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Milieuvergunning USPB
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KAM rule 13, Biosafety

KAM-13 non-GMO (Biological agents that are not genetically modified)

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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	Total 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: added 'In the Environmental Permit (VoH) activities with BA risk category 4 are not permitted, these activities are not allowed at the USPB.'
page 5: Under Comments for clarification, bullet added 'By 'before' (at bullet 2, 3 and 4) is meant: at least 30 days before the start of the work. With a subsequent notification, it is sufficient to provide only the new data.'
page 5: Text modified at category 4 'activity is not permitted, so this work is not allowed at the USPB.
page 6: BA category 4 removed from figure 1.

Introduction

When performing activities with *non genetically modified* biological agents, the 'Arbowet' is applicable and the GMO legislation can be left out of consideration. In that case, this document (KAM-13 non-GMO) will suffice alongside KAM-13-GEN. If *genetically modified* biological agents are concerned, then KAM-13-GMO is applicable. If necessary, use the general part KAM-13-GEN to determine which part is applicable.

Purpose
The purpose of this document (KAM-13 non-GMO) is to promote safe working with *non* genetically modified BA in accordance with the applicable laws and regulations.

Responsibilities
For this, refer to the chapter Internal Organisation.

Laws and regulations

In the Netherlands, on grounds of the 'Arbowet', **activities with BA** are subject to the 'Arbobesluit', which makes no distinction as to *whether or not* BA are *genetically modified*. The 'Arbobesluit' regarding BA focuses on the protection of the employee against undesirable exposure to human pathogens. Practical information can be found in the 'Arbo Informatieblad AI-09 Biologische Agentia'.

The 'Arbo' legislation with regard to biological agents is an elaboration of the EU directive 2000/54/EC 'on the protection of workers from risks related to exposure to biological agents at work'.

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

Risk categories and containment levels

Risk categories

The risk category of a BA is determined by the pathogenicity (the property of causing disease) of the BA, the chance of spread of the BA among the population and the availability of prophylaxis or treatment. There is a (very) great risk with a (very) serious disease, a (very) contagious pathogen, and/or if some form of prophylaxis or treatment is not available. The risk categories are described below (source: AI 09 'Biological Agents').

Category 1: An agent that is unlikely to cause disease in humans.

Category 2: An agent that can cause a disease in humans and can pose a hazard to the safety and health of employees, but which is unlikely to spread among the population, and for which an effective prophylaxis or treatment is available.

Category 3: An agent that can cause a serious disease in humans and can pose a significant hazard to the safety and health of employees and which can spread among the population, and for which usually an effective prophylaxis or treatment is available.

Category 4: An agent that causes a serious disease in humans and poses a significant hazard to the safety and health of employees and which is very likely to spread among the population, and for which usually no effective prophylaxis or treatment is available.

Table 1 shows a simplified representation of the above descriptions.

Category	Pathogenicity	Chance of spread	Prophylaxis/treatment
1	very small	-	N/A
2	present	-	+
3	great	+	+
4	very great	+	-

Table 1. Simplified representation of the risk categories (taken from AI-09).

Remarks on the above categorisation:

- Category 1 actually falls outside the scope of the 'Arbowet', as there is no real risk (see however the following remark).
- The estimation of the risk concerns healthy employees and *may be different for vulnerable individuals*. Consider in this respect e.g. individuals who are pregnant, the elderly or immunocompromised individuals. In this case, consult with the BSO or company doctor.
- The above categorisation primarily concerns the *infectious* risks as a consequence of professional exposure. Toxins and allergens originating from microorganisms fit less well into this categorisation. When working directly with toxins, there is no spread through infection but there is a 'Arbo' risk comparable to a harmful chemical substances risk.

The legally applicable categorisation of microorganisms into category 2, 3 or 4 can be found in **appendix III of the EC Directive 2000/54/EC**. However, this list has no longer been updated since its publication in 2000.

The categorisation of microorganisms in risk categories may be subject to change. Also in **Appendix 4 of the 'Regeling GGO'** there is a list with the classification of microorganisms which is updated regularly. Remarks with the category lists:

- If the categorisation of a BA in one of the lists deviates from the legally applicable EC-categorisation, then the BSO must be consulted.
- The category lists have limitations.
    - EU 2000/54/EC prescribes classifications based on definitions and provides a list of classified biological agents. This list only shows pathogenic micro-organisms that are classified in category 2, 3 and 4. A micro-organism that does not appear on this list is not by definition unclassified and is not automatically category 1, and therefore not necessarily harmless. The 'Arbo wet' provides for the application of the imposed definitions for determining the category of unknown BA, but those definitions are not 'watertight'.
    - The list in Appendix 4 of the 'Regeling GGO' only shows pathogenic micro-organisms classified for GMO work that are classified in categories 2, 3 and 4. A micro-organism that does not appear on this list (nor is it mentioned on Appendix 2 of the 'Regeling GGO') is by definition unclassified and cannot be used for genetic modification: a classification decision must be made first.
- Classification lists from other countries may differ in details. In some cases, specific pathogenic micro-organisms may have been put in a different category, for example, country-specific measures such as vaccinations or a ban on working with a specific pathogenic micro-organism.
- If in doubt, consult the BSO

A great deal of useful information for individual pathogenic microorganisms can be found on the Public Health Agency of Canada website[1]. Although this information has no legal basis in Europe, the information is certainly useful for estimating the risk and for implementing control measures.

Containment levels

The starting point for determining the containment level is the classification of the used organism into one of the risk categories (point 1 below). However, for an adequate classification, a risk inventory and evaluation (RI&E) is required, which can for example result in a lower estimate for an attenuated strain (point 2 below), or a higher estimate with high-risk or large-scale actions (points 3 and 4 below). Thus the containment level is partly defined by:

1. The classification of the specific micro-organism into one of the risk categories.
2. Whether the strain of the micro-organism used has been attenuated, so that the pathogenicity, or contagiousness, is strongly reduced (with the exception of Polio virus).
3. The nature of the intended activities (e.g. can aerosols occur?).
4. The scale of the intended activities.

For activities with BA that are not genetically modified, the international designation for containment levels is often used: Biosafety Level (BSL). The different levels are designated BSL-1, BSL-2, BSL-3 and BSL-4 respectively.

The minimum legal design specifications and work procedures for level 2 are stated in Appendix 4 of this KAM rule.

[1] See http://www.phac-aspc.gc.ca/id-mi/index-eng.php

When working with *non* genetically modified BA of risk category 3, at the USPB they have agreed to follow the minimum legal design specifications and work procedures for ML-III according to the 'Regeling GGO', see KAM-13-GEN and Appendix 5 of this KAM rule.

In the Environmental Permit (VoH), activities with BA of risk category 4 are not permitted, these are not allowed at the USPB.

When working with GMO in the same room, the GMO legislation is leading. For this, see KAM-13-GMO. This applies to all risk levels.

Internal organisation

In general, there are three actors in the organisation with responsibilities, tasks and competences regarding biosafety:

1. **CEO and line management:** According to the 'Arbobesluit', the management is responsible for Occupational Health and Safety. The CEO has ultimate responsibility for Occupational Health and Safety. This is also described in KAM-13-GEN.

2. **BSO/BVF:** The management appoints one or more biosafety officers. The tasks and responsibilities of the BSO/BVF are stated in Appendix 6 of this KAM rule.

3. **Employees:** For this, see KAM-13-GEN.

Notifications and commencement of activities

The following situations require a (renewed) notification to be made to the 'Nederlandse Arbeidsinspectie' before starting with (adjusted) activities with BA (*the text below with five bullets has been copied (and subsequently translated) from the '*Nederlandse Arbeidsinspectie*'*):

- When working with one or more biological agents of category 2, 3 or 4, *or* when this only concerns diagnostic work and no notification has been made previously.
- Before working with one or more biological agents of category 2, 3 or 4 for the first time.
- Also, each time before working with a subsequent category 4 biological agent and each time before working with a subsequent category 3 biological agent if you have provisionally categorised this agent yourself.
- Before working with biological agents for the first time, if this only concerns diagnostic work.
- If fundamental changes have taken place in the processes or procedures that may have consequences for the safety and health of the employees, as a result of which an earlier notification has become obsolete.

Remarks to clarify the above text:

- 'By 'before' (at bullet 2, 3 and 4) is meant: at least 30 days before the start of the work. With a subsequent notification, it is sufficient to provide only the new data'
- The phrase '*a subsequent biological agent*' (third bullet above) means a different species. If in doubt, consult the BSO.
- Explanation per category:
    - For **category 2**, a one-time notification is sufficient for all of the subsequent category 2 agents.

  - For **category 3**, a one-off notification is sufficient for all of the subsequent category 3 agents if the new agents are specifically stated under category 3 in the legally applicable list. If in doubt, consult the BSO. A new notification may be required.
  - For **category 4**, activity is not permitted, this work is not allowed on the USPB.
- All changes in the work (i.e. the room, equipment, employees, procedures or quantities) that are relevant to the RI&E may be a reason for making a renewed notification. If in doubt, consult the BSO.

A one-off notification is sufficient for exclusively diagnostic work. The flowchart in Figure 1 shows whether a new notification is required for non-diagnostic work, assuming that a notification has already been made for another BA of category 2 or 3.

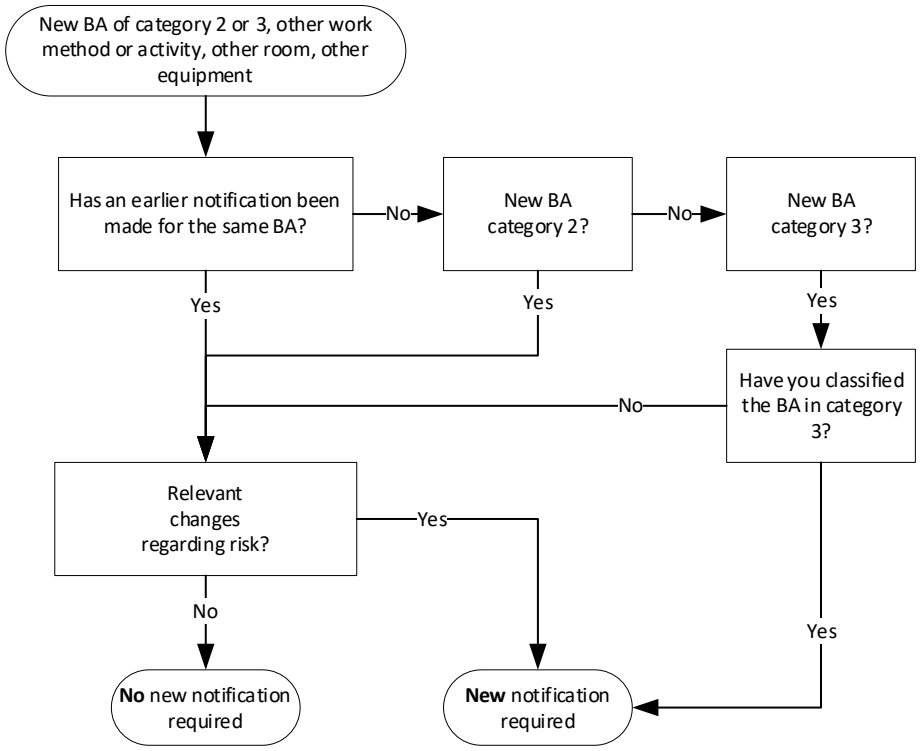

Figure 1. Flowchart for making a notification to the 'Nederlandse Arbeidsinspectie' for non-diagnostic work, assuming that a notification has already been made for another BA of category 2 or 3.

The BSO makes a notification using the 'Kennisgevingsformulier biologische agentia' on the website van de Nederlandse Arbeidsinspectie.

The work may not be commenced for a period of 30 days after the notification has been submitted to the 'Nederlandse Arbeidsinspectie'. Within this period, the 'Nederlandse Arbeidsinspectie'may object or specify additional control measures. However, the responsible researcher must always carry out his own risk assessment.

The responsible researcher (in consultation with the line manager and BSO) also assesses whether the following conditions have been met:

- The work area where the activities will be carried out complies with the minimum legal **design requirements** (see appendix 4 of this KAM rule).
- The employees who will carry out the activities have sufficient **preliminary and additional training, experience and expertise**. Level 3 requires agreement from the BSO.
- There is no increased risk for **other employees** who are working in the same area on another project or with another agent.
- The **line management is aware** of the intended activities and has **given permission** to the BSO to make a notification.
- The **activities and the risk assessment have been discussed with the BSO** and he/she has given approval.
- The employees concerned are adequately protected (see the **vaccination policy of the organisation**).

If necessary, the responsible researcher collects additional information, requests expert advice (internally or externally), or requests/draws up a safety data sheet.

The activities may commence once all conditions have been met.

Education and training

The starting point is that employees working at containment level 2 have had adequate preliminary education that is suitable for the activities to be performed and that they have followed sufficient training. If in doubt, consult the BSO.

Often, Good Microbiological Practice (GMP) is stated as the basis for safe working with microorganisms. A GMP course is sometimes offered in, or forms a part of, vocational training. The BSO platform website (www.bvfplatform.nl) provides information about a range of courses under the heading '*Opleidingen*'.

Information can also be found in chapter 6 of the book '*Veilig werken met micro-organismen, parasieten en cellen in laboratoria en andere werkruimtes*' by the KNVM.

Another useful addition in the instruction video[2] '*Precies zoals het hoort*' about GMP and the GMO regulations, made at the request of the Ministry of I&W in 2011. Of course, specific parts about the GMO regulations are not applicable to activities with BA that are not genetically modified. The second half of the instruction video about the correct use of biosafety cabinets is particularly useful.

Work procedures

See KAM-13-GEN and any additional (local) procedures and instructions per organisation.

[2] For the instruction video, see https://www.youtube.com/watch?v=xbdi95IxUw8

Accidents and Incidents

Examples

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

Procedures regarding non-GMO

The organisations at the USPB site use their own regulations for 'Arbo'-related cases.

Essential notifications concerning non-GMO

The organisations at the USPB site use their own regulations for 'Arbo'-related notifications. Notifications are absolutely necessary after:

- Accidents and incidents with a BA of category 2 or 3 must be reported to line management and the BSO of the organisation in question. The BSO provides for any mandatory forwarding of reports to the OR and external authorities.
- Accidents and incidents with a BA of category 3 involving an infection must also be reported to the 'Nederlandse Arbeidsinspectie' through the BSO.
- If an employee has (potentially) become infected through his or her work, then this concerns an occupational disease and the medical officer must be informed. The medical officer will subsequently report to the Netherlands Centre for Occupational Diseases.
- Accidents and incidents with poliovirus must also be reported to the NAC (National Authority for Containment) through the BSO.

Follow-up

For this, see KAM-13-GEN.

Administration and reports

For this, see KAM-13-GEN.

Monitoring, inspections and enforcement

For this, see KAM-13-GEN.

End of activities

If all activities with a specific type of BA of category 3 have ended (and all stocks have been destroyed), then this must be reported to the line management and the BSO.

Abbreviations and terminology

Where possible, the abbreviations and terminology have been taken from AI-09 'Biological Agents'.

Abbreviations	
BA	Biological agent(s)
BSO	Biosafety Officer
COGEM	The Netherlands Commission on Genetic Modification
GMO	Genetically modified organism(s)
KNVM	Koninklijke Nederlandse Vereniging voor Microbiologie
NAC	National Authority for Containment (Poliovirus)
OR	Ondernemingsraad
RI&E	Risk inventory and evaluation
Stichting- ALt	Stichting Antonie van Leeuwenhoekterrein
SZW	(Ministry of) Sociale zaken en werkgelegenheid

Terminology	
Biological agents (Arbobesluit)	Microorganisms, cell cultures and human endoparasites, *whether or not genetically modified*, which can cause an infection, allergy or toxicity[3].
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 whose genetic material has been altered by genetic technology.
Pathogenic	Causing disease.
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.

[3] 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.

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
- EU richtlijn 2000/54/EG on the protection of workers from risks related to exposure to biological agents at work and EU richtlijn 2019/1833 amending Annexes I, III, V and VI to Directive 2000/54/EC (as regards purely technical adjustments)
- KNVM richtlijn 'Veilig werken met micro-organismen, parasieten, en cellen in laboratoria en andere werkruimten', https://www.knvm.org/activities/biosafety-booklet-knvm
- KAM rules of 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: KAM13 GEN and KAM13 GMO
    - 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
- ISO35001:2019 (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 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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