**Guidance on completion of Risk Assessment for Biological Activity (GM and BioCOSHH Assessment)**

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# Definitions

|  |  |
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| ACDP | Advisory Committee on Dangerous Pathogens |
| BA | Biological Agent |
| BSO | Biological Safety Officer |
| CL | Containment Level |
| COSHH | Control of Substances Hazardous to Health |
| DEFRA/Defra | Department for Environment, Food and Rural Affairs. |
| GM | Genetic Modification (Genetically Modified) |
| GMM | Genetically Modified Micro-Organism |
| GMO | Genetically Modified Organisms |
| GMSMC | Genetic Modification Safety Management Committee |
| MSC | Microbiological Safety Cabinet |
| PI | Principal Investigator |
| SACGM | Scientific Advisory Committee on Genetic Modification |

Biological Material any biologically-derived material or materials which, either by accident or design, contain biological agents which might pose a risk to health and safety or the environment.

This includes

1) The intentional use of biological agents.

2) Use of materials which may incidentally contain such agents;

3) Biological materials which may contain toxic or harmful chemicals;

4) Live animals.

Biological agent A biological agent is defined in COSHH as;

‘*a micro-organism, cell culture, or human endoparasite, whether or not genetically modified, which may cause infection, allergy, toxicity or otherwise create a hazard to human health.’*

This includes:

1. micro-organisms such as bacteria, viruses, fungi, and the agents that cause transmissible spongiform encephalopathies (TSEs);
2. Cell cultures
3. parasites, e.g. malarial parasites, amoebae and trypanosomes; and including the microscopic infectious forms of larger parasites, such as the ova and infectious larval forms of helminths

Hazard Group (HG) Biological agents are classified into four hazard groups according to:

(a) their ability to cause infection;

(b) the severity of the disease that may result;

(c) the risk that infection will spread to the community; and

(d) the availability of vaccines and effective treatment.

Hazard Group (HG) 1 A biological agent unlikely to cause human disease.

Hazard Group (HG) 2 A biological agent that 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 effective treatment available.

Hazard Group (HG) 3 A biological agent that can cause severe human disease and maybe a serious hazard to employees; it may present a risk of spreading to the community, but there is usually effective prophylaxis or treatment available.

Hazard Group (HG) 4 A biological agent that 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. This category is highly specialised.

(Biological agents in Hazard Groups 2 to 4 are listed in The Approved list of biological agents, which can be viewed via the HSE website at <http://www.hse.gov.uk/pubns/misc208.pdf>. The List is not exhaustive and a biological agent that does not appear on it does not automatically fall into Hazard Group 1.

# Responsibilities

**Proposer**

Responsible for ensuring:

* Assessment is completed and approved prior to the start of any work.
* Assessment is suitable and sufficient, considers up-to-date hazard data and complies with this procedure.
* Assessment is recorded and reviewed.
* Assessment is read and understood by all persons carrying out the work.
* Assessment is completed by persons with sufficient knowledge and expertise of the agents and process.

**Genetic Modification Safety Management Committee (GMSMC)**

The GMSMC is responsible for ensuring that any Biological risk assessment submitted to them is reviewed to make sure the work is safe, compliant and current. Duties include:

* Reviewing all Biological risk assessments sent to them. See Appendix 1 for the work flow and approval timeline of GMSMC.
* Maintenance of records of all work carried out.
* To provide guidance, advice and to assist persons carrying out suitable and sufficient biological risk assessments.

Employees, Users, Tenants and visitors

Employees, Users, Tenants and visitors are responsible for ensuring any work to be undertaken is sufficiently assessed.

# Procedure

## General Guidance

The final risk assessment must contain enough background and detail to ensure that a reviewer with limited understanding of the precise nature of the work will not require further information to comprehend the nature of any hazards. All feasible potential hazards must be acknowledged and information must be based on established scientific knowledge where available and duly referenced. Any uncertainty must be acknowledged and dealt with appropriately and lack of evidence does not equal lack of hazard.

It is a legal requirement for risk assessments to be kept for 10 years after the work has ceased. Storage of materials is classed as active work.

The following areas of work **MUST BE** risk assessed and approved **BEFORE** starting any work.

* + - Work involving ‘biological materials’ or 'biological agents'. This will include the use of experimental materials which are likely to contain a biological agent.
    - Work involving genetic modification or work with genetically modified organisms
    - Work with blood or body products.

Biological material/biological agents **MUST NOT** be brought onto the site without prior permission from either the GMSMC or local competent staff (e.g. BSO).

This document will guide investigators through an initial Biological risk assessment for a proposed research project involving biological materials. Consideration must be given to the possible risk of harm or damage to humans, animals and the environment through the proposed work.

Of particular concern are biological materials which will require special containment facilities or licences including

* genetically modified microorganisms, plants or animals.
* human body secretions or tissues
* materials likely to carry human pathogens, parasites or zoonoses
* pathogens which cause disease in plants

As these are generic guidelines, not all sections or questions may be appropriate for all types of work or experiments. If in any doubt please contact a member of the GMSMC as detailed in Appendix 1.

Based on the Biological risk assessment, a **C**ontainment **L**evel (CL) or activity class for the work will be assigned by the GMSMC.

All projects require approval and the completed biological risk assessment should be forwarded to the GMSMC contacts (see Appendix 1) for this purpose. At present, the site can facilitate work up to and including CL2. Copies of the final approved biological risk assessments should be retained by the investigator and the GMSMC.

Depending on the nature of the proposed research further risk assessments, approvals, licences and/or permissions may be required from other regulatory authorities (e.g. DEFRA, Home Office).

Samples obtained from commercial sources, such as purified proteins (e.g. serum albumin), enzymes (e.g. nucleases), nucleic acids (e.g. *E.coli* DNA), blood products (e.g. sera) or other specified extracts (e.g. tryptone) may not require risk assessments, however the material safety data sheets (MSDS) accompanying these products should be examined for any statements referring to hazards, pathogen screening etc.

## Guidance on the completion of the Biological activity risk assessment form

### **3.2.1 Section A: Project overview**

**Applicant:** The person completing the Biological activity risk assessment.

**Project Title:** A short title for the project.

**Name of Project Leader:** The person responsible for this work.

**Organisation:** Detail the organisation which the applicant represents, this maybe an internal organisation e.g. Diamond, RCaH, ISIS, STFC, RFI.

**Contact details:** The contact details of the applicant should be described here. Include a phone number and email address.

**Persons involved in the project:** List all persons who will participate in this work.

**General description of the project, including the aim of the work:** This section is to provide an overview of the aims of the project, any methods and processes that will be used to carry out this work. Try to avoid technical language / jargon so that the description can be understood by a non-expert.

**List all the locations of proposed work:** This should describe where the work will be completed and include locations where samples are handled and stored.

**Is any of the material listed under the following regulations:** If any of the materials used fall under the following legislation specify here

* Specified Animal Pathogens Order (SAPO): Refer to guidance document <http://www.hse.gov.uk/pUbns/priced/hsg280.pdf>
* Schedule 5 of Anti-Terrorism, Crime and Security Act 2001: Refer to legislation <https://www.legislation.gov.uk/ukpga/2001/24/contents>
* Human Tissue Act (HTA 2004: Refer to legislation or contact a member of GMSMC if required

[Human Tissue Act 2004 (legislation.gov.uk)](https://www.legislation.gov.uk/ukpga/2004/30/contents)

**Does this work involve:**

1. **Biological Non-GM activity –** Choose this optionif your work does not involve any genetic modification and uses only wild type biological agents.
2. **Biological GM activity only –** Choose this option if your work involves genetic modification of the recipient organism. Genetic modification includes insertion of non-native genes or alteration of native genes.
3. **Both Biological GM and Non GM activities –** Choose this option if your work involves both the above options.

### **3.2.2 Section B: Project Risk Assessment involving Biological Non-GM activity**

**The nature of the biological material**

1. **Describe the biological materials to be used in the work**

Provide as much information as you have available

* Describe what biological materials will be used
* Specify their origin
* Will the work involve human tissue?

1. **Describe how and from where the materials will be obtained.**

Provide as much information as you have available about where and how the materials will be obtained. E.g. commercial supplier, collaborators

1. **Will the biological material(s) be subject to any form of pre-treatment to reduce risk?**

The way in which biological materials are treated and stored may increase or decrease the hazard. Specify any pre-treatment of the materials e.g. chemical extraction,culturing**,** disinfection, freezing, fixation, autoclaving, heat treatment or other processing which could affect agents present (e.g.inactivate or amplify).

Evidence for treatment of samples must be available where such processing is used as a means of removing pathogens/agents and evidence that this is a validated method (i.e. evidence that it kills the agent).

1. **Where will the biological materials be stored and under what conditions, e.g. frozen, refrigerated, liquid nitrogen?**

List all the possible places where samples will be stored for short term and long term.

**Risks from biological material and biological agents present in the material**

1. **Are there any other biological agent(s) or toxins likely to be present in the biological material that may pose a risk of harm to human health, animals or the environment?**

List all known or possible agents or toxins which will be used or may be present in the biological materials. Include viruses, prions, bacteria, fungi or parasites (such as worms or protozoa). If the biological material also contains a toxin or other biologically active chemical which may pose a risk list it here.

1. **Does the biological material or biological agent(s) present appear on the ACDP Approved List of Biological Agents and, if so, what is its hazard group under COSHH?**

Human pathogens are assigned to a **H**azard **G**roup (**HG 1-4**) depending on their human pathogenicity and effective measures of the treatment against the disease. The HG forms part of the assignment of work to a **C**ontainment **L**evel (**CL1 to 4**) along with other factors. Consult The Approved list of biological agents. <http://www.hse.gov.uk/pubns/misc208.pdf>

1. **Provide information on the mode of transmission, disease caused and symptoms. If any toxins present, please provide information on its likely concentration in the material and at what level has an effect on human health.**

* What is the route of infection by each agent?
* What disease and symptoms are produced?
* Is there an effective treatment for the disease?

**d) Provide information on the likely viability of the biological material and any biological agents present in it**

* Under what conditions will the agent survive, propagate or be killed?
* What disinfectants are effective against the agent?
* Consider the pre-treatment of the material and treatment prior to disposal.

1. **Provide information on any risks posed to the environment, e.g., ability to survive outside the laboratory, effects on the ecosystem**

Describe the consequences of the escape of experimental organisms into the environment.

### **3.2.3 Section C: Project Risk Assessment involving biological GM activity**

**Give the details of all the recipient organisms, vectors used, modifications including altered genes etc.**

The volumes and/or titres of the proposed material and the processes involved in the work must be considered when assessing the work. Explanation of answers must be given, for example, if none or non-applicable then describe why this is the case. Please include the following information-

* Details of all GMM/GMOs to be constructed: Ensure all the intermediate cloning steps and any intermediate GMM/GMOs are considered and not just the final construct.
* Detail the name of the strain(s) to be used, the name of the wild-type organism from which it is derived and the extent to which it is disabled.
* Detail the names of all the vectors to be used and any disabling mutations.
* List of all modifications, including any altered genes. Genes must be identified in such a way that an outside reviewer will have a general idea of their function i.e. providing an acronym may not be sufficient. Where the function is unknown, it may help to provide details of any known homologues.
* Identify the most hazardous GMM constructed considering both human health and the environment. With some projects it may not be clear that any one GMM will be more hazardous than any of the others (e.g. if all class 1 work). If this is the case this should be stated.

**Consideration of potential properties of the GMM/GMO to determine if there are any potential mechanisms by which it could present a hazard to human health and/or the environment.**

1. **Hazards associated with the recipient micro-organism**

Factors to consider

* ACDP Hazard Group
* Disabling mutations
* Mode of transmission
* Disease symptoms
* Host range and tissue tropism
* Available vaccines or chemotherapeutic agents

1. **Hazards arising directly from the inserted genetic material**

Consideration should be given to whether the inserted DNA encodes

* A toxin
* An oncogenic protein
* An allergen
* A modulator of growth or differentiation (e.g. hormone or cytokine)
* A product that could result in potentially harmful biological activity

**Note:** Any human gene may be harmful if over expressed, especially if the over expression is in tissues that do not normally express the protein.

1. **Hazards arising from the alteration of existing pathogenic traits (e.g. alteration of tissue range or tissue tropism)**

Factors to consider

* Does the inserted gene encode a pathogenicity determinant, a penetration factor or a surface component providing resistance to host defence mechanisms?
* Does the inserted gene encode a surface component, envelope protein or capsid protein that might bind to a different receptor to that used by the recipient microorganism?
* Does the inserted DNA (or the plasmid sequence) encode resistance to a drug or antibiotic that might be used for the treatment of an infection?

1. **Potential hazards of sequences within the GMM/GMO being transferred to related micro-organisms (e.g. via gene transfer or recombination, survivability in the environment)**

Factors to consider

* Widespread dissemination of the GMM/GMO
* Could the GMM/GMO survive in the environment for long enough for gene transfer to take place? Consider in the event of a breach of containment.

1. **Potential hazards of the final GMM/GMO (Include consideration of the ability of the GMM to become established in the host and consideration of the probability that rare events will occur)**

Consider the likelihood that, in the event of an exposure, the GMM/GMO could actually cause harm to human health or be a risk to the environment. For example, consider the overall fitness of the GMM/GMO and the probability that rare events like mutation or gene transfer may occur. Where the likelihood of harm is poorly understood, a precautionary approach should be adopted until evidence to the contrary has been obtained.

**Assignment of provisional Containment Level to protect human** health - The requirements of the final containment level must be sufficient to control all the potential harmful properties of the GMM/GMO and offer sufficient protection for human health.

**Assignment of provisional Containment Level to sufficiently protect against harm to the environment** -The requirements of the final containment level must be sufficient to control all the potential harmful properties of the GMM/GMO and offer sufficient protection for the environment.

**Assignment of activity class** - This is done by comparing the containment and control measures (see section D). For further information please refer to table 1a from Schedule 8 of the GMO (Contained Use) Regulations can be found at <http://www.legislation.gov.uk/uksi/2014/1663/schedule/8/made>. The SACGM Compendium of guidance details these measures and can be found at <http://www.hse.gov.uk/biosafety/gmo/acgm/acgmcomp/index.htm>

### **3.2.4 Section D: Control Measures**

**Detail the control measures in place to protect against the risk of harm to human health and environment. Comment on each of the following where applicable.**

1. **Reduction of aerosols;** describe any precautions or controls in place to reduce the production of aerosols e.g use of microbiological cabinet
2. **Waste disposal procedure;** include procedures at all sites where the work will take place
3. **Disinfection procedure;** include specifics at all sites where the work will take place e.g virkon useage not suitable for all processes,
4. **Spills management;** includes management at all sites where the work will take place
5. **Transportation of material(s);** give specific details of transport to be completed including locations
6. **Any other information;** e.g. COSHH assessment for chemicals involved

### **3.2.5 Section E: Documentation, Licences & Approvals**

1. List and attach to the final assessment any supporting documentation, letters, references and/or procedures which support any of the information provided in this assessment. E.g. Codes of practice, journal articles, risk assessments from collaborating institutes
2. Does the import, production and/or use of the biological material require a special licence, notification or specific permission from a legislative body or a council committee? If yes, is this in place and give details.

### **3.2.6 Section F: Signatures and Review**

Signatures

The signatures will be completed after the GMSMC have reviewed the proposal. No work must start before all signatures have been gathered.

Review

All biological risk assessments are subject to review where there is a 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 or periodically depending on the risk.

Low risk (CL1 or GM class 1) at least every two years

Medium risk (CL2 or GM Class 2) at least annually

**Document History**

|  |  |  |
| --- | --- | --- |
| **Issue** | **Date** | **Comment** |
| 1 | 28 June 2011 | New document – Diamond only |
| 2 | 06 December 2013 | Full revision – Joint document |
| 3 | 23 August 2016 | Full revision – Joint Document |
| 4 | 02 October 2018 | Guidance updated to reflect the new merged GM and BioCOSHH assessment form |
| 4.1 | 25 November 2019 | Formatting amendments to reflect the biological activity form. |
| 4.2 | 09 December 2021 | Updating guidance to reflect addition of RFI |

# Appendix 1

**Submission of Biological risk assessments for approval**

Before any biological work starts, a Biological risk assessment must be completed by the person responsible for carrying out the work.

Once a biological risk assessment is submitted to any of the entities of the site (i.e. Diamond, RCaH, ISIS/STFC/BIS or RFI), the GMSM committee (GMSMC) will review this assessment. In the majority of cases this can be done electronically, but may require a GMSMC meeting to discuss the assessment.

The biological risk assessment should be circulated to all entities via the following persons:

Diamond Valerie Loughry ([Valerie.loughry@diamond.ac.uk](mailto:Valerie.loughry@diamond.ac.uk) )

RCaH Zuzanna Lalanne ([Zuzanna.lalanne@rc-harwell.ac.uk](mailto:Zuzanna.lalanne@rc-harwell.ac.uk) )

ISIS

RFI Chelsea Norman ([Chelsea.Norman@rfi.ac.uk](mailto:Chelsea.Norman@rfi.ac.uk))

BIS Mark Roberts (mark.roberts@stfc.ac.uk

This biological risk assessment will then be circulated to all GMSMC members as well as, if required, other relevant persons. This circulation will request the biological risk assessment to be reviewed and any comments to be sent back to one of the above points of contact. A deadline of approximately 2 weeks should be specified on this circulation for comments to be received. The following format in email subject lines should be used: Entity name/year/sequential number e.g. Diamond/2013/001

Once the deadline has passed, all comments received will be collated by the entity where the biological risk assessment has been submitted. If minor comments are received these can be discussed electronically, however a GMSMC meeting can be arranged if required.

Once the biological risk assessment has been reviewed successfully, the assessment can be approved. Part of the approval process involves assigning a reference to the biological risk assessment. Once approved, the biological risk assessment can be circulated to all entities and the proposer for their records.

All biological risk assessments must be reviewed at least every 2 years by the applicant and proposer.

A flow diagram of this process can be found in Figure 1

**Figure 1: Process for approval of Biological risk assessments**



**End of document.**