

GENETICALLY MODIFIED ORGANISMS (CONTAINED USE) REGULATIONS – S.I. NO. 73 OF 2001

GUIDANCE NOTE FOR USERS OF GMOs (CONTAINED USE) IN IRELAND

This Guidance Note has been prepared to provide assistance and guidance to GMO users who wish to apply to the EPA for a consent for the first time contained use and/or the subsequent contained use of Genetically Modified Organisms (GMOs). Nothing in this Guidance Note shall be construed as negating the users statutory obligations or requirements under the Genetically Modified Organisms (Contained Use) Regulations S.I. No. 73 of 2001 or any other enactments or Regulations.

The note is broken down into a number of Sections as follows:

Section 1 – Legislation and Definitions

Section 1 provides information about: the legislation which should be consulted when preparing a notification; definitions; and, techniques which give rise to genetic modification as well as those which do not result in genetic modification and are therefore excluded from the scope of the legislation.

Section 2 – Classification of Contained Use and Risk Assessment

Section 2 provides guidance on how to classify a contained use and some general guidance on the conduct of risk assessments.

Section 3 – Requirements for GMM Notifications

Section 3 sets out the requirements for the first time use of a premises and /or the subsequent contained use of a Class 1, 2, 3 or 4 activity involving Genetically Modified Micro-organisms (GMMs).

Section 4 – Requirements for Other GMO Notifications

Section 4 sets out the requirements for the notification of genetically modified organisms other than micro-organisms i.e. GM plants and animals.

SECTION 1 – Legislation and Definitions

Legislation

Directive 98/81/EC amending Directive 90/219/EC on the contained use of Genetically Modified Organisms (GMOs) was transposed into Irish Law – GMO

(Contained Use) Regulations S.I. No 73 of 2001 - on March 15th 2001. This legislation may be referenced at the following web address; <http://www.irishstatutebook.ie/ZZSI73Y2001.html>

Definitions

The GMO Regulations define **contained use** as '*any activity in which organisms are genetically modified or in which such organisms are cultured, stored, transported, destroyed, disposed of or used in any other way and for which specific containment and other protective measures are used to limit their contact with the general public and the environment*'.

A **genetically modified organism (GMO)** is defined as an organism in which the genetic material has been altered in a way that does not occur naturally by mating or natural recombination or by a combination of both.

GMOs refers to GM plants and/or animals and are inclusive of Genetically Modified Micro-organisms (GMMs). Again in accordance with the legislation micro-organism means '*any microbiological entity, cellular or non-cellular, capable of replication or of transferring genetic material, including viruses, viroids, animal and plant cells in culture*'.

The GMO (Contained Use) Regulations S.I. 73 of 2001 require the classification of all GMM¹ activities into one of four classes - Class 1, Class 2, Class 3 or Class 4 - as appropriate, depending on the level of risk the activity poses to human health or the environment.

A **Risk Assessment** will determine the class (Class 1, 2, 3 or 4) into which the GMM contained use activity will fall. Examples of Class 1 and Class 2 Risk Assessments may be viewed on the EPA Website under GMO Licensing (www.epa.ie).

Techniques which result in genetic modification

Genetic modification occurs through the use of the following techniques:

- 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;
- 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;

¹ Note-this classification is only pertinent for GMM, it is **not** used for GMOs, i.e., GM Plants and animals

- 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, which do not result in genetic modification

1. The following techniques are not considered to result in genetic modification, provided they do not involve the use of recombinant-nucleic acid molecules or GMOs made by techniques/methods other than those set out in paragraph 2:
 - *in vitro* fertilisation;
 - natural processes such as: conjugation, transduction, transformation;
 - polyploidy induction.
2. Organisms resulting from the following techniques or methods of genetic modification are excluded from the requirements of this legislation:
 - Mutagenesis;
 - Cell fusion (including protoplast fusion) of plant cells of organisms, which can exchange genetic material through traditional breeding techniques, provided that the
 - Cell fusion (including protoplast fusion) of cells of any eukaryotic species, including production of hybridomas and plant cell fusions;
 - 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.

SECTION 2 – CLASSIFICATION OF CONTAINED USE AND RISK ASSESSMENT

In accordance with the Contained Use Regulations S.I. No. 73 of 2001, all GMM activities must be classified into one of four classes - Class 1, Class 2, Class 3 or Class 4.

As a preliminary step it is recommended that the user provisionally allocate the GMM to Class 1, 2, 3 or 4. Directive 90/679/EEC and amendments (which classify biological agents known only to infect humans into groups 1 - 4) and S.I. No 146 of 1994 may be referenced for this initial classification.

- a. In general only GMMs which show the following characteristics would be considered appropriate for inclusion in Class 1 as defined in article 14:
- The recipient or parental micro-organism is unlikely to cause disease to humans animals or plants*;
 - The nature of the vector and the insert is such that they do not endow the GMM with a phenotype likely to cause disease to humans, animals or plants*, or likely to cause deleterious effects in the environment;
 - The GMM is unlikely to cause disease to humans, animals or plants*and is unlikely to have deleterious effects in the environment;
- *(this would only apply to animals and plants in the environment likely to be exposed)
- b. Having assigned the GMM to Class 1, 2, 3 or 4 subject to confirmation, article 13 of the GMO Regulations S.I. No 73 of 2001 stipulates the completion of a Risk Assessment (RA) in accordance with the Third Schedule of the same regulations. Users should also refer to the EU Guidance notes for Risk Assessment. The RA serves to identify any risk associated with the contained use activity.
http://europa.eu.int/smartapi/cgi/sga_doc?smartapi!celexapi!prod!celexnumdoc&l g=en&numdoc=32000d0608&model=guichett
- c. Having identified the risks involved it is necessary to assign the appropriate containment level (i.e. Containment level 1, 2, 3 or 4) and other protective measures, which must be applied in order to control that risk. These containment and other protective measures are outlined in the Fourth Schedule of S.I. No. 73 of 2001 and in the tables to the Regulations (Table IA, IB, IC and Table II, Fourth Schedule).
- d. Containment level corresponds directly to Class. Therefore the Class into which the activity will fall may be determined by reference to article 14(1) of the GMO Regulations S.I. No. 73 of 2001 which has been reproduced in Table 1.

Table 1: Article 14(1) showing correlation between Class and containment level

Class 1	Activities for which level 1 containment as set out in the Fourth Schedule is appropriate
Class 2	Activities for which level 2 containment as set out in the Fourth Schedule is appropriate
Class 3	Activities for which level 3 containment as set out in the Fourth Schedule is appropriate
Class 4	Activities for which level 4 containment as set out in the Fourth Schedule is appropriate

So if containment level 1 is deemed appropriate to control the risk posed by the activity then the corresponding GMM will be classified as belonging to Class 1.

- f. The initial classification conducted in step (a) should be revisited, reviewed and confirmed prior to finalisation of the assessment.

Regarding the classification of a GMM activity the following example might be useful in terms of illustration.

Take the example of a user working with a wild type *Clostridium botulinum* strain (classified as a Group 2 biological agent under Directive 90/679/EEC and S.I. No. 146) containing an innocuous DNA insert. Where the RA shows that the genetic modification does not alter the risk to human health and the environment, the containment level to control the risk is level 2 which is the same as that of the wild type *Clostridium botulinum* strain. Therefore, such an activity should be classified as a Class 2 GMM activity. However where the DNA insert constitutes a harmful toxin the activity would be required to be upgraded to another class.

In some cases it may be possible that the GMM will be less hazardous than the parental organism and the Risk Assessment may indicate that the final class may be lower, while in other cases the protective measures might fall between two levels. In those cases the activity must be classified at the higher level.

Many laboratories will be working with level 2 containment measures and will therefore use level 2 containment and other protective measures when the actual risk would only require level 1 measures. Such activities should be classified as Class 1 GMM activities. It is important to remember that classification of GMM activities is based on the containment required to control the risk as outlined in the Risk Assessment and not on the actual containment which is currently in use in a laboratory. The Risk Assessment might indicate that a higher or lower containment level should be used to control the risk and the user must ensure that an appropriate containment level is used to protect human health as well as the environment.

SECTION 3 – REQUIREMENTS FOR GMM NOTIFICATIONS (Part II of S.I. No. 73 of 2001)

First time use of a premises (Articles 16, 18 and 19) (for Classes 1 – 4)

Where a premises is being used for the first time for any GMM contained use activity the user is required to forward a first time use notification to the EPA, in accordance with Article 16 of S.I. 73 of 2001 (Page 16). For first time use of a premises for a Class 2 contained use activity, a notification must also be forwarded to the EPA in accordance with Article 18 of S.I. 73 of 2001 (Page 17). For first time use of a premises for either Class 3 or Class 4 contained use activities, a notification must also be forwarded to the EPA in accordance with Article 19 of S.I. 73 of 2001 (page 18). In practice, for a first time use of a premises for a Class 2 contained use activity, the Article 16 and Article 18 notifications can be submitted together. Similarly, for a first time use of a premises for a Class 3 or 4 contained use activity, the Article 16 and Article 19 notifications can be submitted together.

A notification under Article 16 must contain:

- information as set out in Part A of the 5th Schedule to S.I. No 73 of 2001 (Page 51).

Article 16(1) of S.I. No 73 of 2001 states that a premises shall not be used for the first time unless:

- a notification in respect of such first time use has been given by the user to the Agency;
- a consent for such use has been granted by the Agency; and
- the conditions, if any, attached to the consent have been complied with.

A notification under Article 18 must contain:

- information set out in Part B of the 5th Schedule to S.I. No 73 of 2001 (Page 51)

A notification under Article 19 must contain:

- information set out in Part C of the 5th Schedule to S.I. No 73 of 2001 (Page 52)

Article 19 (2) states that a Class 3 or 4 activity may not proceed unless a consent has been granted by the EPA and the conditions, if any, attached to the consent have been complied with.

The Agency must communicate its decision in writing to the user at the latest 45 days after receipt of the notification in the case of Class 1 and Class 2 activities, and at the latest 90 days after receipt of the notification in the case of Class 3 or Class 4 activities. It should be noted that, in the case of Class 3 or Class 4 activities, the failure of the EPA to issue a decision within 90 days shall not entitle the user to proceed with the activity.

Note: Article 16(4) (page 16) states that '*...a consent granted for the first time use of a premises for a particular class of contained use shall be treated as a consent for the first time use of a premises for that class and for any lower class of contained use and accordingly a further consent shall be required in respect of the first time use of the premises for any higher class of contained use*'. For example, if a user has obtained consent for the first time use of a premises for a class 2 contained use activity, a notification of class 1 contained use activities at the same premises is not required.

Subsequent Use of Premises (for Classes 1 to 4)

Class 1 (Article 17)

Notifications are not required for subsequent Class 1 contained use activities at premises that are in compliance with an article 16 consent for class 1 or higher class contained use activities. However, a user is required to carry out and maintain risk assessments in respect of all subsequent Class 1 contained use activities and these

assessments are to be submitted to the EPA within one month of the end of each calendar year together with a report of the work carried out on the contained use.

Class 2 (Article 18)

A notification in accordance with article 18 must be submitted to the Agency in respect of each Class 2 activity undertaken. The notification must contain:

- information set out in Part B of the 5th Schedule to S.I. No 73 of 2001 (Page 51).

Where the premises has been the subject of a previous notification to carry out a class 2 or higher class of contained use and where the user has complied with any associated requirements, the contained use activity may proceed within 10 days of receipt of the notification. Annual reporting will also apply.

Class 3/4 (Article 19)

A notification in accordance with article 19 must be submitted to the Agency in respect of each Class 3/4 activity undertaken. Such a notification must contain:

- information set out in Part C of the 5th Schedule to S.I. No 73 of 2001 (Page 52).

Under no circumstances may a notifier proceed with a Class 3/4 activity without the prior approval of the Agency.

Where the user submits a notification in respect of a new Class 3/4 activity, having already received a consent in respect of the first time use of a Class 3/4 activity, the Agency must revert within 45 days. Annual reporting will also apply.

Notices (Article 22)

Under Article 22 (Page 19) the notifier is required to give public notice of its proposed contained use of Class 3/4 activities (and Class 2 activities at the discretion of the Agency) in a newspaper circulating in the district in which the proposed activity is scheduled to take place. Members of the public may then make representations in writing to the Agency regarding the notification.

Consents (Article 26)

The Agency will issue its consent with or without conditions or refuse its consent. (Article 26, page 21)

Fees

A notification is not deemed valid until such time as fees are received in respect of a notification. Fees are set out under the 8th Schedule of S.I. No 73 of 2001 (Page 61).

Refund of fees (Article 48)

Article 48 (Page 31/32) permits users to seek a waiver or refund of up to 50% of fees payable in certain limited circumstances. Users applying for such a refund should do so in writing stating their reasons. The granting of a waiver or refund is at the absolute discretion of the Board of the Agency.

Containment measures

Containment measures are set out in Part A and B of the 4th Schedule (Page 42).

SECTION 4 – Requirements for Other GMO Notifications (Part III of S.I. No. 73 of 2001)

A notification of contained use for a GMO (GM plants/animals) must be submitted to the Agency and must contain:

- a risk assessment (refer to article 36(2), (page 28) and Part II of the 7th Schedule (page 58));
- information set out in Part I of the 7th Schedule (page 57).

There is no requirement for the payment of fees in respect of GMO activities.

The contained use activity may commence 45 days after submission of the notification or earlier with the written agreement of the Agency. The Agency is not required to issue the notifier with a consent. The user is required to submit an annual report to the Agency.