KAM rule 13, Biosafety

KAM-13-GMO (Genetically Modified Organisms)

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Rev.	Date	Description	Author	Approved by
3	March 31, 2022	Regular update, laws and regulations checked	Stichting-Alt	Management
2	January 9, 2019	Revision: KAM rule 13 split into three parts (GEN, GMO and non-GMO.)	Stichting-Alt	Management
1	01 July 2016	Version KAM rule 13 BA+GMO of BBio/NVI/RIVM of 2012.	Stichting-Alt	Management

Changes

page 4: the main differences in the latest version of the 'Regeling GGO' are indicated here: the distinction between levels II-k and II-v has been abolished and activities with lentiviral vector systems, which meet the new criteria in accordance with Annex 5 Part I and Part II, on AP-I, ML-I or DM-I scaled.
page 6: In table 1 letters of containment levels explained.
page 8: Replace II-k and II-v with II. Added 'For a number of deviating situations, a 2.8 request can be made to assign a containment level and a category of physical containment to intended activities with GMO.'
BLz.10: figure 2 adapted due to expired distinction II-k and II-v.
page 12: A table 'reports' has been added for the overview.
page 13: References, AI-9 and AI-18 can no longer be ordered as separate copies, there is only an online package with all AI sheets.Page.. : Better definition of terms

Introduction

The GMO laws and regulations distinguish between three work areas:

- **Contained Use** ('Ingeperkt gebruik', IG): GMO activities in areas with containment measures.
- **Introduction into the environment:** GMO activities outside a contained area, such as field trials and gene therapy.
- **Market requests**: GMO activities for admission to the European market.

This document (KAM-13-GMO) is restricted to regulations concerning the **contained use of GMO**. Rules concerning the **introduction into the environment** and **market requests** are not taken into consideration and can be consulted as such in the 'Besluit GGO' and the 'Regeling GGO' (see chapter: Laws and Regulations). The BSO is the first point of contact should introduction into the environment or market requests be concerned.

Purpose

The purpose of this document (KAM-13-GMO) is to promote safe working with GMO in contained areas in accordance with the applicable laws and regulations.

Responsibilities

For this, refer to the chapter Internal Organisation.

Laws and Regulations

Legal framework for GMO

In the Netherlands[1], the 'Besluit genetisch gemodificeerde organismen milieubeheer 2013' (hereafter: **Besluit GGO**) is applicable to **the creation of and activities with GMO** is applicable. The legally applicable version of the Besluit GGO can be found on: http://wetten.overheid.nl/BWBR0035090/

The 'Regeling genetisch gemodificeerde organismen milieubeheer 2013' (hereafter: **Regeling GGO**) is linked to the Besluit GGO. The legally applicable version of the Regeling GGO can be found on: http://wetten.overheid.nl/BWBR0035072/

The Besluit GGO and the Regeling GGO fall under the **'Wet milieubeheer'**. The 'Besluit GGO' gives a general description of the rules to be complied with when working with GMO. The 'Regeling GGO' is an elaboration on the Besluit GGO and contains many practical appendices. See Figure 1 for the mutual correlation.

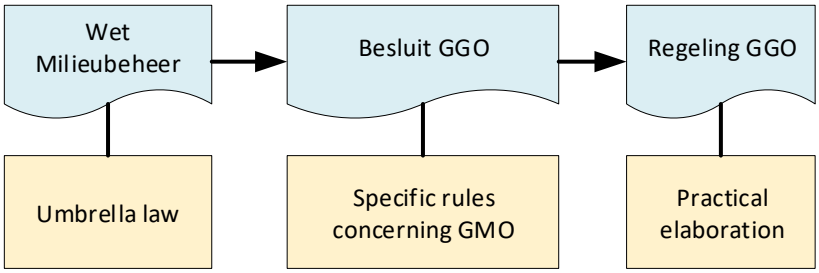

Figure 1. Legal framework for GMO.

The Dutch GMO legislation is an implementation of the **EU directive** 2009/41/EC 'inzake het ingeperkte gebruik van genetisch gemodificeerde micro-organismen'.

See KAM-13-GEN for any additional laws and regulations that may be applicable.

GMO definition in legislation

Article 1.1 of the 'Besluit GGO' states the definition of GMO:

> *An organism, with the exception of human beings, whose genetic material has been altered in a way that is not feasible by natural reproduction or natural recombination.*

Subsequently, the 'Besluit GGO' refers to appendices stating specific techniques with which organisms are obtained, which either **are** (appendix 1 of the 'Besluit GGO') or are **not** (appendix 2 of the 'Besluit GGO') designated as GMO.

It is recommended to carefully study the above definition and the appendices to the 'Besluit GGO' before concluding whether an organism is a GMO. The BSO can advise on this.

Government agencies concerned[2]

The 'competent authority' for GMO is the Ministry of 'Infrastructuur en Waterstaat' (I&W). The monitoring task is exercised by the 'Inspectie Leefomgeving en Transport' (ILT) and by the

[1] Dutch names are used for Dutch laws and regulations, as there are no official English translations available.
[2] Dutch names are used for Dutch ministries and competent authorities.

'Wabo'-competent authority in connection with the environmental permit. Important executive and/or advisory bodies are the 'Bureau GGO' and The Netherlands Commission on Genetic Modification (COGEM).

The '**Inspectie Leefomgeving en Transport' (ILT**, website: www.ilent.nl) monitors compliance with the 'Besluit GGO' and the 'Regeling GGO' and the associated notifications and permits. In practice, this concerns monitoring the use of GMO in laboratories and other work areas (contained use). The monitoring carried out by the 'Wabo' competent authority concerns the design specifications for the work areas.

The **'Bureau GGO'** (website: www.ggo-vergunningverlening.nl) is part of the RIVM and performs a number of GMO-related tasks at the request of the Ministry of I&W:

- Assessing notifications and granting of permits for GMO activities with contained use.
- Point of contact for all parties concerned with activities involving GMO.
- Supporting the Ministry of I&W in its policy.
- Promoting the connection between policy/regulations and feedback from the field.
- Providing information and organising training courses for BSOs.

The **Netherlands Commission on Genetic Modification** (**COGEM**, website: www.cogem.net) advises the government on the environmental risk aspects of GMO and identifies ethical and social aspects of genetic modification. The tasks of the COGEM are laid down in the 'Wet milieubeheer'.

'Regeling GGO 2013'

The current version (January 2022) of the 'Regeling GGO 2013' differs fundamentally from the previous version of January 2019. The main changes are:

- No longer a permit obligation for level II activities.
- Activities with lentiviral vector systems, which meet the new criteria in accordance with Appendix 5, part I and part II, are classified as AP-I, ML-I or DM-I.

The 'Regeling GGO' is subject to change. The BVF/BSO can provide more information about the current regulation.

Risk categories and containment levels

Risk categories

The 'Regeling GGO' categorises microorganisms into (hazard) categories 1 to 4 inclusive, on grounds of the **risk for humans, animals, plants or the environment**. The descriptions of these categories are similar to those of the BA risk categories in the 'Arbowet', which only takes into account the **risk for the employee**. The following risk category descriptions have been copied from the 'Regeling GGO'.

Category 1: a microorganism that at least complies with one of the following conditions:

a. the microorganism does not belong to a type for which representatives are known to be pathogenic for humans, animals or plants.
b. the microorganism has a long history of safe use under conditions for which no special containment measures are taken.
c. the microorganism belongs to a species that contains representatives of category 2, 3 or 4, but the specific strain contains no genetic material that is responsible for virulence.
d. the non-virulent character of the microorganism has been demonstrated by means of adequate tests.

Category 2: a microorganism that can cause a disease in humans or animals, which is unlikely to spread among the population, and for which an effective prophylaxis, treatment or disease control is available, as well as an organism that can cause a disease in plants.

Category 3: a microorganism that can cause a serious disease in humans or animals, which is likely to spread among the population, and for which an effective prophylaxis, treatment or disease control is available.

Category 4: a microorganism that can cause an extremely serious disease in humans or animals, which is likely to spread among the population, and for which no effective prophylaxis, treatment or disease control is available.

The legally applicable categorisation of micro-organisms into categories 2, 3 and 4 which are used for the construction of GMO can only be found in **appendix 4 of the 'Regeling GGO'**. A micro-organism that is not listed in this Annex (and is also not listed in Annex 2 of the 'Regeling GGO') is in principle unclassified and cannot be used for genetic modification: a classification decision must be made first. See also the corresponding chapter in KAM-13 non-GMO.

Classification

Appendix 5 of the 'Regeling GGO' contains guidelines for classification of GMO activities. The classification is partly determined by:

1. The classification of the **host** (microorganism) in one of the risk categories.
2. The nature of the **vector** to be used for inserting a genetic element into the host.
3. The nature of the **insertion**.
4. The nature of the intended **activities** (for example: Can aerosols occur?).
5. The **scale** of the intended activities.

If **appendix 5 of the 'Regeling GGO'** does not suffice, e.g. because there are deviating circumstances or special activities, then an adequate risk assessmentis essential. **Appendix 8 of the 'Regeling GGO'** describes how to carry out an adequate risk assessment. See also the chapter on Notifications and permits.

Containment levels

A specific system for activities with GMO is used in The Netherlands, which is unknown outside the country. Roman numerals I to IV inclusive are used for indication of the containment levels, in combination with letters that indicate the type of activities. Table 1 shows the most relevant indications for the USPB. A complete overview can be found in **Appendix 9 of the 'Regeling GGO'**, which also states the minimum statutory design specifications for all containment levels.

Containment level	Description
ML-I, ML-II, ML-III	Laboratories for activities with genetically modified microorganisms (M for micro-organism; L for laboratories).
D-I	Animal enclosure for genetically modified animals (D for animal).
DM-I, DM-II, DM-III	Animal enclosures in which animals are combined with genetically modified micro-organisms (D for animal; M for micro-organism).
MI-I, MI-II, MI-III	Process installations in which genetically modified microorganisms are applied (I for industrial, process installation > 100 liter).
AP-I	Equipment space.
ODG	Other part of GMO area.

Table 1. Principal indications for containment levels from the 'Regeling GGO'. Level IV has been omitted because it does not occur at the USPB.

Combined area (ML/BSL)

For microbiological laboratories, the control measures for ML-I, ML-II and ML-III are comparable with those for the international indications BSL-1, BSL-2 and BSL-3, which are commonly used for non genetically modified BA.

For work areas where work is done with both non genetically modified BA and GMO, the requirements from the Regeling GGO for that level must be followed. For such work areas, it is better to use the designation from the Regeling GGO (e.g. ML-II), or if preferred, a combination (e.g. ML-II / BSL-2). In this example, the requirements for ML-II are leading.

An indication is required on the door of the GMO work area with at least the following elements:

- The containment level of the area (the minimum legal requirements are described in **appendix 9 of the 'Regeling GGO'**).
- The biohazard symbol (not legally required for level I).
- The names and telephone numbers of at least one person responsible for the area and of the BSO.

Control measures

The purpose of the control measures is to prevent the chance of spreading the GMO in order to limit as much as possible the risk of genetic modification for the environment and for employees. Three types of control measures are taken to minimise this chance of spread:

- **Biological containment**: The use of safe host organisms and vectors, in other words, host organisms and vectors with special characteristics that limit survival and spread in the environment. For this, see **appendix 2 of the 'Regeling GGO'**.

- **Physical containment**: Activities with GMO may only be performed in closed spaces (laboratories, animal enclosures, production areas etc.), which are designated for the purpose and have special facilities and for which the equipment present has to meet certain requirements. These minimum legal requirements are described in **appendix 9 of the 'Regeling GGO'** and it is referred to in Appendix 5 of KAM rule 13.

- **Safe work procedures**: The application of work procedures, using 'good microbiological practice' as a minimum, which limits the spread of GMO. See also the chapter Work procedures.

Internal organisation

For working with GMO, the law distinguishes three actors in the organisation with responsibilities, tasks and competences regarding biosafety:

1. **'Gebruiker':** According to the 'Besluit GGO', the 'User' (formerly permit holder) is the natural or legal person who is responsible for the contained use of GMO. This is the top management of the organisation in question, and has final responsibility for all GMO activities within the organisation.

2. **BSO (Dutch: 'BVF'):** The User appoints one or more biosafety officers (BSOs) who are authorised by the Minister. The tasks and responsibilities of the BSO are stated in Appendix 6 of this KAM rule.

3. **'Onderzoeksleider' (OL) and 'Verantwoordelijk medewerker' (VM):** According to article 8 of the 'Regeling GGO', the User provides for the appointment of:
    a. one or more 'Onderzoeksleiders' (OL) for each distinct group of activities for which notification has been made, or
    b. one or more 'Verantwoordelijk medewerkers' (VM) for each distinct group of activities for which a permit has been granted.

    The OL or the VM has daily supervision of the GMO activities and draws up internal work procedures and safety regulations that are assessed and approved by the BSO. If necessary, the User arranges the further distribution of tasks and responsibilities between the BSO, the OL and the VM.

4. **'Uitvoerend medewerker'**: Employees who carry out activities with GMO, or who monitor them within a group of activities, know the applicable KAM rules and room-specific procedures. They have followed relevant training (assessed by the BSO) that is appropriate for the work that needs to be done. If necessary, these employees are given additional training and support.

Notifications, permits, and commencement of activities

The organisation where GMO work is to be done, will first carry out its own **risk assessment** to define which containment level (I, II, III or IV) and which physical containment category are applicable to the activities. In principle, this is the task of the OL and/or the VM, but the BSO can provide support.

Appendix 5 of the 'Regeling GGO' can be followed for the **standard risk assessment**. If the GMO does not fit in with the rules of appendix 5 of the 'Regeling GGO', or if the applicant is of the opinion that the risk assessment according to **appendix 5 of the 'Regeling GGO'** will not result in the correct classification, then a risk assessment according to **appendix 8 of the 'Regeling GGO'** must be carried out. For a number of deviating situations, a 2.8 request can be made to assign a containment level and a category of physical containment to intended activities with GMO. Moreover, exemption can be requested by means of an Alternative design or workprocedure request ('ATV verzoek') if the design specifications laid down in **appendix 9 of the 'Regeling GGO'** cannot be met (e.g. presence of BHK in ML-II microscope room). The 'Bureau GGO' website offers tools for risk assessment, such as the Risk Assessment Tool and a breakdown of **appendix 5 of the 'Regeling GGO'** into flowcharts[3].

The BSO assesses the risk assessment report. On the basis of the containment level, the BSO determines which procedure should be followed for requesting GMO activities with the 'Bureau GGO'. The **notification procedure** is applicable to levels I and II, and the **permit procedure** is applicable to levels III and IV.

All notifications and permit requests are made **by the OL or VM**, based on the current versions of the forms, which can be found on:
http://www.ggo-vergunningverlening.nl/Ingeperkt_gebruik/IG_downloads.
The **BSO** assesses and signs the form and submits it to 'Bureau GGO'.

'Bureau GGO' sends a **confirmation of receipt** for notifications. In some cases (see the 'Bureau GGO' website), an extended period applies before the activities may commence. A notification may be followed by a decision containing **additional requirements**.

With a permit request, the activities may commence after **receiving the permit**. The permit may contain additional requirements.

The BSO also grants **Internal Permission** (for example by using the example forms Appendix 8 and Appendix 9 of this KAM rule for requesting Internal Permission or for granting Internal Permission for GMO work).

The flowchart in Figure 2 summarises the above, both for new GMO activities and for changes in existing GMO activities.

[3]Risk assessment tool of 'Bureau GGO' see: http://www.ggo-vergunningverlening.nl/Ingeperkt_gebruik/Risicobeoordeling/Hulpmiddelen_bij_de_risicobeoordeling

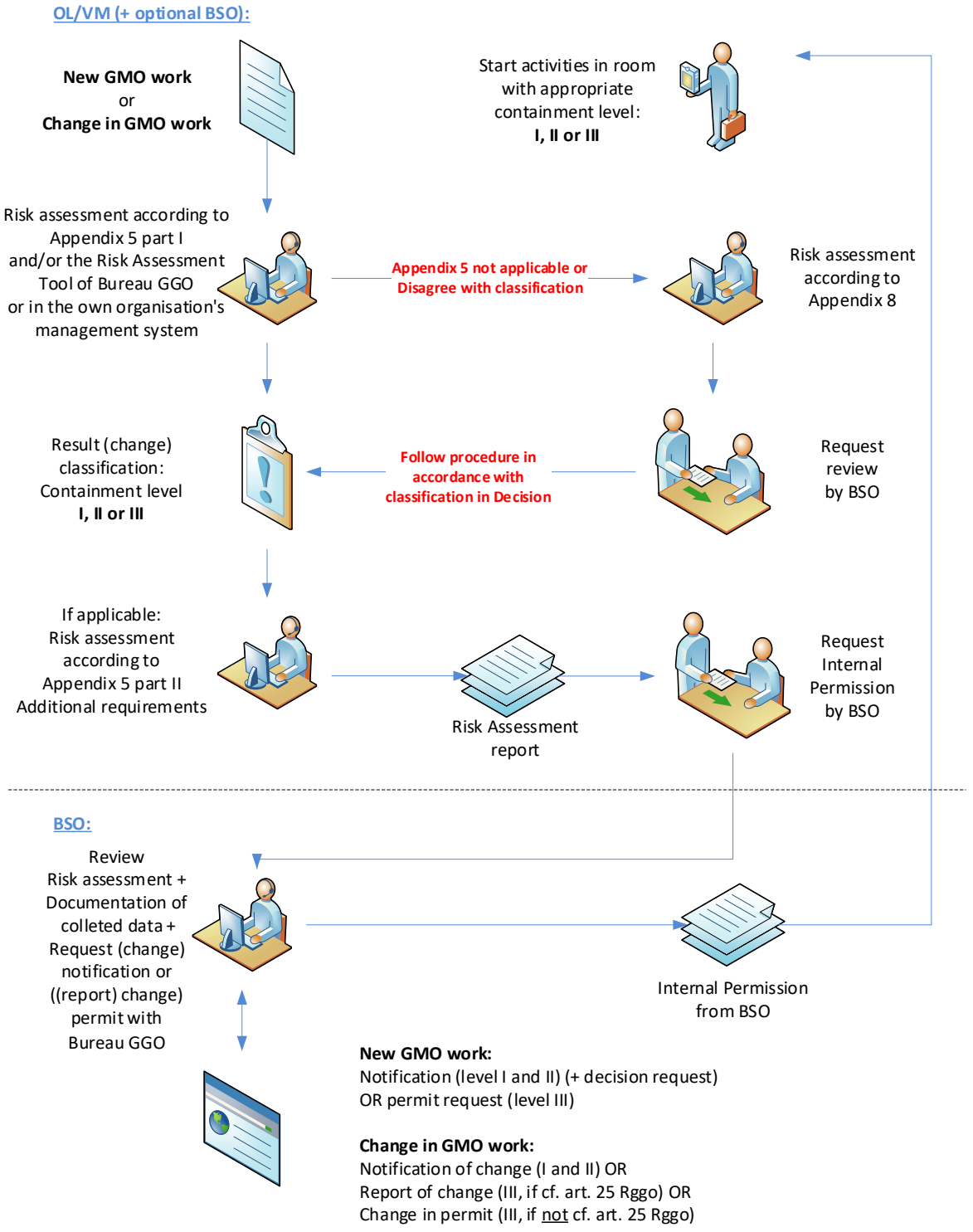

Figure 2. Flowchart for obtaining Internal Permission for new or changed GMO work.

Either the OL or the VM also assesses whether the following conditions have been met:

- The work area where the activities will be carried out complies with the **design requirements** laid down for that level. For level ML-III, this verification is carried out together with the BSO.
- The employees who will carry out the activities have sufficient **preliminary and additional training, experience and expertise**. This is assessed by the BSO, see the example form for verifying the professional competence in Appendix 7 of this KAM rule.
- There is no increased risk for any **other employees** who carry out other activities in the same work area.
- The **line management** has been **informed** about and has **agreed** with the intended activities.
- The **BSO** has not set any **additional requirements**.
- All employees have adequate protection or received vaccinations in line with the vaccination policy applicable at the USPB (available through your own organisation).

If necessary, the employee in question collects additional information, requests expert advice (internally or externally), or requests or draws up a safety data sheet.

The activities may commence once all conditions have been met.

Work procedures

Legally required work procedures

Appendix 9 of the Regeling GGO states the minimum legally required work procedures. For many levels, these are subdivided into:

- General
- During activities
- Terminating activities
- Waste and contaminated material
- Other

Moreover, **appendix 9 of the 'Regeling GGO'** states **additional instructions for specific cases** for a number of levels, e.g. for activities with:

- A bioreactor or FACS equipment
- Certain organisms or strains
- Organisms or strains with certain characteristics

Other work instructions

For this, see KAM-13-GEN and work procedures and instructions of the own organisation.

Accidents and incidents

For examples of accidents and incidents, see KAM-13-GEN.

Procedures regarding GMO

According to the 'Regeling GGO', the User draws up procedures for:

- The immediate internal notification to the BSO of deviations from the legal requirements and the internal procedures.
- The immediate notification to the Minister of all situations in which a serious risk for humans and the environment may arise.

Essential notifications concerning GMO

Notifications are absolutely necessary after:

- Accidents and incidents with GMO must always be reported to the BSO of the own organisation and internally registered.
- Accidents and incidents with a GMO classified at levels 2 or 3 must also be reported to line management and the OR of the organisation in question.
- Accidents and incidents with a GMO classified at level 3 must also be reported to ILT through the BSO.
- Incidents with GMO of all categories where the GMO has been released outside the secondary containment must be reported to the ILT through the BSO.
- (near) incidents with GMOs must always be reported to Stichting-ALt and possibly via the Stichting to the Wabo competent authority.
- KAM rule 15m 'Reporting (near) environmental incidents' describes the procedure regarding reporting and handling (near) environmental incidents to the Stichting-ALt.

Category	Type	Containment level	Internal report to BSO	Report to ILT through BSO	Report to Stichting-ALt	Line management and 'OR'
A	small-scale contamination	I, II and III	X		X	
B	difficult to control contamination	I and II	X		X	Only II
B	difficult to control contamination	III	X	X	X	X
C	(potential) impairment of the barrier of the room	I, II and III	X	X	X	X
D	release of GMO into the environment	I, II and III	X	X	X	X

Table for reports of incidents involving GMOs (source: 'Bureau GGO, melding incidenten ingeperkt gebruik'). Last 2 columns added specific for KAM13.

Follow-up

For this, see KAM-13-GEN.

Administration and reports

According to article 10 of the 'Regeling GGO', the User (management) must provide for an **accessible administration in one place within the establishment**, containing at least (shortened representation of article 10):

- The written appointments, indications, authorities, instructions, procedures and requirements.
- A list of the **notifications** that have been made, stating the OL per notification.
- A list of **permits** issued to the User, stating the VM per permit or permit part.
- A list of notifications and permits that are no longer used.
- An clear overview of the locations where the **risk assessment** reports are kept.
- An **up to date map** of the establishment showing, insofar as is present, the following:
    - The GMO area, including ODG and the rooms where activities with GMO may be carried out, stating the physical containment category and the containment level.
    - Storage locations of GMO and GMO waste and the storage method.
- Results of periodic **inventory** of the organisation units that carry out GMO activities.
- Data, stating the date, regarding:
    - The execution of **internal inspections**.
    - **Incidents**, accidents and deviations from the applicable rules.
    - **Evaluations** and their reports.

For larger organisations, it is obvious that the responsibility for delivering the required data lies with the departments. As the above data must be accessible in one location, it is obvious that the BSO plays a key role in this. The organisations decide in detail how this is arranged.

The 'Gebruiker' (management) also provides for maintaining **detailed up to date data on site** concerning the GMO present and the employees who carry out activities with GMO. See article 10 of the 'Regeling GGO' for the data that is to be made available. The departments within the organisation are responsible for collecting and updating the data. The BSO ensures that this is done correctly.

Monitoring, inspections and enforcement

See KAM-13-GEN for general aspects on this topic. The rules concerning GMO stated below are also followed for non-GMO of category 3.

Internal monitoring

The **OL or VM** has **daily supervision** of the activities with GMO within his or her field of activity. The **BSO** visits the OL or VM on a regular basis. If necessary, the BSO inspects the work areas that are being used together with the OL or VM. The BSO can always carry out an unannounced inspection. The management has final responsibility for the adequate internal monitoring of all GMO activities.

Inspection reports are drawn up of all internal inspections, stating any shortcomings and recommendations. The report is shared and discussed with those concerned. If there are **serious deviations or if there is a significant risk** of exposure, the BSO informs the line management and the top management of this. If there is an **acute hazard**, the BSO is entitled to stop the activities, after which consultations will be held with the line management and the top management, and if necessary a report will be made to the Inspectorate.

If a **new work area** is to be taken into use for GMO activities, then the BSO must inspect it beforehand. A report is also made of this inspection. The risks may change due to changes in the organisation (a relocation, change in activities, change in applied GMOs etc.), and this may result in adjusting the control measures. The BSO must be engaged for advice.

Monitoring and enforcement by the government

On behalf of the Minister, the **ILT** monitors the implementation of the **GMO laws and regulations** (’Besluit GGO’ and ’Regeling GGO’). For contained use, this means among other things that verification is done as to whether the activities have been licenced or notified and that they take place in accordance with the correct work procedures and inside the right work areas. Random inspections are made as to whether the GMOs described in publications have been notified or licenced. The ILT may also check whether periodic internal inspections have taken place and whether the administration is complete and up to date.

Stichting-Alt manages the '**milieuvergunning op hoofdzaken'** (VoH) and is the discussion partner for the relevant monitoring authority (which primarily concerns the work areas and design specifications and not activities with GMOs). The VoH applies to all organisations at the USPB. Stichting-ALt performs inspections within the framework of the VoH on a regular basis. If the topic GMO is on the agenda, then the inspection will take place in proper consultation with the persons concerned.

End of activities

If all GMO activities that fall within a specific notification or permit have ended (and the relevant specific GMOs have been destroyed), then this must be reported to the line management and the BSO. The BSO reports this to 'Bureau GGO'.

If a work area is no longer used for GMO activities, or if it will be used for other GMO activities, then this must be reported to the line management and the BSO, and also to Stichting-ALt.

All changes will be processed in the internal administration.

Guide to the appendices with the 'Regeling GGO'

The 'Regeling GGO' contains a number of appendices containing practical information. KAM rule 13 contains a number of detailed rules and requirements. Moreover, the organisations at the USPB are responsible for more elaborately detailed local or room-specific work procedures. In some cases, it is essential or useful to fall back on the appendices in the 'Regeling GGO'. The appendices in the 'Regeling GGO' are numbered, but they have no title or description. To help find the right appendix quickly, a list is given below of all the numbered **appendices in the 'Regeling GGO'** with a brief description of the contents of the appendix.

1. Transfer and transport of GMO.
2. Combinations of lists (host organisms, vectors, insertions).
3. (reserved)
4. Classification of pathogenic microorganisms in categories.
5. Classification of activities with GMO.
6. Article 2.8 criteria for down scaling GMO activities.
7. List of GMO plants that reach the flowering stage and do not contain any harmful genetic information.
8. Risk assessment in accordance with the basic principles of a risk assessment.
9. Requirements connected with the categories of physical containment and the ODG.
10. Requirements for activities with GMO with a permit under fixed requirements.
11. Table with GMO for classification in category S-I.
12. Correlation tables for naming in decrees.

Abbreviations and terminology

Where possible, the abbreviations and terminology have been taken from the 'Regeling GGO'.

Abbreviations	
BA	Biological agent(s)
BSO	Biosafety officer
BVF	Biologische veiligheidsfunctionaris
COGEM	The Netherlands Commission on Genetic Modification
GMO	Genetically modified organism(s)
ILT	Inspectie Leefomgeving en Transport
IvD	Instantie voor dierenwelzijn (Animal Welfare Body)
I&W	(Ministry of) Infrastructuur en Waterstaat
KeW	Kernenergiewet
KNVM	Koninklijke Nederlandse Vereniging voor Microbiologie
OL	Onderzoeksleider
OR	Ondernemingsraad
RI&E	Risk inventory and evaluation
Stichting-ALt	Stichting Antonie van Leeuwenhoek terrein
USPB	Utrecht Science Park Bilthoven
VM	Verantwoordelijk medewerker
VoH	Vergunning op Hoofdzaken

Terminology	
Biological agents ('Arbobesluit')	Microorganisms, cell cultures and human endoparasites, *whether or not genetically modified*, which can cause an infection, allergy or toxicity[4].
User	Natural person or legal person responsible for the contained use of genetically modified organisms, including the person who intends to carry out the contained use and who will be responsible for that contained use.
Genetic modification	An alteration in genetic material in a way that is not possible by natural reproduction or natural recombination.
Genetically modified organism	An organism, with the exception of human beings, whose genetic material has been altered in a way that is not possible by natural reproduction or natural recombination (*the 'Besluit GGO' refers to appendices stating specific techniques by which organisms are obtained, which either **are** (appendix 1 of the 'Besluit GGO') or are **not** (appendix 2 of the 'Besluit GGO') designated as GMO*).
Onderzoeksleider	person **designated** by the user, in charge of the day-to-day management of each distinct group of notified activities (levels I and II) and in charge of drawing up work protocols ('Regeling GGO' article 8, section 1, under a).
Pathogenic	Causing disease.

[4] According to the 'Arbobesluit', the term Biological Agents also includes substances or structures originating from living or dead organisms (e.g. toxins), as well as prions. The question is whether there is a harmful or adverse effect on humans.

Pathogen	A micro-organism that can cause disease.
Pathogenicity	The property of causing disease.
Prophylaxis	Preventive measure (e.g. vaccination).
Site	Site of the Antonie van Leeuwenhoeklaan 9-13 in Bilthoven, known as the USPB.
Verantwoordelijk medewerker	person **designated** by the user, charged with the day-to-day management of each distinct group of activities for which a permit has been granted and charged with drawing up work protocols ('Regeling GGO' article 8, section 1, under b).
Permit holder	See User.

References

- Arbo-besluit, http://wetten.overheid.nl/BWBR0008498/
- Arbo Informatieblad 09 'Biologische Agentia', only available in an online package with all AI sheets Arbo Informatieblad 18 'Laboratoria', only available in an online package with all AI sheets
- Besluit genetisch gemodificeerde organismen milieubeheer 2013 (Besluit GGO 2013), http://wetten.overheid.nl/BWBR0035090/
- Regeling genetisch gemodificeerde organismen milieubeheer 2013 (Regeling GGO 2013), http://wetten.overheid.nl/BWBR0035072/
- EU richtlijn 2009/41/EG inzake het ingeperkte gebruik van genetisch gemodificeerde micro-organismen, https://eur-lex.europa.eu/legal-content/NL/TXT/?uri=CELEX%3A32000L0054
- EU richtlijn 2001/18/EG inzake de doelbewuste introductie van genetisch gemodificeerde organismen in het milieu, http://eur-lex.europa.eu/legal-content/NL/TXT/?uri=CELEX:32001L0018&qid=1501681605298
- KNVM richtlijn "Veilig werken met micro-organismen, parasieten, en cellen in laboratoria en andere werkruimten"
- KAM-rules Stichting ALt, https://stichting-alt.nl/kam-regels/ :
    - KAM rule 07 Disposal of (hazardous) waste
    - KAM rule 08 Waste from (micro) biological laboratories
    - KAM rule 13 Biosafety: KAM-13-GEN and KAM-13-non-GMO
    - KAM rule 15m Reporting (near) environmental incidents
    - KAM rule 16 Risk statement
    - KAM rule 17 Cadavers and bedding
    - KAM rule 20 Access to lab and production areas
- ISO 14001 Environmental management systems
- ISO 35001:2019 (before CWA 15793) Laboratory Biorisk Management

List of appendices with KAM-13

Appendix 1: Transport of biological materials and other additional laws and regulations
Appendix 2: Basic rules for safe working in microbiological work areas (maximum risk category 2)
Appendix 3: Sequence and examples of control measures
Appendix 4: Design specifications for containment level 2 according to the 'Arbobesluit'
Appendix 5: Minimum statutory design specifications and work procedures for BSL-3 and GMO's activities.
Appendix 6: Tasks and authorisations of the BSO

Bijlage 7: Voorbeeld formulier voor interne toetsing van de vakbekwaamheid van medewerkers (Example form for internal verification of the employees' professional competency
Bijlage 8: Voorbeeld formulier aanvraag interne toestemming GGO-werk (Example form for an application for internal permission for GMO work)
Bijlage 9: Voorbeeld formulier interne toestemming GGO-werk (Example form for internal permission for GMO work)
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