Health and Safety Services

WELLBEING, SAFETY AND HEALTH

UNIVERSITY OF LEEDS

Risk Management of Hazardous Biological Materials

Definitions:

- **Hazardous Biological Material**
- **Incidental contact and Deliberate work**
- **Contained / Uncontained Use**
- **Containment (and containment levels)**
- **Hazard Groups**
- **Human Material**
- **GMP & GOSH**
- **Validated means**

What do we mean by hazardous biological material?

Hazardous biological material is any biologically-derived material or material which, either by accident or design is, or contains:

- **hazardous biological agents** } These can **harm** (i.e. infection, allergy, toxicity) or otherwise
- **hazardous multicellular organisms** } create a hazard to **human** or animal health or the **environment**
- **<u>any</u> genetically modified organism** } Whether or not it can cause harm to health or the environment

What isn't covered:

- Use of naked nucleic acid or plasmids is covered by the hazardous substances protocol. The exception to this is that full-length copies of the genomes of viruses known to be infectious in their own right are considered to be micro-organisms, even when they are not encapsulated or enveloped, and therefore fall within this protocol.
- Deliberate release of biological material (including those genetically modified) into the environment or clinical trials involving the use of biological material are not included in the scope of the hazardous biological materials standard, please speak to the University Biological Safety Contacts.

Hazardous biological agents:	micro-organisms such as bacteria, (e.g. *Salmonella*), viruses (e.g. Hepatitis), fungi (e.g. *Candida*), cell cultures and tissue cultures, agents that cause Transmissible Spongiform Encephalopathies (TSEs), parasites (e.g. malarial parasites, amoebae and trypanosomes).
Hazardous multicellular organisms:	microscopic infectious forms of larger parasites (e.g. the ova and infectious larval forms of helminths, tapeworm, parasitic flukes and nematodes etc.). Other multicellular organisms that can cause **harm** to **human** or animal health or the **environment** (from mosquitoes to American bullfrogs to mink).
Genetically Modified Organisms (GMOs):	<u>any</u> type of biological material that has been artificially altered at a genetic level, regardless of whether or not it can cause harm to health or the environment. They can be plants, animals or more commonly micro-organisms (including bacteria, viruses parasites and fungi). Typically, genetic modification involves nucleic acid sequences (DNA or RNA) being removed, manipulated outside the cell and reinserted into the same or another organism.
Harm:	harm can be caused in a number of ways, either directly by: 1) infecting and causing disease in humans, animals, or plants 2) colonising or displacing within the environment or indirectly: 3) by acting as a reservoir/host/source for hazardous biological materials
Human:	In the context of this protocol, human is taken to mean "healthy" individuals. Where an individual's health status places them at increased risk from hazardous biological material (e.g. weakened immune response) then they will need to be assessed separately.
Environment:	The environment includes the air, water, land, flora and fauna that go to make it up. Environmental damage is caused by the presence of organisms that have escaped and are capable of causing harm to any other living organisms or the environment. This includes: • organisms likely to disturb natural ecosystems, especially derivatives of naturally-occurring species that may have a selective advantage; • non-indigenous organisms that are able to become established and might prey upon native organisms or compete for the niche they currently occupy; • non-indigenous organisms that might consume indigenous organisms and disrupt the ecology; • non-indigenous organisms that express potentially harmful biologically active products, especially if they are likely to be preyed upon.

What do we mean by “incidental contact” and “deliberate work”?

Work activities which expose people, (and possibly animals or the environment) to hazardous biological material can be divided into one of two categories; incidental contact or deliberate work.

Why do we need to categorise our work?

The risk assessment process for the two types of work is best managed separately at the University. Incidental contact is dealt with either by considering the hazards under a COSHH risk assessment or an activity assessment. For deliberate work, a specific risk assessment must be completed and submitted to your local biological safety committee for approval before work can begin.

Incidental contact with hazardous biological material

This is work where exposure to hazardous biological material may occur but only incidentally i.e. the activity does not involve direct work with the hazardous biological material itself (there is no intention to isolate, concentrate or propagate) — it may include almost any task, but, in particular, exposure may be greatest in farming; food preparation; nursing and healthcare; waste handling, engineering and where process waters are used.

Examples of types of work known to be at risk from incidental contact to hazardous biological material include: agriculture (zoonoses, animal wastes, contaminated dusts), food production (zoonoses and food poisoning bacteria in food production), engineering (process waters and coolants), plumbing, printing (process waters and humidifiers), domestic waste and wastewater treatment (contaminated dusts, aerosols, zoonoses), textile handling (contaminated dusts and zoonoses), gardeners, emergency services (blood borne pathogens).

Zoonoses *is any infectious disease that can be transmitted (in some instances, by a vector) from animals, both wild and domestic, to humans or from humans to animals (the latter is sometimes called reverse zoonosis). Many serious diseases fall under this category.*

Deliberate work with hazardous biological material

This is work which involves a deliberate intention to handle hazardous biological materials or where hazardous biological materials are known to be or are likely to be present — this includes laboratory work e.g. pathology, diagnostics, hospital laboratories; veterinary laboratories; research laboratories; also biotechnology where microorganisms form part of the process.

Where work with hazardous biological material is deliberate, then it is further categorised into contained use, and uncontained use.

What do we mean by contained or uncontained use?

Contained Use of hazardous biological materials

Any activity by people that involves hazardous biological material in which measures are taken to limit contact between the material and people or the environment. The vast majority of work at the University of Leeds is contained, if you are unsure how to categorise your work then speak to your University Biological Safety Contacts. The Health & Safety Executive's definition is:

> "*Contained use is, any operation in which any hazardous biological material is cultured, stored, used, transported, destroyed, disposed of, or used in any other way, and for which specific measures (physical, chemical or biological barriers or any combination of barriers) are used to limit their contact with and provide a high level of protection for, the general population and the environment.*"

Examples of contained use facilities include microbiological laboratories, animal houses, greenhouses or industrial production facilities.

Where work is categorised as 'contained use', then the work must be carried out at a "*Containment Level*" that is appropriate to the hazard of the activity. Containment level refers to the physical and management requirements needed to control the hazard.

Uncontained use of hazardous biological materials (Deliberate Release of GM or non-GM)

These are hazardous biological materials (including genetically modified organisms) that are either already in the environment, or are deliberately introduced into the environment (e.g. for experimental purposes). This also includes material placed on the market, for example, as food or for medical purposes (e.g. vaccinations).

If your work comes under the uncontained use category speak to the University Biological Safety Contacts

Uncontained use - Deliberate Release of GMOs

Consent to release a GMO is issued by the Secretary of State for Environment, Food and Rural Affairs under the GMO (Deliberate Release) Regulations 2002 (as amended). Specific consents are issued with strict conditions for conducting and managing each release. It is the GM Inspectorate's responsibility to ensure that consent holders are complying with these conditions by undertaking inspections of GM deliberate release field sites for both experimental ('Part B') and commercial ('Part C') consents. See the DEFRA website for details of the deliberate release approvals process.
In the consents, various conditions such as correct location and size of GM release, monitoring requirements, may be imposed. GM Inspectors must verify that the release is compliant with these conditions, if this is found not to be the case the consent holder will be contacted and the matter investigated further.

Uncontained use - Deliberate Release of non-native species

The Convention on the Conservation of European Wildlife and Natural Habitats requires that each country shall undertake to "strictly control the introduction of non-native species". For more information speak to the University Biological Safety Contacts; see the DEFRA website for details about the control of non-native species.

What do we mean by Containment?

The term "containment" is used in describing safe methods for managing hazardous biological material (i.e. biological agents or genetically modified organisms) in the laboratory environment where they are being handled or maintained. The purpose of containment is to reduce or eliminate exposure of laboratory workers, other people, and the outside environment to potentially hazardous biological agents.

For each Hazard Group of biological agents there are legally defined **minimum** control measures (known as Containment Levels) that reduce exposure to an acceptable level for the biological agents of that Hazard Group. The table below is a summary of the controls needed at the various containment levels in a laboratory, for other types of facilities (e.g. industrial production units, plant growth rooms, animal rooms) speak to the University Biological Safety Contacts for further advice.

🟢 Recommended
🟡 Required where and to the extent the risk assessment shows it is required
🔴 Required

CONTAINMENT LEVEL				CONTAINMENT MEASURES
1	2	3	4	
		🔴	🔴	**Laboratory suite: isolation**
		🔴	🔴	**Laboratory: sealable for fumigation**
EQUIPMENT				
🔴	🔴	🔴	🔴	**Bench impervious to water and resistant to acids, alkalis, solvents, disinfectants, decontamination agents and easy to clean**
🟢	🟢	🔴	🔴	**Floor impervious to water and resistant to acids, alkalis, solvents, disinfectants, decontamination agents and easy to clean**
		🟢	🔴	**Walls and ceiling impervious to water and resistant to acids, alkalis, solvents, disinfectants, decontamination agents and easy to clean**
		🟡	🔴	**Entry to lab via airlock**
	🟡	🔴	🔴	**Negative pressure relative to the pressure of the immediate surroundings**
		🔴	🔴	**Extract air from the laboratory HEPA filtered**
			🔴	**Input air to the laboratory HEPA filtered**
	🟡	🔴		**Microbiological safety cabinet/enclosure**
		🔴		**Procedures with infective materials contained within a cabinet /enclosure**
			🔴	**Class III Microbiological safety cabinet**
🔴				**Autoclave[1] on site for GM material only**
	🔴			**Autoclave[1] in the building for GM material only**
		🔴		**Autoclave[1] in the laboratory suite**
			🔴	**Double ended autoclave[1] required in laboratory**
SYSTEM OF WORK				
🟢	🔴	🔴	🔴	**Access restricted to authorised personnel only[2]**
			🔴	**Access restricted to authorised personnel only[2] via air lock key procedure**
	🔴			**Specific measures to minimize aerosol dissemination**
	🟢	🔴	🔴	**Specific measures to prevent aerosol dissemination**
		🟡	🔴	**Shower**
🔴	🔴	🔴	🔴	**Suitable protective clothing**
		🟡		**protective footwear**
			🔴	**Complete change of clothing and footwear before entry and exit**

	🟡	🔴	🔴	**Gloves**
🟡	🔴	🔴	🔴	**Efficient control of disease vectors (e.g. for rodents and insects) which could disseminate hazardous biological materials**
🟡	🔴	🔴	🔴	**Specified disinfection procedures in place [1]**
WASTE				
		🟡	🔴	**Inactivation of hazardous biological material in effluent from hand-washing sinks and showers and similar effluents[1]**
🔴	🔴	🔴	🔴	**Inactivation of hazardous biological material in contaminated material [1] by validated means for GM material**
	🔴	🔴	🔴	**Inactivation of hazardous biological material in contaminated material [1] by validated means**
		🔴		**Inactivation of hazardous biological material in contaminated material [1] by validated means, with waste inactivated in the laboratory suite**
			🔴	**Inactivation of hazardous biological material in contaminated material [1] by validated means, with waste inactivated within the laboratory**
OTHER MEASURES				
		🟡	🔴	**Laboratory to contain its own equipment**
🟡	🟡	🔴	🔴	**An observation window or alternative is to be present so that occupants can be seen**
🟡	🔴	🔴	🔴	**Safe storage of hazardous biological material[4]**
		🟡	🔴	**Secure storage of hazardous biological material (see LPS 1175 for guidance)**
🟡	🔴	🔴	🔴	**Biohazard signs posted**
🟢	🟡	🔴	🔴	**Written records of staff training[3]**

Information to construct the table above has been taken from *Control of Substances Hazardous to Health Approved Code of Practice and guidance*, and *A guide to the Genetically Modified Organisms (Contained Use) Regulations*.

[1] For information about disinfection, inactivation, and autoclaving see the University Biological Safety Contacts.

[2] For information about restricting access the University Biological Safety Contacts.

[3] It is recommended at the University of Leeds that relevant training records for people are maintained regardless of the containment level; the level of training should be appropriate to the level of risk and the complexity of the operations being undertaken.

[4] Hazardous biological material should be located in a secure area, e.g. the laboratory or laboratory suite in order to prevent unauthorised access. Fridges or freezers (or other storage) used to store hazardous biological material outside the main laboratory area should be lockable.

Categorisation of hazardous biological material into Hazard Groups:

Hazardous biological materials (i.e. biological agents and genetically modified organisms) are classified into defined hazard groups based on the potential level of harm that they can cause to humans, animals or the environment.

Assessment of the inherent risks of biological agents in order to categorise it into one of four hazard groups is made on the basis of factors such as the severity of the disease it causes, the routes of infection, its virulence and infectivity. It will also take into account the existence of effective therapies, immunization, the presence or absence of vectors, quantity of agent and whether the agent is indigenous, as well as possible effects on other species, including plants and animals (see table below). Many hazardous biological agents have already been categorised by Advisory Committee on Dangerous Pathogens, and this classification is therefore legally recognised.

Hazard Group 1	○ is unlikely to cause human disease; and ○ in relation to susceptible animals is unlikely to produce disease or is enzootic and does not produce notifiable animal disease.
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; or ○ in relation to susceptible animals is exotic, novel or produces notifiable diseases; and it has both of the following characteristics: ▪ is of low clinical significance; and ▪ has low likelihood of spread.
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; or ○ in relation to susceptible animals is exotic, novel or produces notifiable disease and it has one or both of the following characteristics: ▪ moderate clinical significance; ▪ moderate likelihood of spread.
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; or ○ in relation to susceptible animals is exotic, novel or produces notifiable disease; and it has one or both of the following characteristics: ▪ the disease has serious clinical significance; ▪ has a high likelihood of spread.

- **Disease** this is referring to disease caused by infection
- **Susceptible animals** are any kind of mammal except man, any kind of four-footed beast which is not a mammal and any species of bird likely to be affected by the biological agent.
- **Novel** means a new strain of biological agent not previously seen.
- **Spread** means the passing of the biological agent from one susceptible animal to another and assumes any necessary enzootic vector is present.

When provisionally categorising biological agents, the agent should be assigned to one of the above Hazard Groups according to its level of risk of infection to humans and according to its level of risk to susceptible animals. Where the biological agent meets the definition in more than one group, the higher group should be assigned.

Human Materials

What are **human materials** – these are any samples obtained from a human; including blood, urine, tissue, faeces, saliva, cerebral spinal fluid, synovial fluid, foetal tissue, amniotic fluid, placenta etc.

What do we mean by **Screened Samples** – are those obtained through the Blood Transfusion Service or from a tissue bank that undertakes screening of their samples for harmful pathogens. Where these samples are proved to be negative for harmful pathogens, the material can be handled at Containment Level 1. When samples are screened and are shown to contain a pathogen, they should be handled at the appropriate Containment Level for that pathogen.

What do we mean by **Unscreened Samples** – human materials that do not come from a screened source must be regarded as potentially infectious (e.g. harbour Blood Borne Viruses (BBV's) such as HIV and Hepatitis B). They must therefore be handled at Containment Level 2 with the additional precautions highlighted in the tables below. If the materials come from a high risk population (e.g. intravenous drug users, or from Sub-Saharan Africa) where the potential for preference of pathogens is higher, the Containment Level should be increased accordingly.
If a sample is shown or discovered to be infected at a later date, then the risk assessment should be revisited and the Containment Level altered accordingly (or the sample correctly disposed of).

What are **Sharps** – these are blunt and sharp needles, scalpel blades, glass pasteur pipettes (short and long form), broken contaminated glassware, glass drug/chemical vials, surgical instruments and glass slides or any other item that may cause cuts or puncture wounds.

General Principles of Good Practice, Good Microbiological Practice (GMP) and Good Occupational Safety and Hygiene (GOSH)

1) Keep workplace and environmental exposure to any biological agent to the lowest reasonably practicable level *(it is also good practice to reduce aerosol and dust generation as part of basic hygiene precautions.)*

The key to this is the use of good practice to achieve a low level of exposure. Standard good practice, such as that set out in the SACGM Compendium of Guidance will normally constitute accepted levels of lowest reasonable practicability.

2) Exercise engineering control measures at source and supplement these with appropriate personal protective clothing and equipment where necessary.

This follows the hierarchy of control measures which requires that if exposure cannot be prevented (by elimination or substitution) exposure is controlled through primary containment in the first instance. Protective clothing is always required, although in some cases this is work clothing rather than specialist laboratory coats or overalls. This is actually a slightly different emphasis to the normal control hierarchy for non-biological material. Microbiological safety cabinets (i.e. engineering control) may not always be required - even though protective clothing is.

3) Carry out routine tests and maintenance controls on protective equipment.

It is important to ensure the integrity of containment and that other control measures are being applied. The frequency and degree of testing/examination of equipment and control measures will be dependent on the level of risk and nature of the activity.

4) Test, where necessary, for the presence of viable process organisms outside the primary physical containment.

Where the risk assessment shows that monitoring for viable organisms outside the primary containment (e.g. culture vessel) is necessary to ensure effective control, this must be undertaken. Monitoring could include both monitoring within the workplace and also in the surrounding environment. In particular, monitoring of waste, especially at the point of disposal, is likely to be necessary when there is any possibility that harm might result from any escape;

5) Provide appropriate training of personnel and to keep suitable records of the training.

The level of training should be appropriate to the level of risk and the complexity of the operations being undertaken.

6) Formulate and implement local codes of practice for the safety of personnel, as required. (In particular local rules should minimise the use of sharp instruments and ensure correct use and disposal. Local codes should also outline procedures designed to protect the environment.)

The content and form of local codes of practice will be dependent on the level of risk and nature of activities being undertaken. They might include: operating instructions for particular equipment; management issues; systems of work; maintenance regimes.

7) Provide washing and decontamination facilities for personnel.

What constitutes appropriate facilities would be dependent on the risk and nature of the work.

8) Keep adequate records.

Keep records of risk assessment, you should also keep records of work that has been undertaken and any modifications to the risk assessment or control measures.

9) prohibiting in the work area eating, drinking, smoking, applying cosmetics or the storing of food for human consumption;

10) prohibiting mouth pipetting;

11) Provide written standard operating procedures where appropriate to ensure safety.

Appropriateness should be with regard to the level of risk and nature of the activity and equipment;

12) Have effective disinfectants and specified disinfection procedures available in case of spillage of biological agents.

Disinfection should reduce the numbers of live organisms by at least 99.999% - ie a 5 log reduction.

13) Provide safe storage for contaminated equipment and materials where appropriate.

Appropriateness must be decided based on the risk.

Inactivation of hazardous biological material by validated means

Inactivation is defined as:

'the complete or partial destruction of hazardous biological material so as to ensure that any contact between the material and humans or the environment is limited to an extent commensurate with the risks identified in the risk assessment and to provide a high level of protection for humans and the environment'.

Inactivation validation can be further defined as "*establishing documented evidence that an inactivation process will consistently reduce hazardous biological materials (organisms) to a pre-established level that is considered safe." The pre-established bio-burden levels must be based on public health codes, regulations, industry guidelines, or a scientifically sound rationale.*"

Hazardous biological material can be inactivated in a number of different ways both physical (e.g. heat, radiation etc.) or chemically (e.g. disinfectants, fumigants etc.). Validation of the effectiveness of these methods used to achieve inactivation is required to prove that inactivation method works.

Validation of physical methods

Examples of inactivation methods include: dry heat, wet heat (i.e. autoclaving), microwave, radiation (e.g. gamma ray, X-ray), incineration.

For Hazard Group 1 and 2 hazardous biological materials, it will normally be sufficient to rely on the manufactures data. For some hazard group 2 materials this may not always be the case particularly where the material is difficult to inactivate (e.g. spore forming organisms).

For hazard group 3 materials, validation will need to be demonstrated and documented.

Validation of disinfectants

For Hazard Group 1 and 2 hazardous biological materials it will normally be sufficient to rely on the manufactures data, providing the recommended concentrations and contact times are used.

For Hazard Group 3 hazardous biological materials, researchers must demonstrate the effectiveness of the disinfectant with the relevant organism under the specific conditions of use.

When considering the means of inactivation the following definitions may be helpful when selecting an inactivation process:

Sterilisation	An inactivation process used to render an object free from viable infectious agents including viruses and bacterial spores (see BS EN 556-1:2001). This is an absolute not a relative term. Sterilisation must not be confused with disinfection.
Log Reduction	The decrease in the number of viable organisms as a result of an inactivation process, so that a 90% decrease equals a 1 log reduction, a 99% decrease equals a 2 log reduction and so on.
Kill curve	A function of survivability of an organism against time at a given concentration for an inactivation process.
Soiling	The presence of other materials in or on the surfaces to be disinfected, this can significantly affect any inactivation process (including sterilisation and disinfection).
Disinfection	This is not an absolute term; it denotes a reduction in the number of viable organisms to an acceptable level, ideally a 5 or 6 log reduction. A particular agent is used to destroy the viability of organisms but does not necessarily kill or remove all of them.