**St George’s Risk Assessment for working with Genetically Modified Microorganisms (GMMs)**

Contents

[Part 1 (Mandatory for work with any GMM) 2](#_Toc61507046)

[1. Title of the project 2](#_Toc61507047)

[2. Purpose of the contained use 2](#_Toc61507048)

[3. Characteristics of the GMOs including the evaluation of foreseeable effects 2](#_Toc61507049)

[4. Description of the most hazardous GMM that will be created/used 3](#_Toc61507050)

[5. Considerations regarding clinical trials 3](#_Toc61507051)

[6. Activity classification (part 1) 4](#_Toc61507052)

[Part 2 (Mandatory for work with GMMs that may represent a hazard to human health or the environment) 6](#_Toc61507053)

[1 – Hazards to human health and control measures 6](#_Toc61507054)

[2 – Hazards to the environment. 7](#_Toc61507055)

[3 – Consideration of the nature of the work to be undertaken and detailed review of control measures. 8](#_Toc61507056)

[4 – Consideration whether there is a need to assign additional measures over and above the provisional level of containment assigned in Part 2 section 1.5 9](#_Toc61507057)

[5 – Is there an emergency plan required under regulation 21 of CU 2014?1 9](#_Toc61507058)

[Part 3 (Mandatory for work with any GMM) 10](#_Toc61507059)

[Final classification of the activity 11](#_Toc61507060)

# Part 1 (Mandatory for work with any GMM)

Please write only in the boxes provided and do not modify the original text.

You can find advise on how to complete this form in <https://bit.ly/3fXsbwg> or by contacting the Biological Safety Officer for Genetic Modification BSO-GM@sgul.ac.uk x5791.

**Note that under no circumstance can GM work begin before having received written notification by the BSO-GM that the work can commence.**

## 1. Title of the project

## 2. Purpose of the contained use

This information should provide background and put the work into context. The purpose of the contained use needs not to be disclosed if this information presents problems in the context of intellectual property rights or commercial activity. However, withholding information will make the review process more difficult.

## 3. Characteristics of the GMOs including the evaluation of foreseeable effects

This section should be completed in detail. If you are making a request for non-disclosure in relation to intellectual property rights, you must include at least general characteristics of the GMM(s) that will allow for the evaluation of the risk assessment.

**3.1 Overview of the GMM(s)**

Describe thegeneral characteristics/use of the GMM(s) involved in the intended contained use together with the scope and boundaries of exactly what work will be done (e.g. Will the GMMs be used to infect other organism or to create further GMOs?).

**3.2 List of recipient or parental organisms**

include name and strain of the organism(s), the names of parental strain(s), and the degree to which they are disabled, e.g. Recipient organism E coli DH5alpha; Parental organism: E coli K12, proven track record of safety, non-pathogenic, thiamine & arginine auxotroph, Lactose non- utilizing.

If the recipient organism is a viral vector (lentivirus, adenovirus, etc.), provide details: e.g. pLenti6/V5-TOPO, 3rd generation lentiviral vector without an WPRE cassette.

**3.3 List of vectors** (cover names, mobilisation regions, and any disabling mutations)

**3.4 Origin and function of the genetic material involved**

Preferably a list of genes or gene families should be included. Genes must be identified in a way that an outside reviewer will have a general idea of their function. A three-letter name may not be sufficient. When the function of the gene is unknown, providing the function of any know homologues may help.

## 4. Description of the most hazardous GMM that will be created/used

State clearly if there are no risks arising from this GMM -it is important to consider risk for both humans and the environment. If you foresee any non-negligible risks, state those risks briefly. They will have to be addressed in detail in Part 2.

## 5. Considerations regarding clinical trials

**5.1 How long will the GMMs persist after administration? Are the patients expected to shed GMMs?**

**5.2 How will the shedding of GMMs be contained and how will it be confirmed that shedding has stopped?**

**5.3 What is the expected mode of transmission of the GMM? Are other modes of transmission possible?**

**5.4 What could the effect of the GMM be in untargeted tissues?**

**5.5 Will samples be taken from the patient? Are these samples expected to contain GMMs? How will the samples be treated?**

**5.6 Identify if there are any steps or procedures that could lead to exposure of other patients, staff, visitors or members of the public and describe control measures.**

## 6. Activity classification (part 1)

**6.1 Are you confident that for the GMMs covered by this assessment there are not harmful properties associated with the recipient strain, the vector or the inserted material?**

Consider this question CAREFULLY. If the answer to this question is ‘No’ or it is in any way unclear, Part 2 of this form needs to be completed. Part 2 is likely to be required for all but the most standard cloning techniques and organisms, such as plasmid amplification in E coli K-12

**Yes** [ ]

**No** [ ]

**6.2 Are you confident that none of the final GMMs could be hazardous to humans or the environment?**

Consider this question CAREFULLY. If the answer to this question is ‘No’ or you are in anyway unsure, Part 2 of this form needs to be completed.

**Yes** [ ]

**No** [ ]

**6.3 If your answer to the previous two questions was ‘Yes’, then you may be confident that the proposed activity can be categorised as ‘Class 1’ as defined in the Genetically Modified Organisms (Contained Use) Regulations 2014.** I**n order to do this, you must be confident that even in the event of a total breach of containment, the consequences to human health and environment will be negligible.** Note that intentional release of GMMs into the environment is an offence under the GMO (Deliberate Release) Regulations 2003.

**Are the proposed activities class 1 as defined in Contained Use Regulations 2014?**

**Yes** [ ]

**No** [ ]

If you are assigning your GM activity to class 1, you do not need to complete Part 2 of this form. Complete Part 3 (Mandatory for work with any GMM) and email the form to the Biological Safety Officer for Genetic Modification (BSO-GM@sgul.ac.uk). The application will be considered by the Genetic Modification Safety Committee (GMSC). Work on the activity cannot commence until the GMSC has reviewed and approved the activity. The GMSC aims to review all assessments within 14 days.

**If you are unsure whether the proposed GM activities can be assigned to class 1, you must complete** Part 2 (Mandatory for work with GMMs that may represent a hazard to human health or the environment) **of this form.**

# Part 2 (Mandatory for work with GMMs that may represent a hazard to human health or the environment)

Evaluation of foreseeable effects

When completing this part of the form, please bear in mind that the regulator (the HSE) will not accept simple statements such as ‘it is not anticipated’ without proper justification and supporting evidence (i.e. references).

This form is designed to assess the hazards presented by the most hazardous GMM identified in point 4 of Part 1. In cases where there are 2 or more hazardous GMMs with quite different properties, 2 or more copies of part 2 should be completed.

## 1 – Hazards to human health and control measures

**1.1 – Hazards associated with the recipient microorganism**

Factors to be considered are [classification of the microorganism by Advisory Committee on Dangerous Pathogens (ACDP)](https://www.hse.gov.uk/pubns/misc208.pdf) and the microorganism’s mode of transmission, dissemination, range of host, and tissue tropism. Consider also whether vaccines or any prophylaxis are available. Information must also be provided on any disabling mutation and whether there is any possibility of the disabling mutation being complemented or reverting.

1.2 – **Hazards arising directly from the gene products**

Consideration must be given to whether the inserted DNA encodes a toxin, an oncogenic protein, an allergen, a modulator of growth or differentiation (hormone or cytokine) or any other protein which may result in potentially harmful biological activity. When the function of the inserted gene is unknown, it may help to describe the function of any known homologues. Please note that any human gene may be harmful if overexpressed, especially if the overexpression is in tissues that do not normally express the protein.

1.3 – **Hazards arising from the alteration of existing traits**

Consider whether the inserted sequence carries a pathogenicity determinant, such as a receptor, a penetration factor or a surface component providing resistance to host defence mechanisms. Also consider whether the sequence carries a protein that may allow a different range of hosts for the microorganism. Consideration may also be given to whether the sequence (or its vector) carries a resistance to a drug or antibiotic that may be used for the treatment of laboratory-acquired infection.

1.4 – **Hazards arising from the transfer of the inserted sequence to other organisms**

Factors to consider include whether the dissemination of the inserted sequence as a result, for example, of either gene transfer or recombination of the GMM with a wild-type organism, would be a matter for concern. Note that the likelihood of gene transfer will increase with the ability of the GMM to persist in the environment even if it cannot prosper there.

1.5 – Assignment of a provisional containment level that is adequate to minimise the risks to human health. (The default containment level will be that assigned by the ACDP to the recipient organism. You should evaluate whether the GMM will represent a greater, lesser, or about the same hazard as its parental organism.)

Containment Level 1 ☐

Containment Level 2 ☐

Containment Level 3 ☐

## 2 – Hazards to the environment.

**2.1 – Hazards associated with the recipient microorganism**

Factors to be considered are whether the recipient microorganism is capable of infecting plants or animals and whether there is any possibility of any disabling mutations being complemented or reverted. In particular, it must be asserted whether the microorganism is regulated under the Specified Animal Pathogen Order [SAPO](https://www.legislation.gov.uk/uksi/2008/944/schedule/1/made).

**2.2 – Hazards arising directly from the inserted product**

Factors to be considered are whether the inserted sequence encodes a plant or animal toxin or a product which inhibits crucial metabolic enzymes in susceptible hosts.

**2.3 – Hazards arising from the alteration of existing traits**

Consider whether the inserted sequence carries a pathogenicity determinant, such as a receptor, a penetration factor or a surface component providing resistance to host defence mechanisms. Also consider whether the sequence carries a protein that may allow a different range of hosts for the microorganism. Consideration may also be given to whether the sequence (or its vector) carries a resistance to antibiotics.

**2.4 – Hazards arising from the transfer of the inserted sequence to other organisms**

Factors to consider include whether the dissemination of the inserted sequence as a result, for example, of either gene transfer or recombination of the GMM with a wild-type organism, would be a matter for concern. Note that the likelihood of gene transfer will increase with the ability of the GMM to persist in the environment even if it cannot prosper there.

## 3 – Consideration of the nature of the work to be undertaken and detailed review of control measures.

**3.1 – Are any of the work procedures likely to generate aerosols?**

If work will involve liquid cultures, it is likely that aerosols will be generated. Please describe what control measures will be applied.

3.2 – **Estimate maximum culture volume (Class 2) or specify the culture volume (class 3)**

**3.3 – Will any sharps be used?**

**Yes** [ ]

**No** [ ]

**3.4 – If the work involves the experimental infection of plants or animals, are they expected to shed GMMs?**

**3.5 – If the work involves the experimental infection of plants, what is known about the likely route of transmission of the GMM?**

Consider for example whether the microorganism is insect-borne or can be carried in run-off water. These are important considerations regarding the type of greenhouse used.

**3.6 – In the case of microorganism with a complex life cycle, will the work involve the propagation of organisms that are in stages in that cycle that are particularly hazardous?**

Examples include the propagation of infective stages of parasites or the release of fungal spores. Consideration should be given to all potential routes of transmission including those that might not occur naturally.

## 4 – Consideration whether there is a need to assign additional measures over and above the provisional level of containment assigned in Part 2 section 1.5

Additional control measures may be necessary:

1 – To protect human health

2 – To protect the environment

3 – To provide additional safeguards to particular work procedures

## 5 – Is there an emergency plan required under regulation 21 of CU 2014?1

Yes ☐

No ☐

If yes, please describe:

# Part 3 (Mandatory for work with any GMM)

**Describe the waste management measures which you will apply**

Describe how solid and liquid waste material will be treated and disposed and what measures will be taken to validate/monitor the inactivation process

**Have your disinfectants being validated under actual conditions of work?**

e.g. are the disinfectants effective under the high levels of protein common in tissue cultre conditions?

**Are all the non-GM risks in this activity adequately covered by up-to-date COSHH risk assessment(s)? If not, a risk assessment must be completed.**

**Yes** [ ]

**No** [ ]

**Does the nature of this work preclude it from being undertaken by any workers who have a serious skin condition or other health problems?**

**Does the nature of this work preclude it from being undertaken by any worker who is pregnant or intends to become pregnant? If so has the pregnancy worker risk assessment been performed. This would be mandatory if YES.**

**Yes** [ ]

**No** [ ]

**Please describe the exit strategy for this activity**

e.g. name the person who will take charge of the activity should the principal investigator leave St George’s or confirm that on leaving the project will be cancelled and ALL GMOs will be moved to a different institution or destroyed.

**Final assignment of containment measures and activity class**

* **The following aspects of this project are assigned to Containment Level 1 and will be undertaken in room(s)** (Provide room numbers.)
* **The following aspects of this project are assigned to Containment Level 2 and will be undertaken in room(s)** (Provide room numbers.)
* **The following aspects of this project are assigned to Containment Level 3 and will be undertaken in room(s)** (Provide room numbers.)

## Final classification of the activity

**The activity class for this work is** (Following CU regulation the minimum activity class should be numerically equivalent to -at least- the maximum Containment Level deemed necessary by risk assessment)

**Class 1** [ ]

**Class 2** [ ]

**Class 3** [ ]

**Has the principal investigator notified this activity to the Director of the relevant institute and received approval to carry out the work?**

**Yes** [ ]

**No** [ ]

Name of the Institute Director:

**Name and email address of the Principal Investigator.**

All the communication regarding this GM activity will be via the PI named here.

**Name, email address, and level of competency of each worker involved in the activity (1 = fully competent, 2 = needs supervisor’s advice and approval before work, 3 = requires direct supervision)**

|  |  |  |
| --- | --- | --- |
| Name | Email address | Competency level |
|  |  |  |
|  |  |  |
|  |  |  |
|  |  |  |
|  |  |  |
|  |  |  |
|  |  |  |

Appendix

1 - An emergency plan is required under regulation 21 when -as a result of a reasonably foreseeable accident- the health or safety of persons outside the premises in which the contained use is undertaken is liable to be seriously affected; or there is a risk of serious damage to the environment from the contained use.