Procedure for requesting a notification/permit for contained use

Introduction

Contained use with genetically modified organisms (GMOs) is governed by the following legal requirements:

- Decree on Genetically Modified Organisms, Environmental Management 2013
- Regulation on Genetically Modified Organisms, Environmental Management 2013
- Environmental Permitting (General Provisions) Act

An assessment must be carried on the basis of the GMO Decree of the potential risks to people and the environment posed by work with GMOs. The GMO Regulation sets out the rules relating to contained use and of GMOs and contains several appendices required for the categorization of work with GMOs. In accordance with the GMO Decree, rooms in which work with GMOs is carried out must be included in the Environmental Permitting (General Provisions) Act.

Definitions

- Contained use: all work carried out in a classified room.
- Classified room: a room to which a containment level has been applied based on the Environmental Management Act.
- Containment level: the containment levels correspond to the four risk classes known for microorganisms. The categorization of microorganisms into four classes is dependent on the properties of the microorganism and the degree to which it is pathogenic to humans, animals, or plants. Class 1 contains apathogenic microorganisms, the higher classes contain increasingly pathogenic microorganisms, with microorganisms in class 4 potentially fatal.
- Category of physical containment (CFI): a CFI is a certain type of workspace e.g. a microbiological laboratory (ML), an animal enclosure (D), or greenhouse (PK) where activities involving genetically modified organisms (GMOs) can be carried out safely. The CFI (e.g. ML-I, D-I, PKa-I) is determined by the type of workspace and the containment level (I, II, III, or IV). Design and work instructions have been established for each CFI, which can be found in Appendix 9 to the GMO Regulation. As the workspace satisfies prescribed design requirements and as work is carried out in accordance with prescribed work instructions, the containment is guaranteed. ML-I, ML-II, D-I, DM-I, DM-II, PC-I, PKa-I, PKb-I, PCM-I, PKM-I, PCM-II, and PCM-II rooms are present at our institution.
- Genetically modified organism: an organism whose genetic material has been modified in a way that is not likely to occur naturally by reproduction or recombination and that has the capacity to multiply or transfer genetic material.

Procedure

GMO Decree and Regulation 2013

In view of the fact that work with GMOs may pose a risk to people and the environment, a risk assessment must be carried out in advance of the work, leading to the assignment of a CFI and containment level offering appropriate protection to human health and to the environment. This risk assessment takes the form of an application for a notification or permit (depending on the outcome of the risk assessment). The notification/permit serves as an account of the risk assessment.

Application for new GMO work

Applications for and changes to notifications and permits are requested from the GMO Office by the BSO. If new GMO work is scheduled, contact must be made with the BSO. The BSO will assess whether or not the work has already been notified or permitted for the legal person. If this is not the case, the BSO will change the existing notification/permit or apply for a new notification/permit. In this case, the researcher must supply the BSO with the requisite information relating to the GMO. The BSO will use the information provided to categorize the GMOs in accordance with Appendix 5 to RGGO2013, complete the correct forms, and send them to the GMO Office with the requisite information.

Special procedures

In some cases, the categorization may mean that a person is not able to carry out work, e.g. because the work cannot be carried out in a biosafety cabinet. In that case, a different categorization of the work may be considered or an adjustment to the work/design instructions, e.g. by imposing additional conditions. Special procedures are available for this purpose.

- 2.8 request
  If a GMO cannot be categorized with the aid of Appendix 5 or it is deemed that a lower containment level offers an appropriate level of protection, a 2.8 request may be submitted. The GMO Office will determine whether or not the GMOs can be handled safely at the desired categorization level. Following approval, the work must be added to a notification of the desired containment level. A 2.8 combination request may be submitted, in which case the 2.8 request is linked directly to a notification or permit. A 2.8 request is valid for the user only.

- ATV request
  Appendix 9 to RGGO2013 contains the standard design and work instructions and additional instructions for special cases. In certain situations, it may not be possible to satisfy the instructions outlined here and a different method of work may be desirable. It may also be the case that the instructions outlined do not afford adequate safety for the work that is to be carried out. In that case, an ATV request must be submitted. The user must submit the request and the ATV decision is valid for the user only.

Information to be supplied by the VM/OL

For all requests, the VM/OL must supply information to the BSO relating to GMOs and the work to be carried out. The VM/OL is expected to supply the following information:

- For hosts and vectors not referred to in Appendix 2 list A1/A2 of RGGO2013, information concerning the origin and genetic composition must be supplied, see form Providing information new vector.
- For cells for which no ATCC number is known, relevant information by means of a publication must be supplied, see form Providing information new cell line.
- For genetically modified animals, information must be provided concerning how the animal was/is being produced. To this end, a description or publication must be supplied. This must make it clear how the construct was made and whether or not homologous recombination or a viral vector has been used.
- For special procedures, the VM/OL must supply a detailed description of the work.

Submitting a request to the IenW (GMO Office)

- The request is sent on behalf of the EB/BoD to the IenM (BGGO) and digitally archived in Corsa with the attachments.
- The GMO Office will assess the request. If necessary, the GMO Office will request additional information and/or submit a query to the EB/BoD if clarification is required. A copy of the response from the IenW will be sent to the BSO. Any questions and the decision of the GMO Office will also be digitally archived in Corsa.

When can work start?

- If a new notification (level I and II) or permit (level II and III) has been applied for, work may only start once the notification/permit has actually been received (approx. 45 days). N.B. The clock is stopped if additional information is requested. The BSO will answer any questions from the IenW in consultation with the OL, if necessary. The BSO will send the response to additional questions to the IenW via the secretariat.
- The GMO Office will ask additional questions a maximum of once. In the event of a persistent lack of clarity, the application will be considered not submitted and must be started again. As such, the submission and response must be carried out with care.
- If a level I notification needs to be changed and the category of physical containment remains unchanged, the BSO will add the new GMOs to the existing notification. The OL must supply all information to the BSO, who will document it.
- If a level II notification is changed, the work may commence as soon as the confirmation of receipt has been received (approx. 1-3 weeks). The GMO Office may, however, prescribe additional work

instructions or may, after the assessment (within 45 days), decide not to agree to the change. In the latter case, the work must be brought to a halt immediately and an improved change must be submitted.

- The same waiting time and procedure applies to a change from a level II or III permit as for a new application.
- Assessment of a 2.8 request takes 45 working days. The GMO Office may stop the clock once if there are questions about the request. The waiting period will then be suspended until additional information has been supplied. A 2.8 decision is always received from the GMO Office specifying the containment level and CFI at/in which the GMOs and work may be carried out. Once the 2.8 decision has been received, the work must still be notified; the work may commence as soon as this has been completed (in accordance with the aforementioned criteria). If a 2.8 combination request is used, a confirmation of receipt will also be received together with the 2.8 decision.
- The same waiting time and procedure applies to a 2.8 decision as for a new application.
- Assessment of an ATV request takes 8 weeks. The GMO Office may stop the clock once if there are questions about the request. The waiting period will then be suspended until additional information has been supplied. In the event of a positive decision from the GMO Office, alternative measures may be included in the notification; once this is complete, work may commence.

Communication with the GMO Office is through the BSO; as soon as the BSO has received a confirmation of receipt or decision, the BSO will amend the administration and inform the researcher of the containment level and the instructions and applicable conditions that apply to the commencement of the work.

Contained rooms

- An overview of all contained rooms is maintained in the central database by the BSO. An overview of the rooms and permitted work is forwarded to the WABO competent authority, the Maastricht local authority, once a year.
- The BSO will carry out an annual check to determine whether or not the contained rooms still satisfy the design requirements.
- If a CFI is to be assigned to a new room or an existing room is to be categorized up to a higher CFI, the room must first be approved by the BSO before the CFI is amended. It is, therefore, important that in the event of renovation, the BSO is involved with the plans promptly so as to ensure that the design requirements can be incorporated into the renovation.

Check of registered work

- The BSO draws up an annual inventory for each department of whether or not changes and additions were made to registered projects that had not yet been reported.
- The BSO can carry out a literature search to determine whether or not work was carried out with GMOs that has not been registered.
- The BSO will check DEC applications/work protocols and give formal approval when transgenic animals are requested, after checking the GMO permit. If the permit is incorrect, the VM/OL will be contacted.
- During audits or interim spot checks, the BSO will check whether or not the work carried out was registered on the notification/permit.

Central archiving

- The BSO archives sent notifications and related correspondence with the GMO Office and the VM/OL and notes from meetings with the VM/OL and other employees (including information concerning training and experience).
- All outgoing correspondence is digitally archived using Corsa.

Responsibilities

- Archiving department (FHML secretariat): archiving of correspondence between the competent authority and institutional board
- BSO: initiating, coordinating, supporting, and assessing statutory requirements relating to GMO work
- VM/OL: registering all work with GMOs with the BSO and complying with internal guidelines relating to GMO work
- Environmental advisor: submitting changes to WM permit

Abbreviations

ABV	Departmental Expert for Biosafety
BSO	Biosafety Officer
CFI	Category of physical containment
D-I	Animal enclosure class I
DEC	Animal Testing Committee
DM-I/II	Animal enclosure where GMOs are used, class I/II
EB/BoD	Executive Board/Board of Directors
GMO	Genetically Modified Organism
IenW	Ministry of Infrastructure and Water Management; executive body: GMO Office
ML-I/II	Microbiological Laboratory Class I/II
OL	Research leader
PC-I	Plant chamber, level I
PCM-I/II	Plant chamber where GMOs are used, class I/II
PKa/b-I	Greenhouse type a/b
PKM-I/II	Greenhouse where GMOs are used, class I/II
Ppm	Parts per million
RGGO13	Regulation on Genetically Modified Organisms, Environmental Management 2013
SMT	Safe microbiological techniques
VM	Responsible Investigator
WABO	Environmental Permitting (General Provisions) Act

References

- Decree and Regulation on Genetically Modified Organisms, Environmental Management 2013, IenW April 2014
- Occupational health and safety information sheet 9: biological agents. SDU publishers, The Hague, 6th edition, 2013
- Occupational health and safety information sheet 18: laboratories, SDU publishers, The Hague, 5th edition, 2010
- Website HSB Maastricht

Further information

For further information, please contact the BSO.