Policy Statement
The University of Dundee is committed to ensuring risks from biological materials are managed effectively by carrying out risk assessments that are comprehensive, proportionate to the level of harm, involve staff and are communicated clearly to staff and students so that they understand their responsibilities.

Arrangements
Reporting lines are detailed in the University Health & Safety policy. Specific responsibilities for managing biological risks are outlined below.

Head of Division (HoD) must have arrangements in place to ensure:

- risk assessments are carried out
- laboratory facilities are adequate
- local rules are drawn up, and implemented
- appropriate waste disposal procedures are used
- necessary licences are obtained
- emergency plans are drawn up if required
- microbiological safety cabinets and autoclaves are tested at least annually
- staff and students receive vaccination and health surveillance if required
- records of an individual’s work with Hazard Group 3 and 4 micro-organisms are kept
- appropriate training is in place
- accidents and spillages involving micro-organisms are investigated and reported to University Biological Safety Adviser (UBSA)
- accident report recommendations are implemented
- spillages of genetically modified micro-organisms (GMM) and escape of genetically modified organisms (GMO) are recorded, investigated and reported to UBSA
- biological safety inspections are carried out at least once a year
- inspection report recommendations are implemented
- notifications are made to the Health and Safety Executive (HSE) if required
- competent Biological Safety Advisers (BSA) are appointed
- these arrangements are reviewed at least annually
**Principal Investigator (PI)** or other delegated competent member of staff must

- carry out risk assessments by completing appropriate forms issued by Safety Services or equivalent forms
- inform staff and students of risks when working with biological agents and control measures to minimise risks
- formulate and implement local rules appropriate for the work being undertaken and facilities available
- ensure staff and students comply with local rules
- obtaining licence to work with animal and plant pathogens if required
- notify and obtain consent from HSE to work with genetically modified organisms if required
- keep records of an individual’s work with Hazard Group 3 and 4 micro-organisms
- draw up emergency plan if required, and instruct staff in contents
- report accidents and spillages of GMM and escape of GMO to BSA
- report accidents and spillages of pathogens to BSA
- train staff

**Staff and students** must:

- follow local rules as instructed
- dispose of waste as instructed
- report accidents and spillages of GMO and pathogens to PI and BSA
- report shortcomings in working procedures to PI and BSA

**Biological Safety Adviser (BSA)** will:

- advise on risk assessments
- advise on local rules
- advise on licences required
- advise on disinfection and waste disposal
- provide list of pathogens to UBSA annually
- ensure microbiological safety cabinets and autoclaves are tested when required
- monitor compliance with local rules on a regular basis, and reporting non-compliance to PI, and if necessary HoS and UBSA
- perform formal biological safety inspections at least once a year as part of an inspection team
investigate accidents, spillages of GMM and pathogens, and escape of GMO reported by staff and students, and notify HoD and UBSA of findings and recommendations

**University Biological Safety Adviser (UBSA) will:**

- draw up policies to ensure all university employees fulfil their statutory duties
- keep copies of genetic modification risk assessments
- ensure risk assessments are reviewed by Genetic Modification Safety Committee if required
- ensure work is notified to HSE if required
- report accidents to HSE if required
- report spillages of GMM and escape of GMO to HSE if required
- keep register of pathogens used in research
- give advice to BSA on any issue
- train BSA in risk assessment
- organise and take minute of Committee meetings

**Biological and Genetic Modification Safety Committees will:**

- comprise Convener, BSA’s and UBSA
- meet twice a year
- report to Health and Safety Sub-committee on risks posed to people and the environment by biological hazards created by the University
- give advice on risk assessments carried out under Genetically Modified Organisms (Contained Use) Regulations 2000
- review accident/incident reports concerning GMO and request a revised risk assessments if required
- review inspection reports.
- authorise work involving genetically modified organisms to proceed after consideration of:
  - the risk assessment
  - laboratory facilities
  - staff and student training and supervision
  - local rules
  - arrangements for testing control measures such as microbiological safety cabinets and autoclaves
  - statutory notification and consent requirements.
**Companies** working with genetically modified organisms within University premises must:

- receive authorisation for the work to commence from the City Campus Biological Safety and Genetic Modification Safety Committee or the Ninewells Genetic Modification and Biological Safety Committee
- submit a risk assessment to the Committee via the UBSA. The risk assessment must document the containment facilities, procedures, and competence of staff to control risks to human health and the environment. Authorisation will only be given if the committee consider risks to human health and the environment are controlled adequately
- cease work immediately if requested by the UBSA or other member of the City Campus Genetic Modification Safety Committee or Ninewells Genetic Modification and Biological Safety Committee.
- comply with Local Rules issued by the University.
- notify accidents involving genetically modified organisms to the UBSA
- notify escape of genetically modified organisms to the UBSA.
- appoint a competent BSA from senior management. The BSA will be responsible for ensuring compliance with Items 1-5 above, and will liaise with the UBSA.
Guidance Note on Management of Biological Safety

Competence, training and supervision

Staff and students working with biological agents must be competent to work safely. Previous work experience in another laboratory or holding a paper qualification does not mean a person is competent to work safely. Competence must be assessed for everyone working in the laboratory and if judged to be inadequate training and a high level of supervision must be given. Training programmes should be tailored for each individual taking into account their level of knowledge, experience and the type of work undertaken. Training should include the following:

- information regarding hazards and safeguards to prevent exposure/infection
- knowledge and understanding of local rules
- knowledge and understanding of disinfection policy
- knowledge and understanding of waste disposal procedures
- knowledge and understanding of emergency spillage procedures
- technical competence for all aspects of the work eg use of microbiological safety cabinet, centrifuges, automatic pipette aids
- securing and sealing microbiological safety cabinet following spill within cabinet, and fumigation procedures
- safe evacuation and sealing of Containment Level 3 laboratory following spill outside cabinet, and fumigation procedures
- safe transport and storage of micro-organisms and genetically modified organisms
- accident/incident reporting including personal injury, near misses, spillages and breakages, escape of GMO, non-compliance with local rules eg wrongly packaged or labelled containers

Written records of training should be kept.

All members of staff and students must be continually supervised until they can demonstrate:

- a satisfactory level of technical competence
- a full understanding of local rules
- correct response to spillage, accident, or another emergency

Inspection

At least once a year as part of the formal inspection of laboratories the inspection team must consider biological safety. The inspection team should include the BSA, School Safety
Representative and Laboratory Manager. The UBSA will be invited to participate in these inspections, and typically will attend six such inspections throughout the year. A typical inspection checklist for a laboratory where biological research is carried out is given in Appendix 1. The inspection team should give a short verbal report to the Head of Division on the inspection day, and also prepare a formal report with a time-scale for remedial actions. This report should be kept in Divisional Safety Files and discussed at the Divisional Safety Meeting.

**Handbooks**
The following Handbooks should be consulted as appropriate before completing a risk assessment:

- Working Safely with Micro-organisms
- Working Safely with Human Blood, Tissues and other Specimens in a Research Laboratory
- Working safely with Genetically Modified Organisms in a Research Laboratory
- Safe Disposal of Biological/Clinical Waste
- Safe use of a Microbiological Safety Cabinet

**Risk Assessment forms**
Forms listed below are available in Appendices:

Appendix 2: USS/Fast Track Genetically Modified Micro-organisms
Appendix 3: USS/Genetically Modified Micro-organisms
Appendix 4: USS/ Gene Therapy
Appendix 5: USS/Genetically Modified Animals
Appendix 6: USS/Micro-organisms
Appendix 7: USS/Human Samples
Appendix 1 Biological Research Laboratory Inspection Report

Location: 

Date: 

Installed by:

Part A. Documentation

<table>
<thead>
<tr>
<th>Item</th>
<th>Satisfactory</th>
<th>Comment</th>
<th>Recommendation</th>
<th>Responsibility</th>
<th>Time-scale</th>
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<tr>
<td>Previous inspection report</td>
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<td>Current risk assessment</td>
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<td>Local rules</td>
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<td>Records of staff training</td>
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<td>Arrangements for out of hours working</td>
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<td>Arrangements for visitors and contractors</td>
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<td>Arrangements for lab cleaning</td>
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<tr>
<td>Waste disposal procedures</td>
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<td>Spillage procedures</td>
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<td>Accident reporting procedure</td>
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<tr>
<td>Microbiological Safety Cabinets tested</td>
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</tbody>
</table>
### Microbiological Safety Cabinet
- fumigation procedure

### Laboratory fumigation procedure

### Autoclave tested

### Autoclave print outs

### Accident plan, including fire brigade

### Individual’s work records

## Part B. Facilities

<table>
<thead>
<tr>
<th>Item</th>
<th>Satisfactory</th>
<th>Comments</th>
<th>Recommendation</th>
<th>Responsibility</th>
<th>Time-scale</th>
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<tr>
<td>Containment Level sign posted at entrance</td>
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<td>Restricted Access</td>
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<td>Storage for dedicated lab coats</td>
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<td>Lab coats clean, washing procedure</td>
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<td>Hand wash, soap and towels available</td>
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<td>Fully stocked first aid box</td>
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<td>Eye wash facility</td>
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<td>Clean and tidy, especially sink</td>
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<td>area</td>
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<td>Disposal of sharps</td>
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<td>Waste bins emptied</td>
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<td>Used glassware/pipettes</td>
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<td>immersed in disinfectant</td>
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<td>Disinfectant readily available</td>
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<td>Sufficient space</td>
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<td>Bench surfaces intact</td>
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<td>Floor clear of obstruction</td>
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<td>Safe storage of consumables</td>
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<td>and chemicals</td>
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<td>Secure storage of infectious</td>
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<td>materials, inventory available</td>
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<td>Liquid nitrogen storage</td>
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<td>Aspirator for liquid waste</td>
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<td>Other, please specify</td>
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</table>
signatures of inspection team

signature: signature:

name: name:

position: position:

signature: signature:

name: name:

position: position:
Appendix 2

Form USS Fast Track Genetically Modified Micro-organisms

This Fast Track Risk Assessment is intended for research involving the genetic modification of a micro-organism, or the use (eg culturing, storing, transportation or disposal) of a genetically modified micro-organism generated elsewhere eg some cell lines.

Genetic modification means ‘the altering of the genetic material in that organism in a way that does not occur naturally by mating or natural recombination or both.’

Micro-organism covers all micro-organisms including bacteria, fungi, protozoa, viruses and viroids, prions, cell and tissue cultures from humans, animals and plants, and full length copies of viral genomes that are known to be infectious even when they are not encapsulated or enveloped.

This fast track form is only applicable for very low risk research eg routine cloning/expression using non-pathogenic strains of *E.coli* or other well characterised non-pathogenic systems (eg *S. cerevisiae*), and transfection of well characterised cell lines.

It is not applicable for any work with human, animal or plant viruses.
It is not applicable for any work with viral vectors.
It is not applicable for work with any micro-organism known to be pathogenic or to have the potential to colonise humans, animals or plants.
If your work involves any of these elements complete the more detailed form ‘USS Genetically Modified Micro-organisms’ available on Safety Services web page.

Note: use of primary cells or work with finite or continuous cell lines that are likely to contain (or may potentially contain) human pathogens requires Form USS Human Samples to be completed.

Contact your Biological Safety Adviser for advice on completing this form if it is not clear what is required.
Part 1. Administrative Details

1. Principal Investigator

2. Division/Centre

3. Laboratory number

4. Short Descriptive Title of Research

Part 2: Host/Recipient

List the types of host/recipient used in the project eg *E.coli K12 line derivatives* (e.g. DH5a, DH10b, TOP10) or *B* strain derivatives (e.g. BL21), well characterised or authenticated finite or continuous cell lines, *S.cerevisiae*.

Does each and every host/recipient have a history of safe use? Can it be classified as disabled or non-colonising? If disabled is it unlikely to revert to wild-type?

**YES or NO**

Part 3: Vector

List the vectors or vector series used in the research or for novel or less well characterised vectors, the vector they were derived from eg derivatives of pUC. Consult the suppliers technical data sheets if in doubt, or consult your Biological Safety Adviser.

Is each and every vector used non-mobilisable (e.g. pUC, pGEM, pCAT, pBluescript II, and *Bacillus* vector pUB110 and their derivatives) or mobilisation defective (e.g. vectors pBR322, pGEX and their derivatives) OR a known derivative of a non-mobilisable or mobilisation
defective vector OR classifiable as a non-mobilisable or mobilisation defective vector. If in doubt check its bom/nic/mob/tra status.

YES or NO

Part 4: Inserted genetic material
Explain the biological functions of the inserts (eg cell surface receptors, protein kinases, transcription factors).

Part 5: Source of inserted genetic material
Describe the source of the genetic material (eg human cDNA library)

Can the source of the genetic material be discounted on the basis that it does not present an additional hazard (eg has the inserted DNA been fully characterised and have all coding sequences been identified?)

YES or NO

Part 6: Resulting Genetically Modified Micro-organism
Based upon the responses in Parts 2 to 5 can the resulting genetically modified micro-organism be considered no more harmful than host/recipient

YES or NO

Part 7: Procedures
Describe any non-standard laboratory techniques that could increase risk (eg large scale culture, significant production of aerosols)
Part 8: Good microbiological practice
Are the working procedures described in the Local Safety Manual sufficient for the level of risk arising from the genetically modified micro-organisms?

Have all staff/students been instructed in the Local Safety Manual rules and regulations?

YES or NO

Part 9: Classification
If you have answered YES to Parts 2, 6 & 8 then you can classify this project as **CLASS 1** and take no further action.

If you have answered NO to some Parts or are unsure then you should complete Form **USS Genetically Modified Micro-organisms**.

Part 10: Informing staff and students
This assessment should be circulated and discussed with all staff/students involved in the research, and this discussion should be recorded.

Please send your completed risk assessment to University Biological Safety Adviser. (i.g.scragg@dundee.ac.uk).

Code Number (to be entered by Safety Services upon receipt of completed form)
Form USS-Genetically Modified Micro-organisms

This form should be completed for research when the fast track risk assessment is not applicable (e.g., work with pathogens, viral vectors or systems expressing a biologically active harmful product such as a toxin).

This form should also be completed for work with:
- animals infected with or exposed to genetically modified micro-organisms;
- large scale work with genetically modified micro-organisms;
- plants infected with or grown alongside genetically modified micro-organisms

Micro-organism covers all micro-organisms including bacteria, fungi, protozoa, viruses and viroids, prions, cell and tissue cultures from humans, animals and plants, and full length copies of viral genomes that are known to be infectious even when they are not encapsulated or enveloped.

Further information about risk assessments can be found at http://www.hse.gov.uk/biosafety/gmo/acgm/acgmcomp/part2.pdf

Information about working safely with genetically modified micro-organisms can be found in Safe Working with Genetically Modified Micro-organisms Handbook.

Contact your Biological Safety Adviser for advice on completing this form if it is not clear what is required.

Part 1. Administrative Details

1. Principal Investigator

2. Division/Centre
Part 3: Hazards to human health

1. Associated with recipient micro-organism
   - List hosts and/or viral vectors.
   - Use a micro-organism that does not infect humans if possible.
   - For human pathogens give Hazard Group assigned by the Advisory Committee on Dangerous Pathogens (ACDP). A current list of pathogens and their Hazard Groups can be found at www.hse.gov.uk/pubns/misc208.pdf. Refer to Safe Working with Micro-organisms Handbook for further information on definition of Hazard Groups.
   - Use a disabled or attenuated micro-organism with reduced pathogenicity if available. Is reversion to wild type likely i.e. is there a single disabling mutation or many; is it a deletion mutant, point mutation or conditional lethal mutant.
   - Is the gene material inserted into site of disabling mutation; if not, why not.
   - For genetically modified viruses that could infect humans it is essential to consider the probability of rare events occurring that overcome disabling mutations, e.g. recombination and reversion frequencies, level of genetic variability.
   - Consider all properties of the micro-organism which may cause harm such as infection, production of toxins, cytokines, allergens, or hormones.

2. Arising directly from the inserted genetic material (toxin, oncogene)
   - List the functions of the genetic material—it is wild type or mutated
   - State if it is known to be harmful e.g. toxin, oncogenic protein, allergen or if it could be harmful e.g. growth factor, modulator of growth or differentiation, kinase, transcription factor. Note that normal genes may be harmful if over-expressed or expressed in tissues that do not normally express the genetic material.
3. Arising indirectly from the inserted genetic material (eg alteration of pathogenicity, host range, tissue tropism, mode of transmission or host range)
   - Could the genetic material alter the properties of the micro-organism (eg enable binding to different receptors, entry or adhesion to a cell)
   - Could the genetic material interfere with host immunity
   - Could the genetic material cause resistance to drugs or antibiotics used to treat an infection

4. Arising from transfer of genetic material to a related micro-organism
   - Is widespread dissemination of the inserted genetic material by gene transfer or recombination of the genetically modified micro-organism with a wild type micro-organism of concern
   - What is the likelihood of transfer (ie is it plasmid or chromosome borne, if plasmid borne consider mobilisation status of plasmid)
   - What is the likelihood of the genetically modified micro-organism surviving in the environment if containment is breached
   - What is the likelihood of selection pressure on the gene leading to persistence and proliferation
   - Is the gene a novel construct or already present in the environment (this includes novel promoters)

Part 4: Assign a provisional Containment Level
   - Identify Containment Level that is appropriate for Hazard Group of recipient (ie level 1 for Hazard Group 1 micro-organisms; level 2 for Group 2, level 3 for Group 3);
   - Assess whether the genetic modification has decreased, increased or had no impact upon hazardous features of recipient and adjust Containment Level accordingly (down, up or no change)
   - If the recipient micro-organism is a pathogen of plants or animals but not humans then it presents no hazard to human health and Containment Level 1 is sufficient to control risks to humans. However, risk to the environment will be considered in a later section (Part 5) and will require a higher containment level.

Select from 1/2/3
Part 5: Hazards to the environment

1. Associated with recipient micro-organism
   - Can it infect members of animal or plant kingdom
   - Is it an animal, fish, bee or plant pathogen—is a license required (contact BSA for advice)
   - Is it a disabled or attenuated pathogen—could the disabling mutation be overcome by complementation or recombination

2. Arising from genetic material
   - Can the genetic material cause harm to the environment either directly or indirectly by alteration of recipient micro-organism or transfer to a related micro-organism

Part 6: Nature of work

1. Brief description of nature of work (include maximum culture volumes)
   List any non-standard laboratory procedures such as inoculation of animals and plants; use of equipment likely to produce aerosols; large scale procedures or the use of high titre virus.

2. Is a microbiological safety cabinet or isolator required to protect against aerosol transmission?  YES / NO

3. Waste Disposal
   - Give full details of how waste containing genetically modified micro-organism is inactivated prior to disposal. The following details are required:
     - amounts and types of waste
     - methods of inactivation;
     - expected degree of kill;
     - confirmation that methods are effective under conditions of use;
     - what happens to the treated waste
     - monitoring arrangements

   - The simplest means of waste disposal is to heat treat in an autoclave with online temperature monitoring or other indicators proving that full steam penetration to the centre of the load occurred. Validation of the autoclave using independent thermocouples must be performed at least annually. If this method is chosen the following statements can be made regarding waste disposal:
• autoclaving, effectively 100% kill, verified using (specify on line temperature recording or indicator used);
• autoclave validated (specify frequency, at least annually) using independent thermocouples.

• If chemical disinfection is used it must be stated that the chemical agent is fully active against the micro-organism being used, and that the conditions of use will not reduce the activity of the chemical agent to an unacceptable level. These statements must be supported: either by data provided by the manufacturer or by undertaking experiments to measure percentage kill or log reduction in viability under the conditions of use.

4. Are sharps required?
• Eg glass Pasteur pipettes, hypodermic needles, scalpels, glass containers

YES / NO-if yes justify use

5. If the work involves experimental infection of animals is it known if the animal will shed the genetically modified micro-organism?
• Consider all possible routes eg expired breath, saliva, urine, faeces

If YES give details and measures to prevent exposure

6. Where will the genetically modified micro-organisms be stored?

7. How will the genetically modified micro-organisms be transported within/between buildings to minimise risk of spillage/escape?

8. Health Surveillance/Vaccination required

YES/NO

It is very unlikely that health surveillance/vaccination will be required since working procedures should prevent infection. It may be appropriate when:
i. there is a reasonable likelihood that an employee may become infected by a pathogen under the conditions of work (eg injection of animals);
ii. there is a valid technique to detect infection, or the onset of disease or there is an effective vaccine available;
iii. you have concerns about the health or immune status of your staff/students;
iv. staff/students have concerns about their health or immune status

Contact University Occupational Health Service (ext 85401) for advice.

9. Emergency Plan

- An emergency plan must be prepared when as a result of a reasonably foreseeable accident the health and safety of people outside the premises is liable to be affected seriously or there is a risk of serious damage to the environment. There are many reasonably foreseeable accidents that could lead to a loss of containment (eg fire) so the key issues to consider are:
  - the potential of the genetically modified micro-organism to cause harm to humans, animals or plants;
  - the possible level of exposure to the genetically modified micro-organism, ie scale of the activity is important;
  - the likelihood of spread to humans, or to the environment

For Class 1 activities an emergency plan will not be required since these genetically modified micro-organism are non-hazardous.

For small scale Class 2 activities an emergency plan is unlikely to be required since the risk of serious harm to people or the environment is low given the number of genetically modified micro-organism involved.

For small scale Class 3 activities it is important to consider whether the genetically modified micro-organism is likely to survive or disperse into the environment.

Required/Not required, if not required for Class 2 or 3 activities give reason

10. Monitoring

- Arrangements for testing the efficacy of measures to control risks must be stated. Typical control measures that require testing are:
  - microbiological safety cabinets. The operator protection afforded by a cabinet should be tested (KI discus test) at least annually at Containment Level 2, and six monthly at Level 3.
  - ventilation system including HEPA filters. This should be tested at least annually to ensure Laboratory is at negative pressure.
• The frequency of safety inspections to ensure control measures are adopted such as wearing of laboratory coats and gloves, no eating and drinking in laboratory and correct waste disposal method is used should be stated. Records of safety inspections should be kept, and be available for inspection.

Part 7: Final classification of project

• Is your provisional Containment Level detailed in Part 4 sufficient for any additional risks detailed in Parts 5 and 6?
• Contact your Biological Safety Adviser for requirements of Containment Level 2 and 3, and HSE notification and consent fees
• Classify your project based upon Containment Level required ie project carried out at Containment Level 2 is Class 2: one at Level 3 is Class 3

Select from Class1/2/3.

Part 8: Additional information and comments

• Eg work with high titre virus will be carried out only by experienced staff, or in a higher standard laboratory managed by a colleague
• Eg Low risk aspects of the project will start in existing laboratory and be transferred to a new facility when it is completed
• Eg Virus infected cells will be obtained from a colleague

Part 9: Informing, instructing and training staff and students

All staff and students should sign the risk assessment to confirm that they have read the risk assessment, and any questions they had about it have been answered.

I have read this risk assessment, and any questions I had about it have been answered.
I have been instructed in the Safety Manual and additional measures required for this work.

Names of staff/students carrying out the procedure, signature, and date
Authorisation
Assessed by person responsible for work

Signature:

Name: Date:

Reviewed by Biological Safety Adviser

Signature:

Name: Date:

Permission granted by Head of Department/School

Signature:

Name: Date:

Please send your completed risk assessment to University Biological Safety Adviser (i.q.scragg@dundee.ac.uk) who will arrange for it to be reviewed by the appropriate Genetic Modification Safety Committee.

Please contact University Biological Safety Adviser if you have not received a response within 5 working days.

Code Number (to be entered by Safety Services upon receipt of completed form)

Classification of Project and comments agreed by Genetic Modification Safety Committee (to be entered by Safety Services)

Select from Class 1/2/3
Appendix 4

Form USS Gene Therapy Trials involving genetically modified micro-organisms

This form should be used when patients are treated with a genetically modified micro-organism. It deals with the risks to staff, students and other people who could be exposed to the genetically modified micro-organism, and risks to the environment. It does not consider risks to the patient-these are considered by the Gene Therapy Advisory Committee (GTAC).


Information about working safely with genetically modified micro-organisms can be found in Safe Working with Genetically Modified Micro-organisms Handbook.

Contact your Biological Safety Adviser for advice on completing this form if it is not clear what is required.

Part 1. Administrative Details

1. Code Number (to be supplied by Safety Services upon receipt of completed form)

2. Final Classification of Project (to be agreed by Ninewells Genetic Modification Safety Committee)

   Select from 1 or 2

3. Division/Centre

4. Principal Investigator
5. Comments by Genetic Modification Safety Committee


Signature:

Name: Date:

6. Informing Ninewells Genetic Modification Safety Committee of progress
Contact University Biological Safety Adviser (Ext 84103, i.g.scragg@dundee.ac.uk) when patients are enrolled, and of any adverse events, or accidental release of genetically modified micro-organism.
Part 2. Trial details

1. Name of Trial

2. Brief Description of Trial

3. Status of Gene Therapy Advisory Committee (GTAC) application

Part 3: Risk assessment for human health

1. Hazards associated with the recipient micro-organism being modified
   - Give details of micro-organism being modified including serotype and genotype.
   - Is the micro-organism wild type or disabled. If disabled explain how and effect upon micro-organism. Note: most disabled micro-organism are unlikely to cause disease and can be categorised Hazard Group 1 eg replication defective E1 deleted Adenovirus, retroviral vectors based on murine, feline and avian groups of retroviruses and MVA and NYVAC strains of vaccinia virus.
   - If wild type and a known pathogen give Hazard Group assigned by the Advisory Committee on Dangerous Pathogens (ACDP). A current list of pathogens and their Hazard Groups can be found at http://www.hse.gov.uk/pubns/misc208.pdf.
   - List properties of micro-organism eg route of infection, infective dose, resistance to heat, dessication, and disinfectants, and prevalence in population.
   - List known effects of micro-organism eg localised inflammation and other immune responses.

2. Hazards arising directly from inserted gene product
   - Outline expected physiological effects of gene product.
   - Outline unexpected physiological effects that could arise eg from high level of expression in cells that do not usually express the gene product.

3. Hazards arising indirectly from inserted genetic material
   - Could the gene product affect existing pathogenic traits of the recipient micro-organism eg infectivity or pathogenicity, overcome a disabling mutation, tissue tropism or host range, susceptibility to human defence mechanisms, susceptibility to prophylaxis or therapy.
4. Hazards arising from recombination/complementation events
   - Is the gene product inserted into site of disabling mutation, if not why not.
   - Describe steps taken to minimise possibility of a disabling mutation being overcome either in manufacture or in a person.
   - Consider the likelihood and consequences of the recipient viral vector or the gene product becoming integrated into a person’s genome.
   - Consider the likelihood and consequences of gene product being transferred to related micro-organisms.

5. Hazards to environment
   - Are there hazards to the environment that have not been considered above eg is genetically modified micro-organism an animal pathogen?

6. Additional hazards to pregnant women, or people with health concerns
   - Consider individuals who may be more susceptible to infection or may have a pre-existing condition eg eczema

7. Assign Class/Containment Level
   - Assign a Containment Level using the following scheme:
     - identify Containment Level that is appropriate for Hazard Group of recipient (ie level 1 for Hazard Group 1 micro-organisms; level 2 for Group 2, level 3 for Group 3);
     - estimate whether inserted gene product has decreased, increased or had no impact upon hazardous features of recipient and adjust Containment Level accordingly (down, up or no change).

   Select from 1 or 2

8. Shedding into environment
   - Consider likelihood of shedding either at site of injection, or in urine, faeces, expired air or other body secretions. Where possible give details of similar studies where shedding has been investigated, and outline steps being taken to monitor shedding in this trial.
9. Facilities and procedures

- List all the rooms where genetically modified micro-organism is stored, handled, administered and where samples that contain or could contain genetically modified virus are processed.
- Detail steps taken to ensure genetically modified micro-organisms are kept secure at all times especially if a shared storage facility is used.

10. Waste Disposal

- Give full details of how all wastes (eg vials, used syringes, dressings) containing genetically modified micro-organisms are inactivated prior to disposal in hospital waste streams. The following details are required:
  (i) amount and type of waste;
  (ii) method of inactivation;
  (iii) expected degree of kill;
  (iv) confirmation that method is effective under conditions of use;
  (v) ultimate form and fate;
  (vi) monitoring arrangements

- The simplest means of waste disposal is to heat treat in an autoclave with on line temperature monitoring or other indicators proving that full steam penetration to the centre of the load occurred. Validation of the autoclave using independent thermocouples must be performed at least annually. If this method is chosen the following statements can be made regarding waste disposal:
  (i) autoclaving, effectively 100% kill, verified using (specify on line temperature recording or indicator used);
  (ii) autoclave validated (specify frequency, at least annually) using independent thermocouples.

- If chemical disinfection eg Virkon is used it must be stated that the chemical agent is fully active against the genetically modified micro-organisms being used, and that the conditions of use will not reduce the activity of the chemical agent to an unacceptable level. These statements must be supported: either by data provided by the manufacturer or by undertaking experiments to measure percentage kill or log reduction in viability under the conditions of use.
11. Transport within building
Detail how genetically modified micro-organisms will be transported within building and the steps taken to ensure they are kept secure at all times eg within two screw capped containers, and for liquids surrounded by absorbent

12. Spillage procedure
   • Detail actions to be taken in the event of a spillage of genetically modified micro-organism

13. Will staff receive any vaccinations or health surveillance
   • It is extremely unlikely that staff will require health surveillance for genetically modified micro-organisms authorised for treating patients.

Part 4: Staff instruction, information and training
All staff (eg Pharmacy staff, Nursing staff, Physicians, Laboratory staff) directly involved with the trial should sign the risk assessment after they have read it and been given the opportunity to ask questions.

Names of people carrying out the procedure, their position (eg Post-Doc, Post-Grad student) signature, and date

Please send your completed risk assessment to University Biological Safety Adviser (i.g.scragg@dundee.ac.uk) who will arrange for it to be reviewed by the appropriate Genetic Modification Safety Committee.

Please contact University Biological Safety Adviser if you have not received a response within 5 working days.
Appendix 5

Form USS Genetically Modified Animals

This form should be completed for work with genetically modified animals. In this context work means the generation, breeding or use of a genetically modified animal, including the use of a genetically modified animal provided by someone else (e.g., commercial supplier, collaborator).

If your work involves inoculating or treating animals (e.g., grafting) with a genetically modified micro-organism (e.g., cell lines, viral vectors) then you must also complete Form USS Fast Track Genetically Modified Micro-organism or Form USS Genetically Modified Micro-organism as appropriate.

If you are in any doubt about which form to complete or the information required then please contact your Divisional Biological Safety Adviser, University Biological Safety Adviser or Biological Services.

Please note that the Home Office and the Health & Safety Executive (HSE) use different definitions. For the purposes of this risk assessment, the HSE definitions are the ones to apply. Thus “animal” means any member of the animal kingdom, not the restricted group of species considered by the Home Office.

A “genetically modified animal” means any individual animal in which specific genetic material has been inserted, or that has inherited this material.

A genetically modified animal is not:

- A dead animal or biopsy material;
- An animal derived from selective breeding of a spontaneous or induced mutation;
- An animal bearing a graft of genetically modified material where the genetic modification is no longer ‘mobile’;
- An animal deliberately infected with a genetically modified micro-organism, unless the germ line is involved and the genetic modification could be passed to future generations by breeding.
Further information about risk assessments can be found at http://www.hse.gov.uk/biosafety/gmo/acgm/acgmcomp/part5.pdf

Information about working safely with genetically modified micro-organisms can be found in Safe Working with Genetically Modified Organisms Handbook.

1) Project leader:

2) Home Office project licence number(s) (where applicable):

3) Resource unit(s) or laboratories where animals are kept:

4) Animal species used:

5) Strain name and nature of genetic modification (please list here or attach the relevant technical appendix from the project licence, if applicable)

6) Please consider the following statements of minimal hazard:
   a. The genetically modified animals are not a greater hazard to human health than their wild-type counterparts (an example of where this would NOT be true is if the genetic modification resulted in the animal species becoming a reservoir for a human pathogen, increased allergenicity, production of toxins or other biologically active agents, or behavioural alterations such as aggressiveness etc.)
   b. The genetic modification will not confer any selective advantage if the animals should escape to the wild (an example of where this would NOT be true is if the genetic modification rendered the animals more resistant to commonly-used pesticides)

7) Do these statements accurately reflect the hazards associated with the strains you have listed? YES NO
If not, please outline your assessment of the hazards on a separate sheet and attach it to this document.

8) Please consider the following statements of risk minimisation and control:
a. Animals will be housed and bred in a resource unit that is secured against non-authorised access;
b. The room door will be closed when animals are handled, so as to prevent escape;
c. There are either no floor drains in the animal room or the drains have tight-fitting covers and/or deep traps;
d. Animals cannot penetrate the perimeter security of the unit; all external doors and fire-escapes are close-fitting, with no gaps for a mouse to escape through;
e. Animal numbers are checked at least once a day and husbandry is by trained staff;
f. Laboratory strains of animals are unlikely to have a reproductive or survival advantage in the wild;
g. Soiled bedding will be disposed of as clinical waste;
h. Animal carcasses will be stored frozen until being uplifted by a waste contractor for incineration.

9) Are these measures sufficient to result in effectively zero risks to human health and the environment?  YES  NO

If not, please describe the additional measures that will be necessary to control the risks on a separate sheet and attach it to this document.

10) I confirm that I have read the statements listed above and they either (a) fully encompass the hazards and risks associated with working with the listed strains of genetically modified animals, or (b) I have attached additional information on the hazards and risks, to be considered by the appropriate Genetic Modification and Biological Safety Committee.

11) I confirm that the following members of my research group will be involved in the work and have been given copies of this risk assessment and have had the opportunity to ask questions.
12) I confirm that a copy of this risk assessment has been given to the manager of the Medical School Resource Unit.

(Signed)

Date

Please send a copy of the Form to the University Biological Safety Adviser (i.g.scragg@dundee.ac.uk) who will arrange for it to be reviewed by the appropriate Genetic Modification Safety Committee.

Please contact University Biological Safety Adviser if you have not received a response within 5 working days.
Appendix 6

Form USS Wild-Type Micro-Organisms

This form should be completed for research involving deliberate culture, propagation or concentration of micro-organisms that are not genetically modified.

Micro-organism means bacteria, viruses including viral genomes, TSE’s, mycoplasmas, fungi, parasites, cell cultures and human endoparasites, that may cause any infection, allergy, toxicity or otherwise create a hazard to human health and/or the environment (e.g., animal and plant pathogens).

Form USS Fast Track Genetically Modified Micro-organisms should be completed for work with very low risk genetically modified micro-organisms or Form USS Genetically Modified Micro-organisms for more hazardous ones. If you have completed one of these forms then you do not need to complete this form for work with the wild type micro-organism.

Contact your Biological Safety Adviser for advice on completing this form if it is not clear what is required.

(a) Part 1: Administrative Details

1. Principal Investigator

2. Division or Centre

3. Laboratory number

4. Short descriptive title of the research
Part 2: Hazard identification

1. Full name of micro-organism including species, subspecies, strain

2. Form in which present (eg spores, culture, diagnostic specimen)

3. Does the micro-organism cause disease or harm to farm livestock (animals and birds), fish, bees or plants? YES/NO

4. If yes, is a licence required, and has one been obtained YES/NO

Contact your Biological Safety Adviser if unsure

5. Is the micro-organism listed in the Approved List of Biological Agents YES/NO

Hazard Groups for micro-organisms are found in the Approved List of Biological Agents published by the Advisory Committee on Dangerous Pathogens. A current list can be found at http://www.hse.gov.uk/pubns/misc208.pdf.

If a micro-organism is not listed it cannot be assumed to be in Hazard Group 1. In these situations the pathogenicity must be assessed based on all the available information, and a provisional Hazard Group assigned. Contact your Biological Safety Adviser for advice in these situations.

6. If yes-what is the Hazard Group 1/2/3/4

7. If no-assign it to a Hazard Group 1/2/3/4

8. If in Group 2 or above, specify consequences of infection (type of illness and severity)
Information about human pathogens can be found at http://www.phac-aspc.gc.ca/msds-ftss/index.html

9. Route of infection and infectious dose

10. Describe nature of work including information about titres and volumes

11. Are there any other hazards of the organisms or its products  
   YES/NO
   If yes, identify type ie toxic/allergenic/oncogenic/carcinogenic/other (specify)

Part 4: Control measures
1. Can a less hazardous (eg disabled/attenuated strain) organism be used  
   YES/NO

2. If yes, why is it not being used?
   Click to insert text

3. Are working procedures described in Safety Manual sufficient for level of risk?  
   YES/NO

4. If no- what additional measures are required?
   Eye or face protection  
   YES/NO

   Disposable gloves  
   YES/NO

   Class 1 Microbiological Safety Cabinet  
   YES/NO

   Class 2 Microbiological Safety Cabinet  
   YES/NO
Work at Containment Level 3

Other (specify)

5. Disinfection Procedures

6. Emergency Procedures

for Hazard Group 3 pathogens describe emergency procedures eg fire or flood (eg who would liaise with emergency services)

7. Waste Disposal Procedures

Part 5: Additional requirements when working with human pathogens

1. Records of exposure kept

Records must be kept when working with Hazard Group 3 and 4 micro-organisms. The records must include the following:

   i. names of employees and when they began and finished the work;
   ii. name of the micro-organism;
   iii. details of work;
   iv. details of accidents and incidents.

2. HSE notified

Research involving B. pertussis, C. diphtheria, N. meningitidis and Hazard Group 3 or 4 micro-organisms have to be notified to the HSE at least 30 days before the micro-organism is obtained. Contact the University Biological Safety Adviser for further details.

3. Health Surveillance/Vaccination required
It is very unlikely that health surveillance/vaccination will be required since working procedures should prevent infection. It may be appropriate when:
i. there is a reasonable likelihood that an employee may become infected by a pathogen under the conditions of work (eg unavoidable open bench work with samples containing flu virus);
ii. there is a valid technique to detect infection, or the onset of disease or there is an effective vaccine available;
iii. you have concerns about the health or immune status of your staff/students;
iv. staff/students have concerns about their health or immune status

Contact University Occupational Health Service (ext 85401) for advice.

Part 6: Good working practice
Are the working procedures described in the Local Safety Manual sufficient for the level of risk arising from working with micro-organisms that are not genetically modified?
YES/NO

Have all staff/students been instructed in the Local Safety Manual rules and regulations?
YES/NO

Please send an unsigned copy of this risk assessment to the University Biological Safety Adviser (i.g.scragg@dundee.ac.uk).

Code Number (to be supplied by Safety Services upon receipt of completed form)

A copy with signatures should be kept by the PI for inspection.
Signatures

Name and Status of Assessor, signature and date

Name of Principal Investigator, signature and date

I have read this risk assessment, and any questions I had about it have been answered. I have been instructed in the Safety Manual and additional measures required for this work:

Names of staff/students carrying out the procedure, signature, and date
Appendix 7

Form: USS/Human Samples

Risk Assessment for Work with Human Blood, Tissues or Specimens

(b) Part 1. Brief outline of work

(c) Part 2. Hazard identification

1. Type of samples

2. Source of samples

3. Pathogens potentially present in these samples and symptoms caused

(d) Part 3. Exposure

1. Estimate likelihood of pathogens being present in these samples

2. Nature of work with samples

3. People who could come into contact with samples
(e) Part 4. Control measures

Can screened samples be used YES/NO

1. If yes, are they being used, and if not why not

2. Avoid use of sharps, if not why not

3. Gloves worn, if not why not

4. Containment Level 2 or 2+ (see Handbook Safe Working with Human Blood, Tissues and other Specimens in Research Laboratories for details of Containment Level 2 and 2+)

5. Additional precautions

Eye protection YES/NO

Apron YES/NO

Class 1 Microbiological Safety Cabinet YES/NO

Class 2 Microbiological Safety Cabinet YES/NO

Other (specify)

6. Disinfection Procedures

7. Waste Disposal Procedures
8. Spillage procedures

9. Local rules formulated and implemented  YES/NO

10. Vaccination available  YES/NO

11. Vaccination offered, if not why not

12. Health Surveillance required  YES/NO

(f) Part 5. Further information and comments

(g) Part 6. Signatures

1. Name and Status of Assessor, signature

2. Name of Principal Investigator, signature

3. I have read the COSHH assessment, and any questions I had about it have been answered. Names of people carrying out the procedure, signature, and date
Guidance

(h) Type of samples

biological agents capable of causing disease often show strong tissue specificity eg liver: hepatitis; lung and sputum: Mycobacterium tuberculosis, neural tissue: agents of transmissible spongiform encephalopathies; blood: blood borne viruses and parasites.

the greatest risk of contacting a blood borne agent is when handling blood but other body fluids and tissues especially those contaminated with blood also present a risk. These include: cerebrospinal fluid, pleural fluid, breast milk, amniotic fluid, vaginal secretions, peritoneal fluid, pericardial fluid, semen, synovial fluid and unfixed tissues and specimens.

samples such as urine, faeces, saliva, sputum, tears, sweat and vomit present a minimal risk of blood-borne infection although they may present other hazards (sputum samples may contain Mycobacterium tuberculosis).

(i) Source of samples

• the prevalence of diseases varies throughout the world and this should be considered in the risk assessment (eg a blood sample from the UK is extremely unlikely to be infected with malaria parasites)

• samples that have been screened for pathogens (eg blood from Blood Transfusion Services or organs suitable for transplantation) present minimal risk. However, screening is not error free and does not guarantee the sample is HIV negative because of the time taken for sero-conversion following infection

• all unscreened samples from any source should be regarded as being infected with a blood borne pathogen.

(j) Nature of the work

• greater risk arises when work involves:
  • handling a large number of samples
  • where volumes are large
  • generation of aerosols, splashes or droplets
• unavoidable use of ‘sharps’
• cultivation of white blood cells may support replication of HIV, and other retroviruses. Titres are unlikely to become significant after 4 days incubation, but if incubation for 4 days or longer is required consider need to work at Containment Level 3
• if continuous cell lines are to be established consider the likelihood of infection with HIV, and other viruses
• cultivation of all cells from patient known or suspected to carry HIV must be carried out at Containment Level 3.

(k) Control measures
• for most research involving blood etc it is possible to assess the risks of ill health and select the appropriate sensible precautions (control measures) to eliminate or at least minimise the risk without recourse to a Containment Level 3 laboratory.
• the greatest risk to control is skin puncture by blood-contaminated sharp objects such as needles, instruments or broken glass. Contamination of open wounds and skin lesions such as eczma, splashing the mucous membranes of the eye, nose or mouth is unlikely.
• low risk work with screened samples samples such as blood from BTS will require less rigorous precautions than samples with a higher risk of being contaminated.
• the set of precautions comprising Containment Level 2 are adequate for screened samples, but work with unscreened samples where there is a possibility that the samples are infected (by far the majority of cases) can take place at Containment Level 2+. These measures are required to prevent percutaneous inoculation, contamination of the skin, mucous membranes and work surfaces.