Arrangements for Work with GeneticallyModifiedOrganisms

Policy

It is the policy of the University that all work involving genetically modified organisms is carried in accordance with Genetically Modified Organisms (Contained Use) Regulations 2014 and in such a way as to prevent undue risk to human health or the environment.

In particular, work will only be carried out after prior assessment of the hazards associated with it and ensuring that suitable facilities, local procedures and organisational arrangements are in place which will reduce risk to low or effectively zero. Work may only be carried out by trained competent workers and will be adequately supervised.

The arrangements described in this document form a part of the University’s Health and Safety Policy. Reference should also be made to the following supporting documents:

Definitions & Scope

Genetic Modification is defined as the altering of the genetic material of an organism by a way that does not occur naturally by mating and/or natural recombination.

Contained Use is any activity involving GMOs where barriers are used to limit contact and protect humans and the environment. These barriers can be

- Physical e.g. a containment laboratory, containers, equipment used to prevent escape of or exposure to a GMO.
- Chemical – use of disinfectants to inactivate or destroy a GMO
- Biological – inherent or engineered characteristics that mean it is attenuated or rendered unable to survive outside a specialist environment.

Contained use includes the process of genetic modification and the subsequent growth, storage, transport and destruction and disposal of GMOs.

Appendix 1 Contains information and examples of;
- Techniques that are considered to constitute genetic modification
- Techniques which are considered not to result in genetic modification
- Techniques to which the Regulations do not apply.

Summary of the Regulations
The principal legislation is the Genetically Modified Organisms (Contained Use) Regulations 2014. [GMCU]. These regulations revoke and replace all previous GMCU regulations and amendments. This covers human health and environmental aspects of work involving genetically modified micro-organisms (GMMs) and human health aspects of work with animals and plants.

The Control of Substances Hazardous to Health Regulations apply to work with biological agents, which includes micro-organisms, cell cultures and human endoparasites that may cause infection, allergy toxicity or other ill-health effect. Biological agents are covered by COSHH in both unmodified and genetically modified form. The requirement under COSHH to prevent or minimise exposure to a biological agent means that for GM activities disabled or attenuated derivatives of pathogenic host and vector organisms must be used wherever possible. These regulations also define the criteria for health surveillance.

Environmental protection aspects of work with GM plants and animals are regulated under the following legislation.

- Environmental Protection Act 1990
- Genetically Modified Organisms (Deliberate Release and Risk Assessment Amendment Regulations 1996
- Genetically Modified Organisms (Risk Assessment) (Records and Exemptions) Regulations 1996

The following schematic summarises the relationship between the aforementioned regulations.
Current Legislation on Contained Use of Genetically Modified Organisms

- Prepare an emergency plan to protect health, safety and the environment. Appendix B describes the circumstances under which such a plan is required.

Key requirements of the GMCU and associated Regulations:

- All contained use involving genetically modified organisms and micro-organisms must be subject to suitable and sufficient assessment of risks to human health and the environment prior to the work commencing. The risk assessment must take into account specific matters laid out in the regulations and assign the contained use to one of four activity classes according to the degree of risk. Use of the University GM risk assessment forms will ensure that these matters are adequately addressed.

- Review of risk assessments where there is reason to suspect the risk assessment is no longer valid or if there has been a significant change in the work. Risk assessment must be kept for at least 10 years after work ceases
• Notification to the Health & safety Executive [HSE] of any CU activities of Class 2 and above and of any changes to a notified project which presents significant change or increase in the risks.

• Obtain advice on risk assessment from a person or a genetic modification safety committee [GMSC] with expertise in risk assessment relating to contained use. Where the risk assessment indicates that the contained use is class 2 or above the advice of the GMSC must be obtained.

• Adherence to the principles of good microbiological practice [GMP] and good occupational safety and hygiene practices [GOSH] in order to ensure risks to human health and the environment arising from the contained use is at the lowest level that is reasonable practicable. These principles are contained in Appendix A.

• Preparation of an emergency plan to protect health, safety and the environment. Appendix B describes the circumstances under which such a plan is required.

The University’s arrangements for review and approval of GM risk assessments and the GMSC structures are detailed in these associated documents.

Roles & Responsibilities:

The Head of School in any School that carries out genetic modification must

• Ensure that appropriate arrangements have been made to ensure that risk assessments are undertaken and advice obtained from the appropriate person or a Genetic Modification Safety Committee where relevant.

• Appoint a suitable Biological Safety Officer to provide local advice on GM assessment and procedures. In larger Schools it may be deemed appropriate to appoint Divisional Biological Safety Officers. [The role of the BSO is described in Appendix D.]

• Ensure that Principal Investigators involved in GM work understand their responsibilities under this policy.

Principal Investigators will normally be head of a research group or in charge of a specific GM research project. Their responsibilities are to

• Ensure that all GM work is covered by a risk assessment that has been reviewed and approved by the GMSC.

• Ensure that contents of the risk assessment and control measures are brought to the attention of individuals working on the project.
Ensure that work is undertaken in accordance with the findings of the risk assessment and that the principles of GMP & GOSH are adhered to.

Ensure that all individuals involved in GM work receive training and are competent to carry out the work and that this is recorded in a robust manner.

Ensure an appropriate level of supervision is maintained.

Ensure that risk assessments are regularly reviewed and any changes are notified to the appropriate GMSC for approval.

Where appropriate [e.g. larger research groups] appoint an individual within the group to co-ordinate GM risk assessments and assist in the annual review of GM risk assessments that is initiated by the Safety Office.

The University Biological Safety Adviser is based in the University Safety Office and oversees and advises on compliance with the relevant legislation, co-ordinates the meetings and activities of the UGMSC and reports to the University Safety Committee on matters relating to activities involving Genetic Modification.

The University Biological Safety Adviser is the main contact with HSE and will administer notifications to the HSE, for activities at class 2 and above.

Any proposal to carry out GM work in locations that are not at that time under the supervision of a GMSC must be notified to the University Biological Safety Adviser in order that appropriate arrangements for local supervision may be established.

Work with animals is also subject to regulation by the Home Office and must be carried out in accordance with the Animals (Scientific Procedures) Act 1986 and within the guidelines outlined by the University.

Organisation

Genetic Modification Safety Committees

The University has established 3 local GMSCs to provide advice on the appropriateness of projects and to review and approve risk assessments from constituent schools/departments. It has also established a main University GMSC [UGMSC] to co-ordinate the activities of local GMSCs and ensure consistency of approach across the organisation. The local GMSCs and areas of coverage are contained in this document.
Submission of Risk Assessment & Project Approval

All work involving genetic modification must initially be subject to an appropriate risk assessment which must then be submitted for approval to the relevant GMSC.

The type of GM work to be undertaken will determine the specific risk assessment form that should be completed.

For the purpose of ensuring a consistent approach to risk assessment the following standard forms have been produced and reside on the Safety Office workspace:

Note **Form 1** is in two parts.
- Part 1 for low risk class 1 activities
- Part 2 must be completed for class 2 or above or where there is doubt about it being class 1

*Note:* Although **knock-out mice** are considered to be self-cloned and therefore not subject to the GMCU Regulations [other than Reg 17 – Principles of Good Occupational Hygiene and Safety] they are subject to the requirements of the other Regulations and therefore an assessment of environmental safety must be carried out.

**Review of risk assessments.**

The UBSA will initiate an annual reminder to PIs to review their assessments. However for class 3 & higher risk class 2 assessments review will be more frequent and formal depending on the nature of the work and degree of risk. This frequency will be assigned at the time of approval.

Where there are changes to the project the risk assessment must be reviewed by the PI to ensure there is no significant increase in the risk and/or the
changes are within the scope of the original assessment. The following changes are considered administrative and will require submission of an amendment form but will be approved by the UBSA/Chair of the GMSC.

- Changes to workers [new starters/leavers]
- Changes to location of work. However if the lab /area has not been approved for GM work this will need to be inspected by the BSO/UBSA and approval given.
- Change to the PI. Where a PI leaves but the work is to continue the Head of School must appoint another PI to oversee the project.
- Records of risk assessments, and any reviews of them, must be kept for at least 10 years following the cessation of the activities to which they relate.

Scientific changes such as introduction of additional host strains, vectors, inserts will require formal approval.

**Health Surveillance**

Much work involving genetic modification has no identifiable health risk. However, some types of GM work may involve a risk of ill health resulting from work exposure to the GM activity in which case health surveillance may be required.

Examples of GM work that may involve a risk of ill health as a result of exposure are:

- Genetically modified micro-organisms derived from biological agents classified in ACDP hazard groups 2 - 4, particularly for example, where modified viruses may exhibit different tissue tropism, or where the agent is less susceptible to therapeutic agents, or where immunised workers may not be fully protected;
- Cloning of oncogenic or tumorigenic sequences, mutant tumour suppresser genes or anti-sense constructs for tumour suppresser genes;
- Work with modified prion protein genes;
- Organisms expressing biologically active molecules such as enzymes, hormones, toxins which may pose risks to health;
- Work with a potential for exposure to cloned human genes which may lead to an immune response and subsequent auto-immune type disease;
- Work that may cause respiratory sensitisation, especially at large scale and with the possibility that fusion proteins or inclusion bodies may enhance sensitisation. The University policy concerning health surveillance for respiratory sensitisers would apply under these circumstances.

Health surveillance will only be appropriate where an identifiable health effect may be related to exposure; and there is a reasonable likelihood that the health effect may occur under the conditions of work; and there are means for
detecting indications of the health effect. If a project risk assessment indicates that health surveillance may need consideration in the light of the above criteria then further advice should be obtained from Occupational Health.

**Records of exposure**

Certain types of work require exposure records to be maintained. Exposure records do not include medical information and are a record of the agents with which an individual has worked over time. These are as follows:

- Hazard Group 3 and 4 biological agents – 10 years after work ceases.
- Agents that can cause delayed onset illness, examples listed below – 40 years after work ceases:
  - Hepatitis B, C, D and unclassified hepatitis viruses,
  - Human papillomaviruses,
  - Human retroviruses and
  - Prion agents.
- Oncogenes and related sequences – 40 years after work ceases.

In the case of work with oncogenes and related sequences a copy of the exposure record to this type of agent should be given to the worker on termination of a contract so the information can be passed to the next employer. Appendix E contains a report that should be issued on termination.
Appendix A

General Principles of Good Microbiological Practice
and of Good Occupational Safety and Hygiene

The general principles of good microbiological practice and of good occupational safety and hygiene are as follows:

a. Keeping workplace and environmental exposure to any genetically modified micro-organism to the lowest reasonably practicable level;

b. Exercising engineering control measures at source and supplementing these with appropriate personal protective clothing and equipment where necessary;

c. Testing adequately and maintaining control measures and equipment;

d. Testing, where necessary, for the presence of viable process organisms outside the primary physical containment;

e. Providing appropriate training of personnel;

f. Formulating and implementing local codes of practice for the safety of personnel, as required;

g. Displaying biohazard signs where appropriate;

h. Providing washing and decontamination facilities for personnel;

i. Keeping adequate records

j. Prohibiting in the work area eating, drinking, smoking, applying cosmetics or the storing of food for human consumption;

k. Prohibiting mouth pipetting;

l. Providing written standard operating procedures where appropriate to ensure safety;

m. Having effective disinfectants and specified disinfection procedures available in case of spillage of genetically modified organisms; and

n. Providing safe storage for contaminated laboratory equipment and materials where appropriate.
Appendix B

Emergency Plans

There are limited circumstances that require an emergency plan. One is required if the nature of the activity is such that in the event of an accident there could be a serious off-site impact to the health and safety of the public or to the environment.

The requirements for an emergency plan may be summarised as follows:-

- **Class 1** – safe, none needed.
- **Class 2** – Unlikely to be serious off-site risks. Not needed for small-scale operations, large-scale operations need to be assessed on a case by case basis but it is very unlikely that one would be needed in most cases.
- **Class 3** – Required for large-scale activities. Small-scale activities must be individually assessed. One may be needed if the GMMs have novel pathogenic traits, likely dispersion routes, susceptible populations or environments.
- **Class 4** – Required for all activities.

Incidents to consider include fire; vehicle collision from adjacent road; failure of fermentation vessel, pipes, seals; and human error.

Should the GMSC consider that an emergency plan may be required then the Safety Office must be consulted as it may be necessary to liaise with external agencies.
Appendix D

The Role of the Biological Safety Officer

The Biological Safety Officer (BSO) fulfils an important role in the local control of genetic modification activities. The BSO is appointed by the Head of School and should have sufficient seniority and authority coupled with extensive knowledge and experience of working within a containment laboratory or with similar practices. In larger Schools Divisional/Departmental BSOs may be appointed. Deputising arrangements will also need to be made.

Examples of matters upon which the BSO may advise or assist the employer to enable them to meet the statutory requirements for work with GMOs, include:

- ensuring that local rules are drawn up and followed for the safety of personnel;
- advising on training of personnel in appropriate microbiological practice (the level of training will depend on the level of work being undertaken);
- investigating accidents, spillage etc. in the laboratory (or other containment facility) and taking what action they consider necessary. Appropriate records and reports should be made;
- the safe storage of modified organisms/harmful or potentially harmful material and ensuring that records of these are kept;
- the appropriate transport of all modified organisms;
- ensuring that appropriate disinfection procedures for the laboratories are in place and followed;
- participating in locally organised inspections;
- methods for testing, when necessary, for the presence of viable process organisms outside the primary containment;
- ensuring that control measures and equipment are tested and maintained at appropriate intervals, for example, by using outside contractors to test and maintain microbiological safety cabinets;
- ensuring appropriate waste disposal procedures are used;
- providing technical support to the GMSC on risk assessment and classification;
- adequacy of arrangements for the physical security of the laboratories.
### Appendix E

**Termination record for individual exposure.**
Control of Substances Hazardous to Health Regulations 1999
Genetically Modified Organisms (Contained Use) Regulations 2000

**Record of Work Involving Oncogenes or other Hazardous Sequences**
at the University of Nottingham

**Name:**

**University Location:**

<table>
<thead>
<tr>
<th>Project Ref No.</th>
<th>Oncogenes Studied</th>
<th>Start date</th>
<th>Stop Date</th>
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<tbody>
<tr>
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**Note to leaving worker.**

The above record summarises your work with oncogenic or other hazardous sequences during your period of work at The University of Nottingham. Employers are required to maintain such records for 40 years after the work.
has been completed. You should give this to your new employer to maintain continuity.
Appendix F

Summary of Notification Requirements

<table>
<thead>
<tr>
<th>Notification</th>
<th>Notification Period</th>
<th>HSE Consent Required?</th>
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</thead>
<tbody>
<tr>
<td>First use of premises</td>
<td>None Work can start</td>
<td>No Work can begin after HSE confirms receipt of application</td>
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<tr>
<td></td>
<td>on receipt of HSE</td>
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<tr>
<td></td>
<td>acknowledgement.</td>
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<tr>
<td>GMMs Class 1</td>
<td>First activity only</td>
<td>No</td>
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<tr>
<td></td>
<td>requires notification</td>
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<tr>
<td>GMMs Class 2 (First Activity)</td>
<td>HS must be notified unless previous work on higher class has already been sanctioned.</td>
<td>No Activity can begin 45 days after HSE confirms receipt of application. Work can begin earlier if HSE consents.</td>
</tr>
<tr>
<td>GMMs Class 2 (Subsequent Activities)</td>
<td>HSE must be notified</td>
<td>No Work can begin after HSE confirmed receipt of application</td>
</tr>
<tr>
<td>GMMs Class 3 and 4 (First Activity)</td>
<td>90 days notice before work commences.</td>
<td>Yes HSE must give consent or say why consent is refused. This will be 30-90 days after HSE confirms receipt of application.</td>
</tr>
<tr>
<td>GMMs Class 3 and 4 (Subsequent Activities)</td>
<td>45 days notice before work commences.</td>
<td>Yes HSE must give consent or say why consent is refused. This will be 30-45 days after HSE confirms receipt of application.</td>
</tr>
<tr>
<td>Non-notifiable GMOs (excluding GMMs)</td>
<td>None, except for first activity</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>Work with plants and animals not likely to harm humans.</td>
<td></td>
</tr>
<tr>
<td>Notifiable GMOs (excluding GMMs)</td>
<td>45 days before work commences</td>
<td>No Activity can start 45 days after HSE confirms receipt of application or say why consent is refused.</td>
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<tr>
<td></td>
<td>Work with plants and animals likely to harm humans.</td>
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</table>

Note. Fees change annually – consult Safety Office for current information

Notification of Plants and Animals

All activities involving genetically modified organisms other than micro-organisms (e.g. plants and animals) must be notified if the GMO has a greater potential to cause harm to human health than the equivalent non-modified organism. There are no notification requirements in relation to environmental risks.

Examples of notification requirements in relation to environmental risks:

- disease to humans including allergenic or toxic effects
- acting as a human disease vector or reservoir
- adverse effects to humans arising from change in behaviour or in physical nature
• adverse effects arising from the inability to treat human disease or offer effective prophylaxis