Introduction

Some micro-organisms used in research within the university may cause harm to humans, animals or plants. Indeed, very often the motivation for study of a micro-organism stems from the need to identify novel interventions to prevent disease during an infection. Such research often involves culturing large volumes of harmful micro-organisms presenting a significant risk to people and the environment. For this reason this Guidance Note must be effectively implemented to control the risk of harm to humans, animals and plants when working with micro-organisms or with material that may contain micro-organisms.

Legislation

The primary aim of legislation is to protect humans and agriculturally important livestock, poultry and crops from pathogenic micro-organisms. Material that potentially carries pathogens is also covered by this legislation (eg plant material, living animals, carcasses, parts of carcasses, cell cultures, body fluids).

Human pathogens

The Control of Substances Hazardous to Health Regulations 2002 (COSHH) require that before starting work with a human pathogen an assessment of risks to health,
and of the actions to ensure any identified risks to health are essentially zero must be carried out. These actions will include:

- identifying suitable measures (safeguards) to prevent or at least minimise exposure
- ensuring these safeguards are effective (i.e., they are being used and are functioning as intended through maintenance, inspection, and testing)
- informing employees of the risks to their health, and of the safeguards to protect their health, and providing instruction and training in their use
- providing health surveillance if there is a reasonable likelihood of an identifiable disease occurring and if surveillance will benefit the health of employees

**Animal pathogens**

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

**Fish pathogens**

Research involving some pathogens of fish is currently notifiable and controlled by Orders under the Diseases of Fish Acts 1937 and 1983, or under the Fish Health Regulations 1992 and 1993.

**Bee pathogens**

The Bees Act 1980 makes provision for the control of pests and disease affecting honey bees. Some diseases of bees are notifiable under the Bees Control Order 1982, and the Importation of Bees Order 1980, as amended 1987 controls honey
bee imports including their pathogens.

**Plant Pathogens**
Research involving plant pathogens and pests comes under The Plant Health (Great Britain) Order 1993. This Order prohibits the importation from countries outside the European Community of any plant (including tree) pathogen or pest that is not already established in Great Britain. The Order also controls the spread of quarantine pathogens and pests within Great Britain. Before starting research with a plant pathogen a licence may be required.

**Genetically modified micro-organisms**
Research involving a genetically modified micro-organism in a laboratory comes under the Genetically Modified Organisms (Contained Use) Regulations 2000. Complying with the Guidance Note on Working Safely with Genetically Modified Organisms will ensure that the COSHH requirements for work with human pathogens are met.

The remainder of this Guidance Note is concerned solely with micro-organisms that infect humans. For further information on working safely with, fish, bee and plant pathogens (current lists of specified pathogens, licence requirements) contact the University Biological Safety Adviser (UBSA).

**Risks to human health presented by micro-organisms**

**Micro-organism**
The term micro-organism means a microbiological entity, cellular or non cellular, which is capable of replication or of transferring genetic material that may cause any infection, allergy, toxicity or otherwise create a hazard to human health (eg bacteria, viruses, fungi, mycoplasma, cell cultures or a human endoparasite).

**Categorisation**
A micro-organism is classified into one of four Hazard Groups using the following criteria:
• Can it cause disease in humans?
• Is it a hazard to healthy laboratory workers?
• Can it spread to other people outside the laboratory?
• Is effective treatment available?

**Hazard Groups**

All micro-organisms must be classified into one of four hazard groups. The four hazard groups are defined as:

**Group 1**
These micro-organisms are unlikely to cause human disease.

**Group 2**
These micro-organisms can cause human disease and may be a hazard to laboratory workers; they are unlikely to spread to people in the community and there is usually effective treatment available.

**Group 3**
These micro-organisms can cause severe human disease, including death, and present a serious hazard to laboratory workers; they may spread to people in the community but there is usually effective treatment available.

**Group 4**
These micro-organisms can cause severe human disease, including death, and present a serious hazard to laboratory workers; they are likely to spread to people in the community, and there is usually no effective treatment available.

Hazard Groups for many micro-organisms are found in the Approved List of Biological Agents published by the Advisory Committee on Dangerous Pathogens.

A current list can be found at http://www.hse.gov.uk/pubns/misc208.pdf

If a micro-organism is not listed in the Approved List it cannot be assumed to be in Hazard Group 1. In these situations the pathogenicity must be assessed according to the categorisation above, and a provisional Hazard Group assigned based on all the available information. If there is uncertainty into which Hazard Group a micro-organism falls then the higher of two possible groups should be used.
The classification of micro-organisms is based solely on the infective hazard to healthy workers and does not take into account toxic or allergenic properties of the micro-organism, or its products. For example, some fungi in Hazard Group 1 such as species of *Penicillium* and *Aspergillus* and the thermoactinomycetes responsible for farmers lung are capable of inducing respiratory sensitisation. These factors must be considered when carrying out the risk assessment to identify appropriate measures to prevent ill health from occurring when working with micro-organisms.

**Routes of infection**

It is important to consider how an infection can occur so that appropriate methods to minimise exposure can be established. Micro-organisms can gain access to the body by:

- ingestion (mouth)
- inhalation (respiratory tract)
- instillation (eyes)
- percutaneous route (skin). Micro-organisms cannot be absorbed through the skin like many chemicals, but can enter the body through damaged skin (cuts and grazes, or puncturing with sharp object) or through mucous membranes.

**Individuals at risk**

The categorisation of micro-organisms is based solely on the infective hazard they present to healthy workers and does not allow for any additional risk caused by pre-existing disease, compromised immunity, pregnancy, the effects of medication or any other relevant factor. All these factors must be considered when carrying out the risk assessment to identify appropriate measures to prevent ill health from occurring when working with micro-organisms.

**Control of exposure to micro-organisms**

Working with micro-organisms presents a risk of harm to people; the higher the hazard group of the micro-organism the greater the severity of harm. Whenever
possible, the most effective method to eliminate the risk is to substitute with a less hazardous micro-organism eg a disabled strain. Frequently, this may not be possible so other control measures must be taken to prevent exposure. Exposure must be kept as low as reasonably practicable taking into account the varying levels of risk to human health posed by different micro-organisms. Thus, for each Hazard Group of micro-organism the Advisory Committee on Dangerous Pathogens has defined as a minimum a set of control measures (known as Containment Levels) that reduces exposure to an acceptable level for micro-organisms of that Hazard Group.

There are three aspects to a Containment Level: management measures, operating procedures and engineering/physical measures. These measures vary for each Containment Level and are described in “The Management, design and operation of microbiological containment laboratories” published by the Advisory Committee on Dangerous Pathogens. Note that these measures become more rigorous as the Containment Level increases. This is in recognition that the acceptable level of exposure to a micro-organism capable of causing disease to the laboratory worker (ie Hazard Group 2) is higher than a micro-organism capable of causing severe disease (possibly death) to the laboratory worker and other people (ie Hazard Group 3).

The direct relationship between hazard group and the minimum level of containment forms the basis of identification of control measures but is not sufficient. Depending upon the characteristics of the micro-organism, the nature of the work and features of the exposed individuals additional precautions may be required eg use of microbiological safety cabinet, use of gloves, avoiding use of ‘sharps’, using sealed centrifuge buckets.

Generally, the direct relationship between the Hazard Group of a micro-organism and the minimum level of containment under which it can be handled must be followed eg Containment Level 2 for Hazard Group 2; Containment Level 3 for Hazard Group 3. However, some Hazard Group 3 micro-organisms where the risk of airborne transmission is low can, in some circumstances, be handled under less
stringent conditions than Containment Level 3. These micro-organisms are listed in a Certificate of Exemption and include:

- some enteric bacteria and mycobacteria eg \textit{E.coli} 0157:H7
- some parasites eg \textit{Plasmodium falciparum}
- some blood borne viruses eg HIV
- agents for human Transmissible Spongiform Encephalopathies

Further information can be found in “Biological Agents: Managing the risks in laboratories and healthcare premises” published by the Advisory Committee on Dangerous Pathogens. Contact the University Biological Safety Adviser for further guidance in safe working with Hazard Group 3 micro-organisms.

In some types of research exposure to a Hazard Group 2, 3 or 4 micro-organism could occur, although there is no intention to culture or use these pathogens as part of the planned research eg work with human blood or tissues. In these cases the level of containment depends upon the likelihood of a pathogen being present:

- where there is uncertainty over the presence of a Hazard Group 2, 3 or 4 micro-organism the work must be carried out at Containment Level 2
- where the presence of pathogen is known or suspected an appropriate level of containment must be used
- where the risk assessment is inconclusive but the work may involve serious risk Containment Level 3 must be used.

Within the University uncertainty over the presence of a pathogen is most likely to occur when human blood and tissues are used in research, and further detailed guidance on this topic can be found in the Guidance Note on Safe Working with Human Blood, Body Fluids and Tissues.

**Additional requirements when working with human pathogens**

\textit{Record of an individual's work with a Hazard Group 3 or 4 micro-organism}

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

- names of employees and when they began and finished the work
• name of the micro-organism
• details of work
• details of accidents and incidents.
These records should be kept for 40 years.

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

Surveillance may be appropriate when:

- there is a reasonable likelihood that an employee may become infected by the pathogen under the conditions of work
- there is a valid technique to detect infection, or the onset of disease
- the employee will benefit.

Records of health surveillance must be kept for 40 years.

Contact the Occupational Health Service for advice on whether health surveillance may be required.

**Vaccination**
Effective vaccines are available for many micro-organisms. If work with such a micro-organism poses a risk to the health of an employee then vaccination should be offered unless the individual is already immune.

Contact the Occupational Health Service for advice on whether vaccination may be required.

**Notification**
Research involving *B. pertussis*, *C. diphtheria*, *N. meningitidis* and Hazard Group 3 or 4 micro-organisms has to be notified to the HSE at least 30 days before the micro-organism is obtained.
Contact the University Biological Safety Adviser for further details.

**Emergency spillage procedures**

For research involving a micro-organism that could cause severe disease (e.g., some Hazard Group 2 (e.g., *B. pertussis*, *C. diphtheria*, *N. meningitides*) and all Hazard Group 3 and 4 micro-organisms) a plan to be followed in the event of spillage must be formulated. Spillage could occur following a fire or flood in a laboratory, or during normal handling. This plan will include:

- decontamination procedures;
- the means of instructing and training staff in these procedures;
- identity of person nominated to liaise with emergency services.

**Instruction, information, training and supervision**

Staff and students working with micro-organisms should be competent to work safely. For a new member of staff, competence should not be assumed but must be verified and, if necessary, training should be provided. Records of training must be kept, and achievements verified.

Training should include the following:

- information regarding hazards and safeguards to prevent exposure/infection
- knowledge and understanding of local rules
- knowledge and understanding of disinfection policy
- knowledge and understanding of waste disposal arrangements
- knowledge and understanding of emergency spillage procedures
- technical competence for all aspects of the work (e.g., use of microbiological safety cabinet, centrifuges, automatic pipette aids)
- securing and sealing cabinet following spill within cabinet, and fumigation procedures
- safe evacuation and sealing of room following spill outside cabinet, and fumigation procedures.
Risk Assessment

An assessment of the risks to people, animals and plants before starting work with micro-organisms, or samples that may contain them, must be completed using Form USS/Micro-organisms or an equivalent. The risk assessment must be specific for the procedures involved in the work and take account of the nature and source of the samples to be handled. The risk assessment should reference the Local Rules that are implemented to prevent infection.

Useful information about common pathogens can be found at http://www.phac-aspc.gc.ca/msds-ftss/index.html.

A checklist that can be used as part of the risk assessment process is given in Appendix 2.

Local rules

They should include procedures for:

- safe handling and transport of micro-organisms within and outside the laboratory
- disinfection of contaminated surface
- safe collection, transport and disposal waste
- secure storage of micro-organisms

An example of a basic set of laboratory rules applicable to all laboratories where micro-organisms are cultured is given in Appendix 3.
Appendix 1: Pathogens requiring a licence under the Specified Animal Pathogens Order 1998 for possession or introduction into an animal

African horse sickness virus
African swine fever virus
Aujeszky’s disease virus
Avian influenza viruses which are:
(a) uncharacterised; or
(b) pathogenic
Babesia bovis, B. bigemina, B. caballi and B. equi
Bacillus anthracis
Bluetongue virus
Bovine leukosis virus
Brucella abortus
Brucella melitensis
Brucella ovis
Brucella suis
Burkholdaria (Pseudomonas) mallei
Classical swine fever virus
Cochliomyia hominivorax
Cowdria ruminatum
Eastern and Western equine encephalomyelitis viruses
Echinococcus multilocularis and E. granulosis
Equine infectious anaemia virus
Equine morbillivirus
Foot and mouth disease virus
Histoplasma farciminosum
Japanese encephalitis virus
Lumpy skin disease virus
Mycoplasma agalactiae
Mycoplasma capricolum sub species capripneumoniae
Mycoplasma mycoides sub species mycoides SC and mycoides LC variants
Mycoplasma mycoides var capri
Newcastle disease virus (avian paramyxovirus type 1) viruses which are:
(a) Uncharacterised
(b) Pathogenic
Peste de petits ruminants virus
Rabies virus and all viruses of the genus Lyssavirus
Rift Valley Fever virus
Rinderpest virus
Sheep and goat pox virus
Swine vesicular disease
Teschen disease virus
Theileria annulata
Theileria parva
Trichinella spirallis
Trypanosome brucei, T. Congolense, T. equiperdum, T. evansi, T. simiae and T. vivax
Venezuelan equine encephalomyelitis virus
Vesicular stomatitis virus
Live viral haemorrhagic disease of rabbits
Appendix 2: Micro-organism Risk Assessment Checklist

Hazard

- Name of micro-organism
- Is it attenuated/disabled or fully virulent
- What is Hazard Group
- Is it an animal pathogen; if yes is a licence required
- Is it a plant pathogen; if yes is a licence required
- What are the symptoms of infection, what complications are possible and what is incidence of disease
- What is mortality rate
- Is chronic infection possible
- Are there any other hazards to humans
- Are there hazards to animals, plants or the environment
- Is effective treatment available
- What is the incubation period
- Is there a carrier state

How is it transmitted and what is route of infection

- Is airborne infection possible
- What is infective dose
- How well can it survive in the environment
- What is its resistance to heat, dessication, and disinfectants

Immune status of staff/students

- Are there risks to pregnant women
- Are other groups at high risk
- Will they have natural resistance to infection
Exposure

- Who is at risk eg, lab staff, cleaners, maintenance staff, visitors
- Who is going to do the work
- How will organism be transported and received?
- How will it be stored
- What quantities and concentration will be used
- How often will it be used
- How will it be cultured
- How will cultures be harvested
- Will they be homogenised and sonciated, are aerosols likely to be generated
- Are ‘sharps’ used
- Will animals be used
- What manipulations will be carried out

Control measures

- Could a less hazardous micro-organism be used
- Could the micro-organism be inactivated
- Where will the work be done
- At what containment level
- How is access restricted
- Is a biohazard sign posted
- Is there a hand wash basin
- Is ventilation suitable
- Are lighting levels adequate
- Is there enough space
- Are floors, wall and ceiling suitable
- Are benches and furnishings suitable
- Is culture facility adequate
- Are microbiological safety cabinets needed
- Are suitable disinfectants available
- How is waste managed
- What are arrangements for cleaning and maintenance
• Are Local Rules available
• Who trains staff/students in Local Rules
• What level of supervision is required
• Is there a spillage procedure
• What protective clothing is required, where is it stored, and how is it cleaned and maintained
• Is vaccination available
• Is health surveillance required
• Are accident/incident reporting procedures in place
Appendix 3: Typical Local Rules

1. The laboratory must be kept tidy and organised such that separate writing and working areas are available.
2. The laboratory door should be kept closed.
3. Eating, chewing, drinking, smoking, applying cosmetics, storing of food and outdoor clothing in the laboratory is forbidden. Workers should avoid touching their mouth or eyes when in the laboratory.
4. Laboratory coats must be worn at all times in the laboratory and removed before leaving. They should be side or back fastening with a high collar and elasticated sleeves and should be stored on a dedicated set of pegs, away from other clothing. The remainder of the body should be protected with suitable clothing.
5. Hands should be washed regularly and always before leaving the laboratory.
6. Mouth pipetting is forbidden.
7. All procedures must be performed so as to minimise production of aerosols: rapid pouring of liquids must be avoided; pipettes used slowly; bottles opened carefully.
8. All workers in the laboratory must cover cuts and abrasions to the skin with a waterproof dressing
9. Sharps must not be used unless there is no alternative. Used sharps must be placed directly into a sharps bin for disposal
10. On completion of work, the workstation and equipment must be cleaned with (appropriate detergent/disinfectant)
11. Waste materials are to be placed in (specify container) and autoclaved before final disposal
12. All specimen containers, glassware and used equipment must be completely immersed in (appropriate disinfectant, concentration and time) before cleaning and disposal.
13. Micro-organisms must be transported in leakproof containers.
14. Surfaces must be disinfected immediately with (appropriate disinfectant, concentration and time) following spillages
15. Accidents

i. In the event of an accident resulting in a wound immediately encourage it to bleed, wash thoroughly but do not scrub, and cover with a waterproof dressing.

ii. In the event of spillage onto skin, or into eyes immediately wash thoroughly with soap and water.

iii. In the event of spillage into eyes immediately irrigate thoroughly with water.

iv. Accidents must be reported to Principal Investigator and Biological Safety Adviser.