a particular containment level, if personnel choose a containment level higher than that which is required by legislation, an explanation should be given to explain the reason for the choice.*

The class into which each organism is placed depends upon the risk assessment and the containment required. As already stated, this risk assessment is made on the basis of risk to human health and the environment. Key factors will be the initial classification that was made on the basis of the hazard identification step and any additional containment measures that have been assigned over and above the minimum requirements appropriate to the initial risk class. To decide on the correct classification for an activity, users must compare the selected measures necessary to control the risk with the appropriate table in Schedule 8 of the Regulations (reproduced in Tables 3 and 4).

NOTE: *It should be noted that these tables contain the phrase 'required where and to the extent the risk assessment shows it is required'. This indicates that the particular item may or may not be required and that deciding the classification of the activity according to this phrase effectively means 'yes or no'. Therefore, if an activity requires level 1 containment but included the need for specified disinfection procedures (which is*

'required where and to the extent the risk assessment shows it is required' at level 1) this would not push the activity into class 2 (which requires specified disinfection procedures).

Similarly, it should be emphasised that the classification is based on the level of containment required to control the risk, not necessarily the level of containment at which you propose to carry out the activity. For instance, the activity may be classified as class 1 based on the containment required to control the risk, but all of the laboratories within the CBE Laboratory Unit meet level 2 requirements. This does not mean that the activity becomes a class 2 activity.

All persons undertaking an activity involving GM must ensure that the exposure of humans and the environment to GMMs is reduced to the lowest level that is reasonably practicable *(see Regulation 17 for explanation)*.

For any activity involving GMMs, in addition to standard containment levels set out in Tables 3 and 4 (reproduced from Schedule 8), the measures taken to comply with the above must include the general principles of good microbiological practice and of good occupational safety and hygiene (GOSH) as set out in Schedule 7 of the regulations.

All persons undertaking an activity involving GMMs must apply the containment measures set out in Schedule 8 (see Tables 3 & 4). If a particular containment measure is not applied, based on risk assessment, this (derogation) must be first justified and agreed by the competent authority.

All persons undertaking an activity involving GMMs must review the containment measures applied at suitably regular intervals and if it is suspected that measures are no longer adequate, the activity class has changed or there is new scientific knowledge.

It is possible to modify the containment procedures based upon the risk assessment. In some circumstances, it may be reasonable to argue in the risk assessment that certain features of the containment procedures are not required. This would be scrutinised closely both by the BHGMSC and the HSE. Extra containment procedures may be added where required. Table 3 sets out the containment measures for activities that are normally considered to be 'laboratory type' both in terms of scale and nature. Table 4 sets out containment and control measures for large scale activities where laboratory type measures are not appropriate. The distinction between Table 3 and 4 is the applicability of the containment measures to the nature of the activity not the purpose of the activity. The requirements of Table 3 might be appropriate for some small scale industrial production.

There is duty for all persons undertaking activities involving GMOs to review the containment measures. Subject to the risk and nature of the activity, low risk routine activities should be reviewed at least every 2 years. For higher risk, less routine activities this should be more frequent e.g. 1 year or less). The appropriate review interval should be considered when the risk assessment is undertaken and recorded on the risk assessment itself. Staff changes should also trigger a review.

4.3.6. Fill in the Appropriate Forms: Notification of Proposed GM Projects

All proposed projects must be submitted to the University BHGM Safety Committee for approval before work commences.

The following describes the arrangements in the University for genetic modification work as required by the relevant regulations. Personnel should have already prepared a Risk Assessment Document which describes the risks to human health and the environment. Depending upon the sort of organism with which personnel wish to work and the risk class that has been determined, personnel are required to fill out one of the following forms (also refer to Section 2, Part 1):

Under the Genetically Modified Organisms (Contained Use) Regulations 2000, as amended 2005, information must be submitted to the HSE for certain types of work involving GMOs; see (i) and (ii) below. Forms CU1 and CU2 must be provided before work begins. A risk assessment and **appropriate fee** must be sent with forms CU1 and CU2. No fee or risk assessment is required with an accident notification, CU3.

The University's BSO must be advised of the intention to make a notification BEFORE these forms are submitted.

Forms may be completed online and sent to notificationofficer@hse.gsi.gov.uk BUT MUST ALSO BE printed, signed and posted to HSE as a signature is required.

- **CU1** - Notification of intention to use premises for genetic modification
- **CU2** - Notification of intention to conduct individual contained use activities involving genetic modification
- **CU3** - Notification of accidents involving Genetically Modified Organisms (Regulation 21)
- **CU4** - Transfer of notified activity form

NOTE: *These forms can be accessed via electronic links in the University Biological Safety Policy document.*

(i) **Genetically Modified Micro-organisms Class 1**

These activities are reported to the BHGMSC on the form that personnel should have used to prepare your GM Risk Assessment. Once the risk assessment has been considered by the BHGMSC, and subject to its approval, authorisation will be issued for Class 1 work which can then commence. Class 1 activities do not have to be notified. If, however, the **first intended activity at new premises** is Class 1, the premises notification must include a risk assessment and form CU1. Under these circumstances, the premises may begin undertaking contained use work as soon as the HSE acknowledges receipt of the notification and the premises have complied with the notification requirements for the first intended activity.

(ii) **Genetically Modified Micro-organisms Class 2, 3 and 4**

At the time of writing, Class 2 work or above is not permitted in the CBE Laboratory Unit. If however a requirement for Class 2 work is identified, all GMO projects classified as activity class 2 or higher must be notified to the Competent Authority (HSE) for approval before work begins.

Along with the GM Risk Assessment personnel are required to fill in form CU2. For work assigned as Class 2 (or higher) the proposal will be sent to the HSE (together with a cheque for the fee) who will consider it and give final authorisation before work can commence.

Any significant change in the risk assessment of a project of class 2 or higher must be notified to the Competent Authority.

Where there is a change that involves *either* raising or lowering the risk; and relocation of the project to different premises, these changes can be notified by letter to the HSE. The re-notification attracts a fee.

Cessation (temporary or permanent) of a project notified to the HSE including the total destruction of GMM stock or complete transfer of GMM away from LU, must be notified to the University BSO. Recommencement must also be notified. LU is required by law (Regulation 15) to notify the HSE of cessation of any project previously notified to them.

4.3.7. Confidentiality and disclosure of notified information

Principal investigators/supervisors of projects that require notification under the Genetically Modified Organisms (Contained Use) Regulations 2000 should be aware of the position on public disclosure of information contained within such notifications made to the Health and Safety Executive (HSE). Whilst this is not a health and safety issue it is one that directly arises from requirements to notify projects under health and safety legislation. The public right of access to the information is under the provisions of the Freedom of Information Act and the Environmental Information Regulations. **It is important that Principal Investigators/Supervisors and Heads of Group are aware of the disclosure provisions since it may have significant effects on patent applications and intellectual property rights.**

All information held by HSE in connection with notifications and inspections is potentially disclosable to anyone who requests it. Furthermore, some parts of notifications are placed on the public register, this is available for inspection at specified local HSE offices and a copy will be available on the internet. Some categories of information can be withheld from disclosure but these are limited. Personal information continues to be protected by the Data Protection Act and is automatically treated as confidential.

The Health and Safety Executive has produced guidance on disclosure of information; available at http://www.hse.gov.uk/biosafety/gmo/guidance/disclosureguidance.pdf and researchers are urged to note its contents, particularly with regard to intellectual property rights and patent applications. Researchers are advised to consult with their Head of Group where appropriate, if they have any concerns about the disclosure provisions in relation to any project that requires notification.

4.4. WASTE DISPOSAL

All laboratory waste likely to contain or be contaminated by GMMs must be treated in such a way as to inactivate GMMs before discharge into the liquid or solid waste streams.

At all containment levels, at whatever scale of activity, material and waste contaminated with GMMs must be inactivated before discharge/waste disposal. The methods chosen (i.e. the level of kill) to achieve this will depend on the risk and the need to limit contact of GMMs with humans and the environment. All GMM waste must be inactivated by validated means according to guidance in the ACGM compendium and the ACDP manual. For more hazardous GMMs 100% kill must be achieved. This should normally involve the disposal of GMM waste through heat inactivation by autoclaving.

For lower hazard GMMs chemical disinfection may be acceptable. Inactivation by chemical disinfection would normally give at least 99.999% kill (i.e. a 5 log reduction in viability) and is suitable only by validated means. The manufacturer's guidelines are acceptable if they provide validation, otherwise this must be provided by the investigator. Thus, glassware, plastic pipettes, culture waste supernatant for example can be disinfected in a phenolic (e.g. Hycolin) a hypochlorite (e.g.Chloros) or a peroxygen compound (Virkon). Once disinfected, plastics can then be incinerated through the normal disposal route. If any live GMMs are present in the waste to be disposed of this must be justified by the risk assessment, particularly if viability is reduced by <99.999%. It is therefore recommended that all waste containing GMMs should be incinerated following any treatment process.

(i) For Activity Class 1 GMMs:

Autoclaving is the preferred method but chemical disinfection where this has been demonstrated to be effective, i.e. under optimal conditions for inactivation can be used. Spillages should be disinfected immediately. Spillages in machinery that could corrode should be treated with 70% ethanol or 60% isopropanol.

- Autoclave Load Testing

Autoclave runs used for waste management must be checked on each occasion by the use of recording strips, data logging, etc. and maintained so as to ensure effective functioning and data recording. There is a need to demonstrate reliable inactivation of GMM waste by validation. Although autoclaves undergo annual performance and safety checks, autoclave cycles may be inconsistent due to the diversity of loads placed within them. Autoclaves which have a load temperature probe and printout of cycle parameters effectively monitor the sterilisation process.

For those autoclaves which do not have these features, an **integrated indicator strip** provides assurance that the correct time and temperature conditions have been achieved. These strips are not dependent upon autoclaving parameters and can be used in all loads. Suitable strips are made by 3M - 3M Comply Thermalog Steam Chemical Integrator

For autoclaves with internal temperature probes - Test strips are not required but printed records of recorded cycle conditions should be retained.

For autoclaves without internal temperature probes - Best practice requires that no viable GMMs are released from containment regardless of the level of risk. The methods chosen for inactivation must be demonstrably effective, either through the adoption of well-accepted standard procedures or, if necessary, by experimental evidence.

The following approach is recommended for Class 1 GMM waste:

As a minimum, a test strip should be placed in the centre of the first GMM load each month (although it is recommended that a test strip be included in every load). This strip should be stored in the records for the autoclave e.g. stapled to a dated record sheet and retained by the autoclave. If the test fails, the cycle must be repeated with a fresh strip.

4.5. ACQUISITION AND STORAGE OF GMOS

All GMOs stored in the CBE Laboratory Unit must be registered with the BHGMSC. This is achieved partly through acceptance of the risk assessment by the committee; however each group is required to provide an inventory of GMOs currently being stored. This inventory must be kept up to date as audits will be performed and a central database maintained by the BHGMSC.

Stored GMOs must be clearly identifiable with the GMO name, classification (risk assessment number), date of storage and the name of the research group. The primary and secondary containment vessels containing the GMOs should also be labelled. The storage system (fridge /freezer etc) should also be identified as containing GMOs if deemed necessary.

4.6. MANAGEMENT RESPONSIBILITY, SUPERVISION AND OTHER DUTIES

4.6.1. Head of Group

The Head of Group is responsible for the safe management of work with genetically modified organisms in accordance with the University Biological Safety Policy.

The duties of the Head of Group for ensuring the safe management of GM work are the same as those for all other aspects of biological safety management within the CBE Laboratory Unit. The Head of Group should sign all GM project notification forms to authorise work on a project to proceed within the unit. The Head of Group must appoint one or more local Genetic Modification Safety Advisors (BGMSA) to assist in discharging these duties.

4.6.2. Principal Investigator

The Head of Group normally delegates the duty to ensure safe working on GM projects to research group leaders and/or other senior staff appropriate to the local departmental arrangements. These management duties include assessment of risk, notification of all work with genetically modified organisms, and ensuring the implementation of the risk control measures required by their assessments. It is the duty of the person supervising the work to ensure that all staff students and visitors are informed of any precautionary measures they must observe.

This delegated duty is the normal pattern for the supervision of work. If the project leader is absent from the CBE they should delegate the day to-day management of the project to a named member of the team who is suitably skilled and experienced to carry out the necessary management duties.

4.6.3. Staff and students

Staff and students engaged on a GM project must observe the risk control measures required as a result of the risk assessment, and take due care for their own safety and that of others. This duty applies to occupational visitors to the laboratory.

These duties are in accordance with, and do not exceed, the duties imposed on employees under the Health and Safety at Work Act 1974. Graduate students are treated for the purposes of this CoP as if they were employees. Visitors to the laboratory who are undertaking work should be treated as if they were employees.

4.6.4. Local (CBE) Genetic Modification Safety Officer.

The local BGMSA is nominated by the Head of Group and advises the HoG in all matters relating to the CBE's genetic modification activities. Where appropriate (e.g. the department exists on more than one site, or where the BGMSA is also involved in a GM project) it may be necessary to appoint one or more deputies. The BGMSA is the main point of contact for CBE on matters relating to the safety use of GMOs.

Advice on specific projects should be sought from the local BGMSA in the first instance. (See also "Record keeping".)

4.6.5. Visitors.

Visitors engaged on the work of a GM project must observe the risk control measures required as a result of the risk assessment, and take due care for their own safety and that of others.

Visitors are defined non-CBE employees, including contractors, maintenance workers, cleaners, etc. (though they might be LU employees) who may be permitted entry to the CBE Laboratory Unit. Contractors and maintenance staff should be provided with relevant safety information including the precautions necessary to ensure their safety while on site. If the visitors are involved in collaborative work, they must be treated as CBE staff. If they are viewing the laboratory or observing work in progress but not participating, they must be provided with personal protective equipment as defined by this code of practice and supervised at all times.

4.7. TRAINING, INFORMATION AND CONSULTATION

All staff and students working with GMOs in the CBE should receive information relevant to the biological materials and systems and are provided with instruction on the use of equipment and the laboratory techniques required for the GM work.

New staff and students should receive such instruction and information as is necessary for them to work safely. This Code of Practice has been prepared to facilitate this; covering the safe use of GM materials.

The findings documented in the risk assessment must be communicated to all who will be affected by the work including visitors and others, where necessary, who may not be directly participating in the work.

A large proportion of the GM work at CBE involves human cells or micro-organisms and therefore this section should be read in conjunction with the safe working procedures for work with cells and micro-organisms detailed in other sections of this CoP.

Where the risk from the GM work is low, as it is in the majority, if not all, of CBE projects, there may be sufficient information in the current Code of Practice to ensure that workers are adequately informed of the precautions they must take.

When introducing new materials and techniques, staff (who may not be directly involved in the work) must be consulted and informed of any implications for their health and safety.

The aim of consultation is to provide information to others who, while they may have no stake in the project, might nevertheless be adversely affected by the work. Matters for consideration include not only health, safety and environmental issues but also the possibility of conflicting or hazardous interactions between the GM project and other biological materials or research projects.

Consultation does not imply veto. However, it is necessary to ensure that all relevant information is gathered for risk assessment purposes. Consultation may involve, for example, the CBE Laboratory Management Committee or other formal staff/student consultative process.

Formal training should be provided to all staff, students and visitors working in the CBE Containment Level 2 Laboratory Unit if identified as necessary. Written records of this training must be kept covering the individual workers and the topics covered in their training.

It is the duty of the supervisor of the laboratory and the principal investigators as fits the circumstances, to devise and implement a training programme for laboratory workers. This should cover good microbiological practice, the workplace hazards and the issues included in the laboratory code of practice. It is not sufficient merely to provide this CoP and leave the worker to read it. At this hazard level, the supervisor should be able to provide evidence of active endorsement and support for safe operating procedures.

4.8. RECORD KEEPING

The person undertaking the activity involving GMOs must keep a record of the risk assessment relating to the activity, and any review and revision of that assessment, for at least 10 years from the date of the cessation of that activity.

The records should cover the identification and location of long-term storage of GMOs. A record of testing and maintenance of equipment provided for safety should also be retained. For Activity Class 1 & 2 projects, the records should include training records.

In practice, the act of undertaking a risk assessment and/or the generation of GM notification forms will generate a sufficient record of the GMO activities within the CBE. This record should be sufficient to:

- allow the persons involved in the activity to check and review the risk assessment as necessary
- provide inspectors an historical audit of activities within the CBE

This information may also be useful to the PI when moving to another organisation. On leaving the CBE, the PI should pass the information to the local BGMSA who may wish to archive it as a CBE record. Under both current and previous regulations, organisations are required to keep GM records for *at least* 10 years.

The local BGMSA should keep records of all CBE projects currently active, including those where GMOs are stored even if no work is at present being undertaken.

The BGMSA should retain records of past GM work when PIs leave the CBE. The BGMSA may keep records of the maintenance and testing of equipment where these records are not held elsewhere in the CBE.

These records may include records of maintenance of equipment provided for safety such as biological safety cabinets, autoclaves and ventilation systems if such records are not kept elsewhere. They may be kept by the Department Safety Officer or by the Laboratory Manager. Such record-keeping need not be duplicated unless this suits the needs of the CBE but records must be available for inspection either by University HS&E Department or by the HSE.

The local BGMSA is *not* responsible for maintaining the records which form part of the supervisor's management of the project but they should take charge, on behalf of the CBE, of records which might otherwise be lost when a PI moves out of the CBE. Of the active projects in the CBE, the BGMSA needs only to keep a summary sufficient to identify the project. It will normally be sufficient to note the title (and project number), supervisor and location of the GM work and its current status (e.g. active, in suspension, completed). These records should be a history of CBE's GM work and are needed for monitoring standards of safety management and statutory compliance. The keeping of records is an important aspect of satisfactory management control.

4.9. INSPECTIONS OF LABORATORIES AND MANAGEMENT PROCEDURES

The University HS&E Department shall undertake periodic inspections of CBE laboratories undertaking GM work to monitor compliance with statutory and organisational requirements and report to the BHGMSC.

The inspections examine laboratory facilities, CBE management systems including records, laboratory procedures for safe working and the supervision of work. It is unlikely that inspections by University HS&E Department will cover subject matter outside of this CoP unless unusual circumstances prevail such as a requirement to alter working practice as a result of incidents or new information received.

4.10. REPORTING OF ACCIDENTS AND INCIDENTS

In accordance with existing LU procedures, any occurrence of spillage, contamination with GMOs or release from containment in such a way as to cause harm, or giving the potential for significant harm to health or damage to the environment must be reported to the University BSO and University HS&E Department without delay.

For the purpose of the guidance in this section, the definition of an accident is taken from regulation 2 of the Contained Use Regulations: "*'accident' means an incident involving a significant and*

unintended release of genetically modified organisms in the course of an activity involving genetic modification which presents an immediate or delayed hazard to human health or to the environment." NOTE: The "unintended release" can be within the laboratory/laboratory unit/facility.

Minor spillages within the CBE Containment Level 2 Laboratory Unit of GMMs being used in Class 1 activities are unlikely to count as significant releases (an exception being a major release of Class 1 GMMs from large scale work). See Section 6 for further details.

4.10.1. Notification of Accidents and Incidents Involving Genetic Modification Activities to the Health and Safety Executive

There is a requirement under the Genetically Modified Organisms (Contained Use) Regulations, as amended 2005, to immediately notify the Health and Safety Executive of any accident or incident involving a significant or unintended release of a GMO that presents an immediate or delayed hazard to either human health and safety or the environment. This requirement is in addition to any notification requirements under RIDDOR (the Reporting of Injuries, Diseases and Dangerous Occurrences Regulations 1995).

It is the responsibility of the University HS&E Department to make notifications to the Health and Safety Executive of any accidents or incidents occurring within the University that require to be notified either under the Contained Use Regulations or RIDDOR. The CBE should not make any such notifications; instead they should contact the University HS&E Department as detailed below.

The CBE should immediately inform, preferably by telephone, the University HS&E Department and the Occupational Health Unit in the event of any accident or incident involving the spillage or release of any genetically modified organisms or micro-organisms or where exposure to a genetically modified micro-organism may have occurred. A full accident record should be prepared and forwarded to the HS&E Department as soon as possible.

The University HS&E Department will decide whether any accident or incident requires notification to HSE, be it under the Contained Use Regulations or RIDDOR. Guidance on notification of accidents involving genetic modification activities is available on HSEs website at http://www.hse.gov.uk/dst/acgm32/paper4.htm), which includes information on which accidents are likely to require notification, what information is required and what happens to the information when a notification is made.

Following notification of an accident under the Contained Use Regulations, it is very likely that one of the Health and Safety Executive's Specialist GM Inspectors will visit to investigate the circumstances of the accident and to confirm that appropriate measures have been taken to ensure there is no recurrence.

4.11. REVIEW OF RISK ASSESSMENTS & NOTIFICATION OF ALTERATIONS

Under the Contained Use Regulations, it is necessary to review the risk assessment where there is reason to suspect that the original assessment is no longer valid or where there has been a significant change in the activity to which the assessment relates.

Minor changes to projects should be brought to the attention of the BGMSA and recorded with the risk assessment/notification for the project. The BGMSA should decide whether these changes should be notified to University HS&E Department (ie BHGMSC).

Minor changes are those which do not alter the level of risk. These can include changes in personnel and relocation to a different laboratory within the GM Centre registration provided that the containment level is the same. Changes in insert, vector and host may also be minor but these must be accompanied by a statement of justification as to why the level of risk is considered to be equal or less.

Significant changes to projects must be notified in advance to the BHGMSC using the existing notification procedure.

A significant change is one where the level of risk has increased (or possibly reduced) and might include: change of scale of operations, change in containment conditions used, change of waste treatment procedures, new data on the behaviour of an organism or relocation to a different building or a different GM centre. Such changes may require alterations to a notification to the HSE.

At the discretion of the BHGMSC and in accordance with a schedule agreed by the Committee, PIs will be asked to revise the risk assessment of existing projects by resubmission of a notification.

If the CBE has active projects dating back many years which were originally submitted on earlier and much less developed notification forms. Over time and in accordance with best practice and legislative requirements, the notification procedure has become more sophisticated. In addition, projects tend to accumulate a number of minor changes and may even change direction. Thus, earlier notifications may bear little resemblance to the current work. It is good safety practice to review risk assessments at suitable intervals and the current notification procedure gives a mechanism for doing this without imposing additional burdens. Resubmissions can retain the original notification number or, if preferred can consolidate existing work under a new GM reference number. Titles can be altered as necessary. It is essential, however, to declare any superseded project as completed so that it can be removed from the register of current projects.

4.12. CARTAGENA PROTOCOL AND EXPORT OF GMOs OR GMMs

It is necessary when exporting GMOs to provide certain information with the materials. This is required by various European Community legislation, for example that on safe handling and transport, and for some exports a requirement of an EC Regulation on transboundary movements (1946/2003) implementing aspects of the Cartagena Protocol on Biosafety to the Convention on Biological Diversity. The EC Regulation is directly applicable in Member States and does not require to be transposed into national legislation. The various provisions apply to export both within and out with the EC and are in addition to any standards and requirements of the country of import which also must be met.

When exporting GMOs for contained use it is necessary to ensure the GMOs are transported safely. The GMOs must be classified, packaged and labelled in accordance with the applicable transport regulations. Guidance on the requirements for the transport of GMOs and biological materials that may contain GMOs is provided in Section 7.

Table 3: Containment Measures for Activities involving Genetic Modification of Micro-Organisms in Laboratories

[Source: abstracted from A Guide to the Genetically Modified Organisms (Contained Use) Regulations 2000, as amended 2005]

Containment measures	Containment level 1		Containment level 2		Containment level 3	
1. Laboratory suite – isolation	Not required		Not required		Required	
2. Laboratory - sealable for fumigation	Not required		Not required		Required	
Equipment						
3. Impervious/easy to clean surfaces	Required for bench		Required for bench		Required for bench and floor	
4. Entry to lab via air lock	Not required		Not required		Required where and to the extent the risk assessment shows it is required	
5. Negative pressure relative to the pressure of the immediate surroundings	Not required		Required where and to the extent the risk assessment shows it is required		Required	
6. Extract and input air in laboratory should be HEPA filtered	Not required		Not required		HEPA filters required for extract air	
7. Use of microbiological safety cabinet/enclosure	Not required		Required where and to the extent the risk assessment shows it is required		Required and all procedures with infective materials required to be contained within cabinet/enclosure	
8. Autoclave	Required on site		Required in the building		Required in the laboratory suite	
System of work						
9. Access restricted to authorised personnel only	Not required		Required		Required	
10. Specific measures to control aerosol dissemination	Not required		Required so as to minimise		Required so as to prevent	
11. Shower	Not required		Not required		Required where and to the extent the risk assessment shows it is required	
12. Protective clothing	Suitable protective clothing required		Suitable protective clothing required		Suitable protective clothing required; Footwear required where and to the extent the risk assessment shows it is required	
13. Gloves	Not required		Required where and to the extent the risk assessment shows it is		Required	

			required			
14. Efficient control of disease vectors (e.g. for rodents and insects) which could disseminate GMMs	Required where and to the extent the risk assessment shows it is required		Required		Required	
15. Specified disinfection procedures in place	Required where and to the extent the risk assessment shows it is required		Required		Required	
	Containment level 1		**Containment level 2**		**Containment level 3**	
Waste						
16. Inactivation of GMMs in effluent from hand wash sinks and showers and similar effluents	Not required		Not required		Required where and to the extent the risk assessment shows it is required	
17. Inactivation of GMMs in contaminated material and waste	Required by validated means		Required by validated means		Required by validated means with waste inactivated in lab. suite	
Other measures						
18. Laboratory to contain own equipment	Not required		Not required		Required, so far as is reasonably practicable	
19. An observation window or alternative to be present so that occupants of lab can be seen	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	
20. Safe storage/transport of GMMs	Required where and to the extent the risk assessment shows it is required		Required		Required	
21. Written records of staff training	Not required		Required where and to the extent the risk assessment shows it is required		Required	

Table 4: Containment Measures for Large Scale Activities involving Genetic Modification of Micro-Organisms in Laboratories

[Source: abstracted from A Guide to the Genetically Modified Organisms (Contained Use) Regulations 2000, as amended 2005]

Containment measures	Containment level 1		Containment level 2		Containment level 3	
General						
1. Viable micro-organisms should be contained in a system which separates the process from the workplace and wider environment (closed system)	Required where and to the extent the risk assessment shows it is required		Required		Required	
2. Closed systems located within a controlled area	Not required		Required where and to the extent the risk assessment shows it is required		Required	
3. Control of exhaust gases from the closed system	Not required		Required so as to minimise release		Required so as to prevent release	
4. 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		Required so as to minimise release		Required so as to prevent release	
5. Inactivation of bulk culture fluids before removal from the closed system	Required where and to the extent the risk assessment shows it is required		Required by validated means		Required by validated means	
6. 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	
7. 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		Required where and to the extent the risk assessment shows it is required		Required	
8. Controlled area sealable to permit fumigation	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	
9. Biohazard signs posted	Required where and to the extent the risk assessment shows it is required		Required		Required	
Equipment						
10. Entry via airlock	Not required		Not required		Required where and to the extent the risk assessment shows it is required	
11. Surfaces resistant to water, acids, alkalis, solvents, disinfectants,	Required for any bench		Required for any bench		Required for bench and floor	

decontamination agents and easy to clean						
12. 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		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	
13. Controlled area maintained at an air pressure negative to the immediate surroundings	Not required		Not required		Required where and to the extent the risk assessment shows it is required	
14. Extract and input air from the controlled area should be HEPA filtered	Not required		Not required		Required where and to the extent the risk assessment shows it is required	
System of work						
15. Access restricted to nominated personnel only	Not required		Required		Required	
16. Decontamination and washing facilities provided for personnel	Required		Required		Required	
17. 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	
18. Personnel should wear protective clothing	Work clothing required		Work clothing required		Required	
19. Written procedures and records of staff training	Not required		Not required		Required	
Waste						
20. Inactivation of GMMs in contaminated material and waste including those in process effluent before final discharge	Required by validated means		Required by validated means		Required by validated means	
21. Inactivation of GMMs 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	

SECTION 5 DISINFECTION & WASTE DISPOSAL PROCEDURES

Under COSHH, specified disinfection procedures are required for work at Containment Level 2. Specified procedures should also be in place for work with Class 1 GMOs in the CBE Laboratory Unit. Disinfection protocols are required for both routine use and for use in the event of spillage or biological material. The following section lays down the general principles and standards for disinfection procedures and the treatment of biological waste within the CBE Laboratory Unit. The guidance in this Code of Practice should be used to prepare local SOPs that reflect local circumstances whilst ensuring that the standards and principles detailed below are met.

Workers within the CBE Laboratory Unit must follow the local policy or SOP and new disinfectants should not be introduced without first consulting the BGMSA. Guidance on the selection and use of disinfectants is given below and supplemented with details of recommended disinfectants given in Annex 9.

5.1. DISINFECTION

Disinfection is used to reduce the number of micro-organisms present to an acceptable level such that the item being disinfected is safe to handle. Disinfection should not be confused with sterilisation, a process that renders an object free from all viable organisms. Both disinfection and sterilisation are methods of decontamination as this is the general term used to reduce microbial contamination to render an item "safe". Cleaning may also be regarded as a decontamination method as it too can remove micro-organisms from a soiled surface. Prior to a choice being made as to whether cleaning, disinfection or sterilisation is required, a risk assessment should be undertaken to determine the level of decontamination necessary for an item.

There are several types of chemical and physical agents that can be used for disinfection; these include chemicals, heat and irradiation. The CBE Laboratory Unit, when handling material that may contain BAs or GMOs, should routinely use chemical disinfection to decontaminate surfaces and equipment, and prevent microbial growth in spent culture fluids etc. A chemical disinfectant should be chosen based on the situation to which it is going to be applied. Before a disinfectant is chosen, or if there is a subsequent change in usage, it should be confirmed that the particular disinfectant is suitable for the intended purpose. It should never be assumed that the disinfectant is active in a particular application without checking i.e. some disinfectants may just prevent growth of bacteria (bacteriostatic) rather than kill them (bactericidal).

Wherever possible the use of disinfectants should be consistent throughout the CBE Laboratory Unit rather than varying between laboratories within the unit although different types of work may need particular types of disinfectant. If possible, the number of different disinfectants used in a laboratory should be reduced to a minimum to avoid mistakes in application. Adequate information and instructions must be given to all workers to ensure they know what disinfectant to use and how to use it.

5.1.1. Factors Affecting the Choice of Disinfectant

(i) The Micro-organism

Disinfectants vary in the spectrum of organisms they can inactivate or kill and do not disinfect against all organisms equally well (Table 5). Disinfectants do not normally kill bacterial spores. A disinfectant which is effective against bacteria may not be as effective against viruses. Some disinfectants are more effective against Gram positive than against Gram negative bacteria. Some disinfectants have a wide spectrum of performance against many organisms.

There are many different proprietary products available and these will vary in how effective they are against different micro-organisms (see Annex 9). Manufacturers of disinfectants should provide advice on the specific antimicrobial activity of their particular products. If the types of micro-organisms in samples or materials handled are unknown then a general purpose disinfectant should be chosen.

(ii) The circumstances of use.

The presence of other materials in or on the surfaces to be disinfected can have an effect on the activity of the disinfectant. The presence of organic material, other chemical agents including soaps and detergents and the pH and temperature can all reduce the effectiveness of the disinfectant.

The concentration of disinfection to be used is likely to vary depending on whether it is used in "dirty" or "clean" conditions, used routinely or in the event of accidents, etc. The disinfection policy/SOP should clearly indicate suitable concentrations for the different applications.

(iii) Surface integrity

Some disinfectants will chemically attack items being disinfected. Disinfectants containing acids, alkalis, electrolytes and hypochlorites can adversely affect metal parts and cause corrosion. Disinfectants containing organic solvents can damage plastic. Manufacturers should provide advice on the suitability of using their products on particular surfaces or materials.

(iv) Hazardous properties of the disinfectant

The potential formation of hazardous/toxic products, either in use or as a result of mixing with other disinfectants must be considered. Most disinfectants have toxic properties and some are also highly corrosive, causing damage if they come into contact with skin or eyes. Some disinfectants e.g. glutaraldehyde and hypochlorites may also have irritant properties and so cause respiratory problems if used in poorly ventilated areas. Some disinfectants may react with other chemicals causing hazardous gases.

Under the requirements of COSHH regulations a risk assessment must be made for the safe handling of disinfectants. Precautions should be given for handling both concentrated disinfectants and in-use diluted solutions. When handling concentrated disinfectants care should be taken to avoid splashing, and goggles or a full-face visor and gloves should be worn. A safety data sheet should be provided by the manufacturer. Any instance of suspected sensitisation must be reported immediately using the University accident reporting system and medical advice must be sought from the Occupational Health Advisor.

5.1.2. Use of Disinfectants

Chemical disinfectants reduce the number of viable micro-organisms to a level below which infectivity is destroyed and the disinfected object rendered safe to handle. Disinfection is not an alternative to sterilisation, but chemical disinfection may, where appropriate, be followed by autoclave treatment or by incineration. Effective disinfection is dependent upon the following; Activity, Length of contact and Concentration

(i) Activity - Stability of Working Solutions

A supply of disinfectants effective against the BAs/GMOs used in the CBE Laboratory Unit must be available for decontamination purposes.

Disinfectants are usually provided in concentrated form and have to be diluted in water to the working strength for use. The manufacturers' instructions should be followed to ensure that the

required concentrations are achieved. Over dilution will render the disinfectant ineffective. Once made up the disinfecting capacity of diluted products tends to deteriorate rapidly with time. The manufacturers should recommend how long the 'made up' solution can be stored for and this should be noted in the disinfection policy or procedure.

Some products contain coloured indicators to show effective disinfecting capacity. If the disinfectant in use does not contain an indicator then a "use by" or expiry date should be clearly marked on the bottle when the solution is made up. Solutions must not be used after the date of expiry.

(ii) Contact time

The manufacturers' data should be checked to ensure that the micro-organism remains in contact for the recommended time. Be aware that disinfectants will not easily penetrate solid material such as tissue and cell pellets; therefore autoclaving may be a better means of inactivation. Chemical disinfectants need to be applied to the item they are disinfecting for sufficient time to enable the disinfection to be effective. Manufacturers should recommend contact times (in combination with concentrations) for various applications and this should be clearly stated in the disinfection policy or procedure. Objects should be fully immersed and air pockets should not be present. Disinfectants should always be used in accordance with the manufacturer's instructions.

(iii) Concentration - Validation of Activity

Where little or no relevant efficacy data is available, (e.g. when working with high titres or with significant quantities of organic material), the effectiveness of disinfectants for use with specific biological agents or GMMs should be determined experimentally to identify the optimal combination of disinfectant concentration and contact time.

For Hazard Group 1 and 2 BAs (and Class 1 GMOs) it will normally be sufficient to rely on the manufacturer's data, providing the recommended concentrations and contact times are used. Disinfection is not as effective as steam sterilisation in destroying viable organisms, nor is it easily monitored. Disinfection is a suitable means of inactivation for the following:

- Reusable items that are heat sensitive
- Liquid wastes and effluents other than cultures containing Hazard Group 2 BAs/GMOs
- Liquid cultures of, and equipment used in association with Hazard Group 1 organisms
- At the end of the work, for decontamination of surfaces and equipment that cannot be autoclaved

5.1.3. Selection of Disinfectant

All disinfectants are by their nature hazardous to human health although the extent varies considerably. Some disinfectants, such as formaldehyde and glutaraldehyde, have irritant and toxic properties, are extremely hazardous and carry a risk of respiratory and/or skin sensitisation reactions. These types of chemical disinfectants must not be used as a general disinfectant in the CBE Laboratory Unit and should be employed only for specialised uses when no suitable alternative is available and subject to a strict COSHH risk assessment.

Before choosing a disinfectant it is important to refer to the manufacturers' data to ensure that the disinfectant will be effective against the organism(s) in question and to determine the recommended concentrations and contact times. Bear in mind when choosing a disinfectant that the **aim is to reduce the titre by at least 5 logs** (a 5-log reduction will theoretically reduce the microbial population from 1 to 0.00001. This provides a 'Sterility Assurance Level' of 10^{-5} or a one in 100,000 probability of a single surviving micro-organism). Also note that large amounts of protein can interfere with chemical inactivation

5.1.4. Information on Specific Types of Disinfectants.

The following types of disinfectants are recommended for use in the CBE Laboratory Unit. Key points to be taken into account when selecting the disinfectant are given. Manufacturers' instructions should be consulted for suitable concentration and contact times. COSHH risk assessments should provide clear guidance on handling precautions needed, particularly when using concentrates. Guidance on the use of other chemical disinfectants is given in Annex 9.

5.1.4.1. Virkon (Peroxygen compound)

Virkon is a commercial disinfectant consisting of a balanced, stabilised blend of peroxygen compounds, surfactant, organic acids and an inorganic buffer system. It has been shown to be effective against a greater range of micro-organisms than Trigene for example. Virkon has a wide range of bactericidal, virucidal, fungicidal and sporocidal activities. For details about Virkon and its applications go to http://www2.dupont.com/RelyOn/en_US/tech_info/europe_techinfo.html. Efficacy data for bacteria, virus, fungi etc can then be viewed via a hyperlink.

Characteristics of Virkon

- Wide range of bactericidal, viricidal and fungicidal activity
- Variable activity against bacterial spores and Mycobacterium spp.
- Corrosivity varies with different products, but less so than hypochlorites
- Made up dilutions have very low toxicity and no irritancy (powders are irritants)
- Built-in colour indicator
- Good detergent properties combines cleaning with disinfection
- Stable for seven days on dilution

Due to its wide spectrum of activity (and evidence base), suitability for use in most applications, the pink indicator to show disinfectant capacity and the high degree of safety to users, Virkon is recommended as the disinfectant of choice for most applications in the CBE Laboratory Unit.

Table 5. Working concentrations of Virkon

	Concentration/instructions	Contact time
Hard surfaces, benches, floors etc. **Safety cabinets**	A solution containing 1% Virkon Metal parts ** 1% Virkon, followed by 70% alcohol	1 hour 10 minutes** 10 minutes
Reusable Plastic or glass vessels	A solution containing 1% Virkon. Rinsed, dried and autoclaved for reuse. Ensure all surfaces are in contact with the disinfectant.	1 hour
Supernatants: Discard, spent media	Aspirated into Presept, minimum of 2500 ppm effective concentration of hypochlorides. Autoclaved before disposal down sink	1 hour
Spillages:	Virkon powder directly onto spill, Scrape mixture into yellow bag for incineration. Swab area with 1% solution	Until liquid absorbed
Skin spillages:	A solution containing 1% Virkon, then rinse well with water.	
Contaminated clothing	Where autoclaving is not possible/appropriate soak in 1% Virkon. [Test small area for colour fastness]	1 hour

i. Contact Times for Virkon Solution Use

A minimum contact time of 10 minutes is recommended by the manufacturer (Fisher Scientific Ltd) for complete disinfection of virus, yeasts and bacteria with Virkon. Virkon has a built-in colour indicator for effective disinfection capacity and contains detergent properties that combine cleaning with disinfection. **Note:** Virkon is stable for 7 days in solution.

**When Virkon comes into contact with protein, chlorine is produced which will cause corrosion of metals. Prolonged exposure of metal can also cause corrosion and therefore metal parts (e.g. centrifuge parts and internal surfaces of BSCs) must not be exposed in excess of 10 minutes.

ii. Precautions in use

Dilute solutions (i.e. 1% Virkon) have low toxicity and no irritancy; however the powdered form is a moderate irritant to eyes and respiratory tract. Inhalation of powder or contact with skin/eyes should be avoided. Virkon is available in tablet and sachet form, thus reducing risk of contact with powder.

5.1.4.2. Alcohols (Ethanol, Industrial Methylated Spirits)

70% Ethanol and 60% iso-propanol have relatively poor efficiency and are susceptible to interference. They can be used as a surface disinfectant for metal parts and surfaces where the use of Virkon may not be possible (e.g. centrifuge parts and internal surfaces of BSCs). Care should be exercised when spraying items with alcohol, as there is a flammability hazard.

Characteristics of Alcohols e.g. Ethanol, Isopropanol, Methanol, Industrial Methylated Spirits (IMS)

- Good bacterial and fungicidal activity
- No activity against spores
- Variable activity against viruses (ethanol less effective against non- enveloped viruses, propanol not effective against viruses)
- Only recommended for limited use (such as on clean surfaces and for flaming forceps etc) - seek alternative wherever possible
- Poor penetration into tissues
- Should only be used on physically clean surfaces as poor penetration of organic matter
- Rapid action
- Alcohols must be diluted to 70-80% before use (100% alcohol is not an effective disinfectant)
- Highly flammable
- Effective against Mycobacterium spp

5.2. DECONTAMINATION AND DISPOSAL OF WASTE

The proper, safe disposal of waste is an important aspect of safeguarding the health and safety of employees and others. This waste is categorised in law and is also subject to legislation relating to transport of hazardous material. The generation and disposal of biological waste are also subject to risk assessment under the COSHH and Contained Use Regulations. Landfill Regulations ban the consignment of infectious clinical waste to landfill.

Procedures for the segregation, decontamination and disposal of clinical/biological waste are designed so as to prevent exposure of staff, the public and the environment to hazardous or potentially hazardous substances in the waste. The pre-treatment, labelling, packaging and disposal of the waste is determined by both the type of the waste (e.g. liquid, solid etc.) and its

composition (eg the likely contaminants). Certain wastes arising from biological laboratories require specialist disposal as healthcare waste because they contain infectious micro-organisms. Some of the wastes may also have components that are regarded as unacceptable to be placed in the general waste stream and these, even if they are rendered non-infectious by some sort of pre-treatment, must always be disposed of as healthcare waste.

Each Head of Group (HoG) is responsible for the management of waste arising in areas under their control. They must ensure all biological wastes produced within the CBE Laboratory Unit are disposed of in accordance with this Code of Practice by incorporating the requirements into clear documented local rules and procedures. There should be documented SOPs or protocols incorporating risk assessment of the biological agents likely to be present in the wastes together with (a) their concentrations, (b) the types and quantities of waste, (c) the treatment and disposal options. SOPs should identify each treatment option and operating parameters or conditions known to kill the agents that may be present under laboratory conditions. Guidance on preparing SOPs for waste treatment is given in “The management, design and operation of microbiological containment laboratories”, ACDP.

Workers must follow the local rules and procedures. Each worker in the CBE has a duty of care, imposed under the Environmental Protection Act, to ensure that waste is managed properly and disposed of safely and in accordance with legal requirements. Each Head of Group must ensure adequate instruction, equipment, training and supervision is provided to enable all workers to observe the duty of care.

5.2.1. Healthcare Waste (historically known as Clinical Waste)

Is defined under the “Healthcare Waste Technical Memorandum (HTM07-01): Safe Management of Healthcare Waste", produced by the Department of Health as waste from natal care, diagnosis, treatment or prevention of disease in humans or animals. This definition also covers wastes produced in non-healthcare environments such as university research and teaching laboratories, including biological waste produced in containment level 1 and 2 laboratories, and including waste from Genetic Modification (GM) following autoclaving by a validated means. Examples include: infectious waste, laboratory cultures, anatomical waste, sharps waste, medicinal waste, laboratory chemicals and offensive / hygiene wastes.

Healthcare Waste that can be classified within the infectious or medicinal waste streams according to the following definitions:

5.2.1.1. Infectious waste

The Hazardous Waste Regulations define infectious as: “*H9: Infectious Substances containing viable micro organisms or their toxins which are known or reliably believed to cause disease in man or other living organisms”.* Waste traditionally known as “clinical waste” on the basis of infection risk is infectious waste, which is known or reasonably suspected to contain pathogens (wild type, cultures or GM) capable of causing infection or disease in humans, animals or plants. WM2 (Reference 18) provides UK guidance on the interpretation and risk-based identification of infectious waste.

According to "Health Technical Memorandum 07-01: Safe Management of Healthcare Waste", infectious substances are classified for transport as Category A or Category B:

- Category A – an infectious substance which is transported in a form that, when exposure to it occurs, is capable of causing permanent disability, life-threatening or fatal disease in humans or animals;
- Category B – an infectious substance which does not meet the criteria for inclusion in Category A.

This classification means that the infectious component of laboratory waste is considered as either Category A or Category B, which determines the requirements for colour-coded segregation, packaging, transport, treatment and disposal.

NOTE: No Category A waste will be produced from the CBE premises. All infectious waste produced from the Laboratory Unit will be classified as Category B.

NOTE: While the majority of waste produced by the CBE Containment Level 2 Laboratory Unit will present little risk to man or the environment e.g. those classified as Hazard Group 1, for practical purposes it will not routinely be segregated from infectious waste (i.e. Hazard Group 2) and hence the entire waste stream (that is, where it includes any quantity of infectious waste) will need to be classified as infectious waste and consigned for appropriate in situ treatment and disposal by incineration.

(i) Microbiological cultures

According to the ADR, the definition of cultures is *"Cultures (laboratory stocks) are the result of a process by which pathogens are intentionally propagated. This definition does not include human or animal patient specimens."* Cultures will include HG2, HG3 or HG4 pathogens as well as Class 2, Class 3 or Class 4 GMMs, whether in liquid (for example broth) or solid form (for example agar plate), or whether initiated from a laboratory stock or patient specimen.

Cultures are associated with high concentrations of micro organisms and a consequent increased risk of infection. This is particularly pertinent when the cultures are treated as waste, since – unlike culture samples, which will be used for further investigative purposes in an appropriate laboratory environment – waste cultures are intended for disposal and discard.

While the HG2 organisms used in CBE are not expected to be on this indicative list, it is important to consider the Category A criteria (that is, form of the cultures – for example their concentration, routes of transmission of the organism, host range, survivability in the environment, the quantity of cultures in any one consignment) before classifying HG2 organisms as Category B waste. Best practice dictates that all cultures of HG2 pathogens be inactivated on-site prior to final disposal because of the increased risk of exposure associated with the higher concentration of biological agents therein.

(ii) Clinical specimens

Clinical specimens are defined (for transport) as *"Patient specimens are human or animal materials, collected directly from humans or animals, including but not limited to, excreta, secreta, blood and its components, tissue and tissue fluid, swabs, and bodily parts, being carried for purposes such as research, diagnosis, investigational activities, disease treatment and prevention."*

Occasionally clinical specimens may be handled in the CBE Laboratory Unit, but the bulk of these specimens will have a low probability of containing pathogens. When clinical specimens are discarded, they will form part of the laboratory waste stream and need to be managed appropriately. The infectivity associated with this waste type is highly variable and needs to be considered as part of a risk assessment.

(iii) Definition of Biological Agents

COSHH defines biological agents as any micro-organisms [virus, bacteria, fungi, yeast etc], cell culture or human endoparasite, which may cause infection, allergy or toxicity or otherwise create a hazard to human health, including any that have been genetically modified. A micro organism is defined as a microbiological entity, cellular or non-cellular, which is capable of replication or of transferring genetic material. Cell culture means the in-vitro growth of cells derived from multi-cellular organisms.

Under the Genetically Modified Organism (Contained Use) Regulations the term biological agent is not used and instead the definition of micro organism is extended to include cell cultures as follows; micro-organism means a microbiological entity, cellular or non-cellular, capable of replication or of transferring genetic material, and includes a virus, viroid, and an animal or plant cell in culture.

- Biological agents are classified into four Hazard Groups (HG's) by COSHH on the basis of their ability to infect healthy humans and the consequences of any infection. The classification scheme is illustrated in the following table, taken from Schedule 3 of the COSHH Regulations. The basic classification system is confined to the answers to the four key questions:

    - Is the agent pathogenic for humans
    - Is the agent a hazard to humans
    - Is the agent transmissible to the community, and
    - Is there effective treatment of prophylaxis available

- The ACDP are responsible for issuing categorisation of biological agents and publishes an Approved List of known pathogens. Amendments may be made to the list from time to time, and the Approved List on HSE's website should be consulted to ensure that the most up-to-date version is used. Only agents in Hazard Groups 2-4 appear on the Approved List. The Approved List is available at http://www.hse.gov.uk/pubns/misc208.pdf

- The categorisation gives an indication of the inherent hazard of the BA's listed, but does not consider the how the agent is used, the amount, titre used or procedures undertaken. Additional risks to individuals or groups that might have reduced or comprised immunity or are pregnant is also not considered, nor is the possible effects on the environment, e.g., on animal or plant life. This must be addressed in risk assessments before commencing work with these agents.

NOTE: *Only Hazard group 1, Hazard Group 2 biological agents and Class 1 GMOs are permissible for use in the CBE Containment Level 2 Laboratory Unit.*

Hazard Group 1 (HG1)	Unlikely to cause human disease. *E.g. Tissues & cell lines of non-primate/non human origin. Human/primate cell lines that are well characterised, authenticated, long established and have long history of safe use [e.g.MRC5, HeLa cells] Disabled/attenuated/non-pathogenic strains of some bacteria and virus.*
Hazard Group 2 (HG2)	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. *E.g. tissues and primary cell lines of human/primate origin. Adenovirus, clostridium, most strains of E.coli*
Hazard Group 3 (HG3)	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. *HIV, Hepatitis B, E. coli 0157, Salmonella typhi.*
Hazard Group 4 (HG4)	Causes severe human disease and may be a serious hazard to employees; it is likely to spread to the community, and there is no effective prophylaxis or treatment available. *E.g. Rabies, Ebola Virus. Use of such agents is not permitted in the University*

5.2.1.2. Medicinal waste

The EWC has entries for medicinal waste in Chapter 18 ("Healthcare Waste") and in Chapter 20 ("Municipal waste"). Medicinal waste is classified into two categories:

- Cytotoxic and cytostatic medicines;
- Medicines other than those classified as cytotoxic and cytostatic.

What is cytotoxic waste?

Only cytotoxic and cytostatic medicines are classified as a hazardous waste, although other medicines often possess hazardous properties and therefore require appropriate treatment and disposal.

Cytotoxic waste is any medicinal product or chemically contaminated biological waste that possesses one or more of the hazardous propertiesH6: Toxic; H7: Carcinogenic; H10: Toxic for reproduction; H11: Mutagenic. This may include drugs from a number of medicinal classes, for example anti-neoplastic agents, antivirals, immunosuppressants, a range of hormonal drugs or research-use non-therapeutic chemicals such as Mitomycin C, Ethidium Bromide etc.

5.2.2. European Waste Catalogue (EWC) Codes

All packaging of CBE Laboratory Unit Healthcare Waste shall be labelled with an appropriate European Waste Catalogue (EWC) code(s) before removal from the facility.

Absolute EWC entries for infectious waste (hazardous property H9) produced by the CBE Laboratory Unit are only found in Chapter 18 of the EWC (18 01 XX Waste from natal care, diagnosis, treatment or prevention of disease in humans and 18.02.XX Waste from research, diagnosis, treatment or prevention of disease involving animals). The relevant EWC code for infectious waste is 18 01 03* and/or 18 02.02*- 'Waste whose collection and disposal is subject to special requirements in order to prevent infection'.

Absolute EWC entries for medicinal waste (hazardous property H6, H7, H10 and/or H11) produced by the CBE Laboratory Unit are found in Chapter 18 of the EWC (as above). The relevant EWC code for medicinal waste is 18 01 08* and/or 18 02 07* - 'Cytotoxic and/or Cytostatic waste'.

5.2.3. Colour Coded Segregation

A colour-coded segregation system shall be used to identify and segregate waste on the basis of waste classification and suitability of treatment/disposal options. This shall identify the type of packaging and packaging colour required for each waste stream. The packaging shall meet the requirements of the Carriage Regulations (UN compliant) where appropriate.

5.2.4. Legislation

The Environmental Protection Act 1990 places a duty of care on the University (and CBE) to handle, treat, store and dispose of all hazardous waste produced. This is further supported by The Environmental Protection (Duty of Care) Regulations 1991.

The Duty applies to any person, who produces, imports, carries, keeps, treats or disposes of controlled waste or as a broker has control of such waste. All waste including Healthcare Waste must be controlled, so it must be secured safely on site. This will prevent the illegal deposit, disposal or treatment of any waste produced. Waste must also be prevented from escaping, i.e. preventing it from being stolen, blown away or leaking. Transfer of waste must be carried out by authorised persons. Different types of healthcare waste must be segregated to comply with

requirements of the Hazardous Waste Directive and prevent incompatible materials or substances from mixing.

The waste producer is responsible for the waste as soon as it is produced until its final disposal or inactivation (cradle to grave). In the case of Healthcare Waste the producer is the CBE Laboratory Unit and the final destination is incineration or alternative technology treatment.

This duty was further extended to segregation and disposal according to the appropriate waste streams determined in the Hazardous Waste Directive 2005. The specific disposal of Healthcare waste is described further by the Department of Health's Environment and Sustainability- Health Technical Memorandum (HTM) 07:01: Safe Management of Healthcare Waste. This document is used as a standard by the HSE for compliance and best practice.

This standard shall form an integral part of the overall waste management strategy of the CBE and shall apply to all healthcare wastes produced by the CBE.

5.2.5. Risk Assessment

The need for the type of treatment and disposal of waste required must be determined within the risk assessment for the work from where the waste will arise. The precise method of treatment and the means and route of disposal shall therefore be identified prior to the work commencing. The risk assessment should identify:

- The category of waste to be produced (EWC Code) and its waste stream segregation.
- Whether the waste can be disposed of either to drain or to the healthcare/clinical waste route without prior sterilisation
- Whether the waste must be sterilised on-site prior to disposal
- Whether the waste can be chemically disinfected prior to disposal
- Whether the waste cannot be rendered safe on-site and therefore must be transported and disposed of as infectious waste
- Whether the waste contains carcinogenic, mutagenic, toxic for reproduction or cytotoxic chemical substances
- The appropriate sighting of the autoclave to be used to sterilise the waste
- How to transport the waste prior to sterilisation, if applicable
- The appropriate final disposal treatment e.g. incineration or microwave treatment and landfill

NOTE: *The CBE policy is to always render waste non-infectious** before it leaves the Laboratory Unit. The procedure used must be known to be effective against the particular micro organisms present and be carried out in accordance with the local SOPs. The risk assessment should state clearly whether it is appropriate to autoclave or disinfect in order to ensure that "infectious" waste is "safe" at point of disposal.*

*** Make safe by reducing the numbers of micro-organisms to an acceptable level (unlikely to cause harm in the event of exposure).*

5.2.6. Segregation of Healthcare Waste

All healthcare waste must be clearly segregated at source in accordance with EWC Codes and whether or not it requires treatment prior to its disposal. This shall identify the appropriate waste stream or disposal route. Precautions must also be taken so as to avoid confusion with other laboratory items such as other empty packaging used for waste disposal. In order to ensure adequate segregation, the following aspects must be considered:

- Staff must be fully aware of the nature of the waste they are handling and with the procedures that must be followed

- Easily distinguishable containers must be provided in adequate quantities
- Sufficient space must be available within the CBE Laboratory Unit i.e. the sterilisation facility or waste collection points, so as to allow sufficient spatial separation from other areas or items
- Clearly demarcated and appropriate areas for the storage of waste must be provided
- A rapid throughput of waste at all stages of its disposal must be ensured
- Access to waste at all stages of its processing must be strictly controlled whether in the laboratory or at the waste collection point
- Clear signage and posters must also be used to inform staff and contractors of procedures

5.2.7. Principles for Treatment of Healthcare Waste Prior to Disposal

(i) In order to control the risks associated with handling and disposal of Healthcare Waste to the lowest levels practicable, any waste known, or reasonably suspected, to be contaminated with biological agents or GMOs **MUST** be rendered safe prior to its discharge i.e. must not leave the premises or control of the Laboratory Manager/Principal Investigator(s) without first being disinfected or sterilized to ensure that they present no harm to others or the environment. Hence, where practicable, all waste that has been in direct contact with the living cells or micro-organisms must be inactivated by validated means before pouring down drains or leaving the site for incineration. Inactivation may be achieved by autoclaving or disinfecting.

(ii) Autoclaving is the preferred means of inactivation for all waste generated in the Containment Level 2 CBE Laboratory Unit. It must be used for waste that cannot be effectively inactivated by disinfection. Such items might include: agar plates, cell/bacterial pellets, small tubes, plastic loops, pastettes, tips and gloves. Cycle times and temperatures will need to be determined for each autoclave and type of load. As a guide 121^0C for 15 minutes is an absolute minimum. This temperature must be achieved at the centre of the load and timing must begin when the entire load reaches the required temperature. Further information on the principles of effective steam sterilisation, safe operation and necessary maintenance and validation checks for autoclaves can be found in Annex 5. If the autoclave is not located in the designated laboratory, some means of identifying the source of the waste must be shown. This will depend on local policy but might include coded ties/tags or origin indicator tape.

(iii) The treatment of waste before disposal falls into three broad categories:

- No pre-treatment: waste of low risk can be disposed of without prior disinfection or sterilisation.
- Chemical disinfection: waste of intermediate risk can be chemically disinfected before disposal. Disinfection is defined as a reduction in the viable organisms present. The extent of this reduction will vary depend on the disinfectant, the target agent and the conditions of use
- Sterilisation: waste of higher risk must be sterilised by autoclaving before disposal. Sterilisation is defined as an 'effectively 100% kill' where less than 1 in 10^6 organisms survive

(iv) **The disposal of liquid waste requires special consideration:** Such waste can contain particularly high concentrations of any agent present, can be difficult to contain and, in the event of spillage, can pose a heightened likelihood of leading to a significant exposure. Therefore, if any liquids are sent out as Healthcare Waste they MUST be disinfected or sterilised as appropriate and must be packaged in such a way that a spillage or leakage cannot occur. In many instances where significant volumes of liquid cultures are produced it will be preferable to dispose of this waste to drain rather than to despatch as Healthcare

Waste. However any liquid waste known or suspected of being contaminated with any biological agents MUST be autoclaved or chemically disinfected by validated means before disposal to drain.

(v) **Special note on liquid waste disposal and disposal to drain in, on or from CBE properties to the street or storm water drains.** There are a number of substances which for a variety of reasons are considered to be too hazardous to be disposed of to drain. This is due to the risk of them getting into either sewers or watercourses and the potential impact of them on human or environmental health.

All substances which fall within either of the categories outlined below are therefore banned from disposal to drain in, on or from CBE properties and MUST be disposed of as Special Waste.

- **Any waste designated as Special Waste:** Any liquid waste which falls under the category of special (or hazardous) waste is automatically banned from disposal to drain. It must be determined at the point of completion of a COSHH assessment whether any waste falls within this category, through the use of the hazardous assessment methodology provided in Annex II.

- **Substances or conditions requiring trade effluent consent:** In addition, there is a specific list of substances or conditions which have been identified through EU or national legislation as being inappropriate for disposal to sewerage without prior notification and approval by the local water company. In this instance, the University would be obliged to obtain a Trade effluent consent in order to allow the disposal of any of these substances to drain. All substances which fall within this list are therefore banned from disposal to drain in on or from CBE properties and MUST be disposed of as special waste. Consult the following for a list of substances:
  http://www.water.org.uk/home/policy/publications/archive/pollution/substance-list-appendix-a/appendix-a-substance-list.pdf

Liquids which do not fall within either of the categories outlined above can generally be safely disposed of to the drain. The responsibility remains with the individual or group producing liquid waste to adequately assess and confirm that their liquid waste is in no way hazardous before disposing to drain. If in doubt, the DSO must be consulted.

(vi) Solid laboratory waste that poses a low risk to human health and the environment and that fulfils the following criteria can usually be disposed as healthcare/clinical waste without prior on-site sterilisation or disinfection. This includes:

- Any waste with EWC Codes 18 01 01 or 18 01 02 EXCEPT for those known or likely to be infected with Hazard Group 3 or 4 biological agents or any class of genetically-modified organisms.
- That which is known or suspected of being contaminated only with biological agents in Hazard Group 1 (as defined under COSHH) UNLESS the agent(s) in question pose a risk to the environment. If the latter applies then such waste must be handled as infectious waste and therefore rendered safe as appropriate.
- Uncontaminated solid waste such as empty glove boxes, hand wash towels or clean plasticware EXCEPT for that originating from within Containment Level 3 laboratories.

(vii) Solid laboratory waste that poses a greater risk to health and safety and must be rendered safe by appropriate means prior to disposal as healthcare/clinical waste includes:

- That known or reasonably suspected of being contaminated with Hazard Group 2 cultures

- All waste known or reasonably suspected of being contaminated with Class 1, Class 2 or Class 3 genetically-modified organisms

NOTE: *The Contained Use Regulations require that all waste from work with GMOs to be decontaminated by fully validated means. This includes waste from Class 1 GMO projects. The organism-specific genetic modification risk assessment must always be consulted for treatment and disposal of GM material waste. Although validated chemical disinfection's may be used in some cases for Class 1 GM waste prior to its final disposal (dependent on activity and risk assessment), autoclaving all GM waste is preferred (further details are provided in Section 4).*

5.2.8. Practice for Handling Waste

Whilst physical control measures such as adequate containment, signage, sterilisation facilities, etc are essential in ensuring that the risks associated with healthcare waste are minimised, particular attention must be given to ensure that the waste is handled correctly. The following measures will be required when handling any healthcare waste (including that not yet made safe by sterilisation or chemical disinfection):

- Placing waste in appropriate containers at the time and place of generation
- Minimising the handling of waste
- Replacing containers before they are overfilled (usually no more than ¾ full)
- Not transferring loose contents from one container to another
- Not stockpiling waste
- Clear and appropriate signage of hazards and labels
- Labelling of waste with the correct EWC code
- Clear segregation of healthcare waste from other waste at all stages of the disposal procedure

NOTE: *At the time of writing, clear labelling of waste through completion of labels on rigid containers and tagging so as to indicate its origin is not required unless it is to be transferred to another facility for treatment. However all healthcare waste should be placed in appropriate colour coded containers and labelled with the appropriate EWC code.*

Handling of Sharps (including broken glass) waste

- The use of sharps, including glass, in biological laboratories must be avoided. Where practical, glass must be replaced with disposable plastics or other sharp less systems.
- If the continued use of sharps is essential, their handling must be minimised. Avoidable handling such as resheathing of needles must be eliminated. Sharps must be placed in properly constructed sharps containers conforming to BS 7320 immediately after use.
- Sharps bins must not be overfilled and must be removed when three quarters full (or to the manufacturers mark). They should not be placed in disposal bags and should be kept separate during storage and transport so that any leaks or penetrations are more obvious.
- Sharps contaminated with any GM material or ACDP Hazard Group 1 or 2 biological agents must be rendered safe by autoclaving prior to their removal from site, unless they are contaminated with cytotoxic/cytostatic substances. Sharps containers must be carefully selected so that they are capable of withstanding such treatment.

5.2.9. On-Site Storage and Transport of Waste

The definition of 'on-site' is; "within the boundaries of the CBE premises". This includes movement of waste within buildings and between buildings e.g. Gas Pods. On-site transportation must be in accordance with local procedures. Waste may only be transported by authorised laboratory staff (or contractors).

- Untreated waste must be transported within the CBE Laboratory Unit i.e. to the autoclave facility, in rigid lidded containers capable of containing leakage- it is not permissible to carry waste in loose bags.
- Treated waste that has been transferred to healthcare waste bags must be transported in rigid containers to the waste deposit point. Rigid containers may consist of lidded boxes carried on trolleys or by hand.
- Re-useable rigid containers should be cleaned and / or disinfected at regular intervals.
- Treated waste may only be transferred from rigid containers or carts at designated deposit / collection points.
- Waste routes around the site must be clearly established, avoiding the need to take waste through 'clean' areas e.g. open plan offices and avoiding difficult traffic routes involving stairs, steep slopes, poor surfaces etc.
- Bulk storage areas are operated on site premises. Bulk storage areas should be reserved or otherwise securely segregated for healthcare waste only, well lit and ventilated, located away from routes used by the public, enclosed and secure, sited on a well drained, impervious hard-standing, accessible only to authorised people, clearly marked with signage.

5.2.10. Personal Protective Equipment

COSHH Regulations require that risks to health be eliminated, prevented or, where this is not reasonably practicable, reduced. Although the use of personal protective equipment should be considered as additional to other control measures, it is likely that even after all reasonably practicable precautions have been taken to reduce the exposure of staff that handle, transfer, transport, treat or dispose of healthcare waste; some personal protective equipment will still be required.

Risk assessments should identify the need for personal protective equipment such as: suitable gloves, lab coat, apron, safety glasses etc when handling healthcare waste receptacles. Emergency situations, such as spillages, should also be addressed in any risk assessments. This might include the need for protective equipment to prevent exposure via routes such as skin contact (for example disposable aprons and gloves) or inhalation (for example respiratory protection and/or face visors).

SECTION 6 EMERGENCY RESPONSE PROCEDURES

6.1. INTRODUCTION

Under Regulation 5 of the Management of Health and Safety at Work Regulations 1999, employers are required to plan, organise, control, monitor and review their health and safety arrangements. Reporting and investigating workplace accidents and ill health forms an essential part of this process. Risk control measures should be put in place to minimise identified risks and to prevent accidents and cases of ill health. The fact that an accident, incident or near miss has occurred may indicate that the existing risk control measures were inadequate.

Definitions

- Accident – Any unplanned event that results in personal injury or damage to property, plant or equipment.
- Incident – Any event or occurrence which might disrupt or interfere with normal operations
- Near misses – Any unplanned event or chain of events in which personal injury or damage to property, plant or equipment has only been avoided by chance.
- Hazard – The potential to cause harm, including ill health and injury, damage to property, plant or the environment or increased liabilities.
- Risk – the probability or chance that a hazard will lead to injury.

6.2. EMERGENCY PLANS

Most accidents and incidents can be avoided with good management systems in place, consisting of initial instruction and training on correct procedures and with ongoing supervision and monitoring. Each Head of Group is responsible for ensuring the health and safety of all persons on the CBE premises and must make appropriate arrangements to minimise the likelihood of accidents, incidents or instances of occupational ill health occurring.

The potential seriousness of accidents involving biological materials should not be underestimated. All workers must be made aware of the consequences should they be exposed to biohazardous materials. Needle stick and sharps injuries, for example, are particularly serious and each Head of Group must ensure all workers handling needles and sharps receive instruction and training on safe procedures. Workers in the CBE Laboratory Unit should refer to and follow the guidance on avoiding sharps and needle stick injuries provided in this CoP.

According to the GMO (CU) Regulations 2000 an emergency plan is required if the risk assessment for activities involving GMOs indicates that, as a result of any foreseeable accident (involving significant and unintended release of GMOs), the health and safety of people outside the premises may be affected or is there is a serious risk to the environment. In practice, an emergency plan is unlikely to be necessary in the CBE Laboratory Unit for most small scale activities or those involving low risk GMOs. Nevertheless the following procedures should be implemented.

Emergency procedures for the CBE Laboratory Unit where biological work is carried out should cover:

- the role, responsibilities and authority of individuals during an emergency;
- training requirements – all new staff should be trained in emergency procedures
- the safety equipment and personal protective equipment to be used;
- first aid arrangements – including the availability of post-exposure prophylaxis if appropriate;

- procedures for cleaning up and disposal of waste;
- procedures for reporting accidents/incidents;
- arrangements for the investigation of incidents/accidents i.e. what happened and why, how it was dealt with and whether any amendments are required to the emergency plan.

Entry into the CBE Laboratory Unit is restricted and contact details of an authorised user must be available in order that they can provide advice and supervised access in the event of an emergency.

6.3. ACCIDENT AND INCIDENT MONITORING

All workers must be made aware of what action they need to take in the event of an emergency and those with specific roles must receive training in order for them to carry out their responsibilities effectively. The University Policy demands the immediate and accurate reporting and investigation of accidents, near misses, occupational ill health and dangerous occurrences. Such matters should be reported to the University HS&E Department on an Accident Report Form (ARF), which is downloadable from; www.lboro.ac.uk/admin/hse/forms/forms.html. No accident should be considered too trivial to report. Near misses that could have had serious consequences should also be reported. Details of the accident reporting system in the University is available on the HS&E Department website.

In the event of an accident or incident occurring, the individual(s) involved must inform the manager/person who has responsibility for the particular area or their immediate supervisor. A local record should be made of all incidents and occurrences with infectious or potentially infectious material involving exposure of individuals. All accidents and incidents that occur should subsequently be reviewed by the individual(s) involved in conjunction with their immediate supervisor. The cause of the accident or incident should be established and action to prevent any recurrence identified. The source of any infection risk (specimen, sample, material etc) should be clearly identified and retained.

Accidents and incidents should also be monitored and reviewed at CBE Management level to identify any improvements that are necessary. However, care must be taken to protect the confidentiality of individuals involved in particular accidents. Any remedial action identified must be implemented and any lessons learnt should be communicated widely within the CBE to others who may benefit from the information. Those incidents or accidents resulting in serious personal injury or significant loss or damage to property will be investigated.

6.3.1. Notification of Accidents and Incidents involving BAs and GM Activities to the HSE

In addition to local reporting of accidents and exposures, in some cases the HSE must be notified under 'Reporting of Injuries, Diseases and Dangerous Occurrences Regulations' (RIDDOR) 1995. These include 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. Accidents or incidents which result in or could result in release or escape of biological agent likely to cause severe human diseases i.e. a HG3 or HG4 agent also have to reported under RIDDOR.

There is a requirement under the Genetically Modified Organisms (Contained Use) Regulations 2000, as amended 2005, to immediately notify the Health and Safety Executive of any accident or incident involving a significant or unintended release of a genetically modified organism that presents an immediate or delayed hazard to either human health and safety or the environment. This requirement is in addition to any notification requirements under RIDDOR. Full details of the information required to be notified to the HSE regarding accidents are given in Regulation 20. **Minor spillages of GMOs being used in Class 1 activities are unlikely to count as significant**

releases of GMOs and will not routinely require notification. This may not be true for GMOs in class 2 and above or for large scale spillages of GMOs for some Class 1 activities.

It is the responsibility of the University HS&E Department to make notifications to the Health and Safety Executive of any accidents or incidents occurring within the University that require to be notified either under the Contained Use Regulations or RIDDOR. The CBE Laboratory Management Committee should not make any such notifications; instead they should contact the University HS&E Department as detailed below.

i. In the event of any accident or incident involving the spillage or release of any genetically modified organisms or micro-organisms or where exposure to a genetically modified micro-organism may have occurred, the local BGMSA and the University HS&E Department must be informed.
ii. A standard University ARF must be prepared and forwarded to the HS&E Department as soon as possible. The University HS&E Department will decide whether any accident or incident requires notification to HSE, be it under the Contained Use Regulations or RIDDOR. The CBE Laboratory Management Committee does not need to make any decision on this.

NOTE: *Guidance on notification of accidents involving genetic modification activities is available on HSEs website at http://www.hse.gov.uk/dst/acgm32/paper4.htm). This includes information on which accidents are likely to require notification, what information is required and what happens to the information when a notification is made.*

NOTE: *Following notification of an accident under the Contained Use Regulations, it is very likely that one of the Health and Safety Executive's Specialist GM Inspectors will visit to investigate the circumstances of the accident and to confirm that appropriate measures have been taken to ensure there is no recurrence.*

NOTE: *For guidelines on how to complete an accident report form, consult the Guidance Note, "Reporting of Accidents, Dangerous Occurrences and Occupational Ill Health - Staff, Students, Contractors and Visitors" (at http://www.lboro.ac.uk/admin/hse/accidents.html.*

6.4. ACTION TO TAKE IN THE EVENT OF SPILLAGE OR ACCIDENTAL RELEASE OF BAs/GMOs

6.4.1. Introduction

At Containment Level 2, COSHH requires that work with any biological agent that could create an infectious aerosol must be undertaken in a BSC. To prevent spillages in the laboratory, the agent or material containing the agent should be adequately contained during storage and transfer procedures from BSCs to other areas of the laboratory.

Accidents encountered within the CBE Laboratory Unit will vary from low hazard, small scale releases of biological agents to other more serious incidents that have potential for generating significant aerosols. Arrangements must be in place for handling major incidents at Containment Level 2, for example a major spill

6.4.2. Assessing the Risks: Hazard Evaluation Prior To Response

The type of spill response required must be determined within the risk assessment for the intended work. The method should therefore be identified prior to the work commencing.

Spills of biologically hazardous materials can be divided into two distinct types - minor and major spills. Minor Spills (including "spot" spills) include spills of minimally hazardous material that do not generate infectious aerosols or where the spill is up to 10 cm in diameter or <10mL. Major spills

include spills of a known or suspected/potentially infectious material, a spill of material which generates infectious aerosols or any spills greater than 10cm in diameter or > 10mL.

Several factors determine whether a spill is minor or major, these include: the amount of aerosols that have been generated from the spill; whether the spill is large or small; the risk group classification of the organism that has been spilled; how infectious or easily transmissible the spilled organism is; whether the spill is confined within a piece of equipment (such as a BSC, incubator, refrigerator, water bath or centrifuge) or unconfined (on the work bench, floor of the laboratory or incubator room); the type of surface where the spill occurred (e.g. absorbent or non-absorbent surface); the area where the spill occurred (e.g. in a contained area such as a microbiology laboratory, or in a public access area such as a corridor or lift). The spill may also involve other hazards not of a biological nature which include: isotopes; chemicals; plant/equipment; electrical equipment; sharps (from broken glass or equipment); liquid nitrogen/low temperature. Identification and assessment of all the risks associated with the spill, both potential and actual, as well as the various factors listed above, must be taken into consideration before any spill clean-up begins.

Contingency plans for dealing with a major spillage in the` CBE Laboratory Unit (splashing/aerosol production) requires that there are contingency plans in place. These contingency plans require a number of different factors/scenarios to be considered to determine the most appropriate course of action:

- Type of agent - the Hazard Group, route of transmission, infectious dose (if known), stability in the environment
- Type of accident - instantaneous or delayed - for example, a dropped flask as compared to a broken centrifuge tube which may be undiscovered until the centrifuge is opened
- Severity of accident - amount and concentration of material that could potentially be released and its form, for example, is aerosol formation likely?
- Numbers of staff potentially exposed - this may depend on location of accident (see below)
- Location within the laboratory - an accident in the open laboratory may require evacuation, as compared to a more 'contained' accident in a biological safety cabinet
- Room air change rate - this needs to be known to enable an assessment to be made of the time needed before staff can safely re-enter the laboratory after a spillage

The amount of material released, and its form coupled with the pathogenicity of the agent as described above has to be considered. Large amounts of material are more serious than a small spill of the same agent. Of secondary importance is the location of the spilled material. If the material is contained inside a piece of equipment or within a vessel, this is a less hazardous situation than if it is spread out all over a surface in an uncontained manner.

In some situations it may not be appropriate for laboratory personnel to clean up a biohazardous spill, for example:

- If an employee has not received appropriate training
- If an appropriate spill kit is unavailable
- If the spill represents a combined hazard i.e. chemical and biological
- If the spill is too large

In these situations, other staff in the laboratory should be notified, the laboratory should be evacuated and advice sought from the Laboratory Manager, BGMSA or Department Safety Officer as to appropriate methods to deal with the spill.

6.4.3. General Provisions

The fundamental rule in dealing with a biological spill is to be prepared. Preparation involves identification of the biohazard risks, both actual and potential, that are involved on the site and determining the types of potential spills or emergencies which can occur. In order to prepare for a biohazard spill, personnel must first:

i. Know the ventilation system serving the laboratory or room, the corridors and the building in order to enable you to know how aerosols or airborne particles would move

ii. Know where BSC exhaust ducting goes after leaving the laboratory area

iii. Know where biohazard areas are and where biohazardous materials are stored and assess what hazard could result in the event of a fire, flood, or explosion

iv. Establish evacuation routes and procedures to be used in the event of an emergency with biohazardous materials

v. Establish rules for safe handling, storage and disposal of biohazardous materials to minimize accidental release and set standards for use to avoid conditions which might lead to an accidental spill

vi. Establish an action plan to be followed should a spill occur. This should consist of a step-by-step procedure to follow if a spill occurs.

vii. Know where Spill Kits are located (which must be present in proximity to the area where biohazardous materials are handled).

viii. Know the procedures for reporting and dealing with exposure to biohazardous materials

ix. Display spillage procedures, relevant to the type of organisms in use in the area, on the laboratory wall (see below). These Emergency Information Posters should provide an easily recognizable and consistent means of displaying essential information about the status and contents of laboratories and facilities, primarily for the benefit of persons attempting to cope with an explosion, fire, natural disaster, or other emergency. Such information is important for the safety of emergency personnel and is often of considerable value in evaluating and dealing with the emergency.

    The posters should contain the following information:

    - The home and office phone numbers of persons responsible for and familiar with the laboratory operations. Essential contact information should also be displayed outside of doors leading into the laboratory areas where there are potential hazards and/or on the wall inside the laboratory area.
    - A floor plan of the room, with sketches of appropriate furniture, BSCs, laboratory benches, storage cabinets.
    - Location of principal storage areas for hazardous materials in the room, by hazard class.
    - Specific emergency instructions or warnings, where necessary.

6.4.4. Post Exposure Prophylaxis

(i) As part of the risk assessment the need and availability of post exposure prophylaxis should be considered. The need for immediate medical treatment will depend on:

- Nature of the agent
- Likely risk of developing disease
- Availability of treatment (including a consideration of maximum time after exposure that treatment can be administered with effect)

(ii) If it is available and appropriate details of any prophylactic treatment should be included in the risk assessment. The need for appropriate drugs and prophylaxis to be readily available must be considered

6.4.5. Immediate Actions

In the event of significant spillage for example (either in terms of scale or hazard presented by the agent or both, which should be identified in the risk assessment) laboratory staff should:

1) Immediately leave the laboratory
2) Remove any contaminated clothing and leave in the laboratory
3) Leave the BSC running or should be switched on before leaving laboratory
4) Secure the door and post warning signs to prevent others entering

6.4.6. Clearing the Laboratory of Infectious Aerosol

(i) Spillages outside the Biological Safety Cabinet

Spills outside biological safety cabinets are complex events. They may be within laboratories where a limited number of persons work or they may be in corridors used by a considerable number of persons. For this reason, all work must be planned to minimize the chance of a spill. Material containing biological agents or GMOs that is being moved in or between laboratories or service areas must be contained.

Spills can involve amounts of material ranging from 1 mL or less, to more than 100 mL. The amount spilled, the physical characteristics of the material and how the spill occurred are important factors in determining the area of involvement. When liquid is spilled, it is generally dispersed as three spill fractions:

(a)The bulk of the liquid that remains in an irregular puddle;

(b) The portion that separates as splashes and rivulets;

(c)The small portion that is separated as airborne particles.

The larger airborne particles settle rapidly, whereas the smaller particles can remain suspended in air for a considerable time and can be transported from the spill site by a ventilation system. In the event of a spill of liquid in the laboratory, it should be assumed that an aerosol has been generated. Disinfection procedures for spills of infectious material must contain the contamination in the affected area. Spills in confined areas, especially cold rooms, require special considerations within SOPs for their use. Common spills, such as from liquid cultures or culture plates, must be treated with a suitable disinfectant.

Biological spills outside biological safety cabinets will generate aerosols that can be dispersed in the air throughout the CBE Laboratory Unit. Appropriate protective equipment must be used when decontaminating spills involving biological agents that require Containment Level 2. This equipment should include a laboratory coat, disposable gloves, disposable shoe covers, and safety goggles and mask or full-face shield. Use of this equipment will prevent contact with contaminated surfaces and protect eyes and mucous membranes from exposure to splattered materials. Since spills of biological materials will happen, it is important to be prepared prior to having to deal with the problem:

(a) In the event of an accident resulting in significant spillage inside the laboratory, the biological safety cabinet should be left to run until the room is cleared of infectious aerosol (see Table 6)

(b) If the agent presents a risk of aerosol transmission (as identified in the risk assessment) the room must be evacuated and cleared of infectious aerosol and then disinfected

(c) Assessing the time for clearing aerosol depends on:
- Concentration of organism in solution spilled
- Quantity of solution spilled
- Room ventilation air change rate

Table 6 can be used to calculate the airborne concentration for a given volume of culture at a given concentration. Table 7 indicates the percentage removal vs number of air changes.

Table 6. Airborne concentration of micro-organism/m^3 vs. volume and initial solution concentration.

	Quantity of solution		
Solution Conc./ml	**Small (<50mL)**	**Medium (50-500mL)**	**Large (>500mL)**
10^{10}	$5x10^6$	$5x10^7$	$5x10^8$
10^9	$5x10^5$	$5x10^6$	$5x10^7$
10^8	$5x10^4$	$5x10^5$	$5x10^6$
10^7	5000	$5x10^4$	$5x10^5$
10^6	500	5000	$5x10^4$

This assumes a worse case scenario where aerosol potential is high but exposure time is short due to immediate evacuation. The aerosol potential is a measure of how much of suspension spilled becomes aerosolised.

Table 7. Number of minutes for a given number of air changes that are required to remove 90, 99 or 99.99% of airborne contaminants.

	Percentage Removal			
Air changes/hour	**90**	**99**	**99.9**	**99.99**
6	23	46	69	115
7	20	39	59	98
8	17	35	52	87
9	15	31	46	77
10	14	28	41	69
12	12	23	35	58
14	10	20	30	50
16	9	17	26	43
18	8	15	23	38
20	7	14	21	35
30	5	9	14	23
40	3	7	10	17

EXAMPLE SPILLAGE

A flask containing 20 ml of a 10^8 spores/ml suspension of Bacillus anthracis is accidentally dropped on the laboratory floor. The laboratory ventilation rate is 12 air changes per hour.

From Table 6, the airborne concentration is 50 000 spores/m3 on leaving the laboratory. From Table 7, after 58 minutes, 99.99% of the airborne spores will have been removed, leaving a concentration of 50 spores/m3. After a further 35 minutes, a further 99.9% of the remaining spores will have been removed, and the concentration will have dropped to 0.05 spores/m3, i.e. the laboratory will be almost free of any airborne spores.

When the laboratory has been rendered safe to re-enter the spill should be contained using absorbent booms and appropriate disinfectant applied [e.g. Virkon powder or Trigene at 10 %] Absorb on paper towels and/or scrape into an autoclave bag. Autoclave prior to disposal.

(ii) Contained Spillage inside a Biological Safety Cabinet.

Droplet-size spills or those up to 1 mL may be treated easily by wiping or flooding with a suitable disinfectant solution. If a larger spill or breakage occurs, more extensive treatment may be needed. The occurrence of a spill in BSC poses less of a problem than a spill in an open laboratory provided that the spilled material is contained within the BSC, provided that the BSC is operating properly.

NOTE: *Fumigation may be required to treat inaccessible sections of the cabinet interior following a spill or for certain HG2/GMO organisms (consult risk assessment).*

(iii) **Contained Spillage inside a Centrifuge, Incubator or Other Equipment**

Specific emergency procedures for dealing with minor and major spillages in equipment should be provided in SOPs. The principles of these procedures may be applied to dealing with confined spills in other pieces of equipment, such as an incubator or refrigerator.

6.4.7. Re-entering the Laboratory

i. Before personnel re-enter the laboratory sufficient time must be allowed for any aerosol to be removed from the room and decontamination/fumigation to be carried out. Table 7 indicates the number of minutes for a given number of air changes required to remove 90, 99 or 99.99% of airborne contaminants
ii. Personnel, who have been properly trained, can then re-enter the laboratory wearing appropriate personal/respiratory protective equipment
iii. The spillage should then be contained if necessary to avoid spreading and an appropriate disinfectant applied.
iv. The spillage and disinfectant should be mopped up with disposable paper towels. Care must be taken with broken glassware.
v. The nature of the spillage will influence the extent of further cleaning required. For example, extensive cleaning of the floor (and laboratory) is likely to be required where a flask has been dropped, as contents will have contaminated areas far away from point of impact. For this reason floors under benches in CBE laboratories should not be cluttered with boxes or other absorbent items
vi. In certain irregular or more markedly hazardous situations (e.g. those involving coincidental radiation or toxic chemical release along with the biohazard incident or those involving large spaces or surface areas of equipment) the local BGMSA or DSO should be consulted to determine which hazard poses the greatest immediate risk to all personnel affected and develop an appropriate response plan to address any and all hazards.

6.4.8. Recording and Reporting Significant Spills

All significant spills should be recorded in a local Spill Record Log. Accidental release/spillage of BAs/GMOs must be reported to the Laboratory Manager and local BGMSA or Department Safety Officer who will advise on the appropriate forms to complete. For Hazard Group 2 or GMOs, where it is possible that this could result in an immediate or delayed risk to human health or the environment this will require a report to be made to HSE. The HS&E Department must be informed immediately.

6.5 MEDICAL INTERVENTION.

In the event of an accident or incident in a CBE Laboratory Unit in which an individual/individuals have been exposed and this could result in an immediate or delayed health effect i.e. hazard exposure from face/eye splash, sharps injury or contact with non-intact skin, workers must take immediate action to reduce the risk of infection developing. However this should not be at the detriment of treating other more serious injuries which should always take priority. The appropriate risk assessments must be consulted as these should contain possible adverse health effects and

detail what immediate action should be taken. The following should be read in context of appropriateness to the particular accident or incident.

i. If First Aid is required at the site of an incident, the nearest First Aider should be located. Where a qualified first aider administers treatment and decides a referral to an A & E Department or walk in centre is called for, but that the condition is not life threatening so an ambulance is not required, a First Aid Taxi Service is available. The procedure for using this service can be found by clicking on the First Aid Taxi Service Guidance Notes (see link http://www.lboro.ac.uk/admin/hse/accidents.html).
ii. Skin exposure – immediately following any exposure to biological agents or materials containing them, irrespective of whether or not the source is known to pose a risk of infection, the site of exposure or contamination e.g. wound or non-intact skin should be flooded with running water and the area washed with soap and water. The exposed skin should be wiped down and scrubbed with paper towels soaked in 70% IMS and rinsed with soap and water. Antiseptics and skin washes should not be used - there is no evidence of their efficacy, and their effect on the body's own defence systems is unknown. Free bleeding of puncture wounds should be encouraged gently but wounds should not be sucked.
iii. Splashes to face (mucous membranes of eyes, nose or mouth) – In the event of biological hazard exposure to the eyes, eyeball and inner eyelid should be flushed with cold water for 15 minutes. The eye should be held open to wash thoroughly behind the eyelids. The local first aider should be contacted to get medical attention promptly.
iv. Sharps injury or broken skin – bleeding should be encouraged and the procedure for skin contamination adopted.
v. Biological Hazard Ingestion and Inhalation – the local first aider should be contacted to get medical attention promptly.
vi. In the event of any accident where exposure to a pathogen, genetically modified micro-organism or potentially infectious material may have occurred the Occupational Health Unit should be informed immediately - it is important that the need for any prophylactic treatment or health surveillance be assessed on a case by case basis by medical personnel.
vii. Outside of normal working hours or in the event of a serious injury requiring medical attention, the Accident and Emergency Department/Minor Injuries Unit of the local hospital should be contacted.

6.6. PREVENTING INJURIES FROM GLASS AND SHARPS

Work with needles, glass and other sharp items presents a risk of sharps injury. If the work involves blood or human tissues, such injuries can lead to life threatening infections such as hepatitis B, hepatitis C and HIV. Such an injury when working with micro-organisms could result in a significant exposure with the risk of a related infection.

In order to minimise the likelihood of accidents arising as a result of poor working practices and to take the correct action in the event of any accident that may occur, all individuals using sharps should be aware of, and use, the following guidance which must be regarded as standard working practice when handling glass, needles and other sharps.

Injuries from broken glass are often sustained while inserting pipettes into pipetting aids or pasteur pipettes into teats; attaching glass to or removing glass from rubber or plastic tubing; removing "frozen" stoppers from glass bottles; breaking glass tubing; and handling or washing up broken glassware. These injuries may be largely avoided by instruction in correct techniques and by ensuring glassware is in good condition (without chips or cracks) before use. Hence;

- Plastic alternatives to glass should be used wherever possible.

- Broken or chipped glassware must be repaired or thrown away
- The application of force or excessive pressure when handling glass items should be avoided in case the item slips or gives way suddenly and breaks.
- Glass items must be carried in a box or something similar to minimise the risk of dropping them.
- Use a needle or sharp item only if it is necessary to do so and then use it only for the purpose it was designed. Always consider less hazardous alternatives wherever possible.
- Once the seal on the sheath of a needle has been broken, carry out any subsequent handling with extreme care and keep handling to a minimum.
- If it is necessary to carry needles or syringes, place them on a tray or in a sealed container.
- Never re-sheath needles following use unless a safe system for doing this has been adopted - never hold the sheath with your fingers as if the needle misses the sheath it will puncture a finger.
- Do not detach the needle from the syringe unless absolutely necessary and a safe system for doing this have been adopted.
- Do not put used needles and syringes on the bench or mixed with other items, only put them in something like a tray and make sure they are clearly visible.
- Do not re-use needles so it is always known what a particular needle has been used for.
- Place used needles and syringes, or any other types of sharps, directly into a sharps bin for disposal. Do not detach the needle prior to disposal.
- Have a sharps bin available at the point of use to enable immediate disposal - it is your responsibility to dispose of the sharps you have used, do not leave them for someone else to clear up.
- Dispose of used sharps only in a sharps bin or container which conforms to British Standard 7320:1990 and is UN type-approved for transport - cardboard-type Cin-Bins do not meet this specification and must not be used.
- Use sharps bins only until the contents reach the fill line marked on the side of the bin - do not overfill, used sharps protruding from bins are very dangerous for those who have to handle them. Never place sharps or sharps bins in plastic bags for disposal - sharps bins are clearly identifiable whereas handlers of bags would not expect them to contain sharps. Putting a sharps bin in a bag is particularly hazardous as it is not readily visible if the lid has come off resulting in sharps being loose in the bag.

6.6.1. Preventing other cuts and abrasions

Cuts from scalpel, razor or other blades, sustained while cutting plastic tubes or tubing; opening packages; scraping off adhesive labels; etc frequently occur because of misuse of scalpel or razor blades, which are not designed for any of these tasks. The following should be observed:

- Use only the correct tool for the job.
- Do not use scalpel blades and razor blades unless absolutely necessary.
- Wherever possible use single unit disposable scalpels rather than changing the blades on a re-useable holder.
- Where a blade is used in a holder, take particular care when changing the blade and avoid holding with fingers and applying force or excessive pressure in case it slips or gives way suddenly.
- Dispose of used scalpels, razors, blades etc in a sharps bin. Use labels that can be easily peeled-off avoiding the need for scraping etc.

6.6.2. Accident Procedures for Glass and Sharps Injuries

Accident procedures, described in a flow chart, should be displayed in all areas where infectious or potentially infectious materials are handled (available on the CBE website).

Needle stick and sharps injuries are potentially very serious and must always be reported, recorded and followed up as described previously. All accidents and incidents should be reported to and recorded by the person responsible for the work: All accidents and incidents that do occur should subsequently be reviewed by the individual(s) involved in conjunction with their immediate supervisor in order to establish the cause of the accident or incident and identify what should be done to prevent any recurrence.

6.7 OCCUPATIONAL HEALTH

Any employee who believes they are suffering from ill health attributable to their work should report this to the Occupational Health Advisor, (in confidence if appropriate). Any manager who considers that an employee is suffering from a work related illness or disease should also report this directly to the University Occupational Health Advisor.

The Occupational Health Unit will provide or arrange any health surveillance identified as being required for a particular work activity (refer to Section 2, Part 1). Each Head of Group is responsible for ensuring the requirement for any health surveillance be considered and determined as part of the risk assessment process. The Occupational Health Unit should be informed immediately in the event of any accident or incident where exposure to a pathogen, genetically modified micro-organism or potentially infectious material may have occurred. This will enable the need for any prophylactic treatment or health surveillance to be assessed on a case-by-case basis by medical personnel.

SECTION 7 STORAGE AND TRANSPORT OF BIOLOGICAL MATERIALS

7.1. STORAGE OF BIOLOGICAL MATERIALS

COSHH regulations require the safe storage of Biological Agents. In addition, storage of GMOs is a 'contained use' activity and as such is subject to the requirements of the Contained Use Regulations. In addition the storage of certain material may be subject to additional requirements under the Human Tissue Act (HTA). Workers should refer to the guidance available at http://www.hta.gov.uk/guidance.cfm and advice should be sought from the BHGMSC via the University BSO to confirm whether the material and work activity falls under the terms of the act.

As a practical guide, general storage requirements in the CBE Laboratory Unit for BAs/GMOs are summarised in Table 8. BAs/GMOs or materials containing them must not be stored outside the CBE Laboratory Unit unless:

- the storage unit (freezer, fridge, controlled temperature room or other container) has a biohazard symbol posted on it,
- the storage unit is locked when not in use (unless access is restricted to the room or area where the storage unit is located),
- access to the storage unit is restricted or controlled to prevent unintentional release of BAs/GMOs into the environment.
- the BAs/GMOs or organisms containing BAs/GMOs being stored outside the facility are double-contained. The primary container must be sealed to prevent the escape or release of the BAs/GMOs and must be labelled. The primary container must be stored in an unbreakable secondary container. In the case of a small storage unit such as a fridge, freezer or liquid nitrogen container, the secondary container may be the storage unit.

7.1.1. Cryopreservation

Cells and tissues can be cryopreserved in a stable state for limited or prolonged periods. The cryopreservation process includes freezing, storage and recovery. Storage in the liquid phase of nitrogen provides the lowest, most stable and most convenient storage temperature, but vapour phase storage is generally considered to be safer. Electrical storage systems provide a very practical and maintenance-free, low temperature storage solution. However, in a multi-user environment, such systems are prone to the effects of temperature cycling in stored material, and in the absence of liquid nitrogen or carbon dioxide back-up systems, they are at high risk in the event of loss of power supply. The failure of liquid nitrogen refilling procedures can result in the loss of valuable cells and tissues, so it is vital that there are effective training and monitoring procedures for the filling and maintenance of liquid nitrogen containers. In addition, it is advisable to store aliquots of important stocks at more than one storage site.

7.1.2. Archive Material

Wherever possible material associated with experiments that are no longer 'active' and are not covered by a current risk assessment should be disposed of. Where archive material has to be kept and is not covered by a current assessment it must be physically segregated from currently used material. The outer container must be labelled to the effect that the material inside must not be used unless a risk assessment is carried out.

Table 8: Guidance on General Storage Requirements for Biological Materials in the Containment Level 2 CBE Laboratory Unit

	Containment Level 2
General Requirements	A nominated individual must maintain an inventory of all organisms stored within the laboratory. It is important that every individual vial/plate/flask can be traced back to a risk assessment.
Labelling requirements for storage vials and growth vessels.	All viable organisms, irrespective of where they are stored/used must be **clearly** labelled with • Parental organism • Classification (Risk Assessment No) • Date of storage • Initials of owner and name of Research Group
Room temperature storage	Only where risk assessment has identified that short term storage on bench is acceptable. Due to the nature of the work such storage is likely to be relatively short term. Vessels, universals, agar plates etc containing liquid cultures must be stored securely in such a way as they are not in danger of being spilt or knocked over. This can be achieved by: • Storing in trays • Use of suitable tube racks • Ensuring cultures /plates are not near the edge of benches or in areas where there is danger of spillage
Fridge/4^{0}C	**Agar plates** must be sealed with parafilm and secured in stacks. **Liquid cultures** must be secured in racks or placed in suitable outer [secondary] containers to reduce risk of spillage. Viable organisms shall be segregated from other non-viable materials in the fridge. The fridge must bear a **biohazard** sign. GMOs should be segregated from non-GMOs
-20^{0}C /80^{0}C	BAs/GMO' are usually contained in small ampoules of 2ml or less. These should be secured in trays within boxes. The box must be appropriately labelled as to its contents and bear a biohazard sign. Viable organisms should be segregated from other non-viable materials in the freezer. GMOs should be segregated from non-GMOs It is recognised that in many cases it will not be practicable to dedicate an entire freezer for this purpose. In these circumstances a shelf or area of the freezer should be designated for storage of BAs/GMOs and should bear biohazard signs. The box must be sealed and leak-proof to contain liquid in the event of freezer failure. On no account must freezers containing HG2 BA or GMOs be located in corridors Transport to the freezer should be by secure means to minimise risk of spillage. The door of the freezer must also have a biohazard sign and the freezer must be kept locked if outside of the facility.

7.2. TRANSPORT OF BIOLOGICAL MATERIALS

The CBE Laboratory Unit is designed to remove the need to transport viable BAs/GMOs any distance. Where this cannot be avoided transport must be such as to avoid or reduce the risk of spillage. All BAs/GMOs being transported **out of** the CBE Laboratory Unit, including transport to storage outside the facility must be transported in accordance with the transport guidelines provided in this section.

The transport of BAs/GMOs must be subject to the requirements for risk assessment. The advice of the local BGMSA and/or BHGMSC should be sought. The risk assessment must take particular account of the risks associated with the transport itself. Key aspects should include appropriate packaging and labelling, the supply of information where appropriate to the person transporting the BAs/GMOs, and consideration of possible accidents and where appropriate emergency measures to be taken. Certain biological materials may be subject to the provisions of the Carriage of Dangerous Goods by Road and Rail regulations (see below for details).

7.2.1. Transport of Biological Materials between and within laboratory areas in the CBE Laboratory Unit.

Particular care should be taken when liquid cultures are being transported within the laboratory or between laboratories within the CBE Laboratory Unit

- Trays and tube racks should be used to carry cultures around the laboratory.
- Small volumes of culture that can easily be carried must be transported within a secondary outer container with a lid. If doors need to be negotiated a trolley should be used or assistance should be sort from a colleague.
- Larger cultures must be moved on a trolley, in a secure manner using additional trays, tube racks and secondary containment as required
- On no account must glass flasks containing viable organisms be carried without the use of secondary containment
- Individuals transporting cultures outside of the laboratory should ensure they have enough absorbent material and gloves are readily available to deal with any spillage

7.2.2. Transport of Biological Materials outside the CBE Laboratory Unit

Certain biological materials fall within the description of dangerous goods for transport by road (ADR), rail (RID) and air (ICAO-IATA). Both national and international legislation demand that stringent requirements are met if the goods are transported by any means. Even if the particular biological material to be transported is not hazardous and does not fall under the description of dangerous goods, the item still must be transported in such a way that they are not likely to leak in transit and trigger safety/security alerts or cause unnecessary concern to anyone who may come into contact with leaked material.

Biological agents or materials that contain or may contain them, because they present an infection risk are allocated to UN Division Class 6.2 - Infectious Substances. For transport purposes, infectious substances are substances which are known or are reasonably expected to contain pathogens. Pathogens are defined as micro-organisms (including bacteria, viruses, rickettsia, parasites, fungi) and other agents such as prions which can cause disease in humans or animals. Pathogens that cause disease in humans are also known as biological agents under COSHH Regulations. A wide variety of different types of biological materials may fall under the classification of infectious substances. These typically include cultures or isolates of pathogenic micro-organisms, most human or animal specimens, some genetically modified micro-organisms, some biological products, and healthcare and medical wastes that have not been decontaminated.

There are 5 steps involved in the transport of biological materials, (1) Classification, (2) Packaging, (3) Labelling (4) Documentation and (5) Transport. A guidance document on the Transport of Infectious Substances is provided in Annex 10, which gives full details of the requirements for transport of BAs/GMOs. This guidance should be regarded as essential reading for all persons in the CBE involved in the transport of biological materials. This guidance is supplemented with summaries of the procedures to be followed by CBE personnel when transporting biological materials. These summaries are provided on the CBE website for convenience/easy reference. Anyone using these summaries should be properly trained to carry out their responsibilities to the required standards and be familiar with the full text of the rest of the transport guidance. They must appreciate the risks involved and have a detailed understanding of the relevant regulations. All persons in the CBE transporting biological materials using these summaries must ensure the materials they wish to transport have been properly classified in accordance with the legislative requirements. **Reference must be made to full text of this guidance as well as the current and up-to-date regulations at the time the shipment is made.**

The guidance provided in Annex 10 summarises the main requirements when transporting the most common types of biological research materials and "transporting" is used in the general sense and should be interpreted as including the sending or taking of such materials by any means. The regulations on which this guidance is based are those governing the transport of dangerous goods by road and air since these are likely to be the most common modes of transport used. The guidance therefore covers the requirements for the transport of biological materials both within the UK and abroad. Where there are significant differences in the requirements for transport by road or air these are clearly identified within the text (where there are only minor differences the higher standard is given to simplify the guidance and procedures for users). In all cases the differences are because of more stringent requirements for transport by air, mainly because of industry standard practices and operational considerations. Usually it will be possible to determine in advance how a package is going to be transported but senders should bear in mind there is the increasing likelihood that packages sent by post or courier within the UK may be put on an internal flight and it is important to ensure the requirements for such journeys are complied with.

Each Head of Group must ensure that all persons undertaking any role in the transport chain are properly trained and have a detailed understanding of the relevant Regulations to ensure they are able to undertake their responsibilities to the required standards. The level of training should be commensurate with those responsibilities. All persons undertaking any role in the transport chain should be properly trained to carry out their responsibilities to the required standards. They must appreciate the risks involved and have a detailed understanding of the relevant regulations. The level of training required varies but should be commensurate with the role and the associated responsibilities and must be recurrent to take account of changes in the regulations. Workers must not carry, consign, package or play any other role in the transport chain if they are not competent to do so.

Any problems occurring during transport, such as leakage or breakage, should be reviewed in order that corrective measures can be taken to prevent any recurrence. If workers in the CBE receive packages that are not properly packaged or labelled they should contact the originator to advise of the problem and ask that any future packages meet the legislative standards.

In conclusion, a reminder of two very important points:

- **The various regulations governing the transport of dangerous goods are complicated and senders of packages must ensure they meet all necessary requirements prior to despatch. If CBE personnel have any doubt as to procedures they must seek further advice, this can be obtained from the local BGMSA or the University BSO.**

- **Even if the particular biological materials CBE personnel wish to transport does not fall under the description of dangerous goods or is transported as an Exempt human or**

animal specimen, the item still must be packed safely for carriage and relevant sections included within this guidance must be followed.

7.2.3. Import and Export Procedures

Movement of certain types of biological material into and out of the UK will require additional documentation, eg a licence, to cover their import/export. This includes:

- items containing products of animal origin
- certain animal and plant pathogens or materials that may contain them
- certain human pathogens and
- items covered by the anti-terrorism legislation

1. Importing and exporting human pathogens

There is no requirement under health and safety law to obtain a licence to import human pathogens into the UK, other than the requirement under COSHH to notify the use of these agents as described below:

Before certain pathogens can be brought onto premises the Health and Safety Executive must be notified at least 20 days in advance of the intention to use or store biological agents in Hazard Groups 2, 3 and 4 at particular premises for the first time. Subsequently the HSE must also be notified of the storage or use for the first time of any agent specified in Part V of Schedule 3 of the COSHH Regulations. Part V of Schedule 3 specifies all Hazard Group 3 and 4 agents, and the Hazard Group 2 agents *Bordetella pertussis, Corynebacterium diphtheriae* and *Neisseria meningitidis*. The University Biological Safety Officer will make any such notifications to the Health and Safety Executive and so must be informed in advance of any intention to bring onto University premises any pathogen that has not been used previously.

Exportation of a human pathogen needs a licence if the pathogen is listed in UK/EC strategic export control lists and the pathogen is being exported to any destination outside of EU.

2. Importing and exporting animal and plant pathogens

Importation of certain animal or plant pathogens, or pests, or any material that may be carrying such pathogens or pests, is strictly controlled by legislation enforced by the Department of the Environment, Food and Rural Affairs (DEFRA). Rigorous licensing requirements are in place for both import and possession of many types of materials. Further information on the controls on animal and plant pathogens is provided in Annex 2. Links are provided to further information from the regulatory authorities from where licence application forms etc can be downloaded. It is the responsibility of the individual importing the material to obtain any licences required.

Importing an animal pathogen from outside of the EU into England and Wales requires a licence under the Importation of Animal Pathogens Order (IAPO) 1980. This legislation covers pathogens and carriers.

- Animal pathogens are defined as: “any collection or culture of organisms or any derivative either on its own or in recombinant form of such collection or culture of organisms which may cause disease in animals or poultry”
- Carriers are defined as: “any living creature except man which may carry or transmit an animal pathogen or the tissue, cell culture, body fluid, excreta, carcase or part of a carcase of such creature by or by means of which an animal pathogen may be transmitted”

If importing an animal pathogen from within EU (or transfer in UK), a licence may be needed under Specified Animal Pathogens Order (SAPO) 1998 before premises can hold/use certain specified pathogens or carriers (see list on DEFRA website).

Certain animal pathogens are listed in UK/EC strategic export control lists and will require an export licence before sending outside the EC.

- If you wish to import any animal products that you know are not infected with an animal pathogen, or have good reason to expect that they are not infected with an animal pathogen, from within or outside of the EC you must apply for a Research Sample Licence using the Defra form IAPPO1. Follow this link to download the form http://www.defra.gov.uk/corporate/docs/forms/ahealth/iapppo1.htm

- If you wish to import such an animal product but it is known or suspected of being infected with an animal pathogen then you must use DEFRA form IM137. Follow this link to download the form http://www.defra.gov.uk/corporate/docs/forms/ahealth/inttrade/im137.htm

- If you wish to import an animal pathogen listed under the Specified Animal Pathogens Order then you must use DEFRA form PATH1. Follow this link to download the form http://www.defra.gov.uk/corporate/docs/forms/ahealth/path1.htm

In all cases the instructions for their submission is stated on the forms themselves.

NOTE: *ALL APPLICATIONS MUST BE REVIEWED BY THE BGMSA AND THE UNIVERSITY BIOLOGICAL SAFETY OFFICER BEFORE SUBMISSION*

3. Importing and exporting GMMs

HSE must be informed (as part of the notification process for Class 3 activities) whether Class 3 GMMs are likely to be subject to any movement entering or leaving the EC.

Under the Cartagena Protocol on Biosafety GMMs destined for contained use are excluded from the majority of the requirements of the protocol, eg advanced informed agreement arrangements, as this is meant primarily for organisms destined for deliberate release. However, when exporting GMOs/GMMs for contained use it is necessary to

- Ensure the GMOs/GMMs are transported safely - The GMOs/GMMs must be classified, packaged and labelled in accordance with the relevant transport regulations.
- Provide certain information in accompanying documentation - Some of the information required, for example contact details for further information and the name and address of the person to whom the consignment is being sent, is already included in paperwork necessary to comply with the transport regulations.
- Provide additional information as follows - a statement that the package contains or consists or GMMs giving a basic description of the host and how it has been modified, any unique identification code(s) assigned to the GMMs if such codes exist and any requirements for safe handling, storage, transport and use. This can be achieved by enclosing a copy of relevant parts of the GM risk assessment. However, you should note you must make an explicit statement that the package contains GMMs and not just assume it is implicit by providing a copy of the GM risk assessment.

4. Importing and exporting biological material sourced from humans

Work with human tissues is subject to control under the Human Tissue Act and activities with certain imported human materials must be carried out only under the authority of a licence. The actual import of the human tissues is not a licensable activity under the Act and since this Act is not

an area covered by health and safety legislation it is not covered further here. Importers should however be aware there are licensing requirements under the Act which may be relevant according to the material and its intended use. Researchers needing further guidance should contact University BSO or local BGMSA who should be able to advise on the requirements regulated by the Human Tissue Authority.

5. Importing and exporting biological material sourced from animals

The regulations covering the import of animal products are in a state of flux. Detailed information and guidance on the requirements for animal products' import licences should therefore be sought from the DEFRA website; http://www.defra.gov.uk/foodfarm/animaltrade/imports/index.htm.

Certain animals and animal derived products can be imported under a "general" licence. A general licence is a published document and importer's do not need to apply for their own copy. Personnel wishing to import such material should familiarise themselves with the licence conditions. They should also refer to relevant Importer Information Notes and may wish to contact the Imports Policy Branch for further guidance and to satisfy themselves that they are complying with the rules.

General licences are available for such animal materials as animal blood and tissues, established animal cell cultures including established lines, animal proteins, antibodies (monoclonal and polyclonal), peptides and polypeptides separated from plasma or serum, tissue cultures, tissues, body fluids or fractions thereof). If the material you wish to import is not covered by any general license, you should apply for apply for an animal health import licence.

Export of products of animal origin within the EU may require an Export Health Certificate and outside of EU, may need a certificate depending on products and requirements of receiving country. Further information is available on the DEFRA International Trade web pages.

In cases where the material to be imported presents minimal risks a licence may not be required. However a letter to accompany the shipment should be obtained from the licensing office to confirm this is the case. Determination on whether or not a licence is required should be by the licensing authority not the importer.

It may be possible for the CBE units to obtain a reasonably generic licence if they are importing similar materials on a regular basis. If this approach is taken due consideration should be given to how best to complete the application form and the practical controls that will be required to ensure compliance on a local basis.

6. Items covered by the anti-terrorism legislation

Items on Schedule 1 of the Chemical Weapons Act are subject to strict controls and an import licence must be obtained from the Department of Trade and Industry. It is the responsibility of the individual importing the material to obtain any licences required.

There are no import licence requirements for many of the controlled agents listed in Schedule 5 of the Anti-terrorism, Crime and Security Act 2001. However those items on the list that do require a specific import licence under other legislation are

- micro-organisms that are animal pathogens requiring an import licence from DEFRA under the under the Importation of Animal Pathogens Order (see section 2 above), and
- the toxins ricin and saxitoxin which need a licence from the DTI since these are on Schedule 1 of the Chemical Weapons Act.

In order to receive items on Schedule 1 of the Chemical Weapons Act it is necessary to comply with the other requirements of this legislation and additional licences to possess the material will be required.

See Section 3 above for the requirements to make advance notification to the Health and Safety Executive of any intention to bring certain human pathogens into the University for the first time.

Before you can bring Schedule 5 materials onto University premises there is the requirement to make a premises notification to the Home Office 30 days in advance of your intention to acquire the materials (unless the premises are already notified). The University BSO must be informed in advance of any intentions to acquire any micro-organism or toxins listed on Schedule 5, and if any notification is required this will be made to the Home Office by the HS&E Department.

Anyone unsure about the potential licensing and notification requirements for any materials they wish to import can contact the local BGMSA or the University BSO for further advice on a case by case basis.

SECTION 8 GUIDANCE AND INFORMATION

The following provides details (and links where available) to regulations, publications and other resources relating to general biosafety.

8.1. REGULATION

1) Control of Substances Hazardous to Health Regulations (COSHH) 2002. SI2002/2677. The Stationery Office. ISBN 0-11-042919-2. Available on HMSO website at http://www.legislation.hmso.gov.uk/si/si2002/20022677.htm
2) The Specified Animal Pathogens Order 2008. S12008/944. The Stationery Office. ISBN 9780110813288 Available on HMSO website at http://www.opsi.gov.uk/si/si2008/uksi_20080944_en_1.
3) Anti-terrorism, Crime and Security Act 2001, Ch24, The Stationary Office 2002, ISBN 0 10 542401 3.
4) Controlled Waste Regulations 1992. SI 1992/588
5) Special Waste Regulations. 1996. SI 1996/972
6) Carriage of Dangerous Goods (Classification, Packaging and Labelling) and Use of Transportable Pressure Receptacles Regulations. 1996. SI 1996/2092
7) Landfill (England and Wales) Regulations. 2002. SI 2002/1559
8) Reporting of Injuries, Diseases and Dangerous Occurrences Regulations 1995. SI 1995/3163, The Stationary Office, 1991, ISBN 0 11 053751 3.

8.2. GUIDANCE

1) Control of Substances Hazardous to Health Regulations 2002 (as amended). Approved Code of Practice and guidance L5 (5th edition). 2005. The Stationery Office. ISBN 0 7176 2981 3. £12.50. [Note - includes the regulations and the supporting ACOPs and guidance].
2) Approved List of Biological Agents. ACDP. 2004. Available on the HSE website at http://www.hse.gov.uk/pubns/misc208.pdf
3) The management, design and operation of microbiological containment laboratories. ACDP. 2001. HSE Books. ISBN 0 7176 2034 4.
4) Biological agents: Managing the risks in laboratories and healthcare premises. ACDP. 2005. Available on the HSE website at http://www.hse.gov.uk/biosafety/biologagents.pdf
5) Protection against blood-borne infections in the workplace: HIV and hepatitis. ACDP. 1995. The Stationery Office. ISBN 0-11-321953-9.
6) Revised advice on laboratory containment measures for work with tissue samples in clinical cytogenetics laboratories. Dept. of Health. 2001. Supplement to: Protection against blood-borne infections in the workplace: HIV and hepatitis. Available on DoH website at http://www.dh.gov.uk/PublicationsAndStatistics/Publications/fs/en
7) Blood-borne viruses in the workplace: Guidance for employers and employees. INDG342. 2001. HSE Books. ISBN 0-7176-2062-X. Available on the HSE website at http://www.hse.gov.uk/pubns/indg342.pdf
8) Safe working and the prevention of infection in clinical laboratories and similar facilities. Health Services Advisory Committee. 2002. HSE Books. ISBN 0-7176-2513-3.

9) Transmissible spongiform encephalopathy agents: safe working and the prevention of infection. ACDP/SEAC. 2003. Available on the Department of Health CJD website at http://www.advisorybodies.doh.gov.uk/acdp/tseguidance/Index.htm

10) BSE – Occupational guidance. ACDP. 2006. Available on HSE website at http://www.hse.gov.uk/pubns/web22.pdf

11) Guidance on the use, testing and maintenance of laboratory and animal isolators for the containment of biological agents. ACDP. 2007. Available on the HSE website at http://www.hse.gov.uk/biosafety/isolators.pdf

12) Safe management of healthcare waste. Health Technical Memorandum 07-01. Department of Health. 2006. Available on the Dept. of Health website at http://www.dh.gov.uk/PublicationsAndStatistics/Publications/PublicationsPolicyAndGuidance/PublicationsPolicyAndGuidanceArticle/fs/en?CONTENT_ID=4140891&chk=qyKX8n

13) Infection risks to new and expectant mothers in the workplace: A guide for employers. 1997.HSE Books. ISBN 0-7176-1377.

14) Biological Agents Bulletins. ACDP. Available on the HSE website at http://news.hse.gov.uk/category/infections-at-work/

15) Infection at work: Controlling the risks. ACDP. 2003 Available on the HSE website at http://www.hse.gov.uk/pubns/infection.pdf

16) Links to further sources of HSE information and guidance on biological hazards at work can be found at http://www.hse.gov.uk/biosafety/information.htm

17) Plant Health Guide for Importers (DEFRA). Available at www.defra.gov.uk/planth/publicat/importer/impguide.pdf

18) Good Cell Culture Practice: ECVAM Good Cell Culture Practice Task Force Report 1, Hartung, T et al, ATLA, 30, pp407-414, 2002.

19) Good Cell Culture Practice: ECVAM Good Cell Culture Practice Task Force Report 2, Coecke, S et al, ATLA, 33, pp261-287, 2005.

20) Health Surveillance under COSHH: Guidance for employers. HSE Books 1995 ISBN 0717607550.

21) Human Tissue Act. Guidance available at http://www.hta.gov.uk/guidance.cfm.

22) The Loughborough University Health & Safety Policy: Biological Safety.

23) Hazardous waste technical guidance WM2. Available from http://www.environmentagency.gov.uk

24) CBE Code of practice & guidance note for work with chemical carcinogens, mutagens, substances toxic to reproduction & cytotoxins.

8.3. GENETIC MODIFICATION PUBLICATIONS

The following provides details (and links where available) to regulations, publications and other resources relating to genetic modification.

8.3.1. Regulations covering Contained Use Activities

For protection of human health and safety and the environment from contained use activities involving genetically modified micro-organisms (including animal and plant cultures):

1) The Genetically Modified Organisms (Contained Use) Regulations 2000. SI2000/2831. The Stationery Office. ISBN 0-11-018676-1. Available on the HMSO website at http://www.opsi.gov.uk/si/si2000/20002831.htm

2) The Genetically Modified Organisms (Contained Use) (Amendment) Regulations 2002. SI2002/63. The Stationery Office. ISBN 0-11-039273-6. Available on the HMSO website at http://www.opsi.gov.uk/si/si2002/20020063.htm
3) The Genetically Modified Organisms (Contained Use) (Amendment) Regulations 2005. SI2005/2466. The Stationery Office. ISBN 0-11-07334-6. Available at the HMSO website at http://www.opsi.gov.uk/si/si2005/20052466.htm
4) Amendment to the Genetically Modified Organisms (Contained Use) Regulations 2000 (On the 21 December 2010 three minor changes will be made to the existing Genetically Modified Organisms (Contained Use) Regulations 2000 (the 2000 Regulations) to insert requirements set out in European Directive 2009/41/EC but not included in the original Regulations. **The impact of these changes were assessed and documented in the minutes of the 5th CBE Safety Committee Meeting on 10th Jan 2011.** A copy of the amending Regulations is available at: http://www.legislation.gov.uk/uksi/2010/2840/contents/made

For protection of the environment from contained use activities involving genetically modified animals and plants (see also relevant sections of the Environmental Protection Act 1990 and associated regulations):

8.3.2. Regulations covering Deliberate Release Activities

1) The Genetically Modified Organisms (Deliberate Release) Regulations 2002. SI2002/2443. The Stationery Office. ISBN 0-11-042858-7. Available on the HMSO website at http://www.legislation.hmso.gov.uk/si/si2002/20022443.htm

8.3.3. Guidance

1) A guide to the Genetically Modified Organisms (Contained Use) 2000. L29. 2000. HSE Books. ISBN 0-7176-1758-0. [Note - includes the regulations and the supporting guidance].
2) SACGM Compendium of Guidance. 2007. HSE Books. Available on the HSE website at http://www.hse.gov.uk/biosafety/gmo/acgm/acgmcomp/index.htm.

   Part 1: Introduction http://www.hse.gov.uk/biosafety/gmo/acgm/acgmcomp/part1.pdf
   Part 2: Risk assessment http://www.hse.gov.uk/biosafety/gmo/acgm/acgmcomp/part2.pdf
   Part 3: Containment and control of activities
   http://www.hse.gov.uk/biosafety/gmo/acgm/acgmcomp/part3.pdf
   Part 4: Genetic modification work involving plants
   http://www.hse.gov.uk/biosafety/gmo/acgm/acgmcomp/part4.pdf
   Part 5: Genetic modification of animals http://www.hse.gov.uk/biosafety/gmo/acgm/acgmcomp/part5.pdf
   Part 6: Guidance on the use of Genetically Modified Microorganisms in a clinical setting
   http://www.hse.gov.uk/biosafety/gmo/acgm/acgmcomp/part6.pdf
3) ACGM Newsletters (from Oct 2000 only numbers 29 onwards remains valid).Available on the HSE website at http://www.hse.gov.uk/biosafety/gmo/information.htm
4) Contained use of genetically modified micro-organisms - Excluding information from the public register. INDG357. 2002. HSE Books. ISBN 0-7176-2380-7. Available on the HSE website at http://www.hse.gov.uk/pubns/indg357.pdf
5) Contained use of genetically modified micro-organisms. INDG86(rev2). 2000. HSE Books. ISBN 0-7176-1771-8. Available on the HSE website at http://www.hse.gov.uk/pubns/indg86.pdf
6) Links to HSE guidance on various topics relating to GM activities. Available at http://www.hse.gov.uk/biosafety/gmo/information.htm

8.4. BIOSAFETY BRITISH STANDARDS

The following British Standards are available from British Standards Institute:

1) BS EN 12469. Biotechnology – Performance criteria for microbiological safety cabinets. 2000. (Supersedes parts 1 and 3 of BS 5726 Microbiological Safety Cabinets, 1992)
2) BS 5726. Microbiological safety cabinets – Information to be supplied by the purchaser to the vendor and to the installer, and siting and use of cabinets – Recommendations and guidance. 2005 (Supercedes parts 2 and 4 of BS 5726 Microbiological Safety Cabinets, 1992.)
3) BS 2646 Autoclaves for sterilization in laboratories, 1993
4) BS EN 12347 Biotechnology - Performance criteria for steam sterilizers and autoclaves. 1998
5) BS EN 12128 Biotechnology - Laboratories for research, development and analysis. Containment levels of microbiology laboratories, areas of risk, localities and physical safety requirements. 1998
6) BS EN 12738 Biotechnology - Laboratories for research, development and analysis. Guidance for containment of animals inoculated with micro-organisms in experiments. 1999
7) BS EN 12740 Biotechnology - Laboratories for research, development and analysis. Guidance for handling, inactivating and testing of waste. 1999
8) BS EN 12741 Biotechnology - Laboratories for research, development and analysis. Guidance for biotechnology laboratory operations. 1999
9) BS 3202 Laboratory Furniture and Fittings, 1991
10) BS 7320 Specification for sharps containers. 1990.
11) BS CWA 15793 Laboratory Biorisk Management Standard 2008.
12) BS EN12740:1999. Biotechnology – Laboratories for Research, Development and Analysis – Guidance for Handling, Inactivating and Testing Waste.

SECTION 9 ANNEXES

ANNEX 1: WORK WITH BLOOD, BLOOD PRODUCTS AND OTHER HUMAN TISSUES

The following provides guidance for work with blood, blood products and other human tissue in research laboratories. It does not cover specific work with blood borne pathogens such as the human immunodeficiency virus (HIV) or hepatitis B virus (HBV). It is not aimed at workers carrying out procedures in clinical settings at the point of contact with patients or volunteers or in any health care situation.

NOTE: *If any of the materials have been, or are going to be, genetically modified then this constitutes genetic modification work and a risk assessment should be made in accordance with the requirements of the Genetically Modified Organisms (Contained Use) Regulations 2000.*

A COSHH risk assessment should be made for all work involving handling of blood, blood products and other human tissues. The risk assessment should be specific for the procedures involved and take account of the nature and source of the samples to be handled. Of particular concern is the possible presence in the material of blood borne viruses (BBVs), most notably hepatitis B virus (HBV) and human immunodeficiency virus (HIV), and other pathogens. The key control measures when working with any blood and human tissues are maintaining good working practice standards and avoiding the use of sharps. Paying particular attention to these precautions will protect against the transmission of all blood borne pathogens by the percutaneous route.

1.1 Nature and Source of Samples

The risk assessment must consider the types of pathogens that may be present in the material given the distribution of specific pathogens within the body, and the likely incidence given the source (be it a donor, patient group, or general population).

All human tissues will be contaminated with blood and should be regarded as potentially infectious for BBVs. Potential HIV contamination in particular should be taken into account when handling materials of these types in the laboratory. Other specimens, provided they are not contaminated with blood, such as urine for example are not regarded as posing HBV or HIV infection risk but may contain various other pathogens. Sputum samples and specimens of lung tissues may contain Mycobacterium tuberculosis. Samples of neurological origin may contain disease-form prion proteins. When assessing likely incidence, the following factors must be considered:

- known medical history of a patient or donor,
- whether the samples are from individuals showing clinical symptoms of infectious disease,
- the incidence of the various pathogens that are endemic in the local population.

Any samples that have not been screened should be regarded as potentially infectious.

It is a requirement under the COSHH Regulations to always consider whether a less hazardous substance, or form of the substance, can be used instead. If it can, then it should be used or justification be given as to why it is not being used. In many cases there will be good reasons for using samples from specific sources since these are the subject of the research. However if material is needed for control purposes or a specific source is not required, then the least hazardous should be used.

Whilst it is acceptable to use ones own blood and that of colleagues for certain work (controls, calibration, etc), these must not be used for the transformation of cells as this may be dangerous if

the individuals come into contact with the transformed materials. Ethical considerations of other types of work are not considered here but should also be taken into account.

NOTE: *Blood is a particularly good medium for supporting the growth of a wide range of pathogens and contamination of the blood due to poor working practices may lead to potentially infective material (although these would be pathogens other than blood borne viruses).*

1.2 Control Measures

The following describes the control measures required for handling primary materials. For work involving tissue culture separate guidance is described in Section 2, Part 4. In some cases tissue culture presents additional risks as some cell culture systems, even those incubated for short periods, may support the replication of any HIV that may be present in the starting material.

All work on unscreened samples must be undertaken at a minimum of Containment Level 2 with the additional precautions below. These precautions supplement the basic Containment Level 2 requirements and are to provide extra protection against percutaneous inoculation, and contamination of the skin, mucous membranes and working surfaces. The rigour with which these control measures are applied should be proportionate to the risk. For higher risk samples, for example those from a source population where the incidence of BBVs is greater than 1% (but the samples are not known or strongly suspected to carry BBVs or other pathogens, see below for further guidance on these), particular effort should be directed at segregating the work from general laboratory activities and avoiding all possibility of percutaneous inoculation

In general, work at Containment Level 2 does not need to be confined to a safety cabinet unless there is reason to believe the specimen contains other pathogens that do require such containment. There is no substantive evidence that supports aerosol transmission of HBV and HIV. However where handling or processing may generate aerosols, large droplets or splashes, appropriate containment control measures must be adopted.

If there is any likelihood that materials are known or strongly suspected to contain Hazard Group 3 or 4 pathogens these must not be brought into the University. The local BGMSA or the University BSO can be contacted for further advice.

EXAMPLE: Sputum samples and specimens of lung tissues from patients suffering from tuberculosis must be handled at Containment Level 3. Where it is known or strongly suspected (clinical indications) that blood borne hepatitis viruses, HIV or HTLV are present then the samples must be regarded as high risk materials and handled at a minimum in a derogated Containment Level 3 facility unless any viruses that may be present are to be concentrated or propagated, either intentionally or otherwise, in which case full Containment Level 3 must be applied.

1.3 Sample Reception

All specimen reception should be undertaken in the laboratory by trained workers. Arrangements should be made to ensure that untrained workers do not inadvertently handle samples particularly if these are received in the postal system.

1.4 Transport of Samples

Detailed advice on how to transport samples safely and the various regulatory requirements in relation to the transport of infectious and potentially infectious materials is available in Section 7.

1.5 Immunisation

All workers handling material that may be infected with HBV will be offered immunisation against the virus, and have their response checked. Non-responders to immunisation will be given further advice by the University Occupational Health Advisor.

1.6 Accidents

Immediately following any exposure the site of exposure e.g. wound or non-intact skin should be washed liberally with soap and water but without scrubbing. Antiseptics and skin washes should not be used - there is no evidence of their efficacy, and their effect on local defences is unknown. Free bleeding of puncture wounds should be encouraged gently but wounds should not be sucked. Exposed mucous membranes, including conjunctivae, should be irrigated copiously with water, before and after removing any contact lenses.

Particular care should be taken to ensure that others in the laboratory do not help with the clear up of accidental spillage (especially where there has been an accident that involves broken glass) if they are not aware of the potential risks and trained in safe working practices.

The source of any contamination (specimen, sample, material etc) should be clearly identified and retained for testing if necessary. Every effort should be made within the CBE to ensure the confidentiality of persons potentially exposed to HIV as a result of an accident.

Accidents should be reported to and recorded by the person responsible for the work. The University HS&E Department and the Occupational Health Unit should be informed immediately in the event of any accident where exposure to a pathogen or infectious material may have occurred. A full accident record should be prepared and forwarded to the HS&E Department as soon as possible

1.7 Additional Comments

The HIV virus is not highly infectious or particularly hardy and studies have shown that the occupational risk of exposure is low. However, following accidental inoculation and seroconversion there is the possibility that the person will go on to develop AIDS. Once this happens the prognosis is very poor. Whilst the length of the illness may vary considerably often interspersed with periods of remission the outcome is usually death. The consequence of infection dictates that all effort must be made to prevent accidental infection.

Where research work within the CBE Laboratory Unit involves the use of human tissues, the following policy must be adopted:

- All potentially exposed staff must receive vaccination against Hepatitis B
- Wherever possible the blood or tissue must be obtained from screened sources, e.g. National Blood Service
- Collaborating clinicians supplying blood or body tissue must be informed in writing by the Head of Group that they must take steps to ensure that they do not provide material from any of the following groups
    - Patients who have been identified as HIV, Hep B positive or from high risk groups such as intravenous drug users etc
    - Patients who are/may be suffering from any life threatening transmissible human disease

- Samples must be clearly labelled and identifiable in the event of the material being involved in any exposure incident. The name of donor, clinician supplying the samples and where appropriate the hospital number of the donor should be recorded.
- Where samples are to be imported from overseas then consideration must be given in the risk assessment to any endemic diseases or parasitic infections that may be endemic in the country of origin, e.g. HIV in certain African states, and to samples which may contain parasites
- All research involving the use of human body parts, including blood and serum must have received ethical approval

1.8 Containment Level 2 with Additional Precautions

All work on unscreened samples must be undertaken at a minimum of Containment Level 2 with the additional precautions given below. These precautions supplement the basic Containment Level 2 requirements and are to provide extra protection against percutaneous inoculation, and contamination of the skin, mucous membranes and working surfaces. The rigour with which these control measures are applied should be proportionate to the risk.

- Protocols for the safe conduct of the work should be agreed and strictly adhered to. Local rules should be drawn up to ensure that working practices take into account the measures necessary to control exposure that may arise from the specific work activity. Laboratory rules, disinfection, waste disposal and emergency procedures must be specified. Each procedure should be conducted in a designated area of the laboratory with sufficient space for working safely
- Work should be conducted at a delineated work station which is clearly identified. Work with higher risk materials should ideally be undertaken in a separate room or, if this is not practicable, within a designated area of a larger laboratory. There should be sufficient room to work safely. Typically this is regarded as $24m^3$ for each worker. There should be enough bench space to ensure the workstation is not cluttered and working practices are not compromised due to lack of space.
- A BSC or other form of primary containment should be used when infected material may be dispersed, by for example, tissue homogenisation, vigorous mixing etc. Any procedures that may give rise to potentially infectious aerosols must be conducted in the cabinet.
- The designated working area should be kept clear of any unnecessary equipment before the work starts.
- Access of unauthorised persons to the working area should be prevented to ensure that the person carrying out the work is free from the risk of disturbance or accidental physical contact with others
- Gloves and other personal protective items appropriate to the task (e.g. eye protection) should be worn throughout the work. If during use gloves become punctured or grossly contaminated they should be removed and disposed of, hands should be washed and clean gloves put on. On completion of handling samples gloves should always be removed and discarded, and hands should be washed. Single use (disposable) gloves should not be re-used. Eye protection (goggles or safety glasses) and a plastic overall should be worn if splashing is likely to occur.
- Lesions on exposed skin should be covered with waterproof dressings. Since infections can occur via lesions in the skin all workers in the laboratory should cover cuts and abrasions with a waterproof dressing. This is particularly important when handling higher risk samples. In addition, good basic hygiene practices, including regular hand washing, must be practised at all times.
- The use of glassware and sharps should be avoided. If this is not feasible then handling procedures should be designed to minimise the likelihood of puncture wounds. Wherever possible glass items should be replaced with plastic alternatives. Glass pipettes must not be used. These measures are particularly important for higher risk samples. If it is necessary to use sharps, then used sharps should be placed directly into a sharps bin. Equipment should

not be put down and transferred later as this increases the risk. Unless safe means have been introduced needles should never be resheathed. All sharps and hypodermic needles must be disposed of directly to a sharps container which conforms to the British Standard 7320: 1990. Sharps bins should not be overfilled, used sharps protruding from bins are very dangerous for those who have to handle them. Sharps and sharps bins must never be placed in plastic bags. All sharps and hypodermic needles must be disposed of directly to sharps containers which conform to the British Standard 7320: 1990. All sharps which may be contaminated with pathogenic organisms should, wherever possible, be autoclaved in their boxes before collection for incineration. The term sharp should be taken to refer to any item that is sharp and not be restricted to needles and scalpels. Commonly used items that could easily cause damage to the skin include all glass items (including microscope slides and cover slips), ampoules, pointed nose forceps, dissection instruments, scissors, wire loops that are not closed circles and gauze grids used in electron microscopy work. This list is not exhaustive and all items should be assessed for sharp edges.

- The bench surface and any equipment used should be decontaminated immediately on completion of a session of work. Ideally, dedicated equipment should be used for work with higher risk materials. Equipment must be fully decontaminated prior to maintenance work. A signed statement should be issued to this effect before maintenance work is allowed.
- A satisfactory disinfection policy must be in operation. Suitable disinfectants, concentrations and contact times should be specified for work involving human blood and/or other tissues. Examples of suitable disinfectants include hypochlorites and Virkon. Use of 70% alcohol is not recommended. Use of glutaraldehyde based disinfectants must be avoided. All surfaces should be disinfected immediately following any spillage, at the end of the working day and before any maintenance or cleaning staff are permitted to work in the area where work with blood or blood products has been carried out. All contaminated waste must be disposed of safely. Local rules must specifically state laboratory procedures and arrangements for disposal of contaminated materials.

1.9 Work with Naked DNA (including Oncogenes and Full Length Viral Genomes)

Specific guidance on risk assessments for genetic modification work involving oncogenic sequences is provided by the Advisory Committee on Genetic Modification (ACGM) in the ACGM Compendium of Guidance which is available on HSE's website at http://www.hse.gov.uk/biosafety/gmo/acgm/acgmcomp/3a1.pdf

The following provides guidance for work that is not regarded as genetic modification work but involves the handling of naked DNA or RNA.

NOTE: *If the naked DNA (or RNA) is to be inserted into another organism (micro-organism, animal or plant) then this constitutes genetic modification work and a risk assessment should be made in accordance with the requirements of the Genetically Modified Organisms (Contained Use) Regulations 2000.*

Work with naked DNA is generally regarded as low risk except when it involves oncogenic sequences or is a full length viral genome (in which case it is also important to consider naked RNA). However, even with these types of naked DNA or RNA the risks are often over-estimated as there needs to be an effective means by which the DNA or RNA can gain entry into a cell and cause harm.

Notwithstanding the above comment, these types of naked DNAs and RNAs would be regarded as "substances hazardous to health" and therefore, in accordance with the Control of Substances Hazardous to Health (COSHH) Regulations, a risk assessment should be undertaken to determine the handling precautions to be adopted whilst working with them and appropriate control measures adopted.

1.9.1 Oncogenes

DNA sequences are regarded as oncogenic if they induce tumours in experimental animals or cause transformation of cells in vitro resulting in immortalisation of cells, escape from normal growth control, or production of tumorigenic cells.

The Advisory Committee on Genetic Modification (ACGM) state "Handling naked oncogenic DNA may involve a potential risk to the operator. Although there is no direct evidence as yet that contact with such DNAs can lead to tumours in humans, its possibility cannot be discounted as evidence does exist for animals."

Further evidence of the potential hazards of naked DNA is highlighted in the ACGM Compendium. Whilst there are few examples of naked DNA producing tumours in animals there was a case where ras induced transformation of mouse skin endothelial cells although this was applied in large doses to scarified skin. Of particular note is the effectiveness of DNA vaccines (injected as naked DNA) as demonstrated in animal models and clinical trials.

In undertaking a risk assessment it is important to consider what is likely happen if the naked DNA were to gain access to the body. Firstly the hazard should be identified and a worst-case scenario of the possible consequences of integration or expression of the DNA should be given. This should then be countered by due consideration of the likelihood that integration or expression would occur and whether any harm would result. The risk should take account of both the potential hazard and the likelihood of harm occurring in the event of exposure. It should also be made clear in the risk assessment whether the work involves a known, full length, functional oncogene or a fragment or altered form of such, or a sequence that may be potentially oncogenic.

At this point is it perhaps useful to make comparison with risk assessments for genetic modification work since it can be seen that risks vary and can increase significantly when oncogenic sequences are used in some types of genetic modification work. This variation in risk is due to changes in the likelihood of harm resulting because of the specific activity. The cloning of an oncogene in disabled E. coli would generally be regarded as low risk warranting Containment Level 1 precautions as the potential to cause harm is usually minimal. However, packaging of the same oncogene in a delivery system such as a viral vector with a host range capable of infecting humans, particularly if the oncogene is linked to strong promoters or enhancer sequences that function in mammalian cells, would present a significantly higher risk and most likely require Containment Level 3 precautions is not permissible in the CBE Containment Level 2 Laboratory Unit.

1.9.2 Microbial DNA

There are two important aspects to consider when nucleic acid is extracted from pathogenic micro-organisms.

Firstly, it is important to consider whether the preparation is likely still to contain any of the intact parent micro-organisms. If nucleic acid is extracted from a culture of a hazard group 3 pathogen then the material should not be removed from Containment Level 3 until a stage in the extraction process when all the parent organisms are known to have been destroyed. Alternatively the culture can be killed first and the extraction can be done elsewhere, however in this case a rigorous validation of the kill method would be required with stringent controls to ensure effectiveness of the procedure on every occasion it is used.

Secondly, not only should an assessment should be made of whether the naked DNA or RNA is infectious once extracted. This is not a concern with bacterial DNA but may be so in the case of some full length viral genomes

Naked viral DNA certainly can be infectious but it is much less so than the intact DNA virus equivalent. Different DNA viruses will have different levels of infectivity as naked DNA, but it would need several orders of magnitude of naked DNA molecules to get one infection to take place in a host cell (assuming it is not being helped by artificial means). This is because the intact virus particles have all the machinery to attach to and penetrate the cell whereas naked DNA has none of this machinery. Also, most DNA viruses carry important enzymes in their structure and these enzymes are required to be present immediately after exposure of the intact virion to the host cell. Naked DNA would not carry these enzymes and would therefore be unable to initiate the early replicative processes. However there are plenty of enzymes in the cell and the virus might be able to use these to initiate its replication without needing its own carried enzymes and so this possibility cannot be excluded albeit with a greatly reduced efficiency.

Positive-stranded RNA viruses are usually described as containing infectious RNA. RNA extracted from flaviviruses and alphaviruses for example, are infectious when inoculated intracerebrally into newborn mice. There is the argument that this means this RNA should be handled at Containment Level 3 in the same way as the normal virus from which it was derived. However this is not proportionate to the actual risk. Naked RNA is extremely labile. It takes only the minutest quantity of RNAse enzyme, which is virtually everywhere in the environment, to destroy the intact molecule. Furthermore, it has been estimated that the number of molecules of RNA that are equivalent to a single infectious unit is approximately $1x10^{10}$ (i.e. approx. 10,000,000,000 RNA molecules are required to initiate an infection that an intact single virus particle can initiate).

If the nucleic acid is an intact full length viral genome that is may be infectious as naked nucleic acid (for example if it were to be injected in a sharps injury), then a precautionary approach should be taken albeit not necessarily to the extent of requiring the same level of containment as the parent virus. Control measures should be directed at providing extra protection against percutaneous inoculation, and contamination of the skin, mucous membranes and working surfaces

1.9.3 Control Measures

The risks associated with handling naked DNA and RNA is generally regarded as low since they are unlikely to traverse the natural defence barriers of the body. In addition naked RNA is extremely labile and rapidly destroyed in the environment. The only occasion naked DNA/RNA is likely to gain access to the body is when the skin is punctured, as in the case of a sharps injury, and the material is effectively injected in to the body. Therefore, of prime importance in the control of exposure is the avoidance of sharps in the manipulative procedures. Particular care must also be taken if the naked DNA/RNA is used in solvents which have the ability to penetrate the skin (this should be detailed in the risk assessment and appropriate gloves selected) or are in membrane fusing agents etc.

If the DNA/RNA is likely to contain harmful sequences then consideration should be given to whether it may be possible to include a stage in the protocol whereby the DNA/RNA is denatured. An example of this type of procedure would be heat treatments in excess of 90^0C. A denaturing stage will eliminate any potential for expression and therefore, the hazard will be minimal. Denaturing techniques should not be confused with protein denaturing steps such as phenol chloroform treatment which do not affect the nucleic acid.

Naked DNA/RNA itself is not regarded as a biological agent and therefore there are no minimum standards to apply in the form of specified containment levels. Therefore, in the case of potentially harmful DNA or RNA, control measures should be assigned commensurate with the risk. The precautions given in Appendix 1 are recommended as a minimum for work with oncogenes and related DNA sequences and full length viral genomes that may be infectious.

As mentioned earlier, if naked DNA or RNA is to be inserted into another organism (micro-organism, animal or plant) then this constitutes genetic modification work and a risk assessment

should be made and appropriate controls measures be assigned for that work in accordance with the requirements of the Genetically Modified Organisms (Contained Use) Regulations 2000.

1.9.4 Precautions applied to work with oncogenes and related DNA sequences and full length viral genomes that may be infectious:

- Access to the CBE Laboratory Unit where potentially harmful DNA/RNA is handled should be limited to authorised personnel and designated workers.
- Persons undertaking work with potentially harmful DNA/RNA must receive basic information and training prior to starting work. They should be trained in good laboratory techniques before commencing work and should be fully aware of the potential hazards of such work.
- Laboratory coats must be worn at all times in the CBE Laboratory Unit and be removed when leaving. These should be kept apart from uncontaminated clothing.
- Bench surfaces should be impervious to water and easy to clean.
- A wash basin must be provided and preferably sited near the exit of the laboratory. The taps should be of a type which can be operated without being touched by hand. Hands must be washed before leaving the laboratory.
- Eating, chewing, drinking, smoking, etc should be forbidden in the CBE Laboratory Unit and mouth pipetting must not take place.
- Potentially harmful DNA/RNA sequences should be handled at designated benches within the CBE Laboratory Unit. These should be kept clear of any unnecessary equipment. On completion of the work there should be a rigorous clear up procedures in place to ensure the area is left safe. All work surfaces must be cleaned after use and waste materials removed.
- Gloves must be worn for all work with potentially harmful DNA/RNA sequences. Gloves should be chosen also taking into account their resistance to any chemicals in use. They should be changed regularly and special attention paid to the danger of glove puncture. Gloves worn for this work should not be worn elsewhere. The use of gloves should not preclude the covering of cuts by suitable dressings.
- Sharps must not be used for potentially harmful DNA/RNA work, except where essential, such as for animal inoculation. Glassware must not be used where plastic alternatives exist.
- All experimental procedures involving potentially harmful DNA/RNA should be performed so as to minimise aerosol production. Procedures which are likely to generate aerosols such as the use of blenders, sonicators, vigorous shaking and mixing etc. must be conducted under effective engineering controls including suitable local exhaust ventilation systems (e.g. fume cupboard or ducted vent over the equipment) if appropriate, or in equipment which is designed to contain the aerosol. The suitability of such systems should be determined as part of the risk assessment. However, the control measures utilised for such work must not accentuate the risk in other workplaces or in the outside environment. Where there may be an additional microbiological hazard, a microbiological safety cabinet must be used.
- Potentially harmful DNA/RNA should be securely stored in marked refrigerators, cupboards or rooms when not in use.
- Arrangements should be made for immediate surface decontamination after spillages. Dilution of spillages with detergent and careful disposal of solid waste by incineration is recommended.
- Wherever possible, potentially harmful DNA/RNA should be denatured or destroyed, for example by breaking into biologically inactive fragments or heat treatment, prior to disposal.
- All accidents or incidents should be reported to and recorded by the person responsible for the work. The University HS&E Department and the Occupational Health Unit should be informed immediately in the event of any accident where exposure to potentially harmful material may have occurred. A full accident record should be prepared and forwarded to the HS&E Department as soon as possible.

NOTE: *Whilst it is not appropriate to assign naked nucleic acids to a specified containment level (since these are not biological agents) the above precautions are comparable to Containment Level 2 standards*

ANNEX 2: CONTROLS ON ANIMAL AND PLANT PATHOGENS

Persons wishing to import or work with animal or plant pathogens, or pests, or any material that may be carrying such pathogens or pests, should be aware that such imports and work are strictly controlled by legislation enforced in England and Wales by the Department of the Environment, Food and Rural Affairs (DEFRA. The primary aim of the legislation is to protect livestock, poultry, crops etc against infection by pathogens knowingly or unwittingly imported into the country and to ensure that any work with such pathogens is kept under appropriate containment. Licences are required for any such activities.

Particular care should be taken to be aware of the legislation when importing material that may potentially carry pathogens. These include all types of plant materials, any living creatures or their tissue, cell cultures, body fluids, excreta, carcases or parts of carcases. Appropriate licences are required to import potential carriers.

There may be circumstances in which it will be difficult to decide whether or not a licence is required. In all such circumstances, the proposed importation should be referred to the appropriate government department for guidance. It is the responsibility of the user to determine whether or not the organism or material to be used is required to have an import licence and/or a licence to keep it, and to apply to the appropriate government department.

Licences will stipulate the necessary containment and control measures required to protect the environment. It is also necessary to assess the risks to people from the proposed work activity and implement appropriate containment and control measures to protect human health and safety under the requirements of the COSHH Regulations. If the pathogen or material is genetically modified then the Genetically Modified Organisms (Contained Use) Regulations also apply and impose additional requirements.

1. Animal Pathogens

i) Importation of animal pathogens

There are regulatory controls which prohibit the importation into Great Britain from outside the European Community of “animal pathogens” or “carriers” without a licence issued by the appropriate Minister. The purpose of this is to protect the British livestock and poultry industries from infection by pathogens knowingly or unwittingly imported into Great Britain.

For further details see the information on animal pathogens on the DEFRA website. The index includes links to definitions under IAPO of “animal pathogen” and “carrier”.

An application form for a licence can be printed off the DEFRA website and details are given in the notes accompanying the form on where to send it once completed.

NOTE: *Other controls apply to animals, animal products or products of animal origin that are subject to EC trade rules. Further details on licensing under animal products' legislation are also available on the DEFRA website via the link above.*

ii) Possession of Specified Animal Pathogens

Regulatory control requires that no person shall have in his possession any “Specified Animal Pathogen” or any “carrier” in which he knows such a pathogen is present, except under the authority of a licence issued by the appropriate Minister. The purpose of this is to prevent the introduction and spread of Specified Animal Pathogens which are not endemic in Great Britain and which if introduced would cause serious disease and economic loss to the livestock industry. All work (including holding/storage) with these organisms requires a licence.

For further details see the information on animal pathogens on the DEFRA website. The index includes links to definitions under SAPO of "specified animal pathogen" and "carrier" and the list of specified animal pathogens. The information also includes links to the DEFRA classification of specified animal pathogens and the containment requirements for work with pathogens in categories 2, 3 and 4, rabies virus and arthropods containing specified animal pathogens.

An application form for a licence can be printed off the DEFRA website and details are given in the notes accompanying the form on where to send it once completed. Prospective applicants should note the SAPO licensing process takes several months as applicants' laboratories are inspected and inspections are not arranged until satisfactory documentation has been provided.

2. Plant Pathogens

There are restrictions on imports of plants, plant produce, plant pests, soil and growing medium from non-European Community countries into Great Britain. These restrictions are there to protect plant health and are implemented in England by the Plant Health (England) Order 2005. These Orders are implemented in England and Wales by the Department of the Environment, Food and Rural Affairs (DEFRA). Licences are required for any such activities. For further information, see the DEFRA Plant Health website.

If the work involves the genetic modification of plants or work with plants that have been genetically modified then a risk assessment should be made in accordance with the requirements of the Genetically Modified Organisms (Contained Use) Regulations 2000. Specific guidance on risk assessments for genetic modification work involving plants is provided by the Advisory Committee on Genetic Modification (ACGM) in the ACGM Compendium of Guidance which is available on HSE's website at http://www.hse.gov.uk/biosafety/gmo/acgm/acgmcomp/

Risks associated with genetic modifications are not considered further here. The following provides guidance for experimental work with plants in laboratories, growth rooms and glass houses and although it is not directed at gardening and similar activities, the same general hazards apply.

The potential hazards associated with handling plants and plant materials must always be considered, and reference made to suitable sources of information to ascertain any precautionary measures required, before the work commences. Some of the hazards associated with exposure to plants and plant associated materials are illustrated by well known common ailments such as hay fever, nettle rash, septic finger and gastric upsets. Hay fever and nettle rash are a result of allergic reaction or irritation. Septic finger can arise from a puncture wound and whilst the micro-organisms which cause disease in plants do not usually cause disease in humans, a break in the skin from a thorn or similar may well introduce more common micro-organisms that can result in localised infection. Some plants are poisonous if ingested and others may have other adverse effects such as hallucinogenic causing mushrooms.

Depending on the nature of the hazard, the application of simple control measures such as wearing gloves or other protective clothing will usually adequately control the risk.

ANNEX 3: GUIDANCE ON USE OF CHEMICALS IN BIOLOGICAL LABORATORIES

1. Hazardous Chemicals and the Law

Enacted under the Health and Safety at Work, etc., Act, the Control of Substances Hazardous to Health (COSHH) Regulations are designed to protect persons against risks to their health arising from exposure to hazardous substances associated with their work. The Regulations are supported by a number of Approved Codes of Practice, the most important of which are the Codes entitled, "Control of Substances Hazardous to Health" and "Control of Carcinogenic Substances"; these are published together in one volume. The Health and Safety Commission has also published a booklet entitled, "COSHH Guidance for Universities, Polytechnics and Colleges of Further and Higher Education."

1.1 Administrative Procedures for Achieving the Safe Use of Hazardous Chemicals

The University is responsible for determining the policy to be adopted for implementing the legislation on the use of hazardous substances at work. The responsibility derives from the Health and Safety at Work, etc., Act, 1974. It is the duty of all Heads of Group to ensure that all aspects of the University Health and Safety Policy are complied with within their area of responsibility.

Each Head of Group must take appropriate measures to ensure that all relevant persons are made aware of any hazards associated with the chemical substances encountered during the course of their work and of the requirements to adopt working procedures designed to keep the risks to their health, and to the health of other persons who might be affected thereby, as low as reasonably achievable. Decisions on how best to work safely with hazardous substances stem from risk assessments. It is illegal to carry out a work activity involving hazardous substances without first making such an assessment.

In addition, the University Health and Safety Policy on safety must be supplemented by local rules relating to specific activities of the CBE, so that when read in conjunction with the Policy, the two parts form an effective means of securing the safe use of hazardous chemicals, as well as of potentially hazardous equipment and hazardous processes.

1.2 Risk Assessments

The hazard of a chemical substance is the set of inherent properties of the material which give it the potential to cause harm. Assessing risk involves examining the extent of the likelihood of a substance causing harm, in the actual circumstances of the work.

The COSHH Regulations require an assessment in respect of any risks to health and safety. A risk assessment comprises:

- Recognition.
- Evaluation.
- Consideration of the steps to be taken to achieve and maintain adequate control.
- Keeping a record, in all but the simplest and most obvious cases.

A risk assessment will be considered to be suitable and sufficient if the detail and expertise with which it is carried out are in accord with the nature and degree of risk arising from the work and the complexity of the work concerned.

It is not necessary to carry out a risk assessment for each separate substance used in any work activity. Thus, in a research laboratory, it is quite permissible to group substances and assess risks and outline precautions for each group. Grouping might be on the basis of chemical properties (i.e. similar hazards) or in the way that substances are used.

This approach to generic consideration of groups of substances or activities is described in the Royal Society of Chemistry booklet, "COSHH in Laboratories". A generic risk assessment, as described above, will not be appropriate for activities involving substances which are extremely hazardous. Individual risk assessments must be formulated in such cases.

1.3 Recording Risk Assessments

All risk assessments other than the simplest, require to be recorded and copies of model COSHH Risk Assessment Forms are available from the University's HS&E Department website. The risk assessment relating to a particular work activity should be produced so that it can be easily understood by persons who need to refer to it. Records of assessments should be maintained locally where the work takes place and should be reviewed, from time to time, to ensure that each is still relevant for the work activity concerned. All risk assessments should be reviewed at least annually.

2. General Laboratory Precautions

2.1 Safe Systems of Work

A safe system of work will generally arise naturally out of the COSHH risk assessment. However, it should be noted that all chemical substances are hazardous in some way or another and thus must be regarded as potentially dangerous materials. When planning new research work, all possible sources of danger must be considered and specialist advice must be sought before commencing experimental work with unknown risks.

2.2 Training and Supervision

All persons studying or working in laboratories where hazardous chemicals are stored, used or prepared must receive information, training and supervision appropriate for the work undertaken, so that risks to the health and safety of all persons involved are controlled.

Academic staff who supervise experimental work carried out by postgraduate students, research assistants and technical staff are required to give careful attention to the health and safety of those under their supervision. This applies not only to work on CBE premises but also to work carried out elsewhere in the University. To fulfil its function, the degree of supervision must have reasonable regard for the level of training and expertise of the staff or students being supervised.

The University has a duty to ensure that postgraduate students do not create unsafe conditions by unauthorised initiatives and supervision must be adequate to meet this requirement. Accordingly, prior to the commencement of any hazardous work or activity, the supervisor should provide, obtain or agree to appropriate procedures which would minimise foreseeable risks and thereafter should keep in regular touch with the student's work. During the absence of the supervisor, a second supervisor should be available to ensure that established health and safety procedures are maintained.

2.3 Good Housekeeping

It has long been recognised that good housekeeping plays an important role in reducing laboratory accidents. The workbench should be kept clean at all times and free from chemicals and apparatus which are not required. The laboratory floor should also be free from obstruction; reagent bottles and apparatus left on the floor can cause serious accidents. Never run in the laboratory or along corridors, never rush through doorways or open doors abruptly and never indulge in horse play; all of these can have serious consequences. Hazardous chemicals, flammable liquids, solid carbon dioxide and cryogenic liquids should never be transported in passenger lifts.

Use only the minimum quantities of chemicals for a particular activity. Only minimum quantities of chemicals should be stored in laboratories.

All chemicals should be clearly labelled and toxic and carcinogenic chemicals must carry a special warning. Labels on reagent bottles must never be altered and, if the contents of a container do not correspond with the printed label, then the label should be removed and the container relabelled. When a chemical is transferred from the container in which it was supplied to another container, as much as possible of the information given on the label of the original container should appear on the label of the repackaged material.

Any spillage of a chemical substance must be cleaned up immediately by persons who are able to take due account of the nature of the materials spilled.

2.4 Closing of Laboratories and Overnight Experiments

The last person to leave a laboratory at the end of the day should check that the gas, water and electricity supplies not in use have been turned off, and that all stocks of flammable reagents and solvents have been returned to their fire-resistant cupboards, cabinets or bins.

Apparatus left running overnight must be clearly marked with the standard University notice, giving the name and telephone number of the person(s) to contact in any emergency. All experiments involving toxic and/or flammable substances must be checked and authorised by an experienced person prior to being left running overnight.

Water connections to experiments left running overnight must be made securely by a screw clip, or similar device and a water failure cut-out switch should be fitted, where appropriate. It is recommended that the apparatus and/or experiment should be operated attended for at least one hour under the conditions it will run unattended overnight.

2.5 Toxic Substances

All experiments involving toxic reagents, products and by-products, particularly when these are gaseous or volatile, should be carried out in an efficient fume cupboard, so as not to endanger other nearby workers. If an efficient fume cupboard is not available, the experiment should not be carried out. Where work with very toxic chemicals is being planned, it is a requirement that the DSO is informed and other workers in the same laboratory notified of the dangers.

2.6 Flammable Reagents and Solvents

A limited batch size of < 0.5 litres of flammable solvents is suggested. Precautions must be taken to minimise the concentration of flammable vapour in the working area and to eliminate all sources of ignition, such as sparking thermostat controllers, etc. Thought must be given to the action required should there be an accident with flammable solvents leading to a fire.

Solvent residues and other combustible materials must not be allowed to accumulate in laboratories. Flammable reagents and solvents must never be poured down drains, but must be collected and arrangements made for their safe disposal. Waste acetone and chloroform must not be mixed, since the mixture can lead to an exothermic reaction.

2.7 Highly Reactive Chemicals and Explosive Reactions

Certain highly reactive chemicals, such as acetylides, azides, diazoalkanes, nitrogen halides, perchlorates, peroxides and polynitro-compounds often behave unpredictably and are prone to decompose explosively.

Protection must be provided against the hazards of explosion, rupture of apparatus from overpressure, sprays or emission of toxic or corrosive materials and flash ignition of vented vapours or gases. Apparatus must be placed so that no-one can be injured if an explosion occurs. Operation within an appropriate fume cupboard is always recommended with the additional protection of a safety screen, which is either fixed or weighted so that it does not become a missile itself during an explosion. If a safety screen is used to protect against an explosion risk during work on the open bench, place the apparatus and the screen so that no-one in the area is at risk from flying debris.

2.8 Storage of Chemical Substances

The reception, storage and distribution of chemicals must be the responsibility of authorised persons only. Regulations governing the storage and labelling of toxic and other hazardous materials must always be observed. Very toxic chemicals, including chemicals with emotive names such as potassium cyanide, etc., must always be kept in secure storage, access to which is available only to nominated key holders. Accurate records of chemicals issued from a secure store must be kept by a nominated person.

Research group leaders and others who are responsible for the acquisition, storage and use of hazardous substances must ensure that this process is subject to a suitably documented system of planning and management. Over-ordering of chemicals must be avoided, in order to obviate the accumulation of unwanted chemicals which subsequently become waste for disposal during and after the implementation of research programmes.

Liquids should never be placed on shelving above head height. Incompatible chemicals should not be stored in close proximity, and in particular, mineral acids and organic solvents should not be stored together. Individual workers should not retain chemicals superfluous to current needs and should return these to the chemical store or, if the materials cannot be used again, make arrangements for their safe disposal.

In order to minimise the risk of a serious laboratory fire, the maximum amount of flammable reagents and solvents etc., stored in any one laboratory should not exceed ten litres. This must be kept in suitable closed vessels, in fire resistant cupboards, cabinets or bins, which may be constructed either of wood or steel. Stores for flammable solvents must be properly labelled and should not be sited adjacent to doors or other means of escape from the laboratory. Containers of flammable solvents should be returned to the storage cupboard, cabinet or bin as soon as possible after use. Reasonable quantities of flammable reagents and solvents may be kept in the open laboratory in suitable closed vessels of volume not greater than 500ml; these small quantities are excluded from the fifty litre storage limit suggested for each room.

Flammable reagents and solvents must never be stored in a refrigerator or freezer unless the internal light has been disconnected and removed and the thermostat control circuit has been modified to be sparkproof. Warning notices must be placed on all refrigerators which are not suitable for storing flammable materials.

2.9 Disposal of Waste Chemicals

The disposal of chemical substances, covered by a number of statutory Regulations. It falls to individual users to ensure that their chemicals are disposed of in accordance with the "Duty of Care", outlined by the Environmental Protection Act. Advice should be taken from the Departmental Safety Officer (DSO) on appropriate waste disposal procedures. The University School of Chemistry is in a position to offer practical help to the CBE, in connection with the safe disposal of waste chemicals, in both solid and liquid form, including solvents.

2.10 Pressurised Gas Cylinders

The chemical properties of a compressed gas that represents a hazard, such as flammability, toxicity or corrosiveness, must always be known and fully understood by the user and all "first time experiments" involving toxic, flammable and/or corrosive gases must be discussed with the DSO. Experiments with such gases must always be conducted in a good fume cupboard which has been assessed by the user to provide adequate protection to the laboratory staff whilst not causing any noxious emissions into the atmosphere.

Only the minimum number of cylinders of compressed gases in actual use should be kept within each laboratory, and all the cylinders must be firmly supported by restraining chains, bench clamps or similar devices. All other cylinders should be kept in a properly constructed well ventilated store, where full and empty cylinders should be separated, and where smoking and the use of naked flames is prohibited. Cylinders of oxidising gases must be kept separate from cylinders of flammable gases, and toxic and/or corrosive gases should always be stored separately. General guidelines for gas cylinder storage are published by the British Compressed Gases Association.

Large gas cylinders should be moved on an approved design of gas cylinder trolley and should never be dragged or slid across the floor by the main valve. Cylinders must be sited at a safe distance from any high risk fire area, and never beside the door or other escape route from the laboratory.

The contents of a pressurised gas cylinder must never be used without the correct regulator and/or valves which must always be fitted by a competent person. The inlet and outlet connections must be free of oil, grease, dirt and fragments of plastic from the "full cylinder" seal. Oil and grease will ignite in the presence of pure oxygen and if the latter is under pressure, an explosion can occur. The valve, the regulator and any other connections at high pressure should always be checked for leaks using a soap or detergent water solution.

Where any gas is to be passed through a reaction vessel a pressure release device and a trap to prevent suck-back should be used. An appropriate arrangement is generally: cylinder: regulator: (valve): suck-back trap pressure relief device: reaction vessel. The main valve of the gas cylinder should always be turned off after use and any excess pressure in the regulator released with caution.

Certain cylinders and their contents require special precautions and the manufacturer's or supplier's instructions must always be followed. For example, acetylene cylinders must always be kept vertically and the regulator must be fitted with an approved design of flash-back arrestor. Copper or copper alloy piping and/or equipment must never be used with acetylene, and supply pressures in excess of 9psi (0.6 bar) must not be exceeded.

2.11 Cryogenic Materials

Liquid oxygen and liquid air are dangerous because substances not normally regarded as easily combustible become highly flammable in their presence. Containers of either should be clearly labelled and not used for any other purpose. Liquid nitrogen or solid carbon dioxide should be used as coolants.

Eye protection, most appropriately in the form of a full face visor, gloves and suitable footwear must always be worn when cryogenic liquids are being handled. Liquid nitrogen should be decanted into Dewar flasks which are designed for this purpose; if domestic thermos flasks are to be used as liquid nitrogen containers they should preferably be made of stainless steel rather than glass.

Materials stored at liquid nitrogen temperature should always be stored in the vapour phase inside the Dewar, rather than the liquid phase, unless the materials are in a container specially designed

for immersion in the liquid phase. Incidents have occurred in which ingress of liquid Nitrogen into samples stored in the liquid phase has taken place. Subsequent transfer of the sample to a higher temperature freezer or to room temperature has led to an explosion, due to over-pressuring of the sample container.

Great care must be taken to ensure that ingress of air into vessels containing liquid nitrogen does not lead to condensation of oxygen. Evaporation of liquid nitrogen and solid carbon dioxide into a poorly ventilated room can lower the oxygen concentration to such an extent that a person entering the room can lose consciousness and die. The use of oxygen depletion monitors should be considered, in vulnerable areas.

2.12 Glass Apparatus

Many serious accidents are caused by careless handling of glass apparatus including glass tubing, rods and thermometers. A protective cloth should always be used when cutting glass tubing, particularly large diameter, or when inserting tubing or thermometers into rubber bungs; a lubricant should be used where appropriate. Cut ends of glass rods and tubing should be fire-polished before use.

All glassware should be examined closely before use and any damaged pieces disposed of or sent for repair. Never return damaged glassware to storage. Always clear up broken glass apparatus immediately. A small piece of plasticine is often useful for collecting slivers of glass. Broken glass must always be placed in a separate bin for disposal. Never allow broken glass into the general waste; someone may be cut very badly through such thoughtlessness. Before undertaking glass blowing repairs or alterations to glass apparatus or experimental systems, ensure that all toxic and/or flammable vapours have been thoroughly purged from the system.

Eye protection is mandatory when operating glass apparatus under vacuum. Thin-walled glass vessels that are to be evacuated should be protected by binding with adhesive tape (half inch wide) leaving gaps of no more than one inch; a metal mesh cover will provide the same protection. The use of plastic mesh covers is not recommended. Evacuated glass dessicators should be protected with a metal mesh cage and should not be transported whilst evacuated. Air should be admitted gradually when a vacuum within glass apparatus is to be released. Never evacuate a badly scratched flask or one with a star crack; apparatus damaged in this way will often fail under vacuum.

All large glass flasks should be supported adequately; it is dangerous to clamp such a vessel only at the neck. Great care is required when handling large pieces of glassware with wet hands. Winchester bottles must never be carried by the neck but should always be transported in properly designed bottle carriers.

Great care is required when freeing stoppers from flasks or bottles, particularly if the contents are hazardous. If a bottle of chemical has been heated by sunlight or as a result of being stored near a burner, hotplate or radiator, the contents should be cooled prior to releasing the stopper; this is particularly important in the case of strong ammonia solutions.

Bottles containing strong acids, particularly perchloric acid, or strong alkalis, must not be placed directly on wooden shelving or bench tops; porcelain or plastic dishes or trays should always be used.

Strong acids, strong alkalis, toxic and radioactive solutions must never be pipetted by mouth; indeed, to fill a pipette with any chemical solution by mouth is to take an unnecessary risk. An approved design of pipette filler should always be used.

Fitting pipette pumps or other pipetting aids incorrectly leads to many glass cut injuries, which are often serious. Pipetting aids should be fitted with great care, utilising suitable lubrication where necessary, and employing a protective cloth, in case the pipette should fracture. Laboratory workers should receive suitable instruction in the correct use of teats and mechanical pipetting devices.

3. Fume Cupboards

In the CBE Laboratory Unit, adequate control of inhalable chemical substances hazardous to health is generally achieved by placing the work inside a fume cupboard, which effectively reduces exposure levels. There are many factors which affect the capability of a laboratory fume cupboard to provide efficient containment for the hazardous chemicals used in any particular experiment; amongst these are:

1. the toxicity of the substance(s) used;
2. the volatility of the substance(s) used;
3. the rate of release within the fume cupboard of any toxic substance(s);
4. the amount of heat generated within the fume cupboard;
5. air draughts within the laboratory;
6. bulky apparatus within the fume cupboard which may distort the air flow;
7. the linear face velocity of the airflow across the front opening.

It is readily apparent from the above list that the only person who can be expected to be able to make a realistic assessment of any particular fume cupboard's performance under experimental conditions is the person using the fume cupboard, for it can only be he or she who can estimate most of the above parameters and their interaction. The following basic rules for using a fume cupboard should always be observed:

- The extract fan must be on when the fume cupboard is in use for experiments and when it contains volatile compounds.
- Fume cupboards used for experimental purposes must not contain any stored chemicals.
- For experimental purposes, each fume cupboard must be totally allocated to the control of one person.
- During the experiment the sash opening should not be set above that at which the face velocity has been measured.
- It must be possible to close the sash quickly without any risk of disturbing apparatus in the fume cupboard.
- The sash should be kept closed during an experimental procedure which might "run away" and cause an explosion.
- Appropriate hazard warnings must be displayed.
- The rate of release of toxic or flammable vapours must be minimised by experimental design.

All laboratory fume cupboards are inspected and tested by Works Division on an annual basis. CBE staff should carry out a brief visual inspection at least weekly.

3.1 Environmental Protection

In addition to considerations as to the suitability of a particular fume cupboard as a means of protecting the laboratory worker, all users of fume cupboards are reminded that it is a legal requirement under the Environmental Protection Act to use the best practicable means for preventing the emission into the atmosphere of noxious or offensive substances, and for rendering harmless and inoffensive such substances as may be so emitted. In this connection, it must be stated that, where at all practicable, a fume cupboard should not be used as primary containment for a recognised experimental hazard. It should instead be regarded as a second (or even third) line

of defence, capable of dealing with an unexpected breach of the primary containment built into the user's experimental setup, to prevent the escape of noxious or offensive fumes, vapours, etc.

A general purpose laboratory fume cupboard should never be used to remove a very toxic substance from the proximity of the user, and simply eject such material into the atmosphere at the other end of the fume cupboard duct. In such specialised instances, the use of more appropriate containment apparatus such as a fully enclosed glove box must be considered. Likewise, the proposed removal of very corrosive vapours or gases etc., by use of a general purpose laboratory fume cupboard, must be carefully considered and only the correct design of fume cupboard for the job chosen, e.g. a fume cupboard with a water washdown or scrubbing facility.

4. Laboratory Hygiene

Laboratory workers who handle hazardous substances should get into the habit of washing their hands frequently, especially before eating and drinking. Food and drink must never be stored or prepared in laboratories or chemical storerooms but should be consumed in designated areas such as canteens and common rooms. Laboratory coats must not be worn on outside the CBE Laboratory Unit.

4.1 Personal Protection

Great care must always be taken to ensure that hazardous chemicals never come into contact with any body surface; this is the key to the safe handling of chemicals. Wherever it is practicable to do so, a safe system of work should always be designed to completely eliminate bodily contact with any hazardous chemical substances. Where it is not possible to handle hazardous chemical substances in a fume cupboard, a glove box or similar environment, personal protective equipment should be used, but only after it has been positively assessed as being suitable protection against the hazard. Obvious instances where appropriate personal protection is required arise during the handling of corrosive acids and alkalis and toxic compounds.

Footwear should be chosen that is suitable for laboratory work; open-toed sandals and plimsoles give little protection to the feet.

4.2 Protective Clothing

All persons working in the CBE Laboratory Unit must wear a properly fastened laboratory coat or overall, where a school risk assessment directs them to do so. Laboratory coats not only offer a degree of personal protection against small spillages and splashes but also protect everyday clothing from contamination. Coats should be regularly laundered and kept in good repair; they must not be worn outside the laboratory, especially not in a common room or library, and never in general or public areas.

Protective gloves, of a type best suited to the particular hazard, should be worn, but their value should be measured against the loss of dexterity and possible danger of internal contamination through pin holes.

The use of latex gloves should be avoided wherever possible and in all cases where there exists a viable and practicable alternative to the use of latex gloves the alternative should be utilised. There are a few instances where the use of latex gloves remains the preferred first choice barrier (e.g. handling of blood-borne viruses, cytotoxic drugs, and some biological hazards). In such cases where the use of latex gloves is indicated the following risk reducing measures must be observed;

1. Only non-powdered latex gloves are to be used, the use of powdered latex gloves is prohibited within this University

2. Where powder free latex gloves are used they should be of good quality and have low extractable (leachable) protein content. Ideally this should be <50mg/g (the glove manufacturer/supplier should be able to supply such technical data).

It should be noted that handling of glassware with wet gloves is hazardous. Disposable polythene gloves are excellent for some purposes since they can be discarded immediately after use. Care must always be taken when wearing contaminated gloves not to handle bottles, switches, and door handles etc. that might next be handled by unsuspecting persons.

A chemical-resistant apron and boots, with the bottom of the apron worn below the top of the boots, will give added protection when handling large volumes of chemicals.

4.3 Personal Protective Equipment

Personal protective equipment, other than mandatory eye protection, is always to be regarded as a second line of defence, and should only be required when the hazard cannot be controlled at source.

4.4 Eye Protection

It is essential to wear suitable eye protection in chemical laboratories at all times. All laboratories where corrosive or toxic materials are being handled in open vessels, or where there is a risk from flying particles or fragments, must be designated as Eye Protection Areas and a mandatory notice requiring eye protection to be worn must be displayed at each door. The legal requirements for eye protection are contained in the Personal Protective Equipment at Work Regulations, 1992.

Safety spectacles provide only the minimum protection from unexpected hazards and they are not an adequate substitute for either goggles or a full face visor. All eye protectors used in CBE laboratories must conform to the relevant British Standard. Persons wearing contact lenses are at particular risk from splashes of chemical substances and must wear extra eye protection. Contact lens wearers are also advised to inform the DSO and local first aider, since the presence of these lenses may complicate first aid to the eyes.

The laboratories are required to have eye wash facilities. Laboratory staff should be instructed in the correct use of the eye wash facilities available.

4.5 Respiratory Protection

Respiratory protection should only be considered necessary when environmental control cannot be used effectively. Thus, work involving toxic gases, hazardous volatile substances and dusts should be kept away from persons by placing such work in a glove box, fume cupboard or other well ventilated zone. When respiratory protection is chosen, it must be selected by relating the hazard to the respirator so that the expected protection to the wearer is fully realised. Half or full face respirators with replacable filters are useful when dusts are being produced. Canister type respirators, fitted with the appropriate filter unit, will protect against toxic vapours, but only against low concentrations. Users must be adequately trained in the correct use and maintenance of such equipment.

Self-contained breathing apparatus provides the best personal protection against toxic gases and hazardous volatile substances, but must never be used by untrained personnel. It is a requirement of the COSHH Regulations that respiratory protective equipment is regularly inspected and tested, with appropriate record keeping, unless the equipment is for short term use (disposable).

5. General Laboratory Services

Laboratory workers should familiarise themselves with the positions of the main laboratory controls for electricity, gas and water, and should ensure that these do not become obstructed by equipment.

Serious floods have resulted from failure to realise that the pressure of mains water can be higher at night compared to during the day. For this reason, all tubing connected to water sources must be securely wired or clipped. Waste water tubing leading to the sink or fume cupboard drain, should be securely wired to a weight or extension metal tube to prevent flooding. Rubber tubing used to connect bunsen burners to the gas supply should also be inspected regularly for perished sections that may leak.

Gas heated apparatus should never be placed directly on to wooden benches without a sheet of non-asbestos insulating board under the apparatus. Gas supplies to oxygen/air torches must be fitted with approved non-return valves.

ANNEX 4: USE & MAINTENANCE OF BIOLOGICAL SAFETY CABINETS [BSCs]

Biological safety cabinets are intended to offer protection to the user and the environment (which will include other people in the laboratory) from the aerosol hazards arising from the handling of infected and other hazardous biological material. Some types of cabinet may also protect the materials being handled in them from environmental contamination and cross contamination within the cabinet. Air discharged from the exhaust of the cabinet, which is either ducted to outside or recirculated into the laboratory, is filtered to remove microbial contamination.

Biological safety cabinets are intended to reduce the risk to the user when handling hazardous biological materials but they do not necessarily protect the user from all hazards involved. There may, for example, also be radioactive, toxic or corrosive substances present. Similarly the exhaust HEPA filters will not remove these types of contaminants from the exhaust air and particular care must be taken to ensure these are not discharged into the laboratory environment from cabinets that are not ducted to outside.

The following describes some of the main factors that should be taken into account in selecting the correct safety cabinet for its intended use, where it should be positioned within the laboratory and venting arrangements. Since biological safety cabinets are pieces of local exhaust ventilation (LEV) equipment for controlling exposure to hazardous substances, there is a statutory requirement under the COSHH Regulations for regular maintenance examination and testing to be carried out at least every 14 months. Further information on this is provided below.

The relevant British Standards covering microbiological safety cabinets are

- BS EN 12469 Biotechnology – Performance criteria for microbiological safety cabinets 2000 (this standard supersedes BS 5726 Microbiological Safety Cabinets 1992, Parts 1 & 3), and
- BS 5726 Microbiological safety cabinets – Information to be supplied by the purchaser to the vendor and to the installer, and siting and use of cabinets – Recommendations and guidance 2005 (this standard supersedes BS 5726 Microbiological Safety Cabinets 1992, Parts 2 & 4),

When purchasing biological safety cabinets or arranging maintenance work they should always check the cabinets and the associated installation and servicing complies with the British Standard specifications.

In relation to safety cabinets, the terms user, worker and operator are synonymous. Materials handled within a safety cabinet are commonly described as the work or, less obviously, as the product.

1. Types of Cabinet

There are three types or "Class" of microbiological safety cabinet, which differ significantly in design and mode of operation. These are referred to as Class I, Class II and Class III cabinets. All provide protection to the user operator protection), with Class II and Class III cabinets also providing a clean working environment to protect the work from contamination (termed product protection).

The British Standard defines the three types of cabinet as follows. A diagrammatic representation of the airflow patterns in the different Classes of cabinet is provided below.

CLASS I - a cabinet with a front aperture through which the operator can carry out manipulations inside the cabinet. It is constructed so that the operator is protected and the escape of airborne particles generated within the cabinet is controlled by means of an inward airflow through the working front aperture, with HEPA filtration of the exhaust air.

NOTE: *This type of BSC will not provide any protection for the product and is suitable for work with all categories of biological agent, except HG4.*

CLASS II - a cabinet with a front aperture through which the operator can carry out manipulations inside the cabinet. It provides both worker and product protection. The escape of airborne particles generated within the cabinet is controlled by means of an inward airflow at the front of the cabinet which is filtered before circulation within it; while the down flow of HEPA filtered air over the working surface protects the work.

NOTE: *This type of BSC is suitable for work with all categories of biological agent, except HG4.*

CLASS III - a cabinet in which the working area is totally enclosed and the operator is separated from the work by a physical barrier (i.e. gloves mechanically attached to the cabinet). Filtered air is continuously supplied to the cabinet and the exhaust air is treated to prevent release of micro-organisms.

NOTE: *The use of Class III cabinets is usually confined to work with biological agents in HG4.*

In both Class I and II biological safety cabinets the inward airflow protects the user by minimising the escape of any airborne particulate contamination generated within the cabinet. In Class II biological safety cabinets the down flow of filtered air affords protection to the work minimising contamination during manipulations. In Class III cabinets the physical barrier protects the user from the work and the air going in to the cabinet is filtered to protect the work.

2. Cabinet selection for particular applications

A risk assessment should be undertaken to determine the Class of cabinet appropriate for a particular work activity. This should take into account the nature of the potential hazards in terms of not only the micro-organisms involved and their route of infection but also the techniques to be carried out and whether protection of the work (product protection) is needed.

The class of cabinet required is not linked to the Containment Level assigned to the work. It is a commonly made mistake to think these are connected and it can lead to inappropriate selection of cabinet. The following sets out some general guidance on selecting a cabinet. Class II cabinets will probably be the cabinets of choice for most applications in the University as these provide both operator (user) and product protection (protection of the work) and so allow for flexibility in future use when the nature of the research work may change. However where an older Class II cabinet is already in situ, care should be taken to ensure its performance is adequate for purpose.

Class I cabinets should be used if procedures within the cabinet are likely to generate a significant aerosol and/or disrupt the air flow pattern within a Class II cabinet and so compromise operator (user) protection. An example would be use of a homogeniser to break up tissues. A Class I cabinet would be preferentially selected over a Class II for work with certain pathogens that infect via the airborne route (for example Neisseria meningitidis) if there is no need for protection of the work (product protection).

Since a Class III cabinet is totally enclosed this offers the highest level of protection to both the user and the work. However, in practice this level of protection tends only to be required for the most hazardous work i.e. for certain Hazard Group 3 and Hazard Group 4 pathogens in Containment Level 3 or 4 facilities.

Some general comments on selections likely at the different containment levels:

- at Containment Level 1 - a cabinet is unlikely to be required for operator (user) protection as any micro-organisms involved are unlikely to cause harm (otherwise the work would be assigned to a higher containment level). Class II cabinets can be used to provide protection of the work (product protection), for example for tissue culture work; a Class I cabinet will not provide product protection. Alternatively a vertical laminar flow cabinet could be used to provide product protection.
- at Containment Level 2 - usually a Class II cabinet would be used to provide both operator (user) and product protection (protection of the work) unless the procedures are likely to generate a significant aerosol or compromise air flow pattern in which cases a Class I cabinet should be used. If a respiratory pathogen is being used then consideration should be given to using a Class I cabinet.
- at Containment Level 3 - select cabinet according to nature of work.

Where operator (user) protection is required for work with hazardous micro-organisms the cabinet should meet the requirements of the current British Standard relating to microbiological safety cabinets (BS EN 12469).

Some manufacturers sell tissue culture cabinets. These are very similar to Class II microbiological safety cabinets but do not meet the full specification of the British Standard and so are less expensive. Whilst these do offer operator protection to the user, since they do not meet the recognised standard the use of tissue culture cabinets is not recommended where operator protection is required for work with hazardous micro-organisms.

There are other types of cabinets or hoods available but these do not provide operator protection, they are designed to protect the work only. Examples of such types of cabinet include laminar flow cabinets. These types of cabinet must not be used if operator (user) protection against micro-organisms is required. Laminar flow cabinets may use either horizontal or vertical laminar flow. Since horizontal laminar flow cabinets blow air from the back of the cabinet across the work and into the face of the user it is entirely inappropriate to use this type for work handling anything other than clean, non-hazardous materials.

Fume cupboards and hoods must not be used to provide operator (user) protection against airborne biological hazards. If there is any doubt as to the suitability of a particular cabinet for use then the local BGMSA or the University BSO should be contacted for advice.

3. Venting Arrangements

It is good practice to discharge the exhaust air from biological safety cabinets to the outside. Within the University the following approaches should be taken:

- In Containment Level 2 facilities, venting via a HEPA filter through a window or wall to the same level is acceptable, provided attention is paid to the position of nearby opening windows or adjacent air intakes. Depending on the building, planning restrictions may prohibit this as an option.
- If it is not possible to vent to the outside, a recirculating cabinet fitted with double HEPA filters on the exhaust may be considered in Containment Level 2 facilities (see note below) providing there are no other hazardous contaminants in the discharged air. Consideration must be given to a safe method of fumigating the cabinet.
- In Containment Level 3 facilities cabinets must exhaust via a HEPA filter to the outside. The output duct must be taken to roof level or alternatively it may exhaust at the same level, providing a double HEPA filter is fitted. If for some reason ducting to atmosphere is not practicable then the University HS&E Department must be contacted for further advice.

NOTE: *In the old British Standard (BS 5726) it was specified that if air is recycled back into the laboratory that it be through two HEPA filters whereas the current British Standard (BS EN 12469) specifies only a single HEPA in the exhaust with the caveat that risk assessment may demand additional requirements. Within the University it is recommended that all recirculating Class II cabinets be installed with double HEPAs on the exhaust to ensure they are suitable for work with all types of micro-organisms. This will need to be specified when the cabinet is ordered.*

4. Siting, Installation and Commissioning

The siting of a biological safety cabinet is extremely important. Air currents and movement of people in the laboratory can adversely affect the performance (operator protection) of a cabinet. Factors to be considered include the proximity of cabinets to doors, windows, ventilation ducts and to movement routes. Positioning of cabinets within laboratories should meet the guidelines set out in the current British Standard (BS5726). For new cabinets the supplier should always visit the site, undertake a site survey and advise on installation and meeting BS5726 prior to contracts being placed. If the proposed sitting does not meet the recommendations set out in BS5726 and there is no suitable alternative then the local BGMSA or the University BSO should be contacted for advice.

Cabinets must be properly installed and commissioned. Prior to use the cabinet must pass the performance tests specified in the British Standard. The test requirements are quite detailed; need specialist equipment and competent persons to undertake the work properly. This therefore forms part of the service offered by the supplier. The CBE should note however that similar requirements apply when cabinets are moved or relocated and so a specialist contractor will need to be appointed to undertake such works.

If a facility chooses to install a cabinet itself then the requirements of the British Standard must be met. A specialist contractor must be appointed to undertake the operator protection (KI Discus) test prior to use. It is strongly recommended that the CBE ask the contractor to comment on the installation at that time, specifically as to whether it meets the BS requirements. Particular points to note are in relation to siting, incorporation of anti blow back valves and the need for additional fans if ducting is longer than two metres or bent in any way.

5. Routine Maintenance, Examination and Test

In order to meet the British Standard specification, cabinets undergo various testing when manufactured. Within the British Standard there are also requirements for tests on installation and regularly thereafter to demonstrate performance under conditions of use.

Most importantly, biological safety cabinets constitute local exhaust ventilation (LEV) systems in that they offer protection to the worker (user) from airborne hazards. As such there is a requirement for regular maintenance, examination and test under the COSHH Regulations. Therefore, all biological safety cabinets should be serviced on an annual basis and undergo examination and test at that time. It is a requirement of the COSHH Regulations that a record be kept for 5 years of the examinations and tests and of repairs. Health and Safety Executive Inspectors are likely to request sight of, or copies of, records during visits to the University.

The certificate should show tests results for:

(i) Volumetric airflow measurements and airflow patterns

These include various measurements of face velocity (inward airflow) at the front aperture and, in Class II cabinets, the velocity of the laminar downflow.

For Class I cabinets the measured face velocity should be between 0.7 m/s and 1.0 m/s at all points. For Class II cabinets this should be not less than 0.4 m/s.

The downflow in a Class II cabinets (not applicable in a Class I) should be between 0.25 m/s and 0.5 m/s.

(ii) Exhaust HEPA filter test

The HEPA filters on the exhaust are there to ensure that any contamination in the airstream is filtered prior to discharge. It is therefore important to check the integrity of the filters to ensure there are no holes and the filter is properly located so there are no leaks around the edges. The test is undertaken by introducing an aerosol challenge to the airstream upstream of the filter and testing to see if there is any penetration downstream.

Filters should have an efficiency of at least 99.995% (or penetration of <0.005%).

(iii) Operator Protection Factor (or KI Discus) Test

As part of the inspection, a containment test for operator (user) protection should be undertaken. This is usually by the KI Discus method where an aerosol of potassium iodide is generated within the operating cabinet and sampling devices are placed in front of the cabinet to capture any aerosol escaping from the working area. The operator protection factor (OPF) is defined as the ratio of exposure to airborne contamination generated on the open bench to the exposure resulting from the same disposal of airborne contamination generated within the cabinet.

When tested in accordance with the British Standard all cabinets in use should have an operator protection factor of at least 1.0×10^5.

Within the University the following approaches should be taken:

- All cabinets must have an operator protection (KI Discus) test included as part of the commissioning process for new or relocated cabinets.
- All cabinets must be tested for operator protection (KI Discus test) on an annual basis, or every six months if in Containment Level 3 facilities.
- Operator protection tests are to be carried out in such a way as to ensure the cabinet and the laboratory are as representative as possible of normal working conditions, that is

    a. with any air conditioning units or other ventilation systems in the laboratory switched on;
    b. with other safety cabinets and fume cupboards within the laboratory switched on;
    c. with the cabinet loaded with a typical arrangement of equipment and samples;
    d. with a person moving around the laboratory, particularly if any pedestrian traffic is near the cabinet; and
    e. with doors (laboratory, nearby incubators and fridges etc) being opened and closed.

Copies of KI Discus test certificates must be kept for at least 5 years (a requirement under the COSHH Regulations).

6. Training and correct use of cabinets

The effectiveness of the biological safety cabinet depends on

- good design;
- suitable installation;
- ongoing maintenance; and
- correct use.

Comments on the first three items in this list have been covered in earlier sections. It is important users of biological safety cabinet are trained in correct use not only in order to understand how the cabinet works but also because poor technique can compromise the operator protection afforded by the cabinet.

Practical training should be provided by local personnel dealing with the specifics of the particular equipment, location, work, etc. Training should be provided to cover

- principles of how the different classes of cabinets work including airflow patterns;
- suitability of different cabinets for particular types of work;
- principles of airflow, operator protection factor and filter penetration tests;
- limitations of cabinet performance;
- how to work at cabinets safely;
- operation and function of all controls and indicators;
- how to decontaminate the cabinet after use (routine cleaning); and
- requirements for fumigation and, where appropriate, how to do this.

Incorrect use of biological safety cabinets can compromise their performance and adversely affect the level of operator protection afforded by the cabinet. Some of the most common factors that users should pay attention to are

- the user should avoid sudden and sweeping movement of their arms to minimise disturbance of the air flow patterns;
- large and bulky equipment should not be placed in the cabinet, nor should equipment be placed on air grilles as both these will disturb air flow patterns;
- centrifuges, including microfuges, should not be placed in a safety cabinet unless an operator protection factor (KI Discus) test has been carried out with it running in situ and it shown not to compromise operator protection;
- bunsen burners should not be used in biological safety cabinets, particularly Class II, because of the concern about the effect of the heat rising from the flame on the laminar downflow of air in the cabinet. However, if they are used, they should be placed towards the back of the cabinet and a low profile type used. If the bunsen is used in conjunction with alcohol etc for flaming, then the alcohol pot should always be placed to the far side of the bunsen in order that any drips from the item being flamed do not drop in the pot and ignite it; and cabinets should always be installed in appropriate locations to ensure any traffic movement within the laboratory does not cause draughts to disturb the airflow patterns at the front of the cabinet and affect performance. Users should be aware of this requirement and should ensure the 1 metre clear behind rule is observed when they are using the cabinet.

7. Fumigation of cabinets

Fumigation must be carried out only by a trained responsible person with adequate knowledge of the procedure and the precautions to be followed.

Fumigation with formaldehyde vapour is the recognised and most commonly used method for this type of fumigation procedures although an alternative system using vaporised hydrogen peroxide is available. It is expected that any fumigation required will be contracted out as necessary.

ANNEX 5: GUIDANCE ON THE USE AND MAINTENANCE OF AUTOCLAVES

There are several different types of hazards associated with the use of autoclaves. The main ones are the pressure vessel hazard, the unloading hazard and failure of a make-safe (cycle to sterilise contaminated waste) process. The following describes some of the main factors that should be taken into account in risk assessments and the types of control measures to be implemented.

The relevant British Standard covering use of autoclaves in laboratories is BS 2646 Autoclaves for Sterilisation in Laboratories 1993. When purchasing autoclaves or arranging maintenance work they should always check the autoclave and the associated installation and servicing complies with the British Standard specifications. Regular maintenance is essential for the continued efficiency and safety of laboratory autoclaves and ancillary equipment. The CBE should have a continuing programme of planned preventative maintenance throughout the life of the autoclave. Where the autoclave is used to make safe waste it is also necessary to validate and monitor the performance of the autoclave.

In addition to ongoing maintenance and validation arrangements, it is a requirement under the Pressure Systems Safety Regulation that autoclaves be periodically examined by a competent person. This examination is necessary in advance of the autoclave being brought in to service and thereafter at appropriate regular intervals. Within the University this is carried out by the University's Engineering Insurers and all autoclaves must be notified to the University's Engineering Insurance Surveyor in order that they can be added to the schedule and arrangements be made for examination. Notification of autoclaves should be made through the University HS&E Department.

1. Operation of Autoclaves

Autoclaves should be operated only by persons who have been trained and instructed in their use. Operation instructions should be provided for the operator and should include details of action to be taken by the operator in the event of a fault or any abnormality in autoclave performance. It is recommended that simple, easy to understand instructions are provided in addition to the detailed manual provided by the manufacturer.

2. Maintenance

The continuing safe and effective use of the autoclave depends on a programme of planned maintenance throughout its life. Maintenance schedules should therefore follow all of the recommendations in the current British Standard. The manufacturer should always be consulted on maintenance intervals. The CBE should have a continuing programme of planned preventative maintenance throughout the life of the autoclave.

When a fault occurs during a make-safe cycle an assessment of risk should be made and appropriate action taken. It may be necessary to disinfect those chamber attachments on which engineering work is to be carried out. During a make-safe process, chamber condensate should be considered to be contaminated with viable micro-organisms.

A contaminated laboratory autoclave should never be returned to the manufacturer for servicing or repair. Decontamination should be carried out in accordance with local safety rules. The use of permit to work systems for maintenance contractors is strongly recommended.

3. Protective Clothing

A protective laboratory coat of side or back fastening style should be worn in the autoclave loading/unloading area(s).

Additional protective clothing should be available in the loading/unloading area(s) to protect the operator. This should include an impervious apron, heat-resistant gauntlet gloves, suitable heavy-duty footwear or overshoes and a full-face visor. The hazards on loading include spills of biohazardous material, broken glass and dropped load contents. The hazards on unloading include splashes and spillage of hot material from the load, hot condensate, hot equipment, broken glass, dropped load contents, and vapour from volatile chemicals.

4. Loading the Autoclave

All materials awaiting autoclaving should be stored safely. Bagged waste materials should be supported in a robust, leak proof container, bags should never be placed directly on the floor.

It should be possible to identify the source of all materials to be autoclaved. A labelling system should be used in order that the waste can be tracked back to the laboratory or area from where it came. This serves two important purposes. Firstly to be able to identify the contents of the waste and what hazards may be present in the event of someone having an accident in which they are exposed to any infectious agents that may be present. Secondly to be able to identify the producer of the waste if there is any problem with it, such as a container is leaking, overfilled, or contains inappropriate items etc, to prevent repetition of bad practice.

Items should be packed in a way that ensures that steam will penetrate the load. Bags should not be sealed; if the tops have been taped or tied the bags should be opened or slashed to allow effective steam penetration.

When some chemicals (including disinfectants) or materials are autoclaved they are likely to produce vapours that could harm persons exposed when opening the door or they may be corrosive to the autoclave. A risk assessment should be made of all items to be autoclaved taking account of this possibility.

5. Unloading the Autoclave

Temperature and pressure indicators and warning lights should be checked to ensure that the autoclave has successfully completed the operating cycle. If a fault is indicated, attempts to open the autoclave should only be made with the authority of the responsible person. It is dangerous to attempt to release the autoclave door mechanism before the chamber is vented to atmosphere or whilst the load contents are at high temperature. No attempt should be made by the operator to override door interlocking safety devices.

The operator should stand clear when opening the door as hot liquid or vapour may escape from the chamber. The operator should also be aware that containers of liquid could be pressurised and may explode, volatile liquids may produce harmful vapour and liquids spilled on unloading may cause scalding. The following measures are designed to minimise the unloading hazard:

- temperature activated door interlocks;
- timer activated door interlocks;
- training and supervision of operators;
- protective clothing; and
- load transfer systems.

After autoclaving, waste containers should be emptied in a safe manner and their contents disposed of or reclaimed as specified by local laboratory rules.

6. Waste Containers

All waste should be placed in waste containers which should be easily transportable, leak proof and of a robust design with solid sides and bottoms. They should allow adequate steam penetration to the contents.

If autoclave plastic bags are used they should be supported in a waste container whilst in the laboratory, during transport to the autoclave and also whilst in the autoclave. The bag should be open during the autoclave cycle so that steam can penetrate its contents. It is recommended that transparent (rather than opaque) autoclave bags be used as this allows the autoclave operator to see if any hazardous materials have been placed in the bag by mistake.

7. Operating Cycles

The operating cycle should take account of heat up times. The time required for the load to reach sterilizing temperature should be determined during validation tests. Typical operating cycle conditions are listed in the table below.

	Min ^{0}C	Max ^{0}C	Min	Max
Liquids Sterilisation	121 115	124 128	- -	15 30
Equipment/Glassware Sterilisation	121 126 134	124 129 138	15 10 3	- - -
Make-safe (waste)	121 126 134	125 130 138	15 10 3	- - -

7.1 Operating Cycles for Liquids Sterilisation

When liquids are sterilised the possibility of adverse effects on the liquid caused by the heat treatment must also be taken into account on selecting a cycle. The operating cycle should be selected to ensure that sterilisation is achieved with minimum damage to the liquid. Microbiological culture media are particularly heat sensitive; the degree of deterioration is related to the length of time the medium is maintained at sterilising temperature; the heat-up and cooling stages also contribute significantly to this deterioration.

Heat-up times should be as short as possible, achieved by uniformly filling the chamber with steam at sterilising temperature. Large volumes of fluids will heat up slowly, therefore volumes of liquids should be kept small; a maximum container volume of 500ml is recommended, larger volumes taking considerably longer to heat up (and cool down).

Cooling loads quickly helps to protect heat-sensitive constituents and also shortens operating cycle times. Air at high pressure may be admitted to ballast the chamber, minimise boiling and prevent bottles exploding. Containers should be loosely capped unless they are specifically designed for sealing. However, sealing bottles can increase the likelihood of explosion during autoclaving and slows cooling.

8. Validation of Autoclave Performance

The purpose of validation is to test the ability of the autoclave effectively to perform the autoclaving process when loaded with user-defined loads. An autoclave cycle can be split into three phases, warm-up, holding and cooling down. Validation should demonstrate that in the holding part of the cycle the necessary temperature has been attained throughout the load and this is held for a

minimum time. Calibration, which should not be confused with validation, compares the temperature set on the dial to the temperature in the chamber.

If an autoclave is used for a waste cycle (also commonly called a make safe or destruct cycle) for loads containing pathogens or harmful genetically modified micro-organisms then validation is required to demonstrate that the process is effective in achieving a 100% kill. A worst case load of simulated waste (i.e. worst case volumes, materials and equipment but not contaminated with pathogens) should be placed in the autoclave for the validation test. Probes are then inserted at various (12) points in the waste and connected to recording equipment. This then shows the temperature at the various points throughout the cycle. The holding part of the cycle commences once all sensors indicate the prescribed sterilizing temperature has been reached. All sensors must then maintain at least that temperature for the prescribed holding time.

Validation must be carried out by a competent trained person using thermometric test equipment that is calibrated and traceable to national standards. The test method is described in British Standard 2646. The use of biological or chemical indicators for this purpose is not acceptable. The use of benchtop autoclaves for waste is not recommended because these cannot usually be validated.

The prescribed operating cycle conditions for a make safe cycle for waste are:

i) at least 121^{o}C (max 125^{o}C) for 15 minutes; or

ii) at least 126^{o}C (max 130^{o}C) for 10 minutes; or

iii) at least 134^{o}C (max 136^{o}C) for 3 * minutes.

*Loads comprising a variety of items and containers do not heat uniformly. Short holding times are therefore subject to large proportionate variations and should be avoided if possible.

Following validation it will be possible to ascertain the settings required on the autoclave to achieve the above conditions. This will vary considerably with many factors including the load characteristics. For example, one particular autoclave may need to be set at 121^{o}C for 50 minutes in order to achieve cycle (i) above whereas another may need to be set at 123^{o}C for 75 minutes to achieve the same. Where dials can be altered by the user, the temperature and time requirements for a waste cycle should be clearly displayed on the autoclave.

Validation must be carried out at least annually and at any other times when the previous test may no longer be valid (such as part of re-commissioning after maintenance work). The person responsible for the autoclave should check certificates and print-outs received for the validation testing to satisfy themselves that the autoclave meets the criteria specified above for the required cycle(s). Validation records should be kept for 5 years. Executive Inspectors are likely to request sight of, or copies of, records during visits to the University.

9. Routine Monitoring of Autoclave Performance

Following validation, autoclave performance should be routinely monitored. Where autoclaves are used for waste containing pathogens, the autoclave should be fitted with chart recorders or print out facilities and these should be checked after each run and kept as part of the autoclave process record.

Autoclave tape and indicators printed on bags do not show the load has been sterilised. These are used only to indicate that a load has been processed since the stripes appears very quickly even at low temperatures. Use of these would not be regarded as an adequate means of monitoring autoclave performance.

ANNEX 6: GUIDANCE FOR UNIVERSITY MAINTENANCE STAFF & CONTRACTORS WORKING IN CBE LABORATORIES

It is recommended that a copy of this information is given to all maintenance staff and contractors whose job involves them entering and working in laboratory areas. This guidance is applicable for work in the biological containment Laboratory Unit of the CBE. It is important that everybody who carries out work in a CBE laboratory unit is fully aware of and understands this information. Entry of maintenance staff and contractors into laboratory areas must be under a permit-to-work system unless in emergency situations where this is not practicable.

1. Introduction

The type of work that is undertaken in laboratory areas is extremely diverse as is the hazard potential of materials or equipment that is used. Work carried out in laboratories often includes the use of substances that are hazardous to health if inhaled, ingested, or touched, these generally being classed as toxic, harmful, irritant, or corrosive. Of course the level of risk to the health of persons exposed to these substances depends upon many factors, these factors being taken into account when undertaking a risk assessment for safe working with hazardous substances.

Clearly maintenance staff and contractors cannot, and indeed must not, be expected to make competent risk assessments as to the hazard potential of working in a specific area of a laboratory, or on an item of laboratory equipment. Such risk assessment can only be undertaken by persons with sufficient technical/academic knowledge of the activities being undertaken and substances/equipment being used. It is therefore imperative that maintenance staff and contractors work only to the permit-to-work system provided and that any safety requirement, including the wearing of specific personal protective equipment (such as gloves, overalls, goggles etc), is adhered to. It is also important that they do not extend work outside the area covered by the permit-to-work without obtaining a new or signed alteration, to the permit from an authorised and competent member of the laboratory staff.

2. General Guidelines

1. Always read and adhere to the safety requirements of the permit-to-work. You must never put your own health or safety, or that of others, at risk by deviating from the prescribed requirements.
2. You should always work protected by coveralls when in laboratory areas and the permit-to-work will tell you if you require to wear disposable coveralls over your normal work wear.
3. If there has been the need for the wearing of disposable coveralls these should be left with someone in the laboratory for disposal and should not be removed from the laboratory area by the maintenance worker or contractor.
4. Where special gloves or eye/face protection is required to protect against a laboratory hazard this should be specified in the permit-to-work. The CBE will supply such specialist types of personal protective equipment.
5. Never extend work outside the area or time covered by the permit-to-work without first gaining a new permit.
6. If you accidentally knock over, spill, or break an item of equipment inform a responsible member of the laboratory staff immediately. Under no circumstances should you attempt to deal with a spillage of laboratory material, no matter how small that spillage is.
7. By using basic hygiene precautions, allied to common sense, and following the simple rules in the permit-to-work, maintenance staff and contractors can carry out their work in laboratory areas safely.

3. Emergency call-out situations

There may be exceptional (e.g. out of hours) emergency situations where the CBE Laboratory Unit has to be entered to conduct emergency repairs, or to make safe a part of a buildings structure, and when there is no competent laboratory staff immediately available to complete a permit-to-work. In such times of emergency certain general and common sense precautions should be observed:

1. If there is a strong odour in the area, or physical evidence that chemicals have been spilled, do not enter the area until a competent member of the laboratory staff arrives and indicates it is safe to enter. Never attempt to clean up chemical spills or spills of other laboratory materials that may be hazardous.
2. If there is a strong odour in the area, or physical evidence that chemicals have been spilled, contact the Security Department and check that a CBE contact has been alerted and is attending, do not enter the area until that competent member of the CBE staff has arrived and indicated that it is safe to enter. In the above situation, should the Security Department operative advise you that they are unable to confirm that a CBE contact is attending, the Security Department operative should be advised of a spill of an unknown laboratory substance and asked to summon the Fire Brigade.
3. Always wear coveralls and gloves. If you intend to use gloves made of an absorbent material such as leather/cotton to protect against a mechanical hazard such as broken glass, wear a pair of disposable gloves beneath them. These will normally be close fitting disposable gloves and may often be found in dispensing boxes on benchtops or in wall dispensers.
4. Do not touch or move anything that does not have to be moved to deal with the immediate emergency. If the emergency situation is such that you can wait for knowledgeable back up, always do so.
5. If you have no alternative but to move bottles or containers containing chemicals do so carefully and take special note of any hazard warning labels on the container denoting that the contents may be toxic, corrosive or flammable as this may have a bearing on where you should place the container once moved (e.g. if you are to undertake hot-work, or place ladders, etc.)
6. In all cases where there has been the need for emergency entry to a laboratory area without a written permit-to-work being issued, for record purposes, a written permit-to-work should be completed subsequently and it should be indicated what verbal instructions had been given.
7. If anyone has any doubts that it is safe to start or to continue to work then they should stop work until the problem is sorted out. In the event of any query that cannot be resolved locally the University HS&E Department can be contacted for advice. The Security Department are able to contact Health and Safety personnel out-of-hours.

ANNEX 7: LONE WORKING GUIDANCE NOTES

This note provides guidance for those completing the Lone Working Risk Assessment Form. This guidance note should be read in conjunction with the general principles of risk assessment outlined in this CoP. In addition, reference should be made to the Health and Safety Executive (HSE) Guidance Leaflet 'Working Alone in Safety - Controlling the Risks of Solitary Work'.

Lone working is not covered by any specific piece of legislation; however a wide range of legislation may apply depending on the nature of the work involved. The Health and Safety at Work etc Act and the Management of Health and Safety at Work Regulations will apply in all instances.

1. What is Lone Working

Lone workers are those who work by themselves without close or direct supervision. This may include those who work alone in a specific area or building or may include mobile workers, who work alone but in a number of locations.

2. Hazard Identification:

Identify all the hazards specific to the lone working activity; evaluate the risks (low/medium/high); describe all existing control measures and identify any further measures required.

Specific hazards should be assessed on a separate risk assessment form and cross-referenced with this document where appropriate. Specific assessments are available for hazardous substances, biological agents, and manual handling operations. Some hazards to consider may include:

Workplace: Identify hazards specific to the CBE workplace/environment, which may create particular risks for lone workers, e.g. remote areas, laboratories, confined spaces.

- Process: Identify hazards specific to the work process, which may create particular risks for lone workers, e.g. work on electrical systems, cryogenic gases, chemical and biological materials
- Equipment: Identify hazards specific to the work equipment, which may create particular risks for lone workers, e.g. manual handling, operation of essential / emergency controls.
- Individual: Identify hazards specific to the individual, which may create particular risks for lone workers e.g. medical conditions, disabilities, expectant mothers, age, inexperienced, etc.
- Other: Specify any additional hazards particular to the lone work.

3. Control Measures

Identify existing control methods, assess their effectiveness and specify any additional controls that may be necessary. Consider alternative work methods, training, supervision, protective equipment/devices, etc. Some measures to consider may include:

- specific information, instruction and training (e.g. emergency procedures, out-of-hours procedures, personal safety training, etc).
- increased communication systems / procedures (e.g. regular pre-arranged contact by e.g. mobile phone)
- increased supervision
- increased security (e.g. cctv, secure access, personal alarms)

4. Persons at Risk:

Identify all those who may be at risk. It is important that these individuals are made aware of the outcome of the risk assessment and informed of all necessary control measures.

5. Training

Identify the level and extent of training required, taking into account the nature of the lone working activity. Consider the knowledge and experience of individuals, particularly young and new workers. Lone workers should be given information to deal with normal everyday situations but should also understand when and where to seek guidance or assistance from others, i.e. unusual or threatening situations, etc.

6. Supervision

The extent of supervision required will depend upon the level of risks involved and the ability and experience of the lone worker. A few examples of supervisory measures which may be useful in some circumstances include:

- Periodic telephone contact with lone workers,
- Periodic site visits to lone workers,
- Regular contact (telephone, radio, etc),
- Automatic warning devices, e.g., motion sensors, etc.,
- Manual warning devices, e.g., panic alarms, etc.,
- End of task / shift contact (i.e. returning keys)

7. Additional Information

Identify any additional information relevant to the lone worker, including emergency procedures, out-of-hours contact details, first aid provisions, etc.

8. Recording of Assessment Details

A Lone Working Risk assessment Form is available on the CBE Website. It is important that the CBE maintain records of risk assessments for inspection. Obtaining a signature from individuals to confirm that they have read and understood the information contained in the risk assessment is advised and should be implemented at the discretion of each CBE Laboratory Management Committee.

ANNEX 8: STORAGE OF SAMPLES IN LIQUID NITROGEN

There is a foreseeable risk that when samples that have been stored in liquid nitrogen are removed from the liquid phase and warmed they might explode. Clearly there is potential for significant physical injury to anyone nearby and in many cases there might also be an associated infection risk. Schools should therefore have robust systems in place to minimise any risk of injury associated with use of such systems.

When plastics are placed in liquid nitrogen they become brittle and shrink due to the effects of the extremely low temperatures. This applies even to those plastics used for cryogenic vials sold specifically for storage of samples in liquid nitrogen. Whilst use of tubes with internal threads and a gasket will improve sealability, it is virtually impossible to achieve a leak proof vial and so when they are placed in the liquid phase it can seep in to the vial. When the vial is removed for thawing the liquid nitrogen warms up quickly and expands and can cause the tube to explode.

This problem is well known and further details are given on the NUNC website at http://www.nuncbrand.com/en/page.aspx?ID=302 along with further advice and guidance on cryogenic storage.

Ideally all samples stored in liquid nitrogen should either be in the vapour phase or, if in the liquid phase, sealed in CryoFlex™ or similar (plastic tubing that is sealed around the tube like a sausage skin). This applies even if tubes sold specifically for storage in liquid nitrogen are used.

HoG should ensure all persons using liquid nitrogen storage facilities in the CBE are made aware of the potential for explosion and use appropriate control measures to minimise the risk:

1. wherever possible any samples being returned to or new samples going in to, storage in liquid nitrogen should either go in the vapour phase or if in liquid phase be sealed in CryoFlex™.
2. when samples stored in liquid phase are removed from storage a face shield must be worn and the samples must be immediately placed into a secondary container with a closed lid (e.g. sandwich box, larger tube) to warm up. Alternatively they could be stored for at least 24 hours in the vapour phase to allow any liquid nitrogen to dissipate from the tube.

Any accident arising from failure of workers to follow these instructions is likely to result in serious injury and probably a prosecution by the Health and Safety Executive. If supervisors or DSO's are not confident workers will follow these precautions, then all samples should be removed (under supervision) from the liquid phase as soon as possible, even if this means samples are lost. If during safety inspections it comes to light that these procedures are not being followed, then again the group concerned should be required to remove their samples again under appropriate supervision

ANNEX 9: INFORMATION ON SPECIFIC TYPES OF DISINFECTANTS

The following types of disinfectants are recommended (in no particular order) for use in containment laboratories. Key points to be taken into account when selecting the disinfectant are given. Manufacturers' instructions should be consulted for suitable concentration and contact times and further details of applications. COSHH risk assessments should provide clear guidance on handling precautions needed, particularly when using concentrates. A summary of the characteristics of the common classes of disinfectant is provided in Table 1 and 2.

1. Virkon (Peroxygen compound)

Virkon is a commercial disinfectant consisting of a balanced, stabilised blend of peroxygen compounds, surfactant, organic acids and an inorganic buffer system and is widely used within the Institute. It has been shown to be effective against a greater range of microorganisms than Trigene for example. Virkon has a wide range of bactericidal, virucidal, fungicidal and sporocidal activities. For details about Virkon and its applications go to http://www.antecint.co.uk/go.htm, then click on 'downloads' button. Efficacy data for bacteria, virus, fungi etc can then be viewed via a hyperlink.

Characteristics of Virkon

- Wide range of bactericidal, viricidal and fungicidal activity
- Variable activity against bacterial spores and Mycobacterium spp.
- Corrosivity varies with different products, but less so than hypochlorites
- Made up dilutions have very low toxicity and no irritancy (powders are irritants)
- Built-in colour indicator
- Good detergent properties combines cleaning with disinfection
- Stable for seven days on dilution

Due to its wide spectrum of activity, suitability for use in most applications, the pink indicator to show disinfectant capacity and the high degree of safety to users, Virkon is recommended as the disinfectant of choice for most University laboratory applications.

2. TriGene

Trigene is a halogenated tertiary amine compound with a blend of surface-active disinfectants and detergents. It is non-toxic and less irritant than Virkon but has not been shown to be effective against as many organisms as Virkon. It is considered effective for fungi. Full details of efficacy data are available online at: http://www.medichem.co.uk/disinfectant_veterinary.html#TriGene%20II

A working concentration of 2% is recommended for disinfection of surfaces, and discard jars. For inactivation of body fluids [blood/urine] and for wiping up spillages use 10% Trigene.

3. Alcohols (Ethanol, Industrial Methylated Spirits)

70% Ethanol and 60% iso-propanol have relatively poor efficiency and are susceptible to interference. They can be used as a surface disinfectant for metal parts and surfaces where the use of Virkon may not be possible. [e.g. centrifuge parts and internal surfaces of BSCs]. Care should be exercised when spraying items with alcohol, as there is a flammability hazard.

Characteristics of Alcohols e.g. Ethanol, Isopropanol, Methanol, Industrial Methylated Spirits (IMS)

- Good bacterial and fungicidal activity
- No activity against spores

- Variable activity against viruses (ethanol less effective against non- enveloped viruses, propanol not effective against viruses)
- Only recommended for limited use (such as on clean surfaces and for flaming forceps etc) - seek alternative wherever possible
- Poor penetration into tissues
- Should only be used on physically clean surfaces as poor penetration of organic matter
- Rapid action
- Alcohols must be diluted to 70-80% before use (100% alcohol is not an effective disinfectant)
- Highly flammable
- Effective against Mycobacterium spp.

4. Aldehydes (Cidex, Formaldehyde, Gluteraldehyde)

Formaldehyde and glutaraldehyde are extremely hazardous chemicals, being both irritant and toxic. Both have maximum exposure limits. They must not be used for general disaffection but may be used for fumigation of CL 3 labs or of specific items of sensitive equipment. A written standard operating procedure is required.

Characteristics of Aldehydes e.g. Formaldehyde, Glutaraldehyde, Cidex

Chemicals such as formaldehyde and glutaraldehyde have irritant and toxic properties and are extremely hazardous. Therefore these types of chemical disinfectants should not be used as a general disinfectant in the laboratory and only be employed only for specialised uses when no suitable alternative is available.

Glutaraldehyde based disinfectants are commonly used for disinfection of instruments that cannot be heat sterilised. Consideration should be given to using a disinfectant such as Virkon instead. If glutaraldehyde is used then extreme care must be exercised in its use.

The use of formaldehyde should be limited to gaseous fumigation for disinfection of, for example, microbiological safety cabinets and laboratories. Suitable alternatives are available for the most applications.

5. Chlorine-containing or generating compounds (Hypochlorite, Chloros, Presept)

Has a rapid action but is inactivated by protein and organic matter, When mixed with acid chlorine vapour is produce. Hypochlorite also reacts with formaldehyde to produce a carcinogenic gas. Solutions decompose rapidly and must be replenished daily.

Characteristics of Chlorine containing compounds e.g. Sodium hypochlorite, Chloros, Presept

Available as solutions of sodium hypochlorite or powdered or tableted sodium dichloroisocyanurate (NaDCC). Do not use household bleaches.

- Wide range of bactericidal, virucidal, and fungicidal activity
- Limited activity against bacterial spores
- Rapid action
- Inactivated by organic matter, particularly if used in low concentration
- Corrosive to some metals and may damage rubber
- Compatible with anionic and non-ionic detergents
- Incompatible with cationic detergents
- Irritant
- Chlorine gas released when mixed with strong acids
- Carcinogenic products produced when mixed with formaldehyde

- One of disinfectants of choice for use against HIV and hepatitis B viruses
- Not very effective against Mycobacterium spp.

Commonly used dilutions (expressed in parts per million available chlorine):

- 1,000 ppm for general wiping of equipment and benches
- 2,500 ppm for discard containers (if required)
- 10,000 ppm for spillages
- 20,000 ppm for work surfaces, including microbiological safety cabinets, where material containing prions/TSE agents has been handled (NaDCC not effective in this context)

6. Phenolics (e.g. Hycolin, Stericol, Clearsol)

Whilst an effective disinfectant, particularly for mycobacterium, phenol is very toxic and can cause skin burns. It will also damage plastic.

Characteristics of Phenolics e.g. Hycolin, Stericol, Clearsol

- Wide range of bactericidal activity
- Good fungicidal activity
- No activity against spores
- Variable virucidal activity - usually poor against non-enveloped viruses
- Compatible with anionic and non-ionic detergents and metals
- Not readily inactivated by organic matter
- May be inactivated by rubber and some plastics
- Contain detergents
- Concentrates are stable but stability is reduced on dilution
- Agent of choice for Mycobacterium spp.
- 20,000 ppm for work surfaces, including microbiological safety cabinets, where material containing prions/TSE agents has been handled (NaDCC not effective in this context)

7. Other Disinfectants

There are many proprietary products available that are sold as disinfectants. The ones described above are suitable for general use in the laboratory for disinfecting surfaces and equipment etc. Manufacturers should clearly specify the types of applications their product is useful for. Skin disinfectants, e.g. Hibiscrub, Hibitane, Betadine, pHisomed, Cidal etc., or household disinfectants, e.g. bleach, are not suitable for use as general laboratory disinfectants.

Table 1: Activity Profile for Common Classes of Disinfectant

DISINFECTANT	ACTIVE AGAINST						
Type	**Vegetative Bacteria**	**Bacterial spores**	**Fungi**	**Envelope Virus**	**Non-enveloped virus**	**Myco-Bacteria**	**Tse & prions**
Peroxygen Compounds e.g. Virkon	+	+	+	+	+	+	-
Hypochlorite e.g. Chloros	+	+	+[1]	+	+	+[1]	+
Phenolics e.g. Hycolin	+	-	+	+	+[2]	+	-
Surface active agents	+	-	+[1]	+[2]	+[2]	-	-
Alcohols e.g. 70% ethanol 60% propanol	+	-	-	+	+	+	-
Aldehydes eg formaldehyde, glutaraldehyde	+	+	+	+	+	+	-

Key:

+ Generally effective **1** limited activity

- Generally ineffective **2** depends on virus

Table 2. Characteristics of Common Classes of Disinfectants

	Adverse properties			Inactivated by		
Type	**Toxicity**	**Corrosive to metal**	**Flammable**	**Organic Matter**	**Detergent**	**Hard water/ salt**
Peroxygen Compounds e.g. Virkon	Irritant	+ On prolonged contact	-	-	-	-
Hypochlorite e.g. Chloros	Toxic Corrosive	+	-	-	+ Cationic	-
Phenolics e.g. Hycolin	Toxic & corrosive	-	-	-	+ Cationic	+
Surface active agents e.g. Cetrimide, Tego	-	-	-	+	+ Anionic	+
Alcohols 70% ethanol 60% propanol	Harmful	-	+	-	-	-
Aldehydes eg formaldehyde, glutaraldehyde	Toxic & Irritant	-	-	-	-	-

ANNEX 10: TRANSPORT OF INFECTIOUS SUBSTANCES AND OTHER BIOLOGICAL MATERIAL OUTSIDE THE CBE LABORATORY UNIT

Micro-organisms that are pathogenic for humans or animals, clinical material sourced from humans or animals that contains (or is likely to contain) pathogenic micro-organisms, some genetically modified micro-organisms/organisms and certain other materials of biological origin are classified as dangerous goods for the purposes of transport. This means that such material has to be classified, packaged, labelled and transported in such a way as to control any risks from exposure to the material during the transport process.

Other biological material, eg DNA, which may not be classified as dangerous for the purposes of transport still needs to be sent in robust packaging so that it doesn't leak during transit and also be appropriately labelled so as to not to give rise to concerns as regards safety or security of the material.

This guidance covers the transport of infectious substances and other biological material from the CBE to elsewhere in the UK and overseas, by any mode of transport in accordance with the various dangerous goods regulations. This guidance should be regarded as essential reading for all persons in the CBE involved in the transport of biological materials. Summaries of the procedures to be followed by CBE personnel when transporting biological materials can be found on the CBE website. However, all persons in the CBE transporting biological materials should always refer to the full text of this guidance at the time the shipment is made.

1. Legislation

The regulations in force in the UK are derived from European Directives which in turn implement international regulations issued by the United Nations. The Carriage of Dangerous Goods and Use of Transportable Pressure Equipment Regulations is the main UK legislation that covers transport by road and rail. The requirements for transport of dangerous goods by air (both domestically and internationally) can be found in the International Civil Aviation Organisation's Technical Instructions.

The approach to safe transport of infectious substances is similar for the different modes of transport but, in general, substances sent via air require more stringent packaging. The law is complex and also subject to regular change. This guidance will make reference to the law but only in respect of providing practical guidance on the transport process.

(i) Transport by road and rail - ADR and RID

The current (at the time of writing) Regulations implement various European Council Directives that in turn apply the European agreements on the international carriage of dangerous goods by road and rail (known as ADR and RID respectively). **These documents are updated regularly and this guidance is based on the provisions in ADR 2007**
(available at http://www.unece.org/trans/danger/publi/adr/adr2007/07ContentsE.html**).**

(ii) Transport by air - ICAO (and IATA)

Technical Instructions for the Safe Transport of Dangerous Goods by Air issued by the International Civil Aviation Organisation (ICAO) are recognised as the legal requirements for the transport of dangerous goods by air. The International Air Transport Association (IATA) incorporates these into the IATA Dangerous Goods Regulations along with operational requirements of member airlines/carriers. All the major airlines are members of IATA.

Anyone in the CBE using air transport that is not under IATA membership should still follow the provisions in the IATA Regulations since this would ensure the legal requirements under ICAO are

met. **This guidance is based on the provisions in the 49th edition of the IATA Dangerous Goods Regulations effective from 1 January 2008.**

(iii) Transport by sea - IMDG

Transport of dangerous goods by sea is regulated under IMDG, the International Maritime Dangerous Goods Code of the International Maritime Organisation. In the event anyone in the CBE wishes to specifically transport biological materials by sea they should contact the local BGMSA or the University BSO for advice.

2. General Principles

Items or articles that are being transported are referred to as goods and those that have certain hazardous properties are defined as "dangerous goods" under the international agreements. The criteria for defining dangerous goods are found in the descriptions of nine UN hazard classes with each class relating to a different type of hazard and some hazard classes being further subdivided into hazard divisions due to the wide scope of the class. Most goods that are transported are not considered sufficiently dangerous to require special precautions during carriage but some have properties which mean they are potentially dangerous if carried. Dangerous goods are liquid or solid substances and articles containing them that have been tested and assessed against internationally-agreed criteria - a process called classification - and found to be potentially hazardous when carried. They are assigned to different Classes depending on their predominant hazard as follows:

Class 1 -	Explosive substances and articles
Class 2 -	Gases
Class 3 -	Flammable liquids
Class 4.1 -	Flammable solids, self-reactive substances and solid desensitized explosives
Class 4.2 -	Substances liable to spontaneous combustion
Class 4.3 -	Substances which, in contact with water, emit flammable gases
Class 5.1 -	Oxidizing substances
Class 5.2 -	Organic peroxides
Class 6.1 -	Toxic substances
Class 6.2 -	**Infectious substances**
Class 7 -	Radioactive material
Class 8 -	Corrosive substances
Class 9 -	Miscellaneous dangerous substances and articles

If the goods to be transported meet the criteria for dangerous goods they have to be classified accordingly and assigned a UN number and proper shipping name by following procedures set out under the UN hazard class specification. The UN numbers and proper shipping names are standardised across the world and recognised internationally as a detailed description of the goods. Each UN number and proper shipping name has an entry in the Dangerous Goods List where the provisions that must be met when transporting the goods are indicated under the various columns. These include any limitations or special provisions that may apply, reference to the applicable numbered Packing Instruction that contains the detailed requirements for packaging the goods, and the labels that have to be affixed to the packages etc. A summary of the key entries for infectious substances in the Dangerous Goods Lists is provided in Appendix 1.

For infectious substances, the classification scheme used in the various transport regulations reflects the risks associated with micro-organisms during transport rather than being based on the hazard group classification scheme used to assess risks to workers whilst handling micro-organisms in the laboratory. As can be seen in the following sections, the definitions and classifications of biological materials for transport purposes are quite complicated. However, it is important to get the classification correct as this determines how the goods should be packaged

and labelled and other transport requirements. It is not acceptable to just be overly cautious and classify more stringently than is necessary since **it is an offence to consign dangerous goods incorrectly classified.**

Some biological materials are transported in chemicals such as ethanol, formaldehyde etc for various scientific reasons. Where the chemicals have hazardous properties it is likely that they will be subject to controls under the transport regulations. Guidance on transporting chemicals is not included here and the DSO, local BGMSA or University BSO should be contacted for further advice on particular consignment requirements.

There are 5 steps involved in the safe transport of infectious materials:

Step 1. Classification

Biological materials that are hazardous because they present an infection risk are allocated to Class 6.2 - Infectious Substances. For transport purposes, infectious substances are defined as anything known or are reasonably expected to contain pathogens ie micro-organisms (including bacteria, viruses, rickettsia, parasites, or fungi) or other agents (such as prions for example) which can cause disease in humans or animals. Pathogens that cause disease in humans are also known as biological agents under COSHH Regulations.

A wide variety of different types of biological materials may fall under the classification of infectious substances. These typically include cultures or isolates of pathogenic micro-organisms, most human or animal specimens, some genetically modified micro-organisms, some biological products, and clinical/healthcare and medical wastes that have not been decontaminated.

All hazardous properties of biological materials must be taken into account during classification. If more than one hazard is present then classification varies depending on the nature of the different hazards and is determined by following rules on the order of precedence. Where biological materials do not carry any infection risk but have other hazardous properties, toxic for example or samples are in chemicals, the material must be classified accordingly.

The flowchart in Figure 1 summarises the Classification process.

Infectious substances in Class 6.2 are assigned to one of the following UN numbers with the corresponding proper shipping names:

- UN 2814 INFECTIOUS SUBSTANCE, AFFECTING HUMANS
- UN 2900 INFECTIOUS SUBSTANCE, AFFECTING ANIMALS only
- UN 3373 BIOLOGICAL SUBSTANCE, CATEGORY B
- UN 3291 CLINICAL WASTE, UNSPECIFIED, N.O.S., or (BIO) MEDICAL WASTE, N.O.S. or REGULATED MEDICAL WASTE.

For UN 2814 and UN 2900, where the infectious substance is carried in liquid nitrogen or is in an animal carcass, the proper shipping name is in some cases amended accordingly. Further advice should be obtained from the local BGMSA or University BSO on a case by case basis if it is necessary to transport in these items.

The UN description for Class 6.2 divides infectious substances into either Category A or Category B and this forms the basis for determining which of the above UN numbers should be assigned as follows:

Category A - an infectious substance which is transported in a form that, when exposure to it occurs, is capable of causing permanent disability, life-threatening or fatal disease in otherwise healthy humans or animals.

- An indicative list of infectious substances that meet these criteria is provided in the regulations. However the table should not be regarded as exhaustive. Other infectious substances, including new or emerging pathogens, which do not appear in the table but which meet the same criteria must be assigned to Category A and if there is doubt as to whether or not a substance meets the criteria it is also to be included in Category A.

- Infectious substances meeting the above criteria and which cause disease in humans or both in humans and animals are assigned to UN 2814 whereas those which cause disease only in animals are assigned to UN 2900.

Category B - an infectious substance that does not meet the criteria for inclusion in Category A.

- Infectious substances in Category B are assigned to UN 3373.

NOTE: *The proper shipping name for Category B infectious substances is Biological Substance, Category B not Infectious substance, Category B.*

NOTE: *Many cultures can be assigned to UN 3373 (further information is given below).*

Exemptions and Exceptions

Certain types biological substances are not subject to the regulatory regime because of the low hazard that they present (unless they have other hazardous properties and so meet the criteria for inclusion in another hazard class for dangerous goods). These include:

- Substances which do not contain infectious substances or substances which are unlikely to cause disease in humans or animals
- Substances containing micro-organisms which are non-pathogenic to humans or animals
- Substances in a form that any present pathogens have been neutralised or inactivated such that they no longer pose a risk to health
- Environmental samples (including foodstuff and water samples) for which there is a low probability that infectious substances are present, or where the concentration of pathogens is at a level naturally encountered and which are not considered to pose a significant risk of infection
- Dried blood spots, collected by applying a drop of blood onto absorbent material, or faecal occult blood screening tests and blood and blood components collected for the purpose of transfusion or preparation of blood products and any tissues or organs for use in transplantation
- Human or animal specimens for which there is minimal likelihood that pathogens are present providing the specimen is packed in a packaging which will prevent leakage and which is marked with the words “Exempt human specimen” or “Exempt animal specimen” as appropriate

The above categorisations and exemptions should be read in conjunction with the following paragraphs which provide additional interpretation and guidance. A simple flowchart is provided in Figure 1 to aid classification. This is supplemented with various examples of how many different types of biological materials should be classified in Appendix 2.

For transport purposes an exposure is defined as occurring when an infectious substance is released outside of the protective packaging, resulting in physical contact with humans or animals. Categorisation of micro-organisms into either Category A or Category B for transport purposes is

not directly related to the hazard group classifications assigned under the COSHH Regulations. Whilst all hazard group 4 pathogens meet the criteria for inclusion in Category A only some of those in hazard group 3 do. It should also be noted that two hazard group 2 pathogens, Clostridium botulinum and poliovirus, are included on the indicative list and there may be others that meet the criteria.

In relation to the different types of biological materials:

(i) Cultures of micro-organisms

For transport purposes cultures are defined as resulting from a process by which the micro-organisms are intentionally propagated. The high concentrations or titres of micro-organisms result in increased risk of infection when exposure to them occurs. They are often also referred to as laboratory stocks or isolates. Cultures of micro-organisms that are infectious for humans and/or animals must be classified for transport as follows:

- Category A infectious substance if the particular micro-organism appears on the indicative list (or for new or emerging pathogens if they meet the Category A criteria) or
- Category B infectious substance if the particular micro-organism does not appear on the indicative list (and does not meet the criteria for Category A)

Cultures of micro-organisms that are not infectious for humans or animals are not subject to control under the various transport regulations. However, when transported they must always be packaged in such a way that they are unlikely to leak in transit

(ii) Clinical samples sourced from humans or animals

This includes blood, other body fluids, excreta, secreta, or tissues being transported for research or diagnostic purposes. Materials from human or animals should be assigned to Category A or B based on the known medical history and symptoms of the source human or animal, endemic local conditions, or professional judgement concerning individual circumstances of the source human or animal. The type of sample (blood, faeces, etc) and the distribution of the organism within the body during an infection may be taken into account in deciding whether the samples are likely to contain pathogens.

All samples or materials collected from humans or animals and which are known or likely to contain pathogens are considered, as a minimum, Category B infectious substances. Assignment to Category A should be made where appropriate. Some (see below) samples from humans or animals are exempt from the regulations subject to complying with specified packaging and labelling requirements. In the regulations such samples or materials are termed Exempt human or animal specimens and the exemption includes materials being transported for research purposes.

Professional judgement must be used to determine whether it is appropriate to transport samples as Exempt human or animal specimen ie specimens where there is a minimal likelihood that pathogens are present. That judgement should be based on known medical history, symptoms and individual circumstances of the source human or animal, and endemic local conditions. For example, samples from healthy individuals, or where there is no reason to suspect that the person is suffering from a severe infectious disease, and the sample is not being tested for the presence of pathogens, would be exempt. The following examples are also given in the regulations – blood or urine tests to monitor cholesterol levels, blood glucose levels, hormone levels or prostate specific antigens; tests required to monitor organ function such as heart, liver or kidney function for humans or animals with non-infectious diseases, or therapeutic drug monitoring; tests conducted for insurance or employment purposes and are intended to determine the presence of drugs or alcohol; pregnancy tests; biopsies to detect cancer; and antibody detection in humans or animals. As indicated above, all samples or materials collected

from humans or animals and which are known or likely to contain pathogens are considered, as a minimum, Category B infectious substances. These may not be transported as exempt specimens.

Dried blood spots, collected by applying a drop of blood onto absorbent material, or faecal occult blood screening tests and blood or blood components which have been collected for the purposes of transfusion or for the preparation of blood products to be used for transfusion or transplantation and any tissue or organs intended for use in transplantation (all in humans) are not subject to control under the various transport regulations.

NOTE: *Important note for air transport: some operators (airlines) apply additional restrictions. These are listed in the regulations as Operator Variations. See for example AF-04 (Air France) and LH-12 (Lufthansa), these airlines will carry blood and tissue samples only if they are packaged and labelled under UN 2814 or UN 2900.*

(iii) Miscellaneous other materials that may contain micro-organisms

There are a variety of other types of materials or samples that may contain infectious substances and a judgement should be made as to whether it is appropriate to assign them to Category A or Category B for transport purposes using the criteria for inclusion as described above. Materials in which there is a possibility, but low probability, that infectious substances are present, or where the concentration is at a level naturally encountered, and which are not considered to pose a significant risk of infection are not subject to control under the transport regulations. Examples would include foodstuffs, water and environmental samples. However, in all cases the nature and individual circumstances of the source material must be considered.

(iv) Genetically modified micro-organisms (GMMs) or genetically modified organisms (GMOs)

These are micro-organisms and organisms in which genetic material has been purposely altered through genetic engineering in a way which does not occur naturally. GMOs/GMMs which meet the definition of infectious substances above must be assigned to either UN 2814 or UN 2900 or UN 3373 as appropriate. These would be genetically modified micro-organisms assessed as requiring containment level 2 or above (based on the risk assessment made under the GM regulations) ie Class 2, because they are harmful, or potentially harmful, to humans and/or animals. The local BGMSA and the University BSO must be informed of any intention to transport (within the UK or abroad) Class 3 GMMs since advance notification must be made to the Health and Safety Executive.

GMMs that do not meet the definition of an infectious substance, but are capable of altering animals, plants or microbiological substances in a way that does not occur naturally are classified as Class 9 (Miscellaneous Dangerous Goods) under UN 3245 and their proper shipping name is 'GENETICALLY MODIFIED MICRO-ORGANISMS'. These would be GMMs which can be handled at containment level 1 but are vectors and can transfer genetic material to other organisms.

NOTE: *this is in relation only to micro-organisms and does not cover, for example, naked nucleic acid, plasmids or liposome gene delivery systems, none of which are controlled under the transport regulations. Vectors which require containment level 2 or above for safe handling in the laboratory must be classified as infectious substances as described in the previous paragraph.*

GMMs which do not meet the definition of an infectious substance and which are not able to alter animals, plants or other micro-organisms are not considered hazardous and are not subject to the provisions of the transport regulations. These would be GMMs which can be handled at containment level 1 and present no significant risks to human or animal health and safety or the environment. They should be packaged in such a way that they do not leak during transport.

GMOs that are not micro-organisms (i.e. plants or animals) and which are known or suspected to be dangerous to humans, animals or the environment are classified in Class 9 - Miscellaneous Dangerous Goods under UN 3245 GENETICALLY MODIFIED ORGANISMS and must be transported in accordance with conditions specified by the competent authority. CBE staff wishing to transport such GMOs should contact the local BGMSA or University BSO for further advice.

Some GMMs and GMOs are authorised for use in certain countries by the competent authority for that country. Where they have been so authorised, e.g. have received a consent for deliberate release into the environment, they are not subject to controls under the transport regulations providing that for any journey, authorisations apply in the country of origin, transit and destination. CBE staff wishing to transport such GMMs or GMOs should contact the local BGMSA or University BSO for further advice.

(v) Naked DNA or Proteins derived from GMMs

Such material eg plasmids, as well as non-modified proteins and other biological material generally, eg antibodies, are not considered hazardous for transport but such material should be packaged in such a way so they do not leak during transport. Depending on the source of the material, it may be subject to import/export control (usually material of animal origin).

(vi) Biological products

Biological products are defined for transport purposes as those products derived from living organisms which are manufactured and distributed in accordance with the requirements of appropriate national authorities, which may have special licensing requirements, and are used either for prevention, treatment, or diagnosis of disease in humans or animals, or for development, experimental or investigational purposes related thereto. They include, but are not limited to, finished or unfinished products such as vaccines.

Biological products transported for the purposes of final packaging or distribution and are for use for personal health care by medical professionals or individuals are not subject to the provisions of transport regulations. Biological products which do not fall under this description and are known or reasonably believed to contain infectious substances and which meet the criteria for inclusion in Category A or Category B are assigned to UN 2814, UN 2900 or UN 3373, as appropriate.

Some licensed biological products may present a biohazard only in certain parts of the world. In that case, competent authorities may require these biological products to be in compliance with local requirements for infectious substances or may impose other restrictions.

It is considered unlikely that the CBE will have a requirement to transport biological products but this section is included here for the sake of completeness. However, if CBE staff wish to transport items they consider would be classified as biological products they should contact the local BGMSA or University BSO for further advice.

(vii) Healthcare Waste

This section is included for the sake of completeness. Within the University disposal of biological wastes is managed and transported in accordance with the procedures set out in the University's Waste Code of Practice to which reference should be made. There should be no need for the CBE to transport healthcare waste themselves but if for any reason they wish to do so they must contact the local BGMSA or University BSO for further advice.

(viii) Decontaminated or treated materials

Materials that have been decontaminated or treated to inactivate any infectious substances that may be present are not subject to control under the various transport regulations (with the exception of some wastes). However, there should be confidence in the degree of inactivation achieved, for example by appropriate testing or by using validated procedures, and where the material was known or suspected of containing Category A infectious substances verification should be particularly rigorous.

(ix) Refrigerated or frozen materials

There is often a requirement to transport biological materials at low temperatures either on wet ice or dry ice. Dry ice is listed in the Dangerous Goods List and is classified in Class 9 - Miscellaneous Dangerous Goods under UN 1845 DRY ICE or UN 1845 CARBON DIOXIDE, SOLID (either of these proper shipping names may be used). For transport by road, dry ice is not subject to the provisions of the transport regulations. In contrast, when dry ice is transported by air various requirements must be met.

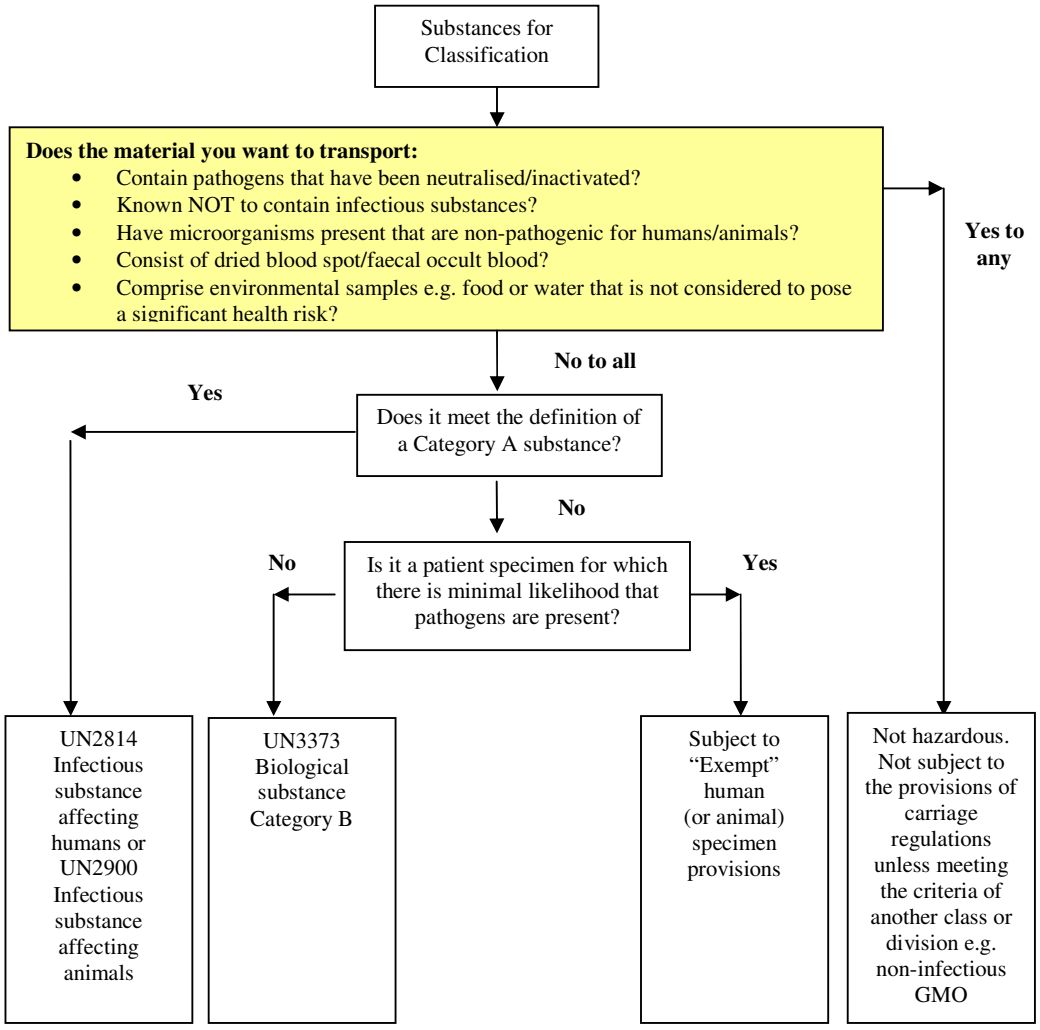
Liquid nitrogen is subject to controls under the transport regulations and wherever possible its use should be avoided for refrigerating infectious substances during transport. Very specialised UN type-approved packing is required to transport infectious substances in liquid nitrogen. CBE personnel should consign infectious substances in liquid nitrogen only if there is no suitable alternative means and must contact the local BGMSA or the University BSO for further advice on the particular consignment requirements.

(x) Samples or materials in chemicals

Some biological materials are transported in chemicals such as ethanol, formaldehyde etc for various scientific reasons. Where the chemicals have hazardous properties it is likely that they will be subject to controls under the transport regulations. Ethanol and formaldehyde are classified as dangerous goods for transport, both being flammable, and formaldehyde also being corrosive. Therefore transport of samples containing surplus liquid of either chemical must meet the necessary transport requirements pertaining to the chemical. Guidance on transporting chemicals is not included here and the local DSO or University BSO should be contacted for further advice on particular consignment requirements. Requirements vary depending not only on the chemical but also on classification of the biological materials due to infectious properties and the mode of transport so advice should be sought on a case by case basis.

Specific examples of how various different types of biological materials should be classified are given in Appendix 2.

Figure 1. Classification Flow Chart (*abstracted from ITA Guidance Document on Infectious Substances***)**



Step 2. Packaging Requirements for Biological Material

The packaging requirements vary depending on the classification of the materials to be transported. The requirements are detailed in the applicable numbered Packing Instruction (PI), as referenced in the Dangerous Goods List against each UN number and proper shipping name. A summary of the key entries for infectious substances in the Dangerous Goods Lists is provided in Appendix 1.

Apart from restrictions on the quantity of materials in packages for air transport, the packing requirements are essentially identical whether the goods are transported by road or by air. However, the road (ADR) and air (IATA) transport regulations use different numbers for the Packing Instructions that in some cases are unfortunately similar – for example ADR Packing Instruction 620 is analogous to IATA Packing Instructions 602. For the sake of clarity the applicable Packing Instructions are referenced below, these have been amalgamated into unified packing procedures for CBE personnel in Appendix 5.

***NOTE**: In various sections the term overpack is used. An overpack is an enclosure used by a single shipper to contain one or more packages and to form one handling unit for convenience of handling and stowage. Each package containing dangerous goods enclosed within an overpack must be properly packed, marked and labelled etc in accordance with the regulations and the overpack labelled as described below. For cooling purposes, an overpack may be used to contain dry ice.*

All infectious substances must be packed using a triple layer system.

- **Primary container** – a primary leak proof (or sift-proof for solids) receptacle containing the infectious substance, wrapped in sufficient absorbent material to absorb the entire fluid content in case of breakage.
- **Secondary packaging** – durable, leak proof (or sift proof) secondary packaging to enclose and protect the primary container.
- **Outer packaging** – secondary packaging is placed in outer shipping packaging with suitable cushioning material to protect content from physical damage during transit.

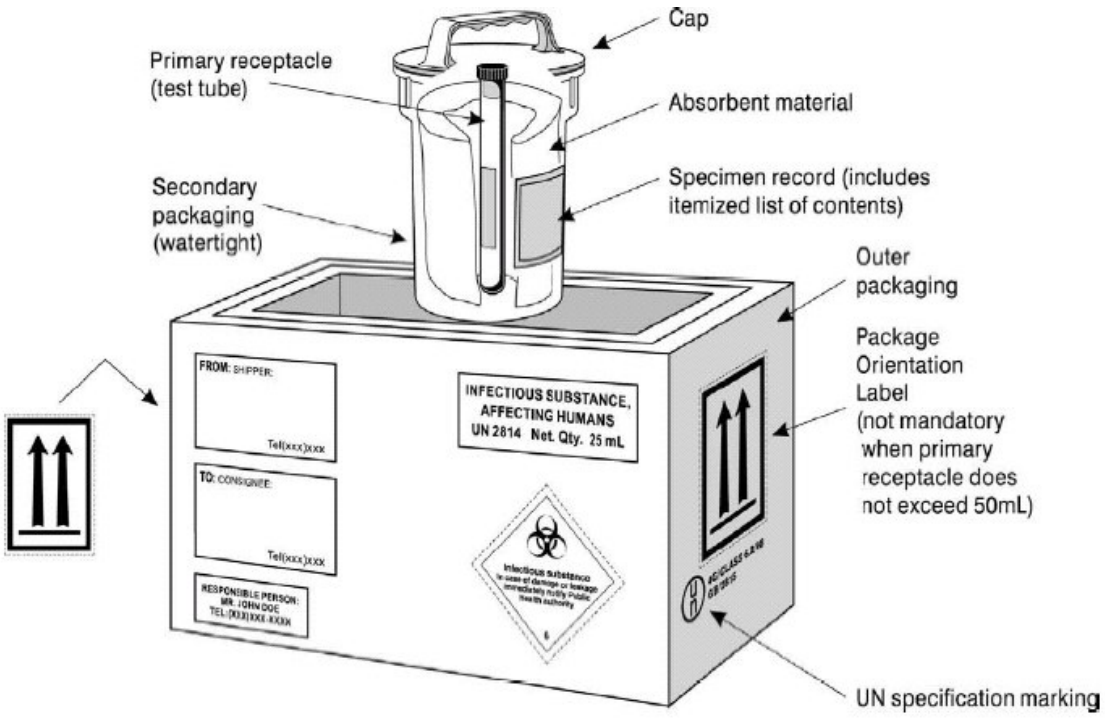


Figure 2. Example of Triple Pack System (for Cat A infectious substances). *Reproduced from IATA guidance document on infectious substances.*

(i) Category A infectious substances assigned to either UN 2814 or UN 2900

Category A infectious substances assigned to either UN 2814 or UN 2900 must be packed in accordance with

- for road transport - ADR Packing Instruction 620
- for air transport - IATA Packing Instruction 602

Packing procedures that meet the packing requirements of both the above Packing Instructions are detailed in Appendix 5 (Procedure 1).

Packaging for Category A infectious substances must meet UN performance requirements for Class 6.2 substances as shown by design type testing. These are known as UN type-approved packaging and they are certified and marked accordingly. Packaging used for Category A infectious substances must be specifically approved for Class 6.2 goods.

For transport by road there are no limits on the quantity of materials contained within either the primary receptacle(s) or the total package. This is in contrast to transport by air where other than for body parts, organs or whole bodies

- on passenger aircraft there is a 50ml/50g limit per package, and
- on cargo aircraft there is a 4L/4Kg limit per package.

In both the above case there is no limit per primary receptacle.

(ii) Category B infectious substances assigned to UN 3373

Category B infectious substances assigned to UN 3373 must be packed in accordance with

- for road transport - ADR Packing Instruction 650
- for air transport - IATA Packing Instruction 650

Packing procedures that meet the packing requirements of both the above Packing Instructions are detailed in Appendix 5 (Procedure 2).

Packaging for Category B infectious substances is not required to be UN-type approved providing it is suitable for its purpose and capable of passing a 1.2 metre drop test. This means that following a drop from a height of 1.2m there is no leakage from the primary receptacle and this should remain protected by the absorbent material within the secondary packaging.

For transport by road there are no limits on the quantity of materials contained within either the primary receptacle(s) or the total package. This is in contrast to transport by air where other than for body parts, organs or whole bodies

- on both passenger and cargo aircraft there is a 4L/4Kg limit per package, with a 1L limit per primary receptacle for liquids whereas for solids the primary receptacle must not exceed the outer packaging mass limit of 4Kg.

(iii) Genetically modified micro-organisms assigned to UN 3245

Genetically modified micro-organisms assigned to UN 3245 must be packed in accordance with

- for road transport - ADR Packing Instruction 904
- for air transport - IATA Packing Instruction 913

Packing procedures that meet the packing requirements of both the above Packing Instructions are detailed in Appendix 5 (Procedure 3).

For transport by road there are no limits on the quantity of materials contained within either the primary receptacle(s) or the total package. This is in contrast to transport by air where

- the maximum quantity in a primary receptacle must not exceed 100 ml or 100 g although there is no total limit per package.

NOTE: *This applies only to GMMs assigned to UN 3245. GMMs assigned to UN 2814 or UN 2900 must be packaged and labelled as Category A infectious substances.*

(iv) Exempt human or animal specimens

Exempt human or animal specimens must be packed in accordance with the packing procedures detailed in the ADR and IATA Regulations. These are specified in the main texts of the regulations rather then within a numbered Packing Instruction and must be followed for any specimen transported under the exemption. Packing procedures that meet the packing requirements of both the ADR and IATA Regulations for exempt patient specimens are detailed in Appendix 5 (Procedure 4).

For transport by road or by air there are no limits on the quantity of materials contained within either the primary receptacle(s) or the total package.

(v) Non-hazardous biological materials

Biological materials that are not classified as dangerous goods must still be packaged in such a way that they do not leak during transport. This can be best achieved by packing in accordance with the procedures set out in Appendix 5 (Procedure 5).

(vi) Refrigerated or frozen materials

Biological materials are frequently transported at low temperatures either on wet ice or dry ice and particular care must be taken to ensure the integrity of the packaging used is not compromised when these melt or dissipate.

Dry ice is assigned to UN 1845 and for air transport must be packed in accordance with IATA Packing Instruction 904 (there is no applicable Packing Instruction for road transport of dry ice and note rather confusingly ADR Packing Instruction 904 is for GMMs). The requirements of IATA PI 904 are included within the procedures for dry ice detailed in various sections in this guidance.

If wet ice is used it should be placed around the secondary packaging in the form of sealed cold packs or similar rather than being loose, and the outer packaging should be leak proof.

Dry ice must be placed only in packaging designed and constructed to permit the release of carbon dioxide gas and to prevent the build up of pressure that could rupture the packaging. If dry ice is used to cool the materials it must be placed around the secondary packaging(s), and the outer packaging (including any overpack) must permit the release of carbon dioxide gas. Dry ice must never be placed in either the primary or secondary receptacle as gas will build up and eventually these will explode with potential to cause very serious damage. Interior supports should be provided to secure the secondary packaging(s) in an upright position after the wet ice has melted or dry ice has dissipated. The primary receptacle and the secondary packaging need to be able to maintain their integrity at the temperature of the refrigerant used.

Insulated products for use with wet ice or dry ice, known as overpacks or thermal control units, are available commercially. Where these are used for packages containing Category A infectious substances, particular care must be taken to ensure that the final packaging combination meets UN performance requirements (i.e. the UN type-approved packaging's are used in accordance with the manufacturer's instructions). Alternatively, UN type-approved products specifically designed for use with wet ice or dry ice are available.

NOTE: *Other dangerous goods must not be packed in the same packaging as Division 6.2 Infectious Substances unless they are necessary for maintaining the viability, stabilising or preventing degradation or neutralising the hazards of the infectious substances. For category A or B infectious substances, if a quantity of 30 ml or less of dangerous goods included in Classes 3, 8 or 9 is packed in each primary receptacle containing infectious substances no other requirements of the ADR or IATA regulations need be met.*

Step 3. Labelling of Packages for Transport of Biological Materials

Packages should be clearly labelled with the delivery address and senders details. For all items assigned to UN 2814 or UN 2900 emergency contact details must be shown on the outer package, this should include a named person, at both where the package is being sent from and where it is going to, and a telephone number. However, in order to facilitate any problems during transport being readily resolved, it is recommended that emergency contact details be shown on all packages containing biological materials.

Labels must be durable and legible and clearly visible on the outside of the packaging. The package must be of such a size that there is adequate space to fix all the required markings and labels. Labels must be located on the same surface of the package affixed adjacent to the consignor's or consignee's address and must not be folded or affixed in such a manner that the same label appears on different faces of the package (i.e. the full label must be on a single face of the package). The package must be of such a size that there is adequate space to affix all required labels (labelling examples are provided in Appendix 6).

Any unnecessary or incorrect labels must not be shown on the outside of the box – for example a box that is pre-printed for infectious substances should not be used if it does not contain these, or if a box has been used before and shows labels that are not relevant to the particular consignment this also should not be used or the labels must be removed or obliterated.

If an overpack is used, it should be marked with the word "OVERPACK" and unless the labels on the packages it contains are clearly visible they must be reproduced on the outside of the overpack.

The following labels must be used as applicable to the contents (refer to all sections to ensure all necessary labels are used):

(i) Category A infectious substances assigned to either UN 2814 or UN 2900

Mark with the appropriate UN number and proper shipping name either UN 2814 INFECTIOUS SUBSTANCE, AFFECTING HUMANS or UN 2900 INFECTIOUS SUBSTANCE, AFFECTING ANIMALS ONLY and add the word liquid or solid as appropriate in lower case and in parentheses at the end of the proper shipping name.

And nearby affixed to the same surface, the hazard warning label for Class 6.2 - Infectious substances as shown below. This must be set at an angle of 45^{o} (diamond shaped), at least 10 cm by 10 cm in size, have black text etc on white background, and a line 5mm inside the edge running parallel to it.

The lower half of the label may, but is not required to, bear the inscriptions “INFECTIOUS SUBSTANCE” and “In the case of damage or leakage immediately notify Public Health Authority”.

It is not necessary to show the technical name, that is the recognised biological (scientific/technical) name of the micro-organism, on the package, but the proper shipping name should be supplemented with the technical name in the accompanying transport documentation.

Emergency contact details (name and telephone number) must be shown on outer packages containing Category A infectious substances.

(ii) Category B infectious substances assigned to UN 3373

Mark with the proper shipping name in letters at least 6 mm high BIOLOGICAL SUBSTANCE, CATEGORY B (the names DIAGNOSTIC SPECIMENS or CLINICAL SPECIMENS are no longer permitted) and adjacent display the following mark

The mark is in the form of a square set at an angle of 45o (i.e. diamond shaped) with each side having a length of at least 50 mm, the width of the line has to be at least 2mm and the letters and numbers at least 6mm high. The background of the mark has to be a contrasting colour to the surface of the package.

NOTE: *For Category B infectious substances, the above diamond does not contain either the biohazard sign or the number 6.*

(iii) Genetically modified micro-organisms assigned to UN 3245

Mark with the UN number and proper shipping name UN 3245 GENETICALLY MODIFIED MICRO-ORGANISMS and nearby affixed to the same surface, the hazard warning label for Class 9 - Miscellaneous dangerous goods as shown below. This must be set at an angle of 45^{o} (diamond shaped), at least 10 cm by 10 cm in size, have black text etc on white background, and a line 5mm inside the edge running parallel to it.

NOTE: *This applies only to GMMs assigned to UN 3245. GMMs assigned to UN 2814 or UN 2900 must be packaged and labelled as Category A infectious substances.*

(iv) Exempt human or animal specimens

Mark as appropriate with the words either EXEMPT HUMAN SPECIMEN or EXEMPT ANIMAL SPECIMEN

(v) Non-hazardous biological materials

Since they are not subject to control under the transport regulations there are no actual labelling requirements for biological materials that are not classified as dangerous goods.

(vi) Refrigerated or frozen materials

If an overpack is used, all required labels described above must also be clearly visible or repeated on the overpack and it be marked with word OVERPACK

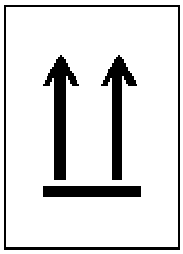
a. Where the package contains dry ice and is transported by road Mark with the words DRY ICE. The UN number and associated hazard label are not required.

b. Where the package contains dry ice and is transported by air mark with the UN number and proper shipping name and the net weight of dry ice UN 1845 DRY ICE ## Kg and nearby affixed to the same surface, the hazard warning label for Class 9 - Miscellaneous dangerous goods as shown below. This must be set at an angle of 45° (diamond shaped), at least 10 cm by 10 cm in size, have black text etc on white background, and a line 5mm inside the edge running parallel to it.

Where dry ice is carried by air in checked or carry-on baggage, the baggage must also be marked with the words DRY ICE 2.5 kg or less of dry ice. A suitable baggage tag should be available from the airline.

(vii) Packages containing liquids

Packages containing liquids must display "Package Orientation" labels. This must be at least 74 x 105 mm in size and show two black or red arrows on a white or suitable contrasting background.



The labels must be affixed or pre-printed on at least two opposite sides to show the proper orientation for the primary(s) to be in the upright position.

NOTE*: whilst they may be used, orientation arrows are not required on packages containing Class 6.2 infectious substances in primary receptacles of not more than 50*

(viii) Packages suitable for cargo aircraft only (quantity restrictions apply on passenger aircraft)

Packages suitable for cargo aircraft only (quantity restrictions apply on passenger aircraft). The Cargo Aircraft Only label must be used if the package is permitted only on cargo aircraft – this would be where it contains more than the quantity allowed on a passenger aircraft. If a package is permitted only on cargo aircraft it should be confirmed prior to despatch that the shipment can be successfully routed and completed using cargo aircraft since would not be an option for some remote places.

The Cargo Aircraft Only label must be affixed on the same surface of the package as, and near, the hazard label. This must be at least 120 x 110 mm in size (or for small packages the dimensions may be halved), and is as shown below. This must be black printing on an orange background.

Step 4. Paperwork/Documentation Requirements

Any carriage of goods subject to controls under the transport regulations must be accompanied by documentation as specified in those regulations. The information required must be clearly legible and for air transport must exactly meet the specified format. The following includes requirements for paperwork included within the package and for paperwork accompanying the package for the carrier etc.

When transporting any biological materials, paperwork (ideally this should be on University headed paper) must be included within the package between the secondary and the outer (attached to the secondary), giving

- the names and addresses of both the consignor (sender) and consignee (receiver), including emergency contact details (name and telephone number) at both ends and
- for dangerous goods, a description of the goods in the following format/order UN NUMBER and PROPER SHIPPING NAME. In addition, for Category A infectious substances assigned to UN 2814 or UN 2900 - the proper shipping name must be supplemented with the technical name (the recognised biological/scientific/technical name of the micro-organism). When the infectious substances to be transported are unknown, but suspected of meeting the criteria for inclusion in Category A and assignment to UN 2814 or UN 2900, the words "suspected Category A infectious substance" in parentheses should be used as the technical name. - an itemised list of contents must be given, to include for each named item the number of tubes and their volume. or
- for exempt human or animal specimens, a simple statement saying what the materials are, that there is minimal likelihood that pathogens are present and that they are exempted under the transport regulations. or
- for non-hazardous biological materials, a simple statement saying what the materials are, that they are non-hazardous and that they are not classified as dangerous goods under the transport regulations.

Written emergency response procedures must also be provided with any package containing biological materials classified under UN 2814, UN 2900, UN 3373 or UN 3245. A standard format is given in Appendix 4.

CBE personnel exporting GMMs or GMOs should see the guidance in Section 4 on the requirements of the Cartagena protocol for such exports which requires additional paperwork to be included. The local BGMSA and University BSO must be informed of any intention by CBE personnel to transport (within the UK or abroad) Class 3 GMMs since advance notification must be made to the Health and Safety Executive.

When using a courier, senders must always give a full description of the goods to the company when initially arranging the shipment, including the relevant UN number(s) and proper shipping name(s), in order the courier is fully aware they will be transporting dangerous goods and ensures the necessary paperwork is completed.

For transport by road of packages containing dangerous goods other than those assigned to UN 3373 as category B infectious substances, the carrier (company transporting the goods) should request that a dangerous goods declaration form be completed. Typically the carrier will provide a copy of the form for completion. The format and information required is similar to that for air transport.

For transport by air of packages containing dangerous goods it is necessary to complete an Air Waybill and, in most cases, a Shipper's Declaration for Dangerous Goods.

Before sending any biological materials abroad, the person sending the goods (the consignor/shipper) should contact the person to whom they are being sent (the consignee) to let them know shipping details and to check that the substance may be legally imported. The person receiving the materials is generally regarded as the importer and the one responsible for obtaining, where necessary, all appropriate permits or licences. Importation of materials into the United States is particularly tightly regulated and there are restrictions even on some items that may be transported as non-dangerous goods. Items requiring an import permit, licence or notification to be made when importing into the UK include items containing products of animal origin, certain animal pathogens or materials that may contain them, all hazards group 4 and a few hazard group 3 pathogens, and items covered by the anti-terrorism legislation. For further information on imports of

animal products and animal pathogens CBE staff should contact the local BGMSA or the University BSO for advice on a case-by-case basis to check whether the item they wish to bring into the UK needs an import licence or is subject to other permissions etc.

Step 5. Methods of Transport

Irrespective of the method of transport the material must first be classified, packaged and labelled in according to the relevant requirements. As indicated at the beginning of this guidance the requirements under the different transport regulations sometimes vary depending on where and how the particular consignment is to be transported. This guidance covers transport of biological materials by road and by air and any significant differences in the requirements are clearly identified. Where there are only minor differences the higher standard is given to simplify the guidance and procedures for users. In all cases the differences are because of more stringent requirements for transport by air, mainly because of industry standard practices and operational considerations. A summary of the key entries from Dangerous Goods Lists applied to the transport of biological samples, cultures and other materials is provided in Appendix 3.

(i) On-site Transport – within and between University Buildings

Any infectious material (including modified) should be transported in appropriate containers ie lidded, leak-proof (or sift proof) containers that can be easily disinfected. Material should not be carried in hands, open trays, pockets or loose in plastic bags.

If material is transported on foot, then the carriage of dangerous goods regulations do not apply, but appropriate containers should still be used (as above). In addition, consideration should be given to the route used to transport the material (eg how many roads need to be crossed, avoidance of crowded public area where possible). Those transporting the material should inform the receiving area when they are leaving and how long they expect to take in case of emergencies.

For transport by road, the transport regulations apply if the goods are transported on the public highway by any means. However, they do not apply to carriage between one part of University premises and another part situated in the immediate vicinity even if a public road separates them. Therefore the regulations do not apply to transport of dangerous goods within the University site. However, even if the regulations do not apply because the journey is as described above, the materials must still be packed in such a way to ensure they do not leak in transit and be appropriately labelled with emergency contact details.

(ii) Transporting Infectious substances or biological material yourself

Researchers often wish to transport or carry biological materials themselves, either on their person or in their bags, when travelling. It is necessary however to comply with the applicable transport regulations and in some case such carriage is prohibited.

Category A infectious substances (those assigned to UN 2814 or UN 2900) – CBE personnel must not transport or carry such materials themselves either in their own, colleagues or University owned vehicles or on any public transport including taxis etc. Therefore University personnel must The only exception to this is when specific arrangements have been put in place to meet the legislative requirements for carrying dangerous goods (member of staff completed the necessary driver training and University vehicle appropriately plated and carrying the necessary equipment etc). The local BGMSA or University BSO should be contacted to discuss these requirements in more detail if required. However, in the vast majority of cases it will be necessary to use a specialist courier with the appropriate licences etc to transport Category A infectious substances.

Category B infectious substances (those assigned to UN 3373), **Exempt human and animal specimens and dry ice** can be transported using public and private transport provided the following steps are taken:

- Material must be packaged, labelled and contain relevant documentation in accordance with the regulations.

- Using public transport - the parcel must be concealed from view eg in a bag and must not be left unattended.

- Using a taxi service - the material must be packed using the triple pack system, but this could comprise the specimen being placed in a leak-proof plastic bag (with absorbent material) and then placed in a rigid, lidded outer container. This outer container must be appropriately labelled. The taxi driver (unaccompanied) should be told that there is no risk to them provided the package is not opened.

- Using private vehicles - if dry ice is required, the minimum amount should be used in a well insulated container. Windows of the car/van should be kept open to provide adequate ventilation during the journey.

The air transport regulations specify that dangerous goods must not be carried by passengers as/or in checked baggage, carry-on baggage or on their person - this applies to both Category A and Category B infectious substances.

Dangerous goods must always be transported as separate packages in the hold and must always be declared (the operator/airline is required to report to the appropriate State authority when undeclared or mis-declared dangerous goods are discovered, this is a serious offence and would be dealt with accordingly by the authorities). If individuals wish to take dangerous goods with them on a journey (as a separate package to go in the hold) they must make advance arrangements with the airline and complete an Air Waybill and, where necessary, a Shipper's Declaration for Dangerous Goods. Individual airlines have different requirements and may require early check in.

Packages containing Exempt human or animal specimens may be carried in checked or carry-on baggage (but not on a person) provided they have been packed and labelled in accordance with the requirements of the transport regulations (as detailed in this guidance). Where dry ice is used in packages containing other dangerous goods (e.g. infectious) the requirements in the previous paragraphs must be met. However, where the dry ice is used to pack perishables which themselves are NOT classified as dangerous goods, then dry ice is permitted on aircraft as checked or carry-on baggage providing the quantity of dry ice does not exceed 2.5 Kg and the package permits the release of carbon dioxide gas. Packages and baggage must be properly labelled as detailed in the previous section above. Passengers are limited to a maximum of 2.5 Kg in carry-on and checked baggage combined. In all cases the operator (airline) must be informed you wish to carry dry ice (specific approval is required to carry it in checked baggage) to ensure ventilation safety procedures are followed. In some cases the operator will apply their own restrictions on carriage of dry ice.

For air transport, some states (countries) and operators (airlines) place additional restrictions or constraints on certain shipments – for example some countries prohibit entry of infectious substances without prior approval by the authorities and some airlines will not carry infectious substances. These restrictions are included within the IATA regulations as state and operator variations. Many airlines require advance arrangements to be made for the transport of dangerous goods. Unless a specialist dangerous goods courier is used, senders of infectious substances are advised to always contact the operator/airline to check on their specific requirements for a particular shipment and to make any necessary arrangements for the consignment.

(iii) Using Couriers

Before sending any infectious substances or other material containing dangerous goods, senders should first check that the courier is able to handle dangerous goods. Some couriers may refuse to handle dangerous goods (because they do not have the necessary authorisations etc) and others may impose additional special requirements

Senders should give a full description of the goods to the courier company when arranging the shipment. This should include the UN number and proper shipping name. Couriers must always be told if the package contains dry ice even if only non-dangerous goods are being transported..

The courier may require you to use their own packaging and should also supply relevant transport documentation for completion, together with instructions on completion; they may ask for additional documentation to meet their own internal safety requirements. If the material is travelling by air, they should also be able to provide advice on any specific requirements of the airline used and/or the destination country. All relevant import or export documentation must be completed.

Using a courier to send material within the UK - check whether any stage of the journey will be undertaken by air so that the correct classification, packaging, labelling and documentation can be completed.

(iv) Using the Postal Services:

Other than Exempt human or animal specimens, infectious substances are not permitted in international mail either to or from the UK. However, only Category A infectious substances are prohibited in the domestic mail and other items may be posted subject to following the special arrangements described below. The following table summarises what is permitted in the mail services:

Category of specimen	International mail	Domestic mail
Category A – UN 2814 or UN 2900	No	No
Category B – UN 3373	No	Yes
Exempt human or animal specimens	Yes	Yes
GMMs - UN 3245	No	Yes
Dry ice - UN 1845	No	No

(i) Royal Mail and Parcelforce National Postal Services

Certain types of dangerous goods cannot be sent by post at all whereas others are accepted only on a restricted basis subject to provisions specified by the national postal authorities. These types of items are referred to by the Post Office as prohibited and restricted goods respectively. Senders of letters and packages containing dangerous goods must always ensure they follow Post Office requirements prior to despatch of such materials in the postal services. By following the information contained in this guidance, the CBE should meet the Post Office requirements.

Most hazardous biological materials may be posted in the domestic mail if packed and labelled correctly under the restrictions imposed by the postal services (as described here and in the rest of this guidance). Only Category A infectious substances (items assigned to either UN 2814 or UN 2900) are prohibited in the domestic mail. Dry ice is also prohibited.

Only recognised laboratories or institutions or certain professional persons are permitted to send hazardous biological materials in the post. Members of the public may only post such materials at

the specific request of such a laboratory or person. Materials sent to or from laboratories within the University of Loughborough for research or associated purposes must meet these criteria.

All biological materials sent by the domestic postal services must be classified, packaged and labelled in accordance with the requirements set out in the relevant sections above. The amount of infectious substances (which includes any items assigned to UN 3373, UN 3245 or Exempt human or animal specimens) that can be sent by post is restricted to a maximum quantity of 50 g or 50 ml per package.

The Royal Mail has produced Safebox™ a purpose designed packaging for sending Category B infectious substances in the postal system with the advantage the package can be posted in a pillar-box. It comes as a complete ready to use kit at a unit cost of around £2.20 including pre-paid postage. This packaging is suitable for sending Category B substances (those assigned to UN 3373) and must not be used for Category A infectious substances (not only because Safebox™ is not UN type-approved for these but also they are not permitted in the mail). Safebox™ is only available through the Royal Mail. Further details are available on the Royal mail website (go to http://www.royalmail.com and search for Safebox)**.**

(ii) Royal Mail and Parcelforce International Postal Service

Any biological materials which are classified as dangerous for carriage (which includes any items assigned to UN 2814, UN 2900, UN 3373 or UN 3245) cannot be sent in the international postal services. Exempt human or animal specimens are permitted if packed and labelled correctly under the restrictions imposed by the postal services (as described here and in the rest of this guidance) restricted to a maximum quantity of 50 g or 50 ml per package.

(v) Security of Transport Process

There are security provisions both in ADR and the IATA regulations requiring measures or precautions to be taken to minimise theft or misuse of dangerous goods at all points of the transport chain. Infectious substances of Category A (i.e. those assigned to UN 2814 or UN 2900) are listed in the regulations as "High consequence dangerous goods". High consequence dangerous goods are those which have the potential for misuse in a terrorist incident and which may, as a result, produce serious consequences such as mass casualties or mass destruction. The need for additional security measures should be considered and implemented as appropriate for such goods.

Some infectious substances are subject to controls under anti-terrorism legislation. The local BGMSA or the University BSO must be contacted in advance of any intention to transport, either by road or air, such materials.

CBE personnel must consider security aspects and the following should be regarded as minimum requirements:

- Packages containing infectious substances must be handed over only to persons and companies (individuals, couriers, airlines etc) that have been appropriately identified.
- Packages awaiting collection, either external for uplift or internal following delivery, must be properly secured and not accessible to the general public.
- Copies of information such as Shippers Declarations, Dangerous Goods notes etc should be retained in a secure location within the CBE

In conclusion, a reminder of two very important points:

- The various regulations governing the transport of dangerous goods are complicated and senders of packages must ensure they meet all necessary requirements prior to despatch. If CBE personnel have any doubt as to procedures they must seek further advice, this should be obtained from the local BGMSA or the University BSO.

- Even if the particular biological materials CBE personnel wish to transport does not fall under the description of dangerous goods or is transported as an Exempt human or animal specimen, the item still must be packed safely for carriage and relevant sections included within this guidance must be followed.

Appendix 1. Indicative List of Infectious Substances included in Category A in any form unless otherwise indicated

UN Number and Name	Micro-organism
UN No. 2814 CATEGORY A Infectious substances affecting humans (HAZARD GROUP 3 or 4, unless indicated)[1]	*BACTERIA* *Bacillus anthracis* (cultures only) *Brucella abortus* (cultures only) *Brucella melitensis* (cultures only) *Brucella suis* (cultures only) *Burkholderia mallei - Pseudomonas mallei* – Glanders (cultures only) *Burkholderia pseudomallei – Pseudomonas pseudomallei* (cultures only) *Chlamydia psittaci* - avian strains (cultures only) *Clostridium botulinum* (cultures only) – HG2 *Coccidioides immitis* (cultures only) *Coxiella burnetii* (cultures only) *Francisella tularensis* (cultures only) *Enterohaemorrhagic E.Coli, serotype O157 & verotoxin producing strains* *Mycobacterium tuberculosis* (cultures only) ***see note* *Rickettsia prowazekii* (cultures only) *Rickettsia rickettsii* (cultures only) *Shigella dysenteriae* type 1 (cultures only) ***see note* *Yersinia pestis* (cultures only) FUNGI Coccidioides immitis VIRUSES Crimean-Congo hemorrhagic fever virus Dengue virus (cultures only) Eastern equine encephalitis virus (cultures only) *Escherichia coli*, verotoxigenic (cultures only)[3] Ebola virus Flexal virus Guanarito virus Hantaan virus Hantaviruses causing haemorrhagic fever with renal syndrome Hendra virus Hepatitis B virus (cultures only) Herpes B virus (cultures only) Human immunodeficiency virus (cultures only) Highly pathogenic avian influenza virus (cultures only) Japanese Encephalitis virus (cultures only) Junin virus Kyasanur Forest disease virus Lassa virus Machupo virus Marburg virus Monkeypox virus Nipah virus Omsk hemorrhagic fever virus Poliovirus (cultures only) Rabies virus (cultures only) Rift Valley fever virus (cultures only) Russian spring-summer encephalitis virus (cultures only) Sabia virus Tick-borne encephalitis virus (cultures only) Variola virus Venezuelan equine encephalitis virus (cultures only)

	West Nile virus (cultures only) Yellow fever virus (cultures only)
UN No. 2900 CATEGORY A Infectious substances affecting animals only (DEFRA RISK GROUP 3 OR 4)	African swine fever virus (cultures only) Avian paramyxovirus Type 1 – velogenic Newcastle disease virus (cultures only) Bluetongue virus[2] Classical swine fever virus (cultures only) Foot and mouth disease virus (cultures only) Lumpy skin disease virus (cultures only) *Mycoplasma mycoides* - Contagious bovine pleuropneumonia (cultures only) Peste des petits ruminants virus (cultures only) Rinderpest virus (cultures only) Sheep-pox virus (cultures only) Goatpox virus (cultures only) Swine vesicular disease virus (cultures only) Vesicular stomatitis virus (cultures only)

NOTE: *The above table should be regarded as an indicative list of infectious substances that meet the criteria for Category A infectious substances and should not be regarded as exhaustive. Other infectious substances, including new or emerging pathogens, which do not appear in the table but which meet the same criteria must be assigned to Category A and if there is doubt as to whether or not a substance meets the criteria it is also to be included in Category A.*

The definition of a Category A infectious substance is one which is carried in a form that, when exposure to it occurs, is capable of causing permanent disability, life-threatening or fatal disease to humans or animals. See section 3 of main text for further guidance.

[1]As defined in COSHH and as classified in the HSC Approved List of Biological Agents
[2]Bluetongue virus is on the indicative list in ADR but not IATA. However, since all shipments involve road transport it should always be classified and transported as a category A infectious substance.
[3]Cultures of *Escherichia coli*, verotoxigenic *Mycobacterium tuberculosis Shigella dysenteriae* type 1 transported by road and intended for diagnostic or clinical purposes **only** may be classified as infectious substances of Category B.

Appendix 2: How Biological Materials should be Classified for Transport

CLASSIFICATION EXAMPLES

The following gives examples of how various biological materials should be classified for transport and is to be read in conjunction with section 3 of the main guidance.

1. Non-hazardous biological materials
Example: antibodies, cell extracts, proteins, plasmids, naked DNA, formalin fixed sections (assuming these are free from any contaminating hazardous agents such as viruses or having other hazardous properties)

Classification: Not classified as dangerous goods for transport

2. Environmental samples
i) Materials in which there is a possibility, but low probability, that infectious substances are present, or where the concentration is at a level naturally encountered (i.e. unlikely to pose a significant risk of infection).
Examples: river water, lake or reservoir water, soil samples, food or feedstuffs

Classification: Not classified as dangerous goods for transport

ii) Similar materials to (i) above but where the likelihood of infectious substances is significantly increased.
Examples: raw sewage, soil samples with heavy faecal contamination, samples of food suspected of causing food poisoning illness

Classification: UN 3373 Biological substance, category B

3. Isolates, samples, cultures, specimens, pellets etc of micro-organisms (non GM)
Laboratory workers commonly use all these terms and, whilst they may not necessarily regard some of them as cultures, many fall within the description in the transport regulations of a “culture”

i) Micro-organisms that are neither human nor animal pathogens. Examples: *Bacillus subtilus*, *Aspergillus niger*, *Staphylococus epidermidis*, bacteriophage

Classification: Not classified as dangerous goods for transport

ii) Human pathogens (including animal pathogens that also infect humans)
a) On Category A indicative list
Examples: *Clostridium botulinum*, verotoxigenic *Escherichia coli*, *Mycobacterium tuberculosis, Burkholderia (Pseudomonas) mallei*, hepatitis B virus, HIV, rabies virus, Dengue virus, Japanese B encephalitis virus, highly pathogenic avian influenza virus

Classification: UN 2814 Infectious substance, affecting humans

b) Not on Category A indicative list
Examples: *Neisseria meningitidis, Salmonella typhimurium, Trichuris trichuria, Candida albicans, Plasmodium falciparum, Trypanosoma brucei*, HTLV, influenza virus, vaccinia virus, CJD agent, BSE agent

Classification: UN 3373 Biological substance, category B

iii) Animal pathogens that do not infect humans
a) On Category A indicative list
Examples: Foot and mouth disease virus, velogenic Newcastle disease virus, vesicular stomatitis virus, *Mycoplasma mycoides*

Classification: UN 2900 Infectious substance, affecting animals only

b) Not on Category A indicative list
Examples: Equine infectious anaemia virus, Avian leukaemia virus

Classification: UN 3373 Biological substance, category B

iv) Any of the above materials that have been treated such that they are no longer infectious (e.g. autoclaved)

Classification: Not classified as dangerous goods for transport

4. Genetically modified micro-organisms (GMMs)
i) GMMs which can be handled at containment level 1, present no significant risks to human or animal health and safety or the environment and are not viral vectors
Examples: disabled *Escherichia coli* with non-hazardous insert, *Saccharomyces cerevisiae* with non-hazardous insert.

Classification: Not classified as dangerous goods for transport

ii) GMMs assessed as requiring containment level 2 or above (based on the risk assessment made under the GM regulations) because they are harmful, or potentially harmful, to humans or animals - classify as for unmodified host

a) Host on Category A indicative list
Examples: *Clostridium botulinum*, HIV, Rabies virus,

Classification: UN 2814 Infectious substance, affecting humans

Examples: Foot and mouth disease virus, velogenic Newcastle disease virus,

Classification: UN 2900 Infectious substance, affecting animals only

b) Host not on Category A indicative list
Examples:, *Neisseria meningitidis, Salmonella typhimurium,* influenza virus, vaccinia virus,

Classification: UN 3373 Biological substance, category B

iii) GMMs that **do not** meet the definition of an infectious substance, **but** are capable of altering animals, plants or microbiological substances in a way not normally the result of natural reproduction (containment level 1 handling precautions for laboratory work)
Examples: disabled retrovirus with non-hazardous insert, disabled baculovirus with non-hazardous insert, disabled adenovirus with non-hazardous insert

Classification: UN 3245 Genetically modified micro-organisms
Note: packaging cell lines expressing viral vectors would also fall under this description.

iv) GM cell lines
a) not containing infectious agents (to humans or animals)

Classification: Not classified as dangerous goods for transport

b) known to contain infectious agents (to humans or animals)

Classification: UN 3373 Biological substance, category B OR if particular agent is on indicative list classify under UN 2814 or UN 2900 as appropriate

c) packaging cell lines expressing replication incompetent viral vectors should be classified on the basis of the viral vector as described in iii above.
v) Other materials used in GM work
Examples: naked nucleic acid, plasmids, liposome gene delivery systems

Classification: Not classified as dangerous goods for transport

5. Samples from humans or animals

i) Blood or tissue samples taken from either humans or animals, not known or suspected of having infectious disease and samples not being tested for presence of pathogens (i.e. minimal likelihood contains pathogens)

Classification: Exempt human specimen OR Exempt animal specimen

However: dried blood spots, faecal occult blood screening tests, nail or hair samples may be classified as follows

Classification: Not classified as dangerous goods for transport

ii) Blood or tissue samples taken from humans in an area where local endemicity is such that a significant proportion may carry a pathogen such as hepB or HIV (and individuals not known or considered likely to have infectious disease caused by a pathogen on the indicative list other than where “cultures only” is specified (see Appendix 2)

Classification: UN 3373 Biological substance, category B

iii) Blood or tissue samples taken from humans known or suspected to be infected with a pathogen such as hepB or HIV (and individuals not known or considered likely to have infectious disease caused by a pathogen on the indicative list other than where “cultures only” is specified

Classification: UN 3373 Biological substance, category B

iv) Blood or tissue samples taken from humans or animals known or suspected to be infected with a pathogen on the indicative list other than where “cultures only” is specified
Examples: diagnosed or clinical signs of ebola, lassa fever

Classification: UN 2814 Infectious substance, affecting humans

v) Blood or tissue samples taken from humans or animals known or suspected to be infected with a pathogen on the indicative list where “cultures only” is specified
Examples: diagnosed or clinical signs of rabies, avian influenza, foot and mouth disease, Newcastle disease (or HIV or hepB as described in iii above)

Classification: UN 3373 Biological substance, category B

vi) Blood or tissue samples taken from humans or animals diagnosed or showing clinical signs of infectious disease caused by a pathogen not on the indicative list e.g. meningitis, glandular fever, canine distemper virus, feline HIV

Classification: UN 3373 Biological substance, category B

vii) Human or animal derived cell lines
a) not containing infectious agents (to humans or animals)

Classification: Not classified as dangerous goods for transport

b) known to contain infectious agents (to humans or animals)

Classification: UN 3373 Biological substance, category B OR if particular agent is on indicative list classify under UN 2814 or UN 2900 as appropriate

Appendix 3: Transport of Biological Samples, Cultures and other Materials - Summary of key entries from Dangerous Goods Lists
(Sources: Road transport - ADR 2007; Air transport - IATA Dangerous Goods Regulations 2008 –CHECK against subsequent amendments)

				ROAD TRANSPORT		AIR TRANSPORT			
UN or ID Number	**Proper shipping name/description**	**Class or Division**	**Hazard Label**	**ADR Packing instruction**	**Max Net Qty/Pkg**	**IATA Packing instruction**	**Max/Net Qty/Pkg Passenger & Cargo aircraft**	**Max/Net Qty/Pkg Cargo aircraft only**	**Special Provisions**
2814	Infectious substance, affecting humans (liquid or solid)	6.2	Infectious Substance	620	No limit	602	50mL or 50g	4L or 4Kg	A81 A140
2900	Infectious substance, affecting animals only (liquid or solid)	6.2	Infectious Substance	620	No limit	602	50mL or 50g	4L or 4Kg	A81 A140
3373	Biological substance, Category B	6.2	[UN3373 diamond]	650	No limit	650	4L or 4Kg	4L or 4Kg	-
3245	GMO or GMM	9	Miscellaneous	904	No limit	913	No limit	No limit	A47
1845	Dry Ice	9	Miscellaneous	-	No limit	904	200 Kg	200 Kg	A48 A151

Special Provisions:
A47 – GMO and GMMs, which meet the definition of an infectious substance and the criteria for inclusion in Division 6.2 must be transported as UN2814, UN2900 or as UN3373 as appropriate
A48 – Packaging tests are not considered necessary
A81 – The quantity limits shown do not apply to body parts, whole organs or whole bodies. Transport in accordance with this Special Provision must be noted on the Shippers Declaration for Dangerous Goods
A140 – For the purposes of documentation, the proper shipping name must be supplemented with the technical name. technical names need not be shown on the package. When the infectious substances to be transported are unknown, but suspected of meeting the criteria for inclusion in Category A and assigned to UN2814 or UN 2900, the words “suspected Category A infectious substance” must be shown, in parentheses, following the proper shipping name on the Shippers Declaration for Dangerous Goods, but not on the outer packaging.
A151 – When dry ice is used as a refrigerant for other than dangerous goods loaded in a unit load device or other type of pallet, the quantity limits per package do not apply. In such case the unit load device or other type of pallet must be identified to the operator and must allow venting of the carbon dioxide gas to prevent a dangerous build up of gas.

Appendix 4: Emergency Response Procedures for Transport of Infectious Substances

(Source: taken from guidance documents produced by the Department for Transport, the Civil Aviation Authority and IATA.)

The following provides a standard format for emergency response procedures when carrying infectious substances. A copy should be provided with any package containing biological materials classified under UN 2814, UN 2900, UN 3373 or UN 3245.

The following information is provided for use by carriers/operators in the event that a package containing infectious substances (of either Category A or B) is involved in an incident resulting in spillage.

1. Mitigation procedures:

DO NOT CLEAN-UP OR DISPOSE OF INFECTIOUS SUBSTANCES, EXCEPT UNDER SUPERVISION OF A SPECIALIST

- Isolate spill or leak area immediately in all directions.
- Keep unauthorized personnel away.
- Obtain identity of substance involved if possible and report the spill to the appropriate authorities.
- Do not touch or walk through spilled material.
- Do not touch damaged containers or spilled material unless wearing appropriate protective clothing.
- Be particularly careful to avoid contact with broken glass or sharp objects that may cause cuts or abrasions that could significantly increase the risk of exposure.
- Damaged packages containing solid CO2 (dry ice) as a refrigerant may produce water or frost from condensation of air. Do not touch this liquid as it could be contaminated by the contents of the package.
- Liquid nitrogen may be present and can cause severe burns.
- Absorb spilled materials with earth, sand or other non-combustible material while avoiding direct contact.
- Cover damaged package or spilled material with damp towel or rag and keep wet with liquid bleach or other disinfectant. Liquid bleach will generally effectively inactivate the released substance.

2. First Aid:

CAUTION: EXPOSED PERSON(S) MAY BE A SOURCE OF CONTAMINATION.

Persons administering first aid should take precautions to avoid personal exposure or secondary contamination of others.

- Move exposed person(s) to a safe isolated area.
- Call emergency medical services.
- If clothing and/or shoes are significantly contaminated, remove and isolate them. However, do not allow this to delay other first aid interventions.
- In case of contact of the substance to skin, eyes, nose or mouth, immediately flush the exposed area with copious amounts of running water. Continue this until emergency medical services arrive. Follow their advice for further decontamination.

- Most effects of exposure (inhalation, ingestion or skin contact) to substance are likely to be delayed.
- Ensure that medical personnel are aware of the substances involved, and take precautions to protect themselves.
- For further assistance, contact the appropriate public health authority.

Emergency contact details for the sender and recipient are provided with the documentation accompanying the package and shown on the package.

Appendix 5: Packing Procedures for Transporting Biological Materials

This Appendix provides packing procedures to be followed by University personnel when transporting biological materials by either road or air. These are fully compliant with the requirements of the applicable ADR and IATA Packing Instructions for the different types of dangerous goods and the requirements of the regulations for exempt patient specimens. Procedures for non-hazardous biological materials are provided to ensure these do not leak in transit and cause concern.

1. Packing procedures for transport of UN 2814 INFECTIOUS SUBSTANCE, AFFECTING HUMANS and UN 2900 INFECTIOUS SUBSTANCE, AFFECTING ANIMALS only
2. Packing procedures for transport of UN 3373 BIOLOGICAL SUBSTANCE, CATEGORY B
3. Packing procedures for transport of UN 3245 GENETICALLY MODIFIED MICRO-ORGANISMS
4. Packing procedures for transport of EXEMPT HUMAN AND/OR ANIMAL SPECIMENS
5. Packing procedures for transport of NON-HAZARDOUS BIOLOGICAL MATERIALS

1. PACKING PROCEDURES FOR TRANSPORT OF UN 2814 INFECTIOUS SUBSTANCE, AFFECTING HUMANS and UN 2900 INFECTIOUS SUBSTANCE, AFFECTING ANIMALS only

The following procedures are compliant with the packing requirements of Packing Instructions 620(ADR) and 602(IATA). However, this MUST be read in conjunction with the main text of the guidance where various other requirements of the Packing Instructions (such as labelling) are detailed. Where there are minor differences in the packing procedures for road and air transport, the more stringent is included here to ensure compliance with both.

Packages must be prepared in such a manner that they arrive at their destination in good condition and present no hazard to persons or animals during transport.

Packaging's that meet UN performance requirements for Class 6.2 substances as shown by design type testing must be used. These are known as UN type-approved packaging and they are certified and marked accordingly.

The packagings must include:

(i) Inner packaging's comprising:

- leak proof primary receptacle(s);
- a leak proof secondary packaging;
- other than for solid infectious substances, an absorbent material in sufficient quantity to absorb the entire contents placed between the primary receptacle(s) and the secondary packaging; if multiple fragile primary receptacles are placed in a single secondary packaging, they must be either individually wrapped or separated so as to prevent contact between them;

(ii) An itemized list of contents, enclosed between the secondary packaging and the outer packaging; and

(iii) A rigid outer packaging of adequate strength for its capacity, mass and intended use. The smallest external dimension must be not less than 100 mm.

For transport by road there are no limits on the quantity of materials contained within the package. For transport by air, other than for body parts, organs or whole bodies, the following limits apply

- on passenger aircraft a limit of 50ml/50g per package,
- on cargo aircraft a limit of 4L/4Kg per package.

Whatever the intended temperature of the consignment, the primary receptacle or the secondary packaging must be capable of withstanding without leakage an internal pressure producing a pressure differential of not less than 95 kPa and temperatures in the range –40 ºC to +55 ºC.

Inner packaging's containing infectious substances must not be consolidated with inner packaging's containing unrelated types of goods. Complete packages may be overpacked in accordance with the provisions of the regulations; such an overpack may contain dry ice.

Other than for exceptional consignments, e.g. large body parts and whole organs which require special packaging, the following specific requirements apply:

Substances consigned at ambient or higher temperatures:

- Primary receptacles must be of glass, metal or plastics.
- Positive means of ensuring a leak proof seal must be provided, e.g. a heat seal, a skirted stopper or a metal crimp seal.
- If screw caps are used, they must be secured by positive means, e.g., tape, paraffin sealing tape or manufactured locking closure.

Substances consigned refrigerated or frozen:

- Ice, dry ice or other refrigerant must be placed around the secondary packaging(s) or alternatively in an overpack with one or more complete packages marked in accordance with labelling requirements.
- Interior supports must be provided to secure secondary packaging(s) or packages in position after the ice or dry ice has dissipated.
- If ice is used, the outer packaging or overpack must be leak proof.
- If dry ice is used, the outer packaging or overpack must permit the release of carbon dioxide gas.
- The primary receptacle and the secondary packaging must maintain their integrity at the temperature of the refrigerant used.

Substances consigned in liquid nitrogen:

- A liquid nitrogen shipper that is UN type-approved for Category A infectious substances must be used.
- Provisions in the regulations for the consignment of liquid nitrogen must also be fulfilled.
- Plastics primary receptacles capable of withstanding very low temperature must be used.
- The secondary packaging must also be capable of withstanding very low temperatures, and in most cases will need to be fitted over the primary receptacle individually.
- The primary receptacle and the secondary packaging must maintain their integrity at the temperature of the liquid nitrogen.

Lyophilised substances:

- May be carried in primary receptacles that are flame-sealed glass ampoules or rubber-stoppered glass vials fitted with metal seals.

Before an empty packaging is returned to the consignor, or sent elsewhere, it must be thoroughly disinfected or sterilized and any label or marking indicating that it had contained an infectious substance must be removed or obliterated.

When goods are to be transported by air, reference should be made to any State or Operator variations that also may apply.

2. PACKING PROCEDURES FOR TRANSPORT OF UN 3373 BIOLOGICAL SUBSTANCE, CATEGORY B

NOTE: *The terms DIAGNOSTIC SPECIMENS or CLINICAL SPECIMENS are no longer permitted.*

The following procedures are compliant with the packing requirements of Packing Instructions 650(ADR) and 650(IATA). However, this MUST be read in conjunction with the main text of the guidance where various other requirements of the Packing Instructions (such as labelling) are detailed. Where there are minor differences in the packing procedures for road and air transport, the more stringent is included here to ensure compliance with both.

The packaging must be of good quality, strong enough to withstand the shocks and loadings normally encountered during transport, including transhipment between vehicles or containers/units and between vehicles or containers/units and warehouses as well as any removal from a pallet or overpack for subsequent manual or mechanical handling.

Packaging's must be constructed and closed to prevent any loss of contents that might be caused under normal conditions of carriage by vibration or by changes in temperature, humidity or pressure.

The packaging must consist of at least three components

(a) a primary receptacle(s);

(b) a secondary packaging; and

(c) a rigid outer packaging.

and an itemized list of contents must be enclosed between the secondary packaging and the outer packaging.

At least one surface of the outer packaging must have a minimum dimension of 100mm x 100mm. The completed package must be capable of successfully passing a drop test where the height of the drop must not be less than 1.2 m. This means following the drop there must be no leakage from the primary receptacle(s) and these must remain protected by the absorbent material, when required, in the secondary packaging.

For transport by road there are no limits on the quantity of materials contained within the package. For transport by air, other than for body parts, organs or whole bodies, the following limits apply to on both passenger and cargo aircraft

- a limit of 4L/4Kg per package, and
- for liquids each primary receptacles must not contain more than 1 L
- for solids each primary receptacle must not contain more than 4 Kg.

Primary receptacles must be packed in secondary packagings in such a way that, under normal conditions of transport, they cannot break, be punctured or leak their contents into the secondary packaging. Secondary packagings must be secured in outer packagings with suitable cushioning material. Any leakage of the contents must not compromise the integrity of the cushioning material or of the outer packaging.

The following specific requirements apply:

For liquid substances:

- The primary receptacle(s) must be leak proof and for air transport must not contain more than 1 L.

- The secondary packaging must be leak proof.
- If multiple fragile primary receptacles are placed in a single secondary packaging, they must be either individually wrapped or separated to prevent contact between them.
- Absorbent material must be placed between the primary receptacle(s) and the secondary packaging. The absorbent material must be in quantity sufficient to absorb the entire contents of the primary receptacle(s) so that any release of the liquid substance will not compromise the integrity of the cushioning material or of the outer packaging.
- The primary receptacle or the secondary packaging must be capable of withstanding, without leakage, an internal pressure of 95 kPa in the range – 40 ºC to +55 ºC.
- For air transport the outer packaging must not contain more than 4L. This quantity excludes ice, dry ice or liquid nitrogen when used to keep specimens cold.

For solid substances:

- The primary receptacle(s) must be siftproof and for air transport must not exceed the outer packaging weight limit.
- The secondary packaging must be siftproof.
- If multiple fragile primary receptacles are placed in a single secondary packaging, they must be either individually wrapped or separated to prevent contact between them.
- If there is any doubt as to whether or not residual liquid may be present in the primary receptacle during transport a packaging suitable for liquids, including absorbent materials must be used.
- For air transport, except for packages containing body parts, organs or whole bodies, the outer packaging must not contain more than 4 Kg. This quantity excludes ice, dry ice or liquid nitrogen when used to keep specimens cold.

Refrigerated or frozen specimens: Ice, dry ice and liquid nitrogen:

- When dry ice or liquid nitrogen is used to keep specimens cold, all applicable requirements of the regulations must be met.
- When used, ice or dry ice must be placed outside the secondary packagings or in the outer packaging or an overpack.
- Interior supports must be provided to secure the secondary packagings in the original position after the ice or dry ice has dissipated.
- If ice is used, the outside packaging or overpack must be leak proof.
- If dry ice is used, the packaging must be designed and constructed to permit the release of carbon dioxide gas to prevent a build-up of pressure that could rupture the packagings.
- The primary receptacle and the secondary packaging must maintain their integrity at the temperature of the refrigerant used as well as the temperatures and the pressures which could result if refrigeration were lost.

Clear instructions on filling and closing such packages must be provided by packaging manufacturers and subsequent distributors to the consignor or to the person who prepares the package to enable the package to be correctly prepared for carriage.

Other dangerous goods must not be packed in the same packaging as Division 6.2 Infectious Substances unless they are necessary for maintaining the viability, stabilising or preventing degradation or neutralising the hazards of the infectious substances. A quantity of 30 ml or less of dangerous goods included in Classes 3, 8 or 9 may be packed in each primary receptacle containing infectious substances. When these small quantities of dangerous goods are packed with

infectious substances in accordance with IATA or ADR Packing Instruction 650, no other requirements of the regulations need be met.

When goods are to be transported by air reference should be made to any State or Operator variations that also may apply.

3. PACKING PROCEDURES FOR TRANSPORT OF UN 3245 GENETICALLY MODIFIED MICRO-ORGANISMS

The following procedures are compliant with the packing requirements of Packing Instructions 904(ADR) and 913(IATA). However, this MUST be read in conjunction with the main text of the guidance where various other requirements such as labelling are detailed.

Genetically modified micro-organisms assigned to UN 3245 must be packed according to the procedures (i.e. triple layer system, see packing procedure 1) for UN 2814 INFECTIOUS SUBSTANCE, AFFECTING HUMANS except that UN type-approved packaging need not be used.

For transport by road there are no limits on the quantity of materials contained within the package. For transport by air, the following limits apply o on both passenger and cargo aircraft no limit per package, but - the maximum quantity in a primary receptacle must not exceed 100 ml or 100 g.

When goods are to be transported by air reference should be made to any Operator variations that also may apply.

4. PACKING PROCEDURES FOR TRANSPORT OF EXEMPT HUMAN AND/OR ANIMAL SPECIMENS

Human or animal specimens for which there is minimal likelihood that pathogens are present are not subject to the transport regulations PROVIDING the specimen is packed in a packaging which will prevent any leakage and which is marked with the words “Exempt human specimen” or “Exempt animal specimen” as appropriate. The following procedures are compliant with the packing requirements of the ADR and IATA Regulations for exempt patient specimens and MUST be followed for any specimen transported under the exemption. However, this must be read in conjunction with the main text of the guidance where details are given on criteria for determining if a specimen can be exempted.

The specimen must be packed in a packaging which will prevent any leakage. The following is required:

(i) The packaging must consist of three components
- a leak-proof primary receptacle(s);
- a leak-proof secondary packaging; and
- an outer packaging of adequate strength for its capacity, mass and intended use, and with at least one surface having minimum dimensions of 100 mm × 100 mm;

(ii) For liquids, absorbent material in sufficient quantity to absorb the entire contents must be placed between the primary receptacle(s) and the secondary packaging so that, during transport, any release or leak of a liquid substance will not reach the outer packaging and will not compromise the integrity of the cushioning material.

(iii) When multiple fragile primary receptacles are placed in a single secondary packaging, they must be either individually wrapped or separated to prevent contact between them.

If such a packaging is used it must be marked "Exempt human specimen" or "Exempt animal specimen", as appropriate.

Whilst the regulations do not specify any minimum standards for the packaging, common sense dictates the packaging must be of good quality, strong enough to withstand the shocks and loadings normally encountered during transport, and closed to prevent any loss of contents that might be caused under normal conditions of carriage by vibration or by changes in temperature, humidity or pressure.

Items should also be packed in accordance with the following:

- for substances consigned at ambient or higher temperatures – primary receptacles should be of glass, metal or plastics. Positive means of ensuring a leak proof seal should be provided, e.g. a heat seal, a skirted stopper or metal crimp seal. If screw caps are used, they should be reinforced with adhesive tape.

  Flame-sealed glass ampoules or rubber-stoppered glass vials fitted with metal seals are suitable primary receptacles for lyophilized substances.

- for substances consigned refrigerated or frozen – wet ice or dry ice should be placed around the secondary packaging(s). Interior supports should be provided to secure the secondary packaging(s) in position after the wet ice or dry ice has melted or dissipated. If ice is used, the outer packaging should be leak proof. If dry ice is used, the outer packaging must permit the release of carbon dioxide gas. The primary receptacle and the secondary packaging need to be able to maintain their integrity at the temperature of the refrigerant used.

- for substances consigned in liquid nitrogen - plastic primary receptacles capable of withstanding very low temperatures need to be used. The secondary packaging should also be capable of withstanding very low temperatures, and in most cases will need to be fitted over the primary receptacle individually. The requirements for the consignment of liquid nitrogen must also be fulfilled. The primary receptacle and the secondary packaging need to be able to maintain their integrity at the temperature of the liquid nitrogen. CBE staff should consign biological materials in liquid nitrogen only if there is no suitable alternative means and do so only in a suitable dry shipper. CBE staff should contact the local BGMSA or the University BSO for further advice.

5. PACKING PROCEDURES FOR TRANSPORT OF NON-HAZARDOUS BIOLOGICAL MATERIALS

Biological materials which are not classified as dangerous goods for transport should still be packaged safely to ensure they do not leak in transit since this would be likely to trigger safety/security alerts and also cause unnecessary concern to anyone who may come into contact with leaked material. This can be best achieved by following the procedures given below which mirror those for exempt patient specimens.

The specimen must be packed in a packaging which will prevent any leakage. The following is required:

(i) The packaging must consist of three components

- a leak-proof primary receptacle(s);
- a leak-proof secondary packaging; and
- an outer packaging of adequate strength for its capacity, mass and intended use, and with at least one surface having minimum dimensions of 100 mm × 100 mm;

(ii) For liquids, absorbent material in sufficient quantity to absorb the entire contents

must be placed between the primary receptacle(s) and the secondary packaging so that, during transport, any release or leak of a liquid substance will not reach the outer packaging and will not compromise the integrity of the cushioning material.

(iii) When multiple fragile primary receptacles are placed in a single secondary packaging, they must be either individually wrapped or separated to prevent contact between them.

The packaging must be of good quality, strong enough to withstand the shocks and loadings normally encountered during transport, and closed to prevent any loss of contents that might be caused under normal conditions of carriage by vibration or by changes in temperature, humidity or pressure.

Items should also be packed in accordance with the following:

- for substances consigned at ambient or higher temperatures – primary receptacles should be of glass, metal or plastics. Positive means of ensuring a leak proof seal should be provided, e.g. a heat seal, a skirted stopper or metal crimp seal. If screw caps are used, they should be reinforced with adhesive tape.

  Flame-sealed glass ampoules or rubber-stoppered glass vials fitted with metal seals are suitable primary receptacles for lyophilized substances.

- for substances consigned refrigerated or frozen – wet ice or dry ice should be placed around the secondary packaging(s). Interior supports should be provided to secure the secondary packaging(s) in position after the wet ice or dry ice has melted or dissipated. If ice is used, the outer packaging should be leak proof. If dry ice is used, the outer packaging must permit the release of carbon dioxide gas. The primary receptacle and the secondary packaging need to be able to maintain their integrity at the temperature of the refrigerant used.

- for substances consigned in liquid nitrogen - plastic primary receptacles capable of withstanding very low temperatures need to be used. The secondary packaging should also be capable of withstanding very low temperatures, and in most cases will need to be fitted over the primary receptacle individually. The requirements for the consignment of liquid nitrogen must also be fulfilled. The primary receptacle and the secondary packaging need to be able to maintain their integrity at the temperature of the liquid nitrogen. CBE staff should consign biological materials in liquid nitrogen only if there is no suitable alternative means and do so only in a suitable dry shipper. CBE staff should contact the local BGMSA or the University BSO for further advice.

Appendix 6: Labelling Examples for Transporting Biological Materials

Figure 1 – shows the labels for a package containing a liquid Category A infectious substance. A combination pack for use with dry ice has been used; the marking in the bottom right corner showing it is UN type-approved packaging. The package contains over 50ml of material and so is restricted to cargo aircraft only because of the quantity limits on passenger aircraft.

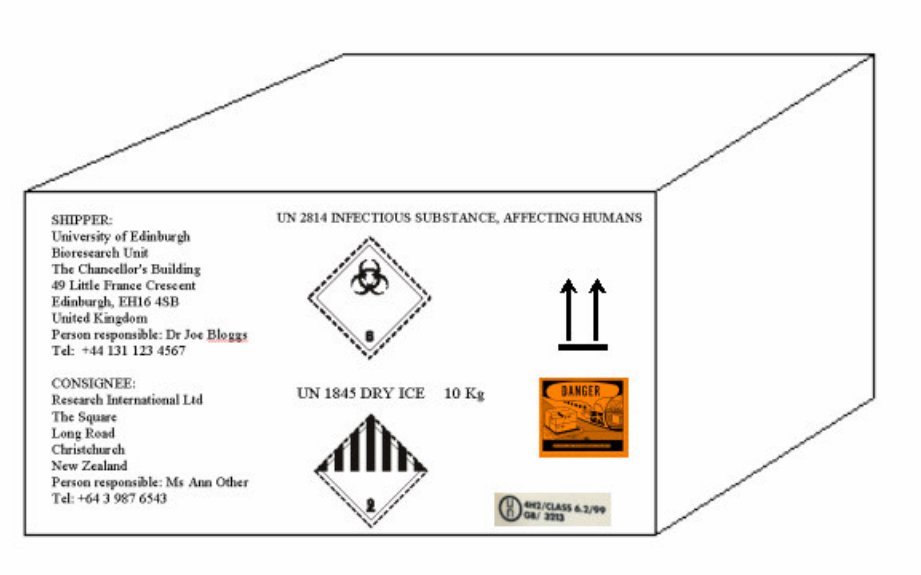


Figure 2 – shows the labels for a package containing a liquid Category B infectious substance. A thermal overpack has been used for the dry ice so the same labels must also be shown on the inner package.

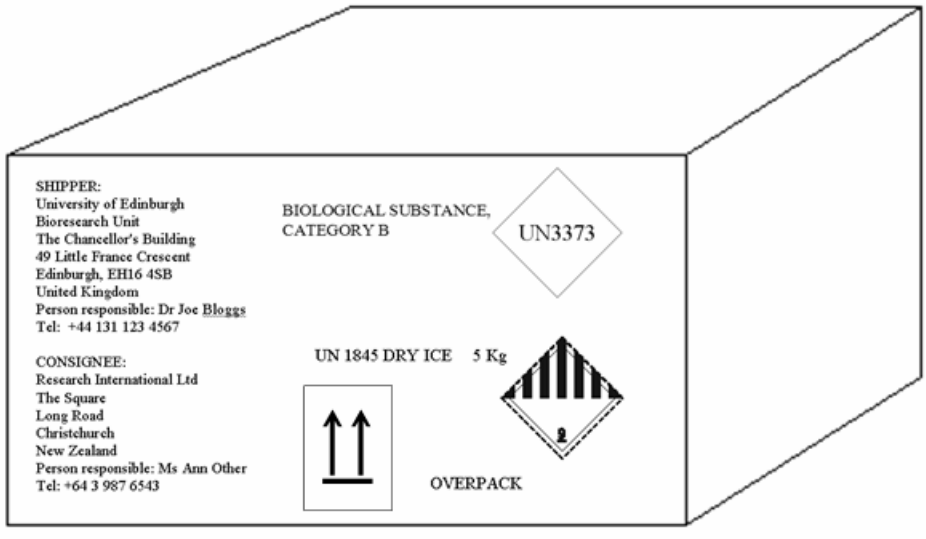


Figure 3 – shows the labels for a package containing an exempt human specimen shipped on dry ice. A thermal overpack has been used for the dry ice so the same labels must also be shown on the inner package

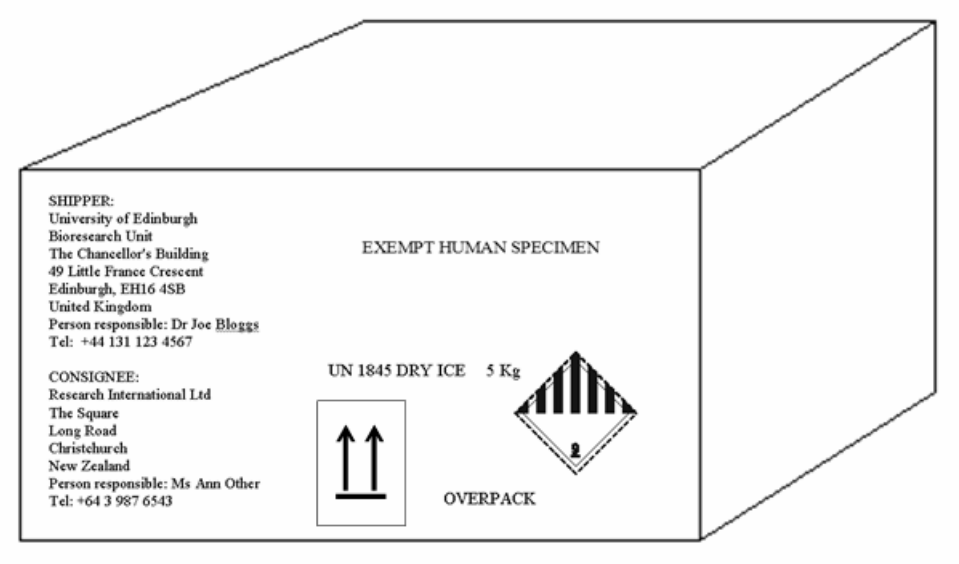
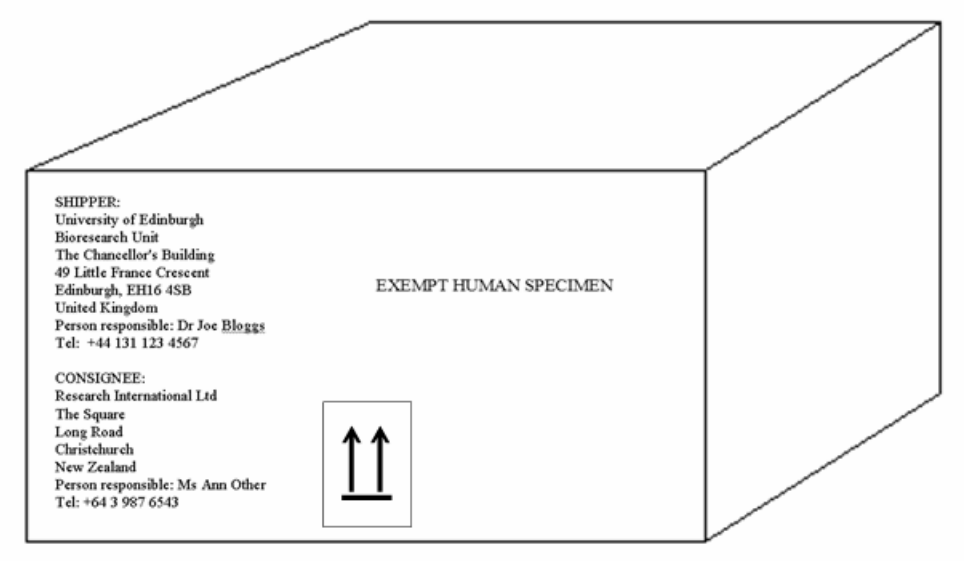


Figure 4 – shows the labels for a package containing an exempt human specimen shipped at ambient temperature



DOCUMENT REVISION HISTORY

(Details of the amendments with reasons to be recorded. The revised CoP must be re-approved by the signing of the cover page

Revision Level	Revision Date	Description of Revision/Change Request	Revised By	New Version Number
1.0	10.01.11	Revised following Annual Review. The following is a brief summary of the revisions: 1. Security statement extended on p1 2. Author surname updated throughout document (Kavanagh) 3. 'must' changed to 'should' on p34, para 1. 4. Clarification on policy for out-of-hours working 5. Removed sub section 2.7.2. Not a regulatory or LU Biological Safety Policy requirement. Annual survey shall provide register of all BA/GMOs held on CBE site. Risk assessment process shall notify BGMSA , BSO and/or BHGMSC of proposal to work with BA/GMO 6. Revised statement to indicate that requirement for eye protection is subject to risk assessment; p58. 7. Section 4.5 (p74) – 'must' changed to 'should' labelling of fridges/freezers with GMO identifier is not mandatory 8. Revised Section 5 'waste handling'. The use of the clinical waste classification system using Groups A to E has been removed, as it is felt that its continued use is inappropriate. The A to E classification system no longer reflects appropriate segregation for treatment or disposal, and does not easily equate to the use of European Waste Catalogue (EWC) codes, which are now mandatory for all waste transfer documentation. Code of Practice for handling of waste revised to incorporate "Healthcare Waste Technical Memorandum (HTM07-01): Safe Management of Healthcare Waste", recommendations, produced by the Department of Health (reference added; p113). **Revision to waste management procedure agreed at CBE Safety Committee Meeting on 15.01.10**. 9. Section 7 & Annex 2 revised to update import and export guidance reflecting changes to DEFRA website 10. Annex 10 revised to include (i) guideline on transport of naked DNA and proteins derived from GMMs (ii) example of triple layer packaging system (ii) clarify guideline for on site transport, personal transport, using couriers. 11. Addition of Revision Record sheet 12. addition of footnote to p6 to indicate that this COP also covers work practices in the CL2 CBE Tissue Engineering Laboratory located in the Wolfson School of Manufacturing & Mechanical Engineering, Loughborough University. 13. Addition of Reference to amendments made to GMO Regulation 2000 on Dec 2010. Addition of footnote to p67 indicating summary of amendments. **Revision agreed at CBE Safety Committee Meeting on 10.01.11**	P.Hourd	2.0