**RISK ASSESSMENT OF ACTIVITIES INVOLVING GENETICALLY MODIFIED MICROORGANISMS & EUKARYOTIC CELL CULTURE SYSTEMS**

and application for approval by RCSI-IBC

This risk assessment;

* is required for any use of Genetically Modified Organisms (Contained Use)
* must be undertaken by the Responsible Person (usually the Principal Investigator (PI) on a project) before work with or storage of GM organisms commences, irrespective of where they were actually made
* must determine a Containment Level for handling the GMM (and thereby assign an activity classification)
* must be reviewed and approved by the RCSI-IBC before work or storage commences
* must be made available for all present and future personnel involved in the GM work to read with records of this kept. Such personnel must also be registered as working with biological agents by the Health and Safety Office
* must be treated as a living document and be reviewed and updated by the PI as required (and the RCSI-IBC consulted if there is a significant change)

The questions on this form are designed to provide the basis for a risk assessment covering the main types of work involving genetically modified microorganisms (GMM) and eukaryotic cell culture systems at the Royal College of Surgeons in Ireland. Alternative forms exist for assessing work involving transgenic animals.

The amount of detail required will vary according to the nature of the hazards and degree of uncertainty in each project, therefore an informed and pragmatic approach should be taken. For commonly used host/vector systems or routine procedures, such as routine cloning in K-12 derivatives of *E. coli* or harmless inserts in replication-deficient adenovirus*,* less detail will usually be required. Where a potential for harm is identified, a more detailed consideration of the risks should be undertaken. Risk assessments, although a legal requirement, are a means to an end, not an end in themselves. They should be fit for purpose and acted upon if they are to help protect people and the environment.

**Please provide the following administrative information**

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| **School/Department/Unit:** |  |
| **Principal Investigator(s):** |  |
| **Project Title:** |  |
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| **Initial Personnel Involved:** | **Experience/training:** |
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| **Give details of arrangements in place for training of present and future personnel:** |
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| **Main facilities to be used for this work:** *(include Containment Level categorisation CL-1, CL-2, or CL-3; this should be consistent with the outcome of this risk assessment)* |
| **Laboratory Work:** |  | **Animal Work:** |  |

**PART 1. OVERVIEW AND PROJECT SUMMARY**

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| **a) Please provide a brief description of the work.** *Include the aims and objectives which will define the scope of the work covered by this risk assessment. Provide enough basic information such that a person with no experience of this area would understand the work proposed.*  |
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| **b) Give brief details of the components of the project for which this risk assessment is being produced:*****Please include details of all vectors and inserts here*** |
| **Host/Vector System:** *specify whether host is wild-type or disabled. State mobilisation status or attenuated nature of the vector, all control sequences (promoters etc) and any sequences conferring antibiotic resistance.* |
| **Insert:** *(what is the normal or expected biological action of the inserted DNA/RNA or transcribed gene product? If this is not known then indicate the types of processes these may be associated with):* |
| **Donor (source) of inserted nucleic acid**: |

**PART 2. RISK ASSESSMENT FOR HUMAN HEALTH AND SAFETY**

Assess the mechanisms by which the activities might pose a hazard to HUMAN health and safety

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| **a) What are the hazards associated with any recipient micro-organism(s)? If you are deliberately infecting animals with the GMM also consider hazards associated with the animal both inherent and after infection**  |
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| **b) What hazards are associated with any cell cultures being used?**  |
| Will you be using primary human or primate cells/ cell lines that are not fully characterised or authenticated; cells with endogenous biological agents; or cells that have been deliberately infected with pathogens | YES / NO / NOT APPLICABLE |
| Give details of any control measures required to protect human health from these unmodified cells. *These measures (e.g. a microbiological safety cabinet) are required to protect humans from the unmodified cell (line) under the Control of Substances Hazardous to Health (COSHH) Regulations*. *They* *do not affect the GM classification. The effect of the genetic modification on the cells and the GM classification will be assessed later on this form.* |
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| A microbiological safety cabinet will be used to protect human health from any endogenous contaminants or pathogens that the cells have been deliberately infected with ? (*This will not affect the GM classification*) | YES / NO  |

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| **c) What hazards does the inserted genetic material pose? Also have the pathogenic traits of the host been altered as a result of insertion?**  |
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| **d) What hazards does the final genetically modified micro-organism and/or eukaryotic cell culture pose? Also assess the likelihood of occurrence and severity of the consequences**  |
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| **ASSIGNMENT OF CONTAINMENT LEVEL TO PROTECT HUMAN HEALTH***Consider the containment level required to control the risks from the wild-type micro-organisms/cell culture system. Guide (Group 1 require min. CL1, Group 2 require min. CL2 etc) and make a judgement as to whether the genetic modification will result in GMMs that are more hazardous, less hazardous or approximately equivalent; then take into account the likelihood of harm occurring and adjust the containment level accordingly. Most cultured cells would be considered equivalent to hazard group 1 and unless the modification increases the risks posed GM activity class 1 should be assigned. However, if you will be working at containment level 2 or above solely because of the nature of the cells or contaminants please state that clearly here.* |
| **CONTAINMENT LEVEL :** | **1, 2 or 3** | **with Good Microbiological Practice and Good Occupational Safety and Hygiene** |
| **OCCUPATIONAL HEALTH CONSIDERATIONS****Specify any requirements or arrangements for immunisation, prophylaxsis, or health surveillance. Also give details of any special requirements for record keeping.**  |
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**PART 3. RISK ASSESSMENT FOR THE ENVIRONMENT**

Assess the mechanisms by which the GMM/GM cell culture might pose a hazard to the ENVIRONMENT (animals, fish, plants *etc*). Environment includes adjacent laboratories and other facilities as well as the wider environment. Please consider the following and provide some justification for your arguments.

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| **a) Consider hazards posed by the recipient and survivability** |
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| **b) Consider whether the stability or survivability of the recipient has been altered by the modification** |
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| **c) Has the infectivity, pathogenicity or host range of the recipient been altered?**  |
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| **d) Could the inserted gene pose a risk to other organisms?**  |
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| **e) Could the GMM or other organisms in the environment acquire harmful sequences and if so what would be the effects ?**  |
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| **f) How likely is it that the hazards will be manifested and how severe might the consequences be? Judge the level of risk to the environment with some justification (high/medium/low/effectively zero).**  |
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| **ASSIGNMENT OF CONTAINMENT LEVEL TO PROTECT THE ENVIRONMENT** *This is to prevent release or minimise the likelihood of the GMM being a threat to the environment. This is based upon your judgement as to the level of risk. If the level of risk is ‘low’ or ‘effectively zero’ then CL-1 may be appropriate, although if the consequences are severe you may wish to consider a higher containment level. Containment measures should be chosen to lower the risk to ‘low’ or ‘effectively zero’.*  |
| **CONTAINMENT LEVEL :** | **1, 2, or 3**  |  |

**PART 4. REVIEW WORK PROCEDURES AND CONTROL MEASURES**

*The requirements of the final containment level must be sufficient to control all the potential harmful properties of the GMM and offer sufficient protection for both human health and the environment. The minimum containment levels set so-far only broadly define the containment measures needed as a function of the properties of the GMM.*

*You should now take into account the nature of the work or any non-standard operations that might increase the risk of exposure or likelihood of release. It may be necessary to implement additional containment and control measures, which may have an impact on the final GM activity class and containment level.*

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| **a) Give details of any work procedures likely to generate aerosols and the precautions to be taken**  |
| **Class of microbiological safety cabinet: I II or III (*if applicable*)**If a microbiological safety cabinet will be used to protect human health solely from any endogenous cell culture contaminants or pathogens that a cell culture has been deliberately infected with and not from any genetic modification then this will not affect the GM classification and notification. |

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| **b) Identify and justify any use of sharps in the work, consider safer alternatives (*e.g.* plastic pasteur pipettes). Specify control measures if sharps are used.**  |
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| **c) Will you be using large (>10 litres) culture volumes? Give maximum culture volumes at any one time.** |
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| **d) Describe any other laboratory operations that may carry additional risks from the GMM and prescribe control measures.** |
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| **e) How will GMMs be inactivated in waste and other contaminated materials? Specify the dilutions of any disinfectants used. Have these methods been validated? How will waste be subsequently disposed of?**  |
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| **f) How and where will GMMs be stored safely? Will they be transported between buildings or elsewhere at any point and if so how will they be contained?** |
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| **g) Does your assessment rely heavily on biological containment or the fact that the GMM is disabled? If so, then monitoring may be required to ensure that this remains effective; how will this be achieved?**  |
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| **h) Emergency procedures – if an emergency plan is required please provide or attach details.**  |
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**PART 5. RECORD OF PERSONNEL INVOLVED**

*Risk assessments should be read by all personnel involved in the assessed work and each person should sign to acknowledge that they understand the assessment. Their qualifications and experiences that make them suitable for this work should also be recorded. All personnel working with biological hazards must be registered with the Health and Safety Office.*

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| **Name** | **Qualifications**  | **Date of completion of Health and Safety Course** | **Signature** |
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**\*\*INTERNAL USE ONLY\*\***

**REVIEW OF RISK ASSESSMENT**

GM (Biohazard) risk assessments should be reviewed annually or earlier if anything about the work has changed or if new information becomes available to ensure that assessments remain valid. Your Biological Safety Officer must also be consulted about any amendments to a project risk assessment as it may be necessary to seek enforcement authority approval.

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| Amendments:      |
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Appendix 1. Lentivirus vectors and GMO risk assessment – specific additional information to be covered as part of the assessment.

* **Lentiviral vectors derived from:**  HIV / SIV / FIV / EIAV /other
* **Type of vector :**1st Generation\* / 2nd Generation\* / 3rd Generation
* **Vector maps have been provided for the committee:** YES / NO\*
* **The *rev* gene has been deleted from the transfer vector and is expressed from a third packaging construct:** YES / NO
* **The viral vector is replication-defective:**  YES / NO\*
* **The SIN system has been incorporated into the vector :** YES / NO\*
* **A helper virus system is being used to deliver the vector or packaging constructs to cells :** YES / NO\*
* **Gene inserts do not consist of potentially harmful transgenes or the biological properties of the gene product are unlikely to cause harm :** YES / NO\*
* **Viral titres in use will be greater than 5x106/ml:** YES / NO
* **Needles will be used to introduce viral vectors into a recipient:** YES\* / NO
* **There will be high levels of expression of the inserted gene in a broad range of cell types:** YES / NO
* **Insertional mutagenesis or provirus transactivation would be of particular concern due to the nature of this work:** YES\* / NO
* **Non-coding sequences that present a particular hazard have been introduced:** YES\* / NO
* **The tissue tropism or host range of the viral vector has been altered or extended by:**
	+ **Pseudotyping:** YES / NO
	+ **Modification of the native *env* gene:** YES / NO\*
* **The potential route(s) for infection by the vector have been altered :** YES / NO
* **Changes to the vector have been made that are likely to affect immunogenicity, posing an additional hazard :** YES\* / NO
* **Changes to the vector have significantly reduced the likelihood of RCV generation :** YES / NO\*
* **The vector contains efficient termination and polyadenylation sequences :** YES / NO\*
* **Stable packaging cell lines are being used :** YES / NO\*
* **Packaging cell lines have been screened for endogenous provirus :** YES / NO\*
* **Hazardous RCV is likely to be generated :** YES\* (stocks must be tested) / NO