The following is a risk assessment form for work with genetically modified organisms (including virus vectors). It is intended to help identify appropriate safe working practices.

The risk assessment form is divided into two parts.

Part 1 is a streamlined form that should be filled in for all projects. If on completion of this part the work was clearly class 1, Part 1 should be all that is needed. For example, it would seem appropriate to allow the majority of work with disabled bacteria, yeast and cultured mammalian cells to proceed on the basis of a risk assessment by the principal investigator (PI) without further input or oversight. Experiments whose entire purpose is to express a protein with a long history of safe use such as LacZ, GUS or the various fluorescent proteins such as GFP, eGFP, YFP etc. would also fall into this category. On the other hand, if the risk assessment was not straightforward, it would be necessary to complete the more detailed format in Part 2.

In particular, if the intention of the experiment is to deliberately and stably express or inactivate a biologically active protein or regulatory molecule, then a careful consideration of whether there is potential risk to the researcher or the environment is required.

Part 2 of the format is designed to assist scientists in undertaking assessments where the issues involved are complex and require detailed consideration. The aim is to take the scientist proposing the work through the process in a logical and systematic way. It is hoped that the structure provided within the format itself will assist researchers in structuring their thought processes and that it will indicate to them those aspects of specific types of work which need to be given particular attention. In this case it may be helpful to ask a colleague to review the risk assessment.

As it stands the form is primarily aimed at risk assessments on modified micro-organisms where human health is the main concern. The form may need modification or expansion before it would be suitable for use in laboratories where environmental issues are the primary concern or where a large proportion of the work involves gene therapy strategies or the use of transgenic animals.

The form can be used to cover a whole project that may include more than one vector system.

RISK ASSESSMENT FOR GENETICALLY ORGANISMS

PART 1
The following sections should be completed by the Principal Investigator/Project Leader

1. Administrative details.			
Faculty		Principal Investigator	
Department		Other staff involved	
2. Title of project			

3 Location of activities *Give details of where different GM activities will take place for both bacterial and virus work e.g. include manipulation, growth, storage, disposal, centrifuges etc.*		
Building		
Activity	**Room**	**Approved Containment Level**

4. Scientific goals and major aims of the project *This information should provide a useful background and put the work in context. If presenting the scientific goals poses problems in relation to intellectual property rights or commercial sensitivity please discuss the issues with the Biological Safety Officer.*

5 Overview of the different types of Genetically Modified Micro-organism (GMM) that will be constructed

This overview should consist of 1 or 2 paragraphs, outlining the scope of the project and setting the boundaries of exactly what work will be done. This overview should be complemented in subsequent sections with lists of recipient strains, vectors and inserts that will be used in the project.

5.1 Details of recipient organism and cell lines

Give the name of the strain, the name of the wild-type organism from which it is derived and the extent to which it is disabled (if at all). Examples might be. E. coli K12 HB101 for bacterial work or Ad5 ΔE1/E3 for a virus vector or ΦNX cells for a packaging cell line. Where Part 2 of the form is to be filled in give sufficient detail to assess any likely hazard. For example details of integrated genes in retrovirus packaging lines.

5.2 Details of vector(s)

For the bacterial component of the work give details of plasmids whether they are non-mobilisable, mobilisation defective or self-mobilisable.

For viral vectors give details of the mechanisms of attenuation, disabling mutations and any built in safety features.

5.3 Function of inserted gene(s)

Genes should be identified in such a way that an outside reviewer will have a general idea of their function i.e. providing a three-letter names is not sufficient and the full name of the gene must be given. Where the function of a gene is unknown, it may help to provide details of any known homologies.

6 Additional work involving animals (including insects and invertebrates)	
Does the work involve **1)** The infection of animals with the GMM? **[*If yes complete a separate risk assessment that considers risks from the animals]*** ***2)*** The production of a genetically modified animal. ***[If yes complete complete a separate risk assessment that considers risks from the GM animals]***	

7 Are you confident that no harm would be caused to humans or the environment from the GMMs described even in the event of a total breach of containment*?* If **YES** you must justify your answer If the answer is `**No'** or you are **in any way unsure**, Part 2 of this form must be completed.

If the GMM meets this criteria and you are able to confidently assign the activity to Class 1 sign the form below and submit to the Departmental Safety Officer. Work should not be started until the BSO has received the form and agrees with the assessment.

Signature of Principal Investigator	Date

PART 2

To be used where a more detailed risk assessment is required. In cases where there are two or more hazardous GMMs with quite different properties two or more copies of PART 2 may need to be completed. However where properties are similar, the information may be suitably included in one.

1 IDENTIFY HAZARDS TO HUMAN HEALTH

1.1 What are the hazards associated with the recipient micro-organism

[bacterial host or viral vector]. Has the organism been assigned to a particular risk group (BMBL/ ACDP). Consider the pathogenicity of the agent i.e. the infectious dose, the natural route of infection, potential outcome of exposure/disease symptoms and stability. Also give details of any disabling mutations and whether there is any possibility of such mutation being complemented or reverting.*

1.2 Identify hazards arising directly from the product of the inserted gene/s

Consider if the gene encodes for a toxin, an oncogenic or allergenic protein, a modulator of growth or differentiation [e.g. cytokine or hormone] or any other protein that may result in a potentially harmful activity. Gene expression regulators and antibiotic resistance genes should also be detailed. The consideration of such cases should include an estimation of the level of expression required to achieve biological or pharmacological activity. In some circumstances normal proteins might be toxic e.g. if expressed in tissues that do not normally express the protein. If the function of the gene is unknown it would be useful to describe the function of any known homologues.

Is more than one gene being inserted in the same vector, if so is there likely to be synergistic effects?

1.3 Identify any hazards arising from alteration of the recipient micro-organisms existing traits (pathogenicity, host range, tissue tropism, mode of transmission, changing host immune response).

Consider the site of insertion of the foreign gene. For viral vectors is the site of insertion the site of primary disablement thus minimising the consequence of recombination with wild type virus? Also consider whether the inserted gene encodes a pathogenicity determinant, such as an adhesin, a penetration factor or a surface component providing resistance to host defence mechanisms. Another important consideration is whether the inserted gene encodes a surface component, envelope protein or capsid protein that might bind to a different receptor to that used by the recipient micro-organism. Consideration should also be given to whether the inserted DNA (or the plasmid sequence) encodes resistance to a drug or antibiotic that might be used for the treatment of a laboratory-acquired infection.

Please also note that deletion of a gene can in some circumstances increase pathogenicity. Are two vectors being used together, if so does this increase the risks?

Also give consideration to the possibility of any disabling mutations being complemented or reverting

2 Assignment of a provisional containment level that is adequate to protect against hazards to human health *This step will involve considering the containment level necessary to control the risk of the recipient microorganism (i.e. the Hazard Group of the recipient micro-organism see ACDP/BMBL*) and making a judgement about whether the modification will result in a GMM, which is more hazardous, less hazardous, or about the same. Sometimes it may help to compare the GMM with the relative hazard presented by other organisms that would fall within the same Hazard Group as the GMM.*

3 Consider the nature of the work to be under taken and review of control measures to be applied.	
Identify procedures likely to generate aerosol [e,g sonicaton. vigorous mixing/shaking, centrifugation.] Will work be carried out in a safety cabinet [MSC] or isolator What type of MSC will be used? Identify any other controls	
Does the procedure require the use of sharps/glass Pasteur pipettes? *Justify use*	
Animal Work Does the work involve a) the infection of animals with the GMM? or b) The production of a genetically modified animal. *If the answer to either of the above is yes complete the relevant additional Animal assessment form [Appendix A or B] and ensure this and the main assessment is forwarded to the manager of the animal facilities as appropriate.*	

4. Treatment of waste *How will waste materials be disposed of? Where procedures are detailed in a local code of practice or other document and are considered adequate it is appropriate to just make reference to the relevant document.*	
Solid waste	
Liquid waste	
Infected animal carcasses	

Validation of Inactivation of waste
Disinfectants
Please give details of the efficacy of the disinfectants used. Ideally these should have been validated under conditions of use (e.g. to show disinfectant is effective in presence of high levels of protein).

Validation systems for autoclaves

5. Emergency procedures

Is an Emergency Plan required in the event of breach of containment? *If yes provide detail.*

Are the standard procedures for spillage contained within local rules adequate? *If not provide details of specific measures. Details of SOPs for spillage of material both within and outside of the safety cabinet need not be given here simply refer to the local rules document.*

6. Occupational health issues
Where health effects have been identified in the advice of the Occupational Health Physician should be sought in relation to completion of this section

	Detail
Does the nature of this work preclude any workers who have a serious skin condition (e.g., eczema) or other health problems that might make them more susceptible to infection (e.g. some kind of immunological defect)?	
Give details of any pre-employment screening, vaccinations or ongoing health surveillance that is required. This may include the provision of medical information cards and exit medicals.	

7. Will the provisional level of containment assigned in Section 2 above be sufficient to protect both humans and the environment?
Additional measures may be needed to protect the environment, to provide the necessary degree of protection for human health or to provide additional safeguards for particular work procedures.
If **NO** – give details of additional measures:

8. Assignment of final containment level and class *Note: For aspects of work involving cell cultures the GM assessment should only focus on the hazard of the cells and their modification [e.g. expression of toxic genes] It is permissible to use a higher containment level than indicated by the class of GM for the cell line without this meaning a higher class of activity.*	
Aspects assigned to Class 1	
Aspects assigned to Class 2	
Aspects assigned to Class 3	

8. SIGNATURES	
The name and signature of the person making the assessment is required. Heads of department may also wish to sign but this is not necessary, however if the assessment is made by a student (undergraduate or postgraduate) or research assistant then their supervisor or PI should also sign.	
Name of Assessor: Signature:	Date:
Name of Reviewer: Signature:	Date:
Head of Department: Signature:	Date: