UNIVERSITY OF BIRMINGHAM

GUIDANCE ON THE MANAGEMENT OF BIOLOGICAL RISKS

GUIDANCE NOTE 1: INTRODUCTION, PRINCIPLES OF PROTECTION AND UNIVERSITY APPROVAL SYSTEM

Introduction

The University Policy on Biological Safety provides the framework for managing risks from work involving biological materials. The aim of the policy is to prevent, or at least to minimise risks to human health and to the environment that arise from activities involving biological materials and to set appropriate standards for control of those risks.

This guidance is intended to help people in a position of responsibility for work with biological materials in Schools and Departments to identify appropriate precautions and to provide guidance on standards to be achieved in reducing the level of risk to an acceptable level. Schools and Departments are required by Policy to have local rules for the handling of biological materials, the guidance contained in this document should assist directly in the production of such notes.

There is a considerable body of official guidance produced and published by the Health and Safety Executive. This document is not intended to replace the official guidance but is intended to supplement it by adding practical detail where necessary.

The relevant requirements of policy are quoted at the head of each part of the guidance.

Application

The Biological Safety Policy applies to the handling, use, transport and storage of biological materials (including organisms that have been genetically modified*). The definition of biological materials in the Policy is as follows:

Any micro-organism, cell culture, parasite, human or animal tissues (including blood, urine and other body products) or plant materials, which may cause infection, allergy, toxicity or other risks to human health or cause a risk to the environment.

(* Including work to produce or construct genetically modified organisms **and** work with organisms already modified.)

Principles of Managing Biological Safety

University Policy requires that:

> *Appropriate measures are provided to ensure that risks arising from activities involving biological materials are eliminated or controlled*

Managing biological safety involves the identification of significant risks (i.e. where there is likelihood that someone, or the environment, could be harmed if precautions are not taken) and ensuring that the appropriate precautions are put in place and maintained. These precautions are known as the control measures. These principles are encoded in the Control of Substances Hazardous to Health Regulations

(COSHH) and the Genetically Modified Organisms (Contained Use) regulations. Compliance with the University Policy and guidance should ensure that the requirements of these regulations are met.

In the case of genetically modified organisms there are additional requirements in relation to processing assessments and notifying the Health and Safety Executive. The procedures for processing assessments are detailed in this document. Assessment forms in MS Word document format are available for downloading from the webpage of the Health and Safety Unit.

Principles of Control

Part of the assessment of risk includes identification of the necessary control measures. In the case of laboratory work the term ***Containment*** is used to describe those control measures. Containment however means more than the physical environment and includes procedures and practice.

Two Health and Safety Commission expert committees, the *Advisory Committee on Dangerous Pathogens* (ACDP) and the *Advisory Committee on Genetic Modification* (ACGM), define hazard categories and levels of containment appropriate for those categories. The schemes for levels of hazard and containment are compatible and both have a system of categorisation into 4 levels. Containment Level 1 (CL1) is the lowest and is for agents that are unlikely to cause harm, while level 4 provides the highest level of containment for agents that cause severe human disease with no treatment and present a high risk to the community. Currently the University has no level 4 containment facilities and work with such agents is not permitted. In practice, most work is usually conducted at level 1 or 2 with a limited amount at level 3. It is good practice to select agents at the lowest hazard level possible for the work.

Deciding On Control Measures

The person supervising the work has the primary responsibility for writing the risk assessment and identifying the control measures for work under their control. This is not done in isolation and there clearly needs to be a match between the facilities and procedures required and those available in the School or Department. There will also be common procedures and facilities that are controlled by the School or Department, which may also need assessing. Clinical waste disposal, autoclave facilities, disinfection regimes, training and transport and storage of material should all be to a common standard.

There is a hierarchy of control measures to be adopted when dealing with exposure to harmful agents. When deciding on the appropriate type of control measure to contain biological materials, the responsible persons doing the project assessments should work from the top of the following list and adopt the highest levels of control that is practicable in the circumstances. In most cases a combination of controls will be necessary.

1. Elimination

Does the work with the hazardous biological material have to be done? Is there a non-hazardous alternative?

2. Substitution

For work with pathogens, allergens, toxic or otherwise hazardous material, does it need to be a hazardous species or strain or could a less hazardous organism or material be used? For example, in undergraduate practicals there may be a non-pathogenic species or strain that could be used instead, or it may be possible to use screened human material instead of unscreened material.

3. Physical enclosure

If hazardous materials have to be used can they be physically contained to prevent exposure to the individual working with them? Where significant aerosols are produced microbiological safety cabinets may be needed, if the aerosol is likely to contain infectious agents. When material is transported outside of the laboratory it needs to be in sealed and leakproof containers.

4. Segregation

The appropriate level of containment facilities (as defined by ACDP and ACGM) should mean that the more hazardous work is segregated from other work and therefore other workers and the environment are protected from exposure. For example work with hepatitis or HIV infected material should be performed in a segregated area away from distractions and with separate dedicated equipment.

5. Procedures

Good technique is critical when handling biological materials, and clear and safe procedures should be in place. For higher risks, Standard Operating Procedures may be appropriate. Routine disinfection and waste disposal procedures are important.

6. Information and Training

Persons working with biological materials need to be trained and competent in technique and procedures. Basic lab rules such as hand washing and prohibitions on drinking and eating need to be instilled.

Signs will be needed to warn people of particular hazards and identify higher risk facilities.

7. Personal Protective Equipment

Where all the above cannot adequately control the risk, personal protective equipment (PPE) may also be necessary. PPE includes gloves, lab coats, goggles, visors, etc. In nearly all cases lab coats will be appropriate as a matter of good laboratory practice. Gloves and other PPE need to be carefully considered on the basis of need and the type required. Provision of PPE is the least reliable form of protection. It requires selection of the appropriate type that fits well, and is then subject to regular checking that it is still functioning correctly. Lab workers must remember to use PPE and supervisors should always check that it in use.

Immunisation is an additional precaution that is recommended and required in certain cases. It does not prevent exposure but does ameliorate the consequences of exposure. It is recommended in the case of work with unscreened human material (Hepatitis B), sewage (Hepatitis A) and work with TB or unscreened sputum.

Maintaining Control Measures

All equipment must be maintained in a safe condition, in particular any equipment that is designed to contain biological agents. The condition of the laboratories and other facilities should be maintained, e.g. impermeable surfaces should remain intact and impermeable.

There are specific requirements in COSHH to test and maintain local exhaust ventilation. In the case of work with biological agents this refers to microbiological safety cabinets, room air HEPA filters and any other extraction equipment that is used. Examination and testing needs to be carried out at least once every 14 months. This guidance provides more information.

Training records should be up to date and there should be an induction system for ensuring that new people are made aware of local arrangements.

PPE needs to be maintained in good and effective condition. Where Respiratory Protective Equipment (RPE) or visors are provided there should be clear allocation of responsibility for their upkeep.

Checking that Standards are being Maintained

Once standards have been identified it is essential that checks are made to demonstrate that they continue to be maintained. Monitoring occurs at a variety of levels. The University Committees for

biological safety carry out inspections from time to time on behalf of the University. These are in addition to local inspections carried out at College and School level.

A key measure of the effectiveness of the arrangements is whether individuals at the bench understand the risks and precautions. Paperwork and assessments need to be in place, and supervisors and the BSO should periodically check that these are up to date.

Reviewing assessments and arrangements

The purpose of review is to learn from experience and improve the arrangements for preventing or reducing risk. For individual assessments a formal review should be carried out after 2 years. However a review must be carried out where the work has changed significantly.

Other Key Guidance

The following official guidance should be read in conjunction with this guidance. Much of this guidance is freely available on the internet and the University's Health and Safety Unit website includes links (see below) to the documents.

Guidance from the Advisory Committee on Dangerous Pathogens (ACDP)

The Approved list of Biological Agents - Available via link on University Health and Safety Unit web pages

Biological agents: Managing the risks in laboratories and healthcare premises - Available via link on University Health and Safety Unit web pages (see below)

The Management, design and operation of microbiological containment laboratories (ACDP 2001): See link on University Health and Safety Unit web pages

Specific ACDP Guidance

Protection against Blood Borne infection in the workplace: HIV and Hepatitis: See link on University Health and Safety Unit web pages:

Transmissible Spongiform Encephalopathy agents: Safe Working and the Prevention of Infection (available on web only at http://www.dh.gov.uk/ab/ACDP/TSEguidance/index.htm /)

Working safely with research animals: Management of infection risks (ACDP 1997) Available from HSE Books

The large scale contained use of biological agents – (ACDP 1998)

Other related guidance

HTM 07-01:The safe management of healthcare waste (Department of Health)

Safe working and the prevention of infection in clinical laboratories and similar facilities (HSAC 2003)

GM Guidance

ACGM Compendium of Guidance - Available via link on University Health and Safety Unit web pages:

A Guide to the Genetically Modified Organisms (Contained Use) Regulations

Health and Safety Unit website:
https://intranet.birmingham.ac.uk/hr/wellbeing/worksafe/biological/index.aspx

Arrangements for Processing Proposals to Work with Biological Materials

University Policy states that:

The use of biological materials requires a risk assessment to be carried out by those responsible for the work.

In addition any work involving:

(i) higher risk categories, i.e. human pathogens of classified by the Advisory Committee on Dangerous Pathogens (ACDP) as being in Hazard Group 2 or above, work with human blood and tissue requiring Containment Level 2;

(ii) animal or plant pathogens requiring a license from DEFRA (Department for the Environment, Food and Rural Affairs);

(iii) all genetically modified organisms; or

(iv) other categories of work or activities notified to Colleges by the Advisory Group on the Control of Biological Hazards.

must be scrutinised by either the University's Advisory Group on the Control of Biological Hazards, in the case of (i), (ii) and (iv) above, or the relevant Genetic Modification Safety Committee, in the case of (iii) above. Details of the procedures for these two groups are outlined below.
NOTE: In addition to the above, Heads of College are encouraged to use the local safety committees to consult with staff on proposals for new work and review of existing assessments.

(i) Work with ACDP Category 2 or Above Organisms, Controlled Plant and Animal Pathogens or Material that May Contain Such Agents.

Risk assessments for this type of work must be submitted to the University Advisory Group for the Control of Biological Hazards via the Biological Safety Officer for the School or Department (a *pro forma* is available). The Advisory Group will consider the assessment, location and the persons working and where appropriate will approve the work. **Work must not start until formal approval has been granted.**

- Work at ACDP level 2 **must not begin** until the assessment has been reviewed by the Advisory Group for the Control of Biological Hazards and the laboratory facilities inspected and approved.
- Work at ACDP level 3 **must not begin** until the assessment, codes of practice and the laboratory facilities have all been reviewed and approved by the Advisory Group for the Control of Biological Hazards. The Health and Safety Executive will also be consulted in advance of work beginning.
- Work with any controlled plant or animal pathogen **must not begin** unless it has been reviewed and approved by the Advisory Group and DEFRA.
- Where work involves the use of a biological agent listed in Part V of Schedule 3 of the COSHH regulations, HSE must be notified at least twenty days in advance of work starting.

* There are currently no ACDP level 4 facilities within the University. Prior consultation with the Health and Safety Unit and the Health and Safety Executive would be required for any work at level 4.
The current ACDP document, *The Approved List of Biological Agents*, classifies biological agents on their ability to cause human infection. Only agents in Groups 2, 3 and 4 are listed. **Those not listed are not implicitly classified in Group 1.**

The minimum containment level must be applied for each project, i.e. for work with HG2 agents, containment level 2 must be applied; for work with HG3 agents, containment level 3 must be applied.

There are some exceptions to this rule, but these will be discussed by the Health and Safety Unit and the Advisory Group for the Control of Biological Hazards at the time of application.

(ii) Work with Genetically Modified Organisms (GMOs)

Work to construct or use genetically modified organisms must be submitted to the relevant Genetic Modification Safety Committee via the Biological Safety Officer (a *pro forma* is available). **All** work with GMOs **must** be approved in advance. The approval procedure will vary according to the Class of work to be undertaken:

- For Class 1 projects involving Genetically Modified Micro-organisms (GMMs) and any work with transgenic animals or plants that do not pose a greater risk to human health than their unmodified counterparts, the assessment must be reviewed and approved by the local GMSC before work may commence.
- For Class 2 GMM work the project must be reviewed and approved by the local GMSC and notified to the Health and Safety Executive. An acknowledgement of receipt of the notification must be received from the HSE before work may commence.
- For Class 3 GMM work and any work with genetically modified animals and plants that pose a greater risk to human health than their unmodified counterparts, the project must be reviewed and approved by the local GMSC, notified to the HSE and approved by the HSE in writing before work may commence.

* There are no ACGM level 4 facilities within the University. Prior consultation with both the Health and Safety Unit and the Health and Safety Executive would be required for any work at level 4.

The legal definition of Genetic Modification is complex and needs careful scrutiny. As with pathogen work the assessment should be made in consultation with the BSO. *Pro formas* are provided to aid the assessment process and completed forms should be submitted for scrutiny by the appropriate GMSC by the Health and Safety Unit, via the BSO. A central record of assessments is kept by the Health and Safety Unit. All notifications are processed by the Health and Safety Unit.

Anti-Terrorism, Crime and Security Act

This Act requires the notification of certain agents and toxins to the Home Office, prior to acquisition and use in the laboratory. The Health and Safety Unit will notify the Home Office of any notifiable agents/toxins held, and their location within the University. The storage arrangements for such materials are subject to inspection by local police.

Work with any of the pathogens or toxins listed below should be notified to your local Biological Safety Officer in the first instance. You should provide the following information:

- Name of pathogen/toxin;
- Quantity (mg) if a toxin is used;
- Location of use (room and building);
- An indication of the number of people who will be handling the substance

This information will be passed to the Health and Safety Unit for notification to the Home Office. The facilities will be inspected by local Counter-terrorism Security Advisers (CTSAs), and advice given on how to meet the required security standard for that Schedule 5 substance. As a <u>minimum</u> this will usually require:

- Material to be protected from unauthorised access by <u>at least one</u> robust security measure (security standard doors, storage cabinets, padlocked freezers, etc)
- Ability to move substances or upgrade security in the event of an increased threat level

- Provision of appropriate security plans
- Personnel security measures
- Inventories of stocks to be kept and updated, when a substance is used or destroyed

Additional security measures may include intruder detection alarms with a response from the University's Security Services.

Notifiable Biological Agents under the Control of Substances Hazardous to Health Regulations

Hazard Group 2

Bordetella pertussis
Corynebacterium diptheriae
Neisseria meningitidis

Hazard Group 3

Any Hazard Group 3 agent.

Notifiable Pathogens And Toxins Under *Anti-Terrorism, Crime And Security Act*

Schedule 5 Listed Items

Bacteria	
Bacillus anthracis Brucella abortus Brucella canis Brucella melitensis Brucella suis Burkholderia mallei (Pseudomonas mallei) Burkholderia pseudomallei (Pseudomonas pseudomallei) Chlamydia psittaci Clostridium botulinum Enterohaemorrhagic Escherichia coli (serotype 0157 and verotoxin producing strains)	Francisella tularensis Multiple-drug resistant Salmonella paratyphi Mycoplasma mycoides mycoides Salmonella paratyphi A, B C Salmonella typhi Shigella boydii Shigella dysenteriae Shigella flexneri Vibrio cholerae Yersinia pestis

Rickettsiae	
Coxiella burnetii Rickettsia prowazeki Rickettsia rickettsii Rickettsia typhi (mooseri)	

Toxins	
Abrin Botulinum toxins Clostridium perfringens epsilon toxin Clostridium perfringens enterotoxin Conotoxin Modeccin toxin Ricin Saxitoxin Shiga and shiga-like toxins	Staphylococcal enterotoxins Tetrodotoxin Viscum Album Lectin 1 (Viscumin) Volkensin toxin

Viruses (Affecting humans)	
Chikungunya Virus Congo-Crimean haemorrhagic fever virus Dengue fever virus Dobrava/Belgrade virus Eastern equine encephalitis virus Ebola virus Everglades virus Getah virus Guanarito virus Hantaan virus Hendra virus (Equine morbillivirus) Herpes simiae (B virus) Influenza viruses (pandemic strains) Japanese encephalitis virus Junin virus Kyasanur virus Lassa fever virus Louping ill virus Lymphocytic choriomeningitis virus Machupo virus Marburg virus Mayaro virus Middleburg virus	Mobala virus Monkey pox virus Mucambo virus Murray Valley encephalitis virus Ndumu virus Nipah virus Omsk haemorrhagic fever virus Polio virus Powassan virus Rabies virus Rift Valley fever virus Rocio virus Sabia virus SARS Coronavirus Sagiyama virus Sin Nombre virus St Louis encephalitis virus Tick-borne encephalitis virus (Russian Spring-Summer encephalitis virus) Variola virus Venezuelan equine encephalitis virus Western Equine encephalitis virus West Nile fever virus Yellow fever virus

Viruses (Affecting animals other than humans)	
African horse sickness virus African swine fever virus Bluetongue virus Classical swine fever virus Contagious bovine pleuropneumonia Foot and mouth disease virus Goat pox virus Hendra virus (Equine morbillivirus) Highly pathogenic avian influenza (HPAI)	Lumpy skin disease virus Newcastle disease virus Peste des petits ruminants virus Rift Valley fever virus Rabies and rabies-related Lyssaviruses Rinderpest virus Sheep pox virus Swine vesicular disease virus Vesicular stomatitis virus

In addition:

1. Any reference to a micro-organism includes:
   (a) intact micro-organisms;
   (b) micro-organisms which have been genetically modified by any means, but retain the ability to cause serious harm to human or animal health;
   (c) any nucleic acid deriving from a micro-organism listed in this Schedule (synthetic or naturally derived, contiguous or fragmented, in host chromosomes or in expression vectors) that can encode infectious or replication competent forms of any of the listed micro-organisms;

(d) any nucleic acid sequence derived from the micro-organism which when inserted into any other living organism alters or enhances that organism's ability to cause serious harm to human or animal health.

2. Any reference in this Schedule to a toxin includes:
   (a) any nucleic acid sequence coding for the toxin, and
   (b) any genetically modified micro-organism containing any such sequence.

3. Any reference in this Schedule to a toxin excludes any non-toxigenic subunit.

* There is an exemption in place for holding small quantities of certain toxins, but the Health and Safety Unit will advise on this upon notification.

Legal Definitions

The Genetically Modified Organisms (Contained Use) Regulations

The Genetically Modified Organisms (Contained Use) Regulations define the application of the regulations and also give a legal definition of *genetic modification*.

Application

These regulations apply to activities **involving** genetically modified organisms. Thus activities where no modification is taking place but where previously modified organisms (from whatever source) are being used come under the requirements of these regulations. For example, work on transgenic animals or modified *E.coli* provided commercially or by collaborators will be subject to the requirements.

Genetic Modification

Regulation 2 defines genetic modification:-

"genetic modification" in relation to an organism means the altering of the genetic material in that organism by a way that does not occur naturally by mating or natural recombination or both and within the terms of this definition -

(a) genetic modification occurs at least through the use of the techniques listed in Part I of Schedule 2; and

(b) the techniques listed in Part II of that Schedule are not considered to result in genetic modification.

Schedule 2 of the Contained Use Regulations

Schedule 2 of the regulations gives examples of techniques to which the regulations do and do not apply.

Part I Examples of techniques constituting genetic modification

(1) Examples of the techniques which constitute genetic modification ..... are -

(a) recombinant DNA techniques involving the formation of new combinations of genetic material by the insertion of nucleic acid molecules, produced by whatever means outside the cell, into any virus, bacterial plasmid or other vector systems so as to allow their incorporation into a host organism in which they do not occur naturally but in which they are capable of continued propagation;

(b) techniques involving the direct introduction into an organism of heritable material prepared outside the organism including micro-injection, macro-injection and micro-encapsulation; and

(c) cell fusion or hybridization techniques where live cells with new combinations of heritable genetic material are formed through the fusion of two or more cells by means of methods that do not naturally occur.

Part II Techniques which are not considered to result in genetic modification

(2) The following techniques are not considered to result in genetic modification if they do not involve the use genetically modified organisms made by techniques other than those listed in Part III or the use of recombinant nucleic acid molecules, namely -

(a) in vitro fertilisation;

(b) conjugation, transduction, transformation or any other natural process; and

(c) polyploidy induction.

Part III Techniques to which these Regulations do not apply

(3) These Regulations (except Reg 17- Principles of environmental and occupational safety) shall not apply to the following techniques of genetic modification providing they do not involve the use of recombinant nucleic acid molecules or of genetically modified organisms other than those recombinant nucleic acid molecules or genetically modified organisms produced by one or more of the following techniques of genetic modification -

(a) mutagenesis

(b) cell fusion (including protoplast fusion) of prokaryotic species which can exchange genetic material through homologous recombination;

(c) cell fusion (including protoplast fusion) of cells of any eukaryotic species, including production of hybridomas and plant cell fusions;

(d) self-cloning where the resulting organism is unlikely to cause disease or harm to humans.

Self cloning means the removal of nucleic acid sequences from the cell of an organism which may or may not be followed by reinsertion of all or part of that nucleic acid (or a synthetic equivalent), whether or not altered by enzymic or mechanical processes, into cells of the same species or into cells of phylogenetically closely related species which can exchange genetic material by homologous recombination; and

Self cloning may include the use of recombinant vectors, with an extended history of safe use in the particular organism, to manipulate and reinsert the nucleic acid sequences, but the vectors shall not consist of any genetic elements other than those designed for vector structure, vector replication, vector maintenance or marker genes.