University College Dublin

Guide To The Use Of Genetically Modified Organisms In UCD

This document is designed to provide University staff and students with guidance on the contained use of genetically modified material in the context of existing legislation, regulatory requirements and University procedures.

Notwithstanding the provisions of the genetically modified regulations, genetically modified biological agents still need to be handled in a safe manner in accordance with applicable Biological Safety Workplace Regulations. Further information on this aspect of the use of genetically modified entities (and indeed all biological entities) can be found in the UCD Biosafety Manual.

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UCD SIRC Office

Contents

Revision History

- Rev. 0 issued February 2007
- Rev. 1 issued January 2008.
- Rev. 2 issued May 2022 (Significant format and layout updates).

Part 1.0 Introduction To The Contained Use Of Genetically Modified Organisms

1.1 Definitions and Terminology

- The contained use of genetically modified material is subject to the provisions of the Genetically Modified Organisms (Contained Use) Regulations (S.I. No. 73 of 2001**)** (as amended by SI 442 of 2010). This legislation lays down the requirements for the licencing, safe use and containment of GM's.
- **Genetically Modified Microorganism (GMM)** means any microorganism in which the genetic material has been altered or modified in a way that does not occur naturally by mating or natural recombination, or by a combination of both. See Appendix 1 and the First Schedule of the legislation for further details of what does and does not constitute genetic modification.
- **Genetically Modified Organism (GMO)** means any organism in which the genetic material has been altered or modified in a way that does not occur naturally by mating or natural recombination, or by a combination of both. See Appendix 1 for further details of what does and does not constitute genetic modification.
- In this guide the term **GMM** is used to refer to modified microbiological entities and cell lines; the term **GMO** is used to refer to modified whole plants and animals; whilst the term **GM** is used to refer to all genetically modified entities
- The **Environmental Protection Agency (EPA)** is the competent authority for overseeing the licencing and contained use of GM materials in Ireland. See EPA for further details. Queries on the contained use of GM material from a regulatory perspective can be sent to licensing@epa.ie
- **Contained Use** of GM materials means their use in a location physically separated from the wider environment, i.e. indoors
- A **Consent** is the term used to describe the licence issued by the EPA to the users of GM materials. No person may use a GM material without such a consent being in place. This extends to persons who both modify the organisms themselves or use commercially available or donated strains. Further information on consents and how to obtain same is outlined below.
- Every person carrying out any activity involving the contained use of a GM must ensure that all appropriate measures are taken to avoid adverse effects on human health and the

environment. Users must apply the principles of good microbiological practice and good occupational safety and hygiene.

- It should be noted that notwithstanding the provisions of the GM regulations, genetically modified biological agents will still need to be handled in a safe manner in accordance with applicable Biological Safety Workplace Regulations. Further information on this aspect of the use of genetically modified entities (and indeed all biological entities) can be found in the UCD Biosafety Manual.

1.2 GM Consents

No person may use genetically modified material without first having obtained a consent from the EPA. The process for obtaining the various classes of GM consents are outlined below in Sections 2 and 3.

In respect of GM Consents the following must be noted:

- EPA consents are issued to named persons / Principal Investigators working in designated areas, not to Schools or individual laboratories. Consequently a School or a multiuser laboratory cannot obtain a single consent to cover all work undertaken therein.
- The person named on the consent must be actively involved in the oversight of the work. Consequently a Head of School or a Technical Officer for example cannot be named as a consent holder for work carried out by a group in their School or laboratory over which they do not have direct supervisory control.
- Significant changes in the use or risk profile of GM material need to be notified to the EPA. These include the use of new laboratories not notified in the original application, a change of named consent holder, a change in the classification of the GM, etc.
- The use of all GMO's and GMM's requires a consent from the EPA, regardless of the source of the material or who modified it
- GMO and GMM consents cannot be 'combined', they are different documents

2.0 Use Of Genetically Modified Microorganisms (GMMs)

2.1 Persons Applying For A Consent For The First Time For The Use Of A GMM

Persons who are applying for the first time for a consent to use a GMM should follow the steps below:

1. Carry out a risk assessment to establish what Class of GMM is in use. There are 4 classes of GMM ranging from Class 1 (Low Risk) to Class 4 (Very High Risk). As a rule as long as the modification does not increase the virulence or pathogenicity of the organism or cell line then the wild type classification can be used.
2. There are sample risk assessments on the EPA website for Class 1 and Class 2 GMM's. When completing the risk assessment researchers must adhere to the layout and numbering system of these sample risk assessments.
3. When completing a GMM risk assessment particular attention must be paid to how the GMM will be contained, how both human health and environmental integrity will be protected and in particular how waste materials will be inactivated. Details on what a risk assessment should address are outlined in the Third Schedule of the legislation.
4. Once complete the risk assessments can be sent to sirc@ucd.ie for review. This is required before the EPA will consider any application.
5. SIRC Office will review the risk assessment and if necessary seek additional advice on same (usually only required for the use of higher risk materials).
6. Once comments have been made / the risk assessment approved, it can then be submitted by the applicant to the EPA (licensing@epa.ie) along with the required fee and a completed Additional Information Document (Fifth Schedule).
7. Note that if the fee is not paid in advance then the EPA will not review the submission. The fee for a submission is €250 for a Class 1 GMM; €1,875 for a Class 2 GMM; and €4,500 for a Class 3 GMM. The EPA does not issue invoices for fees, however they can if needed issue an email confirming the need to pay the fee (licensing@epa.ie). UCD Finance are familiar with the need to pay these fees in the absence of any invoice.
8. The EPA will review the submission and if happy will issue a consent. They have 45 days in which to do so for Class 1 and 2 applications; and 90 days for Class 3 applications. If they seek further information the clock will stop. Note that if a quicker turnaround time is required this can be requested.

If you are planning on modifying a Class 3 microorganism you are advised to contact the SIRC Office as early as possible for advice at sirc@ucd.ie as there are other significant requirements around obtaining Class 3 GMM consents.

2.2 Persons Who Already Hold A GMM Consent

A consent granted to a user for a particular class of contained use of a GMM may also be treated as a consent for any further use of any lower class of GMM by the same user in the same lab(s), and accordingly an additional consent will not be required. However depending on the Class of GMM in use there may still be a need to notify the EPA about its use and pay a 'subsequent use' fee – see below.

If a user has obtained consent for the use of a Class 1 or a Class 2 GMM, a further consent and notification to the EPA is not required for the use of any additional Class 1 GMM's by the same user in the same laboratory / laboratories. The use of the Class 1 GMM must still be risk assessed and the risk assessment retained on file.

A notification must be submitted to the EPA in respect of each Class 2 activity undertaken. Where a user has an existing consent to carry out either Class 2 or 3 contained use, and they wish to use a new Class 2 GMM, then they must submit a risk assessment, an Additional Informaton Document (Fifth Schedule), and pay the 'subsequent use' fee (€625). Once the application has been fully submitted use of the new Class 2 GMM can proceed after 10 days.

No use of a 'new' Class 3 GMM can take place without the explicit approval of the EPA. A full application must be made for same, albeit with a lower 'submission use' fee (€1,500).

2.3 Classification and Containment of GMM's

As part of the risk assessment required to obtain a consent, GMM's must always be classified into one of four classifications. These four classifications range from Low Risk (Class 1) up to Very High Risk (Class 4). In this respect the classification system is very similar to that used under the health and safety legislation for biological materials.

As laid out in the Contained Use Regulations a GMM must only be used in a laboratory or facility that meets the standards required for such laboratories, i.e. a Class 2 GMM can only be used in a Class 2 compliant lab. The design criteria for laboratories and other facilities holding GMM's is outlined in the Fourth Schedule of the legislation.

As referred to above a key part of the GMM risk assessment process is establishing and applying a class to the GMM. As a general rule as long as the modification does not increase the virulence or pathogenicity of the organism or cell line then the wild type classification can be used. However users should review the risks to human health and the environment posed by the GMM and confirm that the containment measures for that class as outlined in the Fourth Schedule of the legislation are adequate to contain the GMM and protect human health.

2.4 GMM Risk Assessments & Risk Assessment Templates

In respect of GMM's the EPA has prepared sample risk assessments for Class 1 and Class 2 GMM's that can be found on the EPA website. The layout and numbering system used in these sample documents must be replicated in a user's own GMM risk assessment. Failure to so do may lead to difficulties and a delay in obtaining a GMM consent.

2.5 Additional Information Document (Fifth Schedule)

As part of the submission to be made to the EPA for a consent an Additional Informaton Document (Fifth Schedule) as well as a risk assessment must be submitted. The EPA has developed a template for this information which can be found on the EPA website.

2.6 Annual Reports – GMM Users

All users of Class 2 and 3 GMM's must submit an annual report to the EPA by the end of March every year detailing their use of GMM's for the preceding calendar year. A template for same can be found on the EPA website. Those who only use Class 1 GMM's do not need to submit an Annual Report.

Part 3.0 Use Of Genetically Modified Organisms (GMOs)

3.1 Applying For A Consent

Persons who wish to use a GMO must apply for a consent for every GMO that they use. The procedure for doing is as follows:

1. Carry out a risk assessment using a developed UCD template (EPA approved).
2. There is no need to classify the GMO. However the risk to the environment from the use of the GMO must be assessed. In particular attention must be paid to how the GMO will be contained.
3. Once complete the risk assessments can be sent to sirc@ucd.ie for review. This is required before the EPA will consider the risk assessment.
4. The SIRC Office will review the risk assessment and if necessary seek additional advice on same (usually only required for the use of higher risk materials).
5. Once comments are made / the risk assessment approved, it can be submitted by the applicant to the EPA along with a completed Additional Information Document (Seventh Schedule).
6. There is no fee for a GMO consent submission.
7. Work with the GMO can begin 45 days after the submission has been made as at this time consent can be assumed. Note that if a quicker turnaround time is required this can be requested.

3.2 Containment of GMO's

GMO's, unlike GMM's, do not need to be classified. Instead, as part of the risk assessment the risk to the environment from their usage must be assessed and the appropriate containment measures identified in order to prevent the accidental release into the environment of the GMO.

3.3 GMO Risk Assessments & Risk Assessment Templates

UCD has developed a GMO Risk Assessment Template which can be used to make the submission to the EPA. This risk assessment must be submitted to the EPA for every GMO in use irrespective of whether the user has a pre-existing consent for the use of other GMO's.

3.4 Additional Information Document (Seventh Schedule)

As part of the submission to be made to the EPA for a consent an Additional Information Document (Seventh Schedule) as well as a risk assessment must be submitted.

3.5 Annual Reports – GMO Users

All users of GMO's must submit an annual report to the EPA by the end of March every year detailing their use of GMO's for the preceding year. A template for same can be found on the EPA website.

Appendix 1. Definitions Of Genetic Modification

Techniques Considered To Result In Genetic Modification

i. Recombinant nucleic acid techniques involving the formation of new combinations of genetic material by the insertion of nucleic acid molecules produced by whatever means outside an organism, into any virus, bacterial plasmid or other vector system and their incorporation into a host organism in which they do not naturally occur but in which they are capable of continued propagation.
ii. Techniques involving the direct introduction into a micro-organism of heritable material prepared outside the micro-organism including micro-injection, macro-injection and micro-encapsulation.
iii. Cell fusion or hybridisation techniques where live cells with new combinations of heritable genetic material are formed through the fusion of two or more cells by means of methods that do not occur naturally.

Techniques Not Considered To Result In Genetic Modification

The following techniques are not considered to result in genetic modification, provided they do not involve the use of recombinant-nucleic acid molecules or GMO's made by techniques / methods other than those set out below:

i. *in vitro* fertilisation;
ii. natural processes such as: conjugation, transduction, transformation;
iii. polyploidy induction.

Exclusions From Provisions Of The GM Regulations

Organisms resulting from the following techniques or methods of genetic modification are excluded from the requirements of this legislation:

i. Mutagenesis
ii. Cell fusion (including protoplast fusion) of plant cells of organisms, which can exchange genetic material through traditional breeding techniques
iii. Cell fusion (including protoplast fusion) of cells of any eukaryotic species, including production of hybridomas and plant cell fusions
iv. Self-cloning consisting in the removal of nucleic acid sequences from a cell of an organism which may or may not be followed by reinsertion of all or part of that nucleic acid (or a

synthetic equivalent) with or without prior enzymic or mechanical steps, into cells of the same species or into cells of phylogenetically closely related species which can exchange genetic material by natural physiological processes where the resulting micro-organism is unlikely to cause disease to humans, animals or plants. Self-cloning may include the use of recombinant vectors with an extended history of safe use in the particular micro-organisms.