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Contained Use of Genetically modified Micro-organisms

Provisions of the Swedish Work Environment Authority and General Recommendations on the Implementation of the Provisions

The Swedish Work Environment Authority
112 79 Stockholm, Telephone 010-730 90 00
E-mail: arbetsmiljoverket@av.se
www.av.se

Translation

In the event of disagreement concerning the interpretation and content of this text, the printed Swedish version shall have priority.

Provisions and general recommendations adopted by the Swedish Work Environment Authority are published in the Swedish Work Environment Authority's Statute Book (AFS).

Provisions are binding rules. General recommendations have a legal status different from that of provisions. General recommendations are not binding but contain recommendations on the implementation of the provisions which state how someone can or should act in a certain respect. They may, for example, inform on appropriate ways of fulfilling the requirements and point to practical solutions.

Please note that references to statutes always give the original number of the document concerned, regardless of any subsequent amendments and reprints.

Concerning amendments to and reprints of Provisions of the Swedish National Board of Occupational Safety and Health and of the Swedish Work Environment Authority, reference is made to the latest Statute Book Register of provisions and general recommendations.

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Provisions and general recommendations of the Swedish Work Environment Authority on the Contained Use of Genetically Modified Micro-organisms

The Swedish Work Environment Authority's Statute Book

Provisions and general recommendations of the Swedish Work Environment Authority on the Contained Use of Genetically Modified Micro-organisms;

Decided on 27 September 2011.

AFS 2011:2

The Swedish Work Environment Authority prescribes[1] the following supported by the Genetically Modified Organisms (Contained Use) Ordinance (2000:271) and establishes the following general recommendations.

Scope

Section 1
These provisions apply to the contained use of genetically modified micro-organisms, with the derogations indicated in Sections 3 and 5 of the Genetically Modified Organisms (Contained Use) Ordinance (2000:271).

Definitions

Section 2
The terms and expressions used in these Provisions have the same meanings as in Chap. 13, Sections 3-7 of the Swedish Environmental Code (1998:808) and Section 2 of the Genetically Modified Organisms (Contained Use) Ordinance (2000:271). Otherwise the terms and expressions stated below have the following meanings.

GMM	Genetically modified micro-organism as defined in the Genetically Modified Organisms (Contained Use) Ordinance (2000:271).

[1] Cf. the European Parliament and Council Directive 2009/41/EC of 6 May 2009 on the contained use of genetically modified micro-organisms (OJ L125, 21.5.2009, page 75, Celex 32009L0041)

Donor organism	An organism from which genetic material is transferred to another organism.
Recipient organism	a) An organism which has received foreign genetic material. b) Each of the organisms jointly contributing to a GMM in cases where it is impossible to tell which organism is the donor or recipient.
Vector	A virus, plasmid or other type of carrier capable of transmitting foreign genetic material to a recipient organism.
Containment level	The sets of protective measures which are adapted to GMM uses with similar risks on a defined level in accordance with the tables in appendix 2.
A GMM use	A contained use of GMM which, in a not insignificant manner, differs from other contained uses in respect of which GMMs are being used or in respect of the methods for production or use of them.
A GMM activity	A F, L or R activity in accordance with Section 2 of the Genetically Modified Organisms (Contained Use) Ordinance (2000:271), within its own premises, with one nature of the activity and with a leader of the activity.
Premises	The premises including the technical devices used in the GMM activities.
Nature of the activity	The nature of the GMM activity, defined by which protective measures are necessary in accordance with appendix 2 B, that is; large scale activities, laboratory, animal or plant activities or, when no other table is applicable, other activities.
Operator	In these provisions it is the legal or natural person who conducts one or more GMM activities.
Decontamination	Treatment of material, cultures and surfaces in order to kill or inactivate GMMs.

General recommendations: "Micro-organism" is in the definition of GMM "any microbiological entity, cellular or non-cellular, capable of replication or of transferring genetic material, including viruses, vi-

roids, and animal and plant cells in culture", see Section 2 of the Genetically Modified Organisms (Contained Use) Ordinance (2000:271).

Examples of micro-organisms according to the definition are bacteria including *Actinomycetes*, *Rickettsia* and *Cyanobacteria*, micro-fungi such as yeast and mould, microalgae, protozoans and cells in eukaryotic cell cultures. Also included are inferior reproductive units which can only reproduce with the aid of a host organism.

Appendix 1 part A in the Directive 2009/41/EG state examples of methods which give rise to GMM. Part B of the same appendix describes methods which are normally not considered to give rise to GMM.

"Operator" is normally the same as an employer with an organization number.

Investigation for assessment of necessary protective measures

Section 3

In order to conduct the investigation for assessing the potential risk of damage that shall precede the contained use of GMM, pursuant to Chapter 13, Section 8 of the Swedish Environmental Code, the operator shall follow the procedure indicated in appendix 1.

The result of the investigation shall form the basis of the selection of containment level and other protective measures.

General recommendations: In accordance with Chapter 13, Section 8 of the Swedish Environmental Code, contained use shall be preceded by an investigation which shall form the basis for assessing the potential risk of damage. The potential risks of damage must be avoided, why also an assessment of what protective measures are necessary is made in connection to the investigation.

The investigation shall be made in accordance with scientific knowledge and proven experience. This may mean that the operator needs to bring expertise into the organization if such is not available. In a larger organization, it may be appropriate to form a Biosafety Committee with collected comprehensive competence which can be advisory in investigations and assessments.

When conducting the investigation in accordance with appendix 1, different classification systems can be used in support. Criteria for classification of human pathogenic micro-organisms can be found in

the Swedish Work Environment Authority's Provisions on Microbiological Work Environment Risks – Infection, Toxigenic Effects, Hypersensitivity. Classification systems for plant and animal pathogens can also be of use. Such systems can give an indication of the containment level that is needed for the use of corresponding GMM.

Documentation

Section 4
The investigation and assessment in accordance with Section 3 and appendix 1 shall be documented.

The documentation shall be available within the GMM activity and must be shown on request from the Swedish Work Environment Authority.

General recommendations: When working with well-known GMM with small risks, the documentation does not need to be as extensive as when the risk is assessed to be great. When working with something new and unfamiliar, the documentation needs to be more extensive. If any information in the investigation or the assessment of the needs for protective measures have been changed at the regular review in accordance with Section 13 of the Genetically Modified Organisms (Contained Use) Ordinance (2000:271) this must also be documented. The documentation can be made in writing or in digital form.

Containment level, protective measures

Section 5
Contained use of GMM shall be conducted on at least the containment level which has been established in the procedures in appendix 1. If any protective measures in accordance with a higher containment level are necessary, then the higher containment level shall be applied.

The Swedish Work Environment Authority can grant exceptions to the rules in the first paragraph. In such cases, the Swedish Work Environment Authority can decide that not all of the protective measures in accordance with the higher containment level are necessary or that a combination of protective measures from table 1 and 2 in appendix 2 shall be implemented in the specific case.

General recommendations: In some cases there are already certain protective measures effective which are equivalent to a higher containment level than that which is really necessary in accordance with the investigation. But those protective measures do not govern which containment level is necessary. It is only the protective measures which have been deemed necessary in accordance with Section 3 that determines the lowest containment level.

When applying for an exception in accordance with the second paragraph, it is important that the investigation in accordance with Section 3 shows that the protective measure is not necessary.

Section 6

The basic protective measures and working methods, as set forth in appendix 2 A shall always be applied. The protective measures in accordance with the tables in appendix 2 B shall be applied based on the results of the investigation and assessment in accordance with Section 3.

At containment level 2 and higher, there shall be written handling and safety instructions pertaining to how the work is to be conducted and for measures in the event of unwanted events.

General recommendations: When preparing handling and safety instructions, the manual "WHO Laboratory Biosafety Manual" can be of use. Additionally, experiences from work places similar to one's own can provide guidance.

However, it is important that the local circumstances and the risk assessment at the individual work place form the basis for the design of the instructions and that the instructions are used by the staff.

There may be a need for different instructions for different categories of staff. It is important to not neglect the dishwashing, cleaning and other service staff. Special instructions may also be required for security guards and such like.

Classification for notification and application for permits

Section 7

Based on the containment level established from the procedure in appendix 1, each GMM use shall be part of a GMM activity which is classified as either a F, L or R activity in accordance with the following:

Necessary containment level	Classification
1	F activity
2	L activity
3 or 4	R activity

***General recommendations*:** The classification of GMM activities is primarily used for determining which regulations regarding notification and permits to adhere to. Such regulations can be found in the Genetically Modified Organisms (Contained Use) Ordinance (2000:271) and in Sections 14-16 and in appendices 3-5 in these provisions.

F, L and R activities are defined in Section 2 of the Genetically Modified Organisms (Contained Use) Ordinance

Signage and marking

Section 8

Warning signs shall be posted at the entrances to facilities or work areas with contained use of GMMs at containment level 2 or above as per Section 5 and appendix 2. Materials, including containers and other equipment which contains GMM, shall also be marked.

Signs and marking shall display a biohazard symbol as indicated in the Swedish Work Environment Authority's provisions on signs and signals for health and safety at work, along with information on the containment level and necessary additional information. Information which is commonly known where material, containers and other equipment are used can be excluded; if doing so poses no risk to health and environment.

General recommendations: Whether signs are necessary at all entrances and working areas depends on the set-up of the location; which GMMs are used; what kind of activity is conducted and which protective measures are being implemented. The most important thing to consider is that those using the facilities have no doubts regarding the containment level.

The biohazard sign is used even when there is no risk of employees becoming infected, e.g., when working with animal or plant pathogens at containment level 2 or higher.

In the Swedish Work Environment Authority's provisions on microbiological work environment risks – infection, toxigenic effects, hypersensitivity; there are rules and recommendations on signage and

marking. It is advisable to adhere to these rules as closely as possible, also when handling animal and plant pathogens which are not harmful to humans.

Waste, decontamination and cleaning

Section 9

Waste and other material consisting of or containing GMMs shall be handled in accordance with predefined routines in order to avoid risks to health and the environment. The party transporting or disposing of such material shall be informed in advance about the material, the risks associated with its handling and the need for protective measures.

General recommendations: When the GMM waste has been neutralized, it can be treated as domestic waste or hazardous waste, depending on the rest of the contents.

When transporting GMM waste that has not been neutralized, transportation rules must be adhered to regarding e.g. packaging and marking; please refer to provisions issued based on the Transport of Dangerous Goods Ordinance (2006:311).

Section 10

Cleaning and decontamination shall be performed to the extent necessary to prevent the GMM causing damages to health or environment, and in general in accordance with that which is stipulated in appendix 2.

General recommendations: The agents and methods necessary for decontamination depend on the GMM use in question. Heat treatment is the method of first preference where possible. When choosing a chemical treatment method the effect of the agent on the GMMs used must be considered, as well as any harmful health effects the agent might cause in e.g. the event of inhalation or by skin contact.

It is important that spillage of GMM is securely and promptly dealt with.

Decontamination is necessary prior to reparations and maintenance of equipment which may be subject to GMM contamination, such as centrifuges and cultivation equipment. The equipment should in such cases have an enclosed certificate of decontamination.

Training and knowledge

Section 11
The operator shall see to it that the person directing the work, and everyone who may come in direct contact with the GMM, has received the proper training and has sufficient knowledge of the GMMs used, of the risks these organisms can entail, and how these risks are to be avoided.

> ***General recommendations***: Besides the party working directly with GMM, others can come into contact with GMM, e.g., cleaning staff, service staff and animal handlers. What constitutes suitable training and sufficient knowledge depends on factors such as, which GMMs are being used, how these are used and on the task the party is performing. For animal handling staff it may be sufficient to have knowledge of whether the animal can secrete GMM or not and potential risks if GMM is secreted. The party who are genetically modifying infectious agents in risk class 3 needs, as a rule, to have undergone scientific or medical training.

Contingency plan and reporting

Section 12
A contingency plan for GMM activities in the event of an unintentional escape of GMM which can entail serious immediate or delayed harm to humans or to the environment needs to be established in accordance with Section 31 of the Genetically Modified Organisms (Contained Use) Ordinance (2000:271).

The concerned authorities and others who may be affected are to be informed of the contents of the plan.

> ***General recommendations***: What constitutes an accident in this context is defined in Section 2 of the Genetically Modified Organisms (Contained Use) Ordinance (2000:271). Which authority to inform depends on where the activity takes place and what risks are involved. The local rescue services need to be notified but other authorities may also need to be notified. Companies in close proximity and the public may need to be informed depending on the location of the facility.
>
> If the GMM is an infectious agent which can cause serious harm to humans and thus it constitutes a need for a contingency plan in accordance with the Swedish Work Environment Authority's Provisions

on Microbiological Work Environment Risks – Infection, Toxigenic Effect, Hypersensitivity; it is appropriate that the plans are combined and correspond with each other.

Section 13
In the event of an accident, the Swedish Work Environment Authority and other concerned authorities shall, immediately or within 24 hours, be notified of

1. the detailed circumstances of the accident,
2. the identity and quantity of the GMMs which are no longer contained,
3. all information necessary for assessing the impact of the accident on health and the environment, and
4. the rescue measures which have been taken.

General recommendations: What constitutes an accident in this context is defined in Section 2 of the Genetically Modified Organisms (Contained Use) Ordinance (2000:271). Depending of the nature of the accident, the authorities concerned may be the local rescue services, the local Environment and Public Health Committee etc. in accordance with the contingency plan.

Notification and application for permits

Section 14
In notification of an F activity as referred to in Sections 15 and 23 of the Genetically Modified Organisms (Contained Use) Ordinance (2000:271), the particulars indicated in appendix 3 shall be submitted to the Swedish Work Environment Authority.

Section 15
In notification of an L activity and new uses of GMM as referred to in Sections 15 and 25 of the Genetically Modified Organisms (Contained Use) Ordinance (2000:271), the particulars indicated in appendix 4 shall be supplied to the Swedish Work Environment Authority.

Section 16
In notification application for permit of an R activity and new uses of GMM as referred to in Sections 15 and 26 of the Genetically Modified Organisms (Contained Use) Ordinance (2000:271), the particulars indicated in appendix 5 shall be supplied to the Swedish Work Environment Authority.

Amendments and updates of submitted information

Section 17

The following applies to amendments in the GMM activity: Amendment of a piece of information which in appendices 3-5 have been marked with an asterisk (*) shall be submitted as an update in accordance with Section 22 of the Genetically Modified Organisms (Contained Use) Ordinance (2000:271). An amendment of a piece of information which have been marked with two asterisks (**) may not be submitted as an update. For this type of amendment, a new complete notification or application shall be submitted.

> ***General recommendations***: For practical reasons, the Swedish Work Environment Authority usually proposes a time during the year for an update to be submitted in accordance with Section 22 of the Genetically Modified Organisms (Contained Use) Ordinance (2000:271). The proposal is made in connection with administration of notifications and permit applications for contained use of GMM. If nothing has changed, there is no need to submit an update.
>
> Note that the Swedish Work Environment Authority shall be notified as soon as possible of any amendments which may be of tangible significance for the risks, in accordance with Section 21 of the same ordinance.

Entry into force and provisional regulations

These Provisions enter into force on 1 January 2012 when the National Board of Occupational Safety and Health's Provisions (AFS 2000:5) on Contained Use of Genetically Modified Micro-Organisms are repealed.

An activity which has been notified under the old statute need not be notified again under the new statute. Permits issued under the old statute are still valid. The old statute is valid for the administration of matters submitted to the Swedish Work Environment Authority prior to 1 January 2012 but which have still not been determined.

MIKAEL SJÖBERG

Claes Trägårdh Anna Middelman

Principles to be followed for the investigation and assessment in accordance with Section 3, determination of containment level in accordance with Section 5 and classification in accordance with Section 7

A. Factors to take into consideration in the investigation and assessment

The following is considered as potentially harmful effects:

- Disease to humans, including allergenic or toxic effects.
- Disease to animals or plants.
- Harmful effects due to the impossibility of treating a disease or providing an effective prophylaxis.
- Harmful effects due to establishment or dissemination in the environment.
- Harmful effects due to the natural transfer of inserted genetic material to other organisms.

B. Principles to be followed in the investigation, assessment and classification

1. The investigation begins by identifying any potentially harmful effects connected to GMM, see appendix 1 A. When doing so it is necessary to identify the recipient organism's and, if necessary, the donor organism's, harmful properties and the potentially harmful properties associated with the vector and/or introduced material, such as every change of the recipient organism's existing properties. If no harmful properties can be identified in accordance with appendix 1 C, point 2 can be excluded.
2. If any potentially harmful effects have been identified, the severity of the identified potentially harmful effects shall be assessed along with the probability of them arising due to the GMMs intrinsic properties.
3. The next step in the investigation is to identify the factors in the specific GMM use which may increase the probability of the potentially harmful effects arising or for GMM to be released into the environment. The following factors must be taken into account:
   - The nature of the activity, e.g., its scope and direction.

- Which methods are being used.
- The characteristics of the environment likely to be exposed.
- The possibility of decontamination of GMM in waste and waste water.

4. Based on the results from the investigation in points 1 to 3, an assessment is made of which protective measures are needed to keep the GMM contained and protect human health and the environment.
5. The protective measures chosen shall be compared to the protective measures in the applicable table in appendix 2, in order to determine on which containment level the GMM use needs to be conducted.
6. The containment level necessary determines the classification for the GMM activity which the GMM use needs to be conducted in.
7. Finally the correct choice of containment level (and thereby classification) is confirmed by examining whether the protective measures are sufficient for GMM not to cause any harm to health and environment and that they can be kept contained.

C. Criteria for which GMM can be used at containment level 1

In general, it is only GMM which presents the following characteristics that can be eligible for use at containment level 1.

- The recipient organism is not likely to cause disease in humans, animals or plants.
- The vector or inserted material does not endow the genetically modified micro-organism with a phenotype likely to cause disease in humans, animals or plants or likely to cause harmful effects in the environment.
- The properties of the resultant genetically modified micro-organism are such that it is unlikely to cause disease in humans, animals or plants or otherwise cause harmful effects on the environment.

Protective measures and working methods to be implemented in accordance with Section 6

A. Basic protective measures and working methods

In order to maintain the containment and work in a safe manner, the measures in the applicable table in appendix 2 B, good microbiological practice and the points below should be adhered to:

- GMM with the lowest possible risk to health and environment, having taken into account the circumstances, is chosen.
- The work is planned, organized and conducted so that exposure to GMM is maintained at the lowest practical level possible in the work place and in the environment.
- Technical protective measures are taken at the source and are supplemented with appropriate personal protective equipment when necessary.
- Protective measures and equipment are maintained and tested regularly.
- The presence of process organisms outside the (large-scale) closed system is investigated when necessary.
- The staff is educated and trained in a suitable manner.
- Biosafety committees or sub-committees are established if necessary.
- Adequate records are kept.
- It shall be prohibited to eat, drink, apply cosmetics, use tobacco products or handle foodstuffs within the work area.
- Mouth pipetting shall be prohibited.
- Efficient disinfectants and routines for disinfection shall be in place in case of spillage.
- Contaminated equipment or materials shall be safely stored when necessary.

B. Protective measures for the contained use of GMMs at various containment levels

Table 1

a) Protective measures at contained use of GMM in laboratory, animal and plant activities

Protective measures	Containment level 1	Containment level 2	Containment level 3	Containment level 4
Facilities and equipment				
1. Facilities which are separated from other areas in the same building or located in a separate building	No	Demarcated from other activities	Yes	Yes, in its own building or as an isolated unit
2. Entrance through an airlock only, preferably with doors which only open one at a time	No	No	Yes, in the event of airborne infection or if required in accordance with the investigation in Section 3	Yes
3. The room has negative pressure relative to the pressure of the immediate environment	No	No	Yes, in the event of airborne infection or if required in accordance with the investigation in Section 3	Yes
4. The room is sealable for fumigation	No	Yes, if required in accordance with the investigation in Section 3	Yes	Yes
5. Separate ventilation system with HEPA filtration of extract air in the facility	No	No	Yes, extract air in the event of airborne infection or if required in accordance with the investigation in Section 3	Yes, extract air and supply air. For virus not trapped by HEPA filter, further measures are necessary.
6. Observation window or the equivalent provided, so that occupants can be seen	Yes, if required in accordance with the investigation in Section 3	Yes, if required in accordance with the investigation in Section 3	Yes	Yes

Protective measures	Containment level 1	Containment level 2	Containment level 3	Containment level 4
7. Surfaces resistant to water, acids, alkalis, solvents and disinfectants and are easy to clean	Bench	Bench, floor	Bench, floor	Bench, floor, walls, ceiling
8. Facility equipped for hand-washing	Yes	Yes, preferably which can be manoeuvred without touching with hands and hand disinfectant	Yes, which can be manoeuvred without touching with hands and hand disinfectant	Yes, which can be manoeuvred without touching with hands and hand disinfectant
9. Waste water from sinks, showers, floor drains and similar drains can be disinfected	No	No	Yes, if there is a risk of GMM being released into the drain	Yes
10. Microbiological safety cabinet	No	Yes, for handling infected material if there is a risk of significant aerosol generation or if required in accordance with the investigation in Section 3	Yes	Yes
11. Alarm system provided to indicate whether any technical safety equipment is out of order	No	Yes, for safety cabinets or if required in accordance with the investigation in Section 3	Yes	Yes
12. Reserve power supply provided for technical safety equipment in the laboratory	No	No	Yes, if required in accordance with the investigation in Section 3	Yes
13. The own equipment is kept within the restricted area	No	Yes, if required in accordance with the investigation in Section 3	Yes	Yes
Work routines				
14. Sign with a biohazard symbol	No	Yes	Yes	Yes

Protective measures	Containment level 1	Containment level 2	Containment level 3	Containment level 4
15. Specific measures to control aerosol dissemination	Yes, if required in accordance with the investigation in Section 3	Yes, aerosol dissemination is minimised	Yes, aerosol dissemination is prevented	Yes, aerosol dissemination is prevented
16. Restricted access	No	Yes, access only for persons informed of the risks	Strict, access only for authorised staff. Locking routines	Strict, access only for authorised staff. Locking routines
17. GMM is stored in a manner so that no one will be exposed by mistake or unauthorized persons can access the material	Yes, if required in accordance with the investigation in Section 3	Yes	Yes	Yes
18. Protective clothing is used	Yes, appropriate protective clothing, in general laboratory coat	Yes, appropriate protective clothing which is removed when leaving the working area	Yes, full-cover protective clothing which is removed when leaving the working area, special footwear when necessary	Yes, full change to protective clothing and special footwear. Full change of clothes when leaving the working area
19. Gloves are used	No	Yes, if required in accordance with the investigation in Section 3	Yes	Yes
20. Shower after finished work	No	No	Yes, if required in accordance with the investigation in Section 3	Yes
21. Efficient pest control (e.g., for rodents and insects)	Yes, if required in accordance with the investigation in Section 3	Yes	Yes	Yes

Protective measures	Containment level 1	Containment level 2	Containment level 3	Containment level 4
Waste and decontamination routines				
22. Autoclave	In connection to the facility, if other satisfactory decontamination is not available	In connection to the facility	Within the facility, possibly double-sided	Double-sided within the facility
23. Used material with GMM is decontaminated before it is washed, reused, discarded	Yes, with a method chosen depending on the results of the investigation in Section 3	Yes, with a method chosen depending on the results of the investigation in Section 3	Yes, before it leaves the laboratory	Yes, before it leaves the laboratory
24. Waste containing GMM is decontaminated	Yes, with a method chosen depending on the results of the investigation in Section 3	Yes, with a method chosen depending on the results of the investigation in Section 3	Yes, before it leaves the laboratory	Yes, before it leaves the laboratory
25. Special routines for measures at spills and other unwanted events	Yes	Yes, in writing	Yes, in writing	Yes, in writing

b) Amendments of and additions to table 1 a for contained use of GMM in animal activities

Protective measures	Containment level 1	Containment level 2	Containment level 3	Containment level 4
Measures that amends corresponding point in table 1 a				
1. Isolated animal unit (building or a separate area within a building which contains one or more animal facilities[2] as well as other areas, such as changing rooms, showers, autoclaves or food storage)	Yes, if required in accordance with the investigation in Section 3	Yes	Yes	Yes

[2] Animal facility: a facility intended for keeping animals or for performing minor surgical operations on animals and where the animals are kept in appropriate enclosures, e.g., cages, stalls or other facilities.

Protective measures	Containment level 1	Containment level 2	Containment level 3	Containment level 4
7. Surfaces which are resistant to water, acids, alkalis, solvents, decontaminants and are easy to clean	Bench if such is available, and otherwise if required in accordance with the investigation in Section 3	Bench if such is available, floors	Bench if such is available, floors and walls	Bench if such is available, floors, walls and ceiling
Measures which are supplements to table 1 a				
26. Animal facilities which are demarcated with lockable doors	Yes, if required in accordance with the investigation in Section 3	Yes	Yes	Yes
27. Isolators or equivalent containment has HEPA filter	No	Yes, if required in accordance with the investigation in Section 3	Yes	Yes
28. Material and equipment are designed to facilitate cleaning and decontamination	Yes, if required in accordance with the investigation in Section 3	Yes	Yes	Yes
29. Measures to limit the risk of animals escaping outside the demarcation	Yes	Yes	Yes	Yes
30. Incineration of animal bodies	Recommended	Yes	Yes	Yes, on location, unless sterilization has occurred with a validated method prior to transfer to an incinerator
31. Litter and waste is decontaminated	Yes, if required in accordance with the investigation in Section 3	Yes	Yes	Yes

c) Amendments of and additions to table 1 a for contained use of GMM in animal activities

Protective measures	**Containment level 1**	**Containment level 2**	**Containment level 3**	**Containment level 4**
Measures that amends corresponding point in table 1 a				
1. Greenhouse or growth-room: structure with walls, a roof and a floor designed and used for growing plants in a controlled and protected environment	Yes, if required in accordance with the investigation in Section 3	Yes	Yes	Yes
2. Entry through airlock only	No	Yes, if required in accordance with the investigation in Section 3	Yes	Yes
3. Efficient pest control (e.g. for rodents and insects)	Yes	Yes	Yes	Yes
Measures which are supplements to table 1 a				
32. Permanent structures with continuous waterproof covering, designed to prevent entry of surface-water run-off and with lockable doors	No	Yes	Yes	Yes
33. Control of contaminated run-off water	Yes, if required in accordance with the investigation in Section 3	Yes, so that run-off is minimised if dissemination of GMM can occur through the ground	Yes, so that run-off is prevented	Yes, so that run-off is prevented
34. Procedures which prevent the dissemination of GMM at transfer of living materials between different locations, e.g., greenhouse/growth room and laboratory	Yes, to minimise the dissemination of GMM	Yes, to minimise the dissemination of GMM	Yes, to prevent the dissemination of GMM	Yes, to prevent the dissemination of GMM

Table 2

Protective measures for contained use of GMM in large-scale activities

Protective measures	**Containment level 1**	**Containment level 2**	**Containment level 3**	**Containment level 4**
Contained system and other technical equipment				
1. Viable GMM is contained in one or more closed systems so that the process is kept separate from the surroundings	Yes	Yes	Yes	Yes
2. Extract air from closed systems is controlled	Yes, if required in accordance with the investigation in Section 3	Yes, the dissemination of GMM is minimised	Yes, the dissemination of GMM is prevented	Yes, the dissemination of GMM is prevented
3. Seals are designed so that release of GMM is minimised or prevented	Yes, if required in accordance with the investigation in Section 3	Yes, minimised	Yes, prevented	Yes, prevented
4. Alarm system provided to indicate whether any technical safety equipment are out of order	No	Yes, if required in accordance with the investigation in Section 3	Yes	Yes
5. Reserve power supply provided for technical safety equipment in the laboratory	No	No	Yes, if required in accordance with the investigation in Section 3	Yes
Facilities and other equipment				
6. Closed systems are located within a controlled area	Yes, if required in accordance with the investigation in Section 3	Yes	Yes	Yes
7. Access to the controlled area through airlock only	No	Yes, if required in accordance with the investigation in Section 3	Yes	Yes

Protective measures	Containment level 1	Containment level 2	Containment level 3	Containment level 4
8. The controlled area is maintained at an air pressure negative to the immediate surroundings	No	Yes, if required in accordance with the investigation in Section 3	Yes, if required in accordance with the investigation in Section 3	Yes
9. Separate ventilation system with HEPA filtration of the air	No	Yes, if required in accordance with the investigation in Section 3	Yes, extract air and otherwise if required in accordance with the investigation in Section 3	Yes, extract and supply air
10. Special measures for minimising air pollutions	Yes, if required in accordance with the investigation in Section 3	Yes, if required in accordance with the investigation in Section 3	Yes, if required in accordance with the investigation in Section 3	Yes
11. The controlled area is sealable for fumigation	No	Yes, if required in accordance with the investigation in Section 3	Yes	Yes
12. Surfaces which are resistant to water, acids, alkalis, solvents, decontaminants and are easy to clean	Bench if such is available	Bench if such is available, floors	Bench if such is available, floors and walls	Bench if such is available, floors, walls and ceiling
13. Facility equipped for hand-washing	Yes	Yes, preferably which can be manoeuvred without touching with hands and hand disinfectant	Yes, which can be manoeuvred without touching with hands and hand disinfectant	Yes, which can be manoeuvred without touching with hands and hand disinfectant
14. Waste water from sinks, showers, floor drains and similar drains can be disinfected	No	No	Yes, if there is a risk of GMM disseminating from the drain	Yes
15. The own equipment is kept within the controlled area	No	Yes, if required in accordance with the investigation in Section 3	Yes	Yes

Protective measures	Containment level 1	Containment level 2	Containment level 3	Containment level 4
Work routines				
16. Sign with biohazard symbol	No	Yes	Yes	Yes
17. Aerosol formation during sample collection, adding, extracting or transfer of materials is limited	Yes, if required in accordance with the investigation in Section 3	Yes, minimised	Yes, prevented	Yes, prevented
18. Restricted access	No	Yes, access only for persons informed of the risks	Strict, access only for authorised staff. Locking routines	Strict, access only for authorised staff. Locking routines
19. Protective clothing used within the controlled area	Yes, special protective clothing	Yes, special protective clothing	Yes, full-cover protective clothing, special footwear when necessary	Yes, full change to protective clothing and special footwear. Full change of clothes when leaving the working area
20. The staff takes a shower before leaving the area	No	No	Yes, if required in accordance with the investigation in Section 3	Yes
21. Efficient pest control (e.g., for rodents and insects)	Yes, if required in accordance with the investigation in Section 3	Yes	Yes	Yes
22. GMM is stored in a manner so that no one will be exposed by mistake or unauthorized persons can access the material	Yes, if required in accordance with the investigation in Section 3	Yes	Yes	Yes
Waste and decontamination routines				
23. The entire volume from the closed system can be taken care of and be decontaminated at the event of an accident	Yes, if required in accordance with the investigation in Section 3	Yes	Yes	Yes

Protective measures	**Containment level 1**	**Containment level 2**	**Containment level 3**	**Containment level 4**
24. Used material or waste with GMM is decontaminated before it is washed, reused, discarded	Yes, with a method chosen depending on the results of the investigation in Section 3	Yes, decontamination through validated methods for inactivation	Yes, decontamination through validated methods for inactivation	Yes, decontamination through validated methods for inactivation
25. Decontamination of larger amounts of culture fluid, including the process drainage, before the fluid leaves the closed system for further handling	Yes, with a method chosen depending on the results of the investigation in Section 3	Yes, decontamination through validated methods for inactivation	Yes, decontamination through validated methods for inactivation	Yes, decontamination through validated methods for inactivation
26. Special routines for measures at spillage and other unwanted events	Yes, if required in accordance with the investigation in Section 3	Yes, in writing	Yes, in writing	Yes, in writing

Information to be provided in notification of an F activity

The information below shall be submitted when notifying an F activity in accordance with Sections 15 and 23 of the Genetically Modified Organisms (Contained Use) Ordinance (SFS 2000:271).

When making amendments in a GMM activity, the following is applicable:

- Amendment of information which has been marked with * is submitted as an update in accordance with Section 22 of the Ordinance.
- Amendment of information which have been marked with ** entails the submitting of a new complete notification.

1. The operator's
   - name and address *
   - organisation number **
2. Biosafety committee or equivalent guidance if such exists *
3. The premises where the GMM is to be used:
   - street address and city **
   - summary description of the premises (optional: blueprints or sketches)*
   - demarcation of the premises, e.g., with house number, floor level or room number *
4. Organisational affiliation and distribution of responsibility *
   - the department, institution etc. which is responsible for the F activity
   - persons with responsibility for the F activity's supervision and/or safety in accordance with environmental as well as work environment legislation
     i. name, contact details and organisational affiliation
     ii. assigned task for supervision and/or safety; also state position if relevant
     iii. education and qualification for the task/tasks
5. Description of the F activity
   - nature of the activity (in accordance with the definition in Section 2) **
   - detailed description of the nature of the activity (basic or corporate research, teaching, pilot studies, production, diagnostics, other) *
   - which types of GMM are being handled (groups of organisms) *
6. Description of waste management *
   - which type of GMM waste is generated

- how the GMM is neutralized in the waste
- in applicable cases: recipients of waste containing non-neutralized GMM and how information on GMM is submitted to those recipients

7. Summary of the investigation and assessment in accordance with Section 3 and details on which table of protective measures in appendix 2 is being implemented.

Information to be provided in notification of an L activity and new GMM uses

The information below shall be submitted when notifying an L activity and new GMM uses respectively in accordance with Sections 15 and 25 of the Genetically Modified Organisms (Contained Use) Ordinance (SFS 2000:271).

When making amendments in a GMM activity, the following is applicable:

- Amendment of information which has been marked with * is submitted as an update in accordance with Section 22 of the Ordinance.
- Amendment of information which have been marked with ** entails the submitting of a new complete notification.

A. Notification of an L activity

1. The operator's
   - name and address *
   - organisation number **
2. Biosafety committee or equivalent guidance if such exists *
3. The premises where the GMM is to be used:
4. street address and city **
   - summary description of the premises, with blueprints or sketches *
   - demarcation of the premises, e.g., with house number, floor level or room number *
5. Organisational affiliation and distribution of responsibility *
   - the department, institution etc. which is responsible for the L activity
   - persons with responsibility for the L activity's supervision and/or safety in accordance with environmental as well as work environment legislation
     i. name, contact details and organisational affiliation
     ii. assigned task for supervision and/or safety; also state position if relevant
     iii. education and qualification for the task/tasks
     iv. which GMM use or uses the responsibility relates to
6. Description of the L activity
   - nature of the activity (in accordance with the definition in Section 2) **

- detailed description of the nature of the activity (basic or corporate research, teaching, pilot studies, production, diagnostics, other) *
- the scale, i.e., approximate volumes of GMM used on one and the same occasion, in one vessel (stated in one of the intervals <100 l, 10-100 l, 100-500 l, >500 l) *[3]

7. Protective measures: which table in appendix 2 is being implemented **
8. Written handling and safety instruction *
   - joint for all GMM uses within the activity
   - for each separate GMM use within the L activity, when required.

For each one of the GMM uses present in the L activity

9. Details on the GMM use
   - own designation for the GMM use
   - the part of the premises being used, e.g., room number *
   - the protective measures in applicable table (see appendix 2) chosen on the basis that they are required in accordance with the investigation in section 3 *[3]
10. Description of the GMM use including the purpose of the use and expected results **
11. Information on the biological material
    - the GMM/recipient organism used **[4]
      i. identity
      ii. properties before and after genetic modification *
    - the vector/equivalent which is used **[4]
    - inserted genetic material
      i. donor organism/origin *
      ii. intended function/intended functions *[5]
12. Summary of the investigation and assessment in accordance with Section 3.

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[3] The information may be amended as an update only if the protective measures needed still are collected from the same table and containment level.

[4] If another ”species”/equivalent is used, it will be included in its own GMM use.

[5] The information may be amended as an update only if the protective measures needed have not been changed.

B. New GMM use

The information below shall be submitted when notifying a new GMM use in an L activity which has already been notified and received a ID number from the Swedish Work Environment Authority.

1. The ID number received form the Swedish Work Environment Authority for the L activity in which the GMM use shall be included
2. Person responsible for the supervision of the GMM use and/or safety in accordance with environmental as well as work environment legislation, if other than responsible for the L activity *
   - name, contact details and organisational affiliation
   - assigned task for supervision and/or safety; also state position if relevant
   - education and qualification for the task/tasks
3. Details on the GMM use
   - own designation for the GMM use
   - the part of the premises being used (e.g., room number) *
   - the protective measures in applicable table (see appendix 2) chosen on the basis that they are required in accordance with the investigation in section 3 *[3]
   - handling and safety instructions for the GMM use, where applicable *
   - if differences compared to the previously notified L activity, the following is specified:
     i. handling of waste *
     ii. approximate volumes *[4]
4. Description of the GMM use including the purpose of the use and expected results. **
5. Information on the biological material
   - the GMM/recipient organism used **[4]
     i. identity
     ii. properties before and after genetic modification *
   - the vector/equivalent which is used **[4]
   - inserted genetic material
     i. donor organism/origin *
     ii. intended function/intended functions *[5]
6. Summary of the investigation and assessment in accordance with Section 3.

Information to be provided when applying for an R activity and new GMM uses

The information below shall be submitted when applying for a permit for an R activity and new GMM uses respectively in accordance with Sections 15 and 26 of the Genetically Modified Organisms (Contained Use) Ordinance (SFS 2000:271). If the GMMs in question are infectious agents in risk class 3 or 4 in accordance with the Swedish Work Environment Authority's Provisions on Microbiological Work Environment Risks – Infection, Toxigenic Effects, Hypersensitivity; the permit application is required to be supplemented in relevant parts in accordance with the provisions.

When making amendments in a GMM activity, the following is applicable:

- Amendment of information which has been marked with * is submitted as an update in accordance with Section 22 of the Ordinance.
- Amendment of information which have been marked with ** entails the submitting of a new complete notification.

An update is not applicable when a permit has become invalid.

A. Application for permit for an R activity

1. The operator's
   - name and address *
   - organisation number **
2. Time period for which the permit is applied for[6]
3. Biosafety committee or equivalent guidance if such exists *
4. The premises where the GMM is to be used: **
   - street address and city
   - detailed description of the premises with blueprints or sketches
   - demarcation of the premises with room number, floor level and, where relevant, house number etc.
   - description of the technical facilities which are significant for the safety as well as planned and implemented technical control measures of significance for safety
5. Any prior permits in the premises:

[6] A permit is usually granted for three years and a maximum of five years.

- the Swedish Work Environment Authority's ID number for previously approved R activity in the premises
- when applying for renewal of a previous permit, a report on how any previous conditions have been med is to be submitted

6. Organisational affiliation and distribution of responsibility *
   - the department, institution etc. which is responsible for the R activity
   - persons with responsibility for the R activity's supervision and/or safety in accordance with environmental as well as work environment legislation
     i. name, contact details and organisational affiliation
     ii. assigned task for supervision and/or safety; also state position if relevant
     iii. education and qualification for the task/tasks
     iv. which GMM use or uses the responsibility relates to
7. Description of the R activity
   - nature of the activity (in accordance with the definition in Section 2) **
   - detailed description of the nature of the activity (basic or corporate research, teaching, pilot studies, production, diagnostics, other) *[7]
   - the greatest total volume which will be handled in one occasion within the R activity *[7]
8. Description of waste management *
   - which type of GMM waste is generated
   - how the GMM is neutralized in the waste
   - other information on waste management which is of importance to environment and health
9. Protective measures: which table and containment level in appendix 2 is being implemented **
10. Written handling and safety instructions *
    - joint for all the GMM uses within the R activity
    - for each separate GMM use within the R activity
11. If a contingency plan is required in accordance with Section 12, the following information is submitted: *
    - risk sources and circumstances by which accidents can occur
    - the specific risks that may arise on the basis of the location of the premises

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[7] The information may be amended as an update only if the protective measures needed still are collected from the same table and containment level.

- conceivable consequences for health and the environment if an accident occurs
- the preventive measures taken, e.g., safety equipment, alarm systems and containment methods
- procedure and plans for control of the protective measure's continued efficiency
- description of the information submitted to the wmployees regarding contingency and accidents
- assurance that competent authorities with the task of implementing rescue measures have been informed about the contingency plan.

For each one of the GMM uses present in the R activity

12. Details on the GMM use
    - own designation for the GMM use
    - the part of the premises being used (state room number) *[8]
    - the greatest total volume which will be handled in one occasion and the greatest volume that will be cultivated *[8]
13. All protective measures implemented in accordance with the applicable table (see appendix 2) **
14. Description of the GMM use including the purpose of the use and expected results *[8]
15. Information on the biological material and documentation of the investigation and assessment in accordance with Section 3
    - the GMM/recipient organism used **[9]
    i. identity
    ii. properties before and after genetic modification
    - the vector/equivalent which is used **[9]
    i. identity
    ii. properties relevant for the investigation and assessment in accordance with Section 3
    - inserted genetic material: *[8]
    i. donor organism/origin
    ii. intended function/intended function
    - copy of the documentation of the investigation and assessment in accordance with Section 3.

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[8] The information may be amended as an update only if the protective measures needed have not been changed.

[9] If another "species"/equivalent is used, it will be included in its own GMM use.

B. New GMM use

The information below shall be submitted when applying for a permit for a new GMM use in an R activity which has already been permitted and received a ID number from the Swedish Work Environment Authority.

1. The ID number received from the Swedish Work Environment Authority for the R activity in which the GMM use shall be included
2. Persons responsible for the supervision of the GMM use and/or safety in accordance with environmental as well as work environment legislation, if other than responsible for the R activity *
   - name, contact details and organisational affiliation
   - assigned task for supervision and/or safety; also state position if relevant
   - education and qualification for the task/tasks
3. Details on the GMM use
   - own designation for the GMM use
   - the part of the premises being used (state room number) *[8]
   - the greatest total volume which will be handled in one occasion and the greatest volume that will be cultivated *[8]
   - handling and safety instructions for the GMM use *
   - if differences compared to the previous permit for the R activity, the following is specified:
     i. handling of waste in the use *
     ii. changes in the contingency plan and assurance that concerned authorities have been notified *
4. All protective measures being implemented in accordance with applicable table (see appendix 2) **
5. Description of the GMM use including the purpose of the use and expected results *[8]
6. Information on the biological material and the documentation of the investigation and assessment in accordance with Section 3
   - the GMM/recipient organism used **[9]
     i. identity
     ii. properties before and after genetic modification
   - the vector/equivalent which has been used **[9]
     i. identity

ii. properties relevant for the investigation and assessment in accordance with Section 3

- inserted genetic material: *[8]

i. donor organism/origin

ii. intended function/intended functions

- copy of the investigation and assessment in accordance with Section 3.