

**Statute book of the Swedish National Board of
Occupational Safety and health**



AFS 2000:5

**CONTAINED USE OF
GENETICALLY MODIFIED
MICRO-ORGANISMS**

**Provisions of the Swedish National Board of Occupational Safety and
Health on Contained Use of Genetically Modified Micro-Organisms,
together with General Recommendations on the implementation of the
Provisions**

Translation

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

AFS 2000:5

The Swedish Work Environment Authority was formed through a merger of the Swedish National Board of Occupational Safety and Health and the Labour Inspectorate, on 1st January 2001.

Provisions adopted by the Swedish Work Environment Authority are published in the Statute Book of the Swedish Work Environment Authority. Provisions earlier published in the Statute Book of the Swedish National Board of Occupational Safety and Health simultaneously still apply. Both Statute Books' names are abbreviated AFS.

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 (in Swedish). A list of Ordinances, General Recommendations, Directions and Notices is also published in English.

Swedish Work Environment Authority
SE-171 84 SOLNA , Sweden

Telephone: +46 8 730 90 00
Telefax: +46 8 730 91 67
Publishing Services, telefax: +46 8 735 85 55

www.av.se

AFS 2000:5

List of contents

Provisions of the Swedish National Board of Occupational Safety and Health on Contained Use of Genetically Modified Micro-Organisms

Scope, Section 1	5
Definitions, Section 2	5
Risk Assessment, Section 3	6
Classification and containment level, Section 4	6
Documentation, Section 5	7
Containment and other protective measures, Section 6 - Section 7	7
Facilities, fittings, equipment and control, Section 8 - Section 9	8
Signage and marking, Section 10 - Section 11	8
Cleaning, decontamination and transfer of contaminated material, Section 12.....	8
Section 13.....	9
Personal protective equipment and hygiene, Section 14 - Section 15.....	9
Knowledge, Information and Instructions, Section 16.....	9
Illnesses, accidents and incidents, Section 17.....	10
Emergency plan, Section 18.....	10
Notification and application for permits, Section 19.....	10
Section 20.....	11
Section 21	11
Charges, Section 22.....	11
Liability, Section 23	11
Entry into force	12
Appendices to the Provisions	
Appendix 1	
Principles to be followed for the assessment of risk and selection of containment and other protective measures.....	13
Appendix 2	
Criteria for the classification of an activity with GMMs as an F, L or R activity as provided in Section 4.....	16
Appendix 3	
Containment and other safety measures to be taken pursuant to Section 7	17
3 A. Good microbiological practice.....	17
3 B. Containment and other protective measures for the contained use of GMMs at various containment levels.....	18
Table 1 a Containment and other protective measures for laboratory activities..	18
Table 1b Containment and other protective measures, over and above those indicated in Table 1a, when working with animals deliberately infected with GMMs	22
Table 1 c Containment and other protective measures over and above those indicated in Table 1a when working with plants deliberately infected with GMM	23
Table 2 Containment and other protective measures for large-scale processes	24
Appendix 4	
Information to be provided in notification of F activity	27
Appendix 5	
Information to be provided in notification of L activity and of new use within previously notified L activity	28

Appendix 6	
Information to be provided in permit application for R activity and for new use within R activity for which permit previously has been issued	29
General Recommendations of the Swedish National Board of Occupational Safety and Health on the implementation of the Provisions on Contained Use of Genetically Modified Micro-Organisms	31
Background.....	31
Guidance on individual Sections	31
Guidance on Section 1	31
Guidance on Section 2.....	33
Guidance on Section 3.....	35
Guidance on Section 4 and 5.....	36
Guidance on Section 6.....	37
Guidance on Section 7 and 8.....	38
Guidance on Section 9, 10 and 11	39
Guidance on Section 12 and 13	40
Guidance on Section 14 and 15	41
Guidance on Section 16.....	42
Guidance on Section 17 and 18	44
Guidance on Sections 19- 22.....	45
Guidance on the Appendices to the Provisions.....	45
Recommendations with reference to App. 1, concerning risk assessment.....	45
Recommendations with reference to App. 2, concerning F,L or R classification of activities	48
Recommendations with reference to App. 3A concerning good microbiological practice	48
Recommendations with reference to App. 3B, concerning containment and other protective measures at different containment levels.....	49
Guidance on Apps. 4-6, concerning information to be provided in connection with notification and permit application	54
Appendices to the Recommendations	
Appendix A Guidance on interpreting the definition of GMMs in Section 2	58
Appendix B Summary of administrative procedures for activity involving contained use of GMMs, together with a comparison with the rules applying to biological agents	59
Information from the National Board of Occupational Safety and Health concerning other relevant rules and national authorities	61

Provisions of the Swedish National Board of Occupational Safety and Health on Contained Use of Genetically Modified Micro-organisms



Adopted 22nd May 2000

Published 28th June 2000

The following Provisions are issued by the National Board of Occupational Safety and Health pursuant to the Genetically Modified Organisms (Contained Use) Ordinance (SFS 2000:271)¹

Scope

Section 1

These Provisions apply to the contained use of genetically modified micro-organisms, subject to the exceptions indicated in Sections 3 and 5 of the Genetically Modified Organisms (Contained Use) Ordinance (SFS 2000:271).

A party conducting an activity coming within the scope of the exceptions in Section 3 of the Ordinance shall, however, on the basis of the assessment which, pursuant to Chap.13, Section 8 of the Environmental Code, shall precede such activity, see to it that the activity is planned, organised and conducted in accordance with Section 6 of these Provisions.

Definitions

Section 2

The terms and expressions used in these Provisions have the same meanings as in Chap.13, Sections 3-7 of the Environmental Code (1998:808) and Section 1 of the Genetically Modified Organisms (contained used) Ordinance (SFS 2000:271). Otherwise the terms and expressions stated below have the meanings given.

<i>GMM</i>	Genetically modified micro-organism as defined in the Genetically Modified Organisms (Contained Use) Ordinance.
<i>Donor organism</i>	An organism from which genetic material is transferred to another organism.
<i>Recipient organism</i>	(a) An organism which has received foreign genetic material,

¹ Cf. Council Directive 90/219/EEC of 23 April 1990 on the contained use of genetically modified micro-organisms (OJ L 117, 8.5.1990, p.1, Celex 390L0219) last amended through Council Directive 98/81/EC (OJ L 330, 5.12.1998, p.13, Celex 398L0081).

AFS 2000:5

- (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.

<i>Vector</i>	A virus, plasmid or other type of carrier capable of transmitting foreign genetic material to a recipient organism.
<i>Insert</i>	Genetic material inserted in a recipient organism with the aid of a vector or by some other technique.
<i>User</i>	The party conducting an activity, or more than one activity, involving contained use of genetically modified micro-organisms.
<i>Decontamination</i>	Treatment of material, cultures and surfaces in order to kill or inactivate GMMs.
<i>Primary containment measures</i>	Protective measures to prevent GMMs spreading on working premises.
<i>Secondary containment measures</i>	Protective measures taken to prevent GMMs spreading outside working premises.

Risk Assessment

Section 3

In the assessment which, pursuant to Chap.13, Section 8 of the Environmental Code, shall precede contained use of GMMs, the user shall follow the procedure indicated in App.1 in order to assess what risks to health and the environment the use may entail.

The user shall have access to the competence needed for an all-round risk assessment.

The risk assessment shall form the basis of the selection of containment and other protective measures.

Classification and containment level

Section 4

The classification of an activity as an F activity, L activity or R activity under Section 8 of the Genetically Modified Organisms (Contained Use) Ordinance (SFS 2000:271) shall be based on the criteria set forth in App.2.

With reference to the containment and other protective measures needed in order for the activity not to cause harm to health or the environment, it shall be deemed to belong to one of the containment levels 1-4 as stated in App.3, Section B. If one or more containment and other protective measures are needed at a higher containment level

than other containment and protective measures, the activity belongs to the higher containment level unless otherwise decided by the supervisory authority.

Documentation

Section 5

The risk assessment shall be documented in such a way that it is possible to judge whether the relevant factors affecting the choice of containment and other protective measures have been taken into account. Documentation shall also exist which clearly shows that the review and updating of the risk assessment and the assessment of containment and other protective measures to be carried out under Section 13 of the Genetically Modified Organisms (Contained Use) Ordinance (SFS 2000:271) have been carried out.

The documentation shall be available for presentation at the request of the Supervisory Authority.

Containment and other protective measures

Section 6

The activity should be planned, organised and conducted in such a way that exposure to GMMs is at the lowest level practicable in the facility and its surroundings.

In this connection the measures indicated in (a)-(d) shall be considered in the order given.

- (a) GMMs shall be selected which entail as little risk to health and the environment as the activity permits.
- (b) Working methods, processes and technical devices shall be selected and designed in such a way that the risk is reduced and exposure to GMMs is counteracted.
- (c) Containment and other protective measures are taken at source, so that no-one is exposed to the risks associated with the activity.
- (d) Work is confined to a particular time or place. Only personnel needed for this work are present.
- (e) Personal protective equipment is used.

Section 7

General principles of good micro-biological practice, as set forth in App. 3A shall be applied to all contained use of GMMs.

In addition, containment and other protective measures shall be applied in accordance with the relevant table and containment level in App. 3B, unless otherwise decided by the supervisory authority following presentation of a risk assessment.

AFS 2000:5

Facilities, fittings, equipment and control

Section 8

Facilities, fittings and equipment shall be designed in such a way that risks associated with the use of GMMs are avoided, the spread of GMMs is limited and the cleaning and decontamination necessary are facilitated.

Section 9

Control and maintenance shall be carried out to the extent necessary in order to prevent GMMs harming health and the environment.

If necessary, the occurrence of GMMs outside the primary and secondary containment shall be checked.

Signage and marking

Section 10

Warning signs shall be put up at the entrances to facilities or working areas with contained use of GMMs at containment level 2 or above as per Section 4 and App.3. Signs shall display a biohazard symbol as indicated in the Provisions of the National Board of Occupational Safety and Health on Safety Signs and Warning Signals at Workplaces (AFS 1997:11), an indication of the containment level, where relevant the text "Smittrisk" (infection risk) and other additional information that is needed. Signs referring to containment levels 3 and 4 as referred to in App. 3 shall also include information concerning access restrictions.

Section 11

In connection with contained use of GMMs at containment level 2 or above, as referred to in Section 4 and App. 3, materials, including containers and other equipment containing GMMs shall be marked. The marking shall contain a biohazard symbol as indicated in the Provisions of the National Board of Occupational Safety and Health on Safety Signs and Warning Signals at Workplaces (AFS 1997:11), an indication of the containment level, where relevant the text "Smittrisk" (infection risk) and other particulars necessary to prevent GMMs causing harm to health or the environment. Marking with such particulars as are common knowledge at the place where they occur may be excluded, if this can be done without any risk to health and the environment.

Cleaning, decontamination and transfer of contaminated material

Section 12

Cleaning and decontamination shall be carried out to the extent necessary in order to prevent GMMs causing harm to health or the environment. The methods used shall be designed so as to avoid the spreading of GMMs.

Active agents and methods for decontamination shall be used when necessary. Special routines shall exist for dealing with spillage.

Section 13

Waste and other material consisting of or containing GMMs shall be handled in accordance with predefined routines, in such a way that risks to health and the environment are avoided. The party transporting or disposing of such material shall be informed in advance concerning the material, the risks associated with its handling and the need for containment and other protective measures.

Personal protective equipment and hygiene

Section 14

Good personal hygiene shall be observed by anyone who may come into contact with GMMs. The equipment needed for this purpose shall be readily available. In connection with work entailing a risk of infection, a means of skin decontamination and hand-washing facilities shall be provided in immediate conjunction with the workplace. No procedures entailing a risk of GMMs entering the mouth may occur.

Section 15

Protective clothing shall be used as indicated in App.3. Protective clothing shall be stored separately from private clothing. Protective clothing and other personal protective equipment shall be removed when leaving the workplace. They shall be managed and stored in such a way that the spread of GMMs is avoided.

Protective gloves shall be used for work entailing a risk of skin contact with GMMs if the work can entail ill-health. Protective gloves shall be used on other occasions when needed.

Respiratory protective equipment shall be used for work entailing a risk through the inhalation of GMMs, if technical measures are not sufficient to prevent such air contamination causing ill-health.

Other suitable personal protective equipment shall be used when necessary.

Knowledge, information and instructions

Section 16

The user shall see to it that the person directing the work and everyone who may come to be exposed has sufficient knowledge of the GMMs occurring in the activity, of the risks with the activity which these organisms can entail, and how these risks are to be avoided.

Written handling and safety instructions on the way in which the work is to be conducted so that GMMs will not cause harm to health or the environment shall be given to those who in the course of the activity come into contact with GMMs at containment level 2 or above as per App. 3 and otherwise when necessary. Measures to be taken in the event of unwanted occurrences which can lead to human beings or the environment being subjected to harmful exposure shall always be included in the instructions. These measures shall be practised regularly. The user shall ascertain that the instructions have been understood and are complied with.

AFS 2000:5

Illnesses, accidents and incidents

Section 17

The user shall see to it that routines exist for

- (a) reporting to the supervisory staff on
 - ill-health which may be connected with the GMMs used,
 - accidents and incidents caused by them and capable of entailing a risk to health or the environment,
- (b) interaction with those concerned, in order to investigate the causes of what has happened.

Containment and other protective measures, routines or instructions shall if necessary be modified in order to avoid a repetition of the occurrence.

Contingency plan

Section 18

In connection with R activity, the user shall draw a contingency plan for measures to be taken in the event of an inadvertent escape which can entail serious immediate or delayed danger to human beings in or outside the plant or to the environment. The plan shall ensure that the Municipal Rescue Service and the Environment and Health Protection Committee, together with others who may be affected, are informed of what needs to be done in the event of an accident. The plan shall also ensure that the information is commonly available and is updated at appropriate intervals.

The supervisory authority for contained use of GMMs, the Municipal Rescue Service and the Environment and Health Protection Committee shall, in the event of an accident, be informed immediately concerning

- the more detailed circumstances of the accident,
- the identity and quantity of the GMMs which have escaped,
- all information necessary for assessing the impact of the accident on health and the environment, and
- the rescue measures which have been taken.

Notification and application for permits

Section 19

In notification of an F activity as referred to in Sections 15 and 23 of the Genetically Modified Organisms (Contained Use) Ordinance (SFS 2000:271), the particulars indicated in App. 4 shall be supplied to the supervisory authority.

AFS 2000:5

Section 20

In notification of an L activity as referred to in Sections 15 and 25 of the Genetically Modified Organisms (Contained Use) Ordinance (SFS 2000:271), the particulars indicated in App. 5 shall be supplied to the supervisory authority.

Section 21

In application for permit for an R activity, as referred to in Sections 15 and 26 of the Genetically Modified Organisms (Contained Use) Ordinance (SFS 2000:271), the particulars indicated in App. 6 shall be supplied to the supervisory authority.

Charges

Section 22

In connection with notification and application for permit relating to activities as referred to in Sections 19-21 of these Provisions and for inspection, the following charges are payable to the supervisory authority.

1. A basic charge of SEK 2,000.
2. For time in excess of 4 hours devoted to inspection or handling directly relating to the matter in hand, SEK 800 per hour.

The charge shall on no account exceed the following amounts:

Permit for R activities	SEK 50,000
Notification of L activities	SEK 20,000
Notification of F activities	SEK 15,000
Inspection, per premises	SEK 30,000

The supervisory authority may order a reduction of the charge if there are special reasons for so doing.

Liability

Section 23

Chap. 29 of the Environmental Code contains stipulations concerning fines or imprisonment for unauthorised environmental activity (Section 4), obstruction of environmental control (Section 5) and inadequate environmental information (Section 6).

AFS 2000:5

Entry into force

These Provisions enter into force on 1st October 2000.

The Ordinance of the National Board of Occupational Safety and Health (AFS 1994:46) containing Provisions on Contained Use of Genetically Modified Micro-Organisms is repealed with effect from the same date.

KENTH PETTERSSON

Thorleif Joelson

Göran Lindh

Principles to be followed for the assessment of risk and selection of containment and other protective measures

This Appendix describes the principles to be followed in the assessment of risk and the selection of containment and other protective measures as referred to in Section 3. During this process special attention shall be paid to the factors enumerated in App. 1B.

A. Procedure

1. The first stage in the risk assessment process is to identify any harmful properties of the biological material.

To this end, the harmful effects, which may be associated with the recipient and, where appropriate, the donor organism shall be identified. The harmful effects which may be associated with the vector or inserted material shall also be identified.

2. Assessment of any harmfulness which may be associated with the GMM resulting from the genetic modification.

The harmful effects which could arise as a consequence of the recombination or transformation of the genetic material should be identified. In the final assessment a balance shall be struck between the harmful effects identified in point 1 (including the extent to which they can be expressed in the new structure) and any new harmful effects which have been identified for the resultant GMMs. In order to gauge the realism of the risk assessment performed, a comparison should be made with other organisms which have known risks. App. 2 contains criteria concerning the properties which a GMM must at least present in order to be deemed to constitute no risk or a negligible risk in connection with contained use in an F activity.

In hazard identification and assessment of the biological material, all available knowledge shall be taken into account, including comparisons with existing classification systems for human, plant and animal pathogens and mandatory information from the supplier.

If, in the hazard comparison with other organisms, it is found that the level of risk does not appear to be correct, the assessment shall be reviewed.

3. An assessment shall be made of the containment and other protective measures needed for the prevention of harmful effects on health and the environment. The selection of containment and other protective measures shall be based on an assessment of the consequences and likelihood of harmful effects resulting from the effect of the activity as a whole. In this connection, the following shall be taken into account.

- (a) The assessment, as referred to in points 1 and 2, above, of the harmful effects which can occur as a consequence of the biological material and the GMM to be used.

AFS 2000:5

- (b) The characteristics of the environment which may, in the event of accidental release, be exposed to the GMM used, and any known biota which may come to be affected in such a case.
- (c) The characteristics of the activity, its scale and nature.
- (d) Non-standard operations and conditions which may affect the risk, e.g. the inoculation of animals with GMMs or the use of equipment likely to generate aerosols.

Consideration of the items set forth in point 3 may increase, reduce or leave unaltered the risk and the need for containment and other protective measures indicated by the preliminary assessment of the inherent properties of the organism as per points 1 and 2.

The containment and other protective measures shall be chosen which are needed in order to minimise the risks with an adequate margin of safety, having regard to the outcome of the risk assessment. The containment and other protective measures chosen shall be compared with containment and other protective measures in the applicable tables in App. 3 in order to establish the containment level as referred to in Section 4.

As a final check, an assessment is made of the risks occurring in the activity in the event of the containment and other protective measures chosen being applied. If the protection proves to be insufficient, further containment and other protective measures need to be taken.

B. Factors to be considered in the assessment

1. The following are regarded as potentially harmful effects:
 - (a) Disease in human beings, including infection, allergenic or toxic effect and a potential for causing cancer, together with the severity and transmissibility of these diseases and harmful effects.
 - (b) Disease in animals or plants.
 - (c) Deleterious effects due to the impossibility of treating a disease or providing an effective prophylaxis.
 - (d) Deleterious effects due to harmful substances formed by GMMs.
 - (e) Deleterious effects due to establishment or dissemination in the environment.
 - (f) Deleterious effects due to the natural transfer of inserted genetic materials to other organisms.
2. Assessment of risks, classification of activity and selection of containment and other protective measures are based on the following:
 - (a) Identification of potentially harmful effects, in particular those associated with
 - the recipient organism,
 - the donor organism (as long as the donor organism is used during the operation)
 - the genetic material inserted,
 - the vector,
 - the resultant genetically modified micro-organism, GMM.

AFS 2000:5

- (b) The characteristics of the activity
- (c) The severity of the potentially harmful effects
- (d) The likelihood of the potentially harmful effects being realised.

Criteria for the classification of an activity with GMMs as an F, L or R activity as provided in Section 4

When it is uncertain whether an activity pertains to a lower or higher category, the higher category applies.

F Activity: An activity involving contained use of GMMs and entailing a negligible risk or none at all of harm to human health and the environment. This includes activities where containment and other protective measures at containment level 1, as per the relevant Table in App. 3, are applicable and where the GMM to be used presents at least the following characteristics.

- No recipient organism is likely to cause disease to humans, animals or plants.
- The vector or insert do not endow the genetically modified micro-organism with a phenotype likely to cause disease to humans, animals or plants or likely to cause deleterious effects in the environment.
- The properties of the resultant GMM are such that it is unlikely to cause disease to humans, animals or plants or otherwise to cause deleterious effects in the environment.

The effects referred to are those which are possible in the environment which the organism may come into contact with in the event of accidental release.

If one or more of the containment and other protective measures at containment level 2, as per the relevant Table in App. 3, are needed, the activity is assigned to category L, unless otherwise resolved by the supervisory authority.

L Activity: An activity with contained use of GMM in which there is a low risk of harm to human health and the environment. This category comprises activities meeting all of the following criteria:

- The activity does not belong to category F.
- Containment and other protective measures at containment level 2 as per the relevant Table in App. 3 are sufficient.
- The volume of culture handled at any one time does not exceed 500 litres.

If one or more of the containment and other protective measures at containment levels 3 or 4 as per Table 1 or on containment level 2 or above in Table 2 of App. 3 is needed, the activity is assigned to category R, unless otherwise resolved by the supervisory authority.

R Activity: An activity with contained use of GMMs where there is a moderate or high risk of harm to human health and the environment. This includes all activity not belonging to categories F or L.

Containment and other safety measure to be taken pursuant to Section 7

A. Good microbiological practice

Good microbiological practice means:

- not eating, drinking, applying cosmetics, using tobacco products or handling foodstuffs within the working area,
- observing cleanliness and tidiness,
- not pipetting by mouth or otherwise working in such a way that a GMM is liable to enter the mouth,
- avoiding formation and spread of aerosols, spillage and spatter,
- handling syringes and sharp objects which have been in contact with body fluids or infected material in a safe manner and not using both hands to replace the protective cover of the syringe,
- handling waste in a safe manner,
- handling cultures in closed vessels,
- using protective clothing in but not outside the working area,
- being prepared for accidents.

B. Containment and other protective measures for the contained use of GMMs at various containment levels

Table 1 a

Containment and other protective measures for laboratory activities

A Containment and other protective measures		B C D E Containment levels			
		Level 1	Level 2	Level 3	Level 4
Facilities and equipment					
1.	Isolation	No	Segregated from other activities	Yes	Yes, in separate building or as a completely isolated unit in a building for other activities
2.	Entry to lab by airlock only	No	No	Yes, in the event of airborne infection or otherwise, subject to risk assessment	Yes
3.	Biohazard sign	No	Yes	Yes	Yes
4.	Separate ventilation system with HEPA filtration of extract air	No	No	Yes, in the event of airborne infection or otherwise, subject to risk assessment	Yes, and also HEPA filtration of input air. For virus not trapped by HEPA filter, additional air handling measures etc.
5.	The laboratory has negative pressure relative to the pressure of the immediate environment	No	No	Yes, in the event of airborne infection or otherwise, subject to risk assessment	Yes
6.	The laboratory is sealable for fumigation	No	Optional, subject to risk assessment	Yes	Yes

AFS 2000:5

A Containment and other protective measures		B C D E Containment levels			
		Level 1	Level 2	Level 3	Level 4
7.	Hand-washing facilities provided	Yes	Yes, preferably with hands-free control and hand disinfection	Yes, with hands-free control and hand disinfection	Yes, with hands-free control and hand disinfection
8.	Shower directly adjoining lab	No	No	Optional, subject to risk assessment	Yes
9.	Surfaces resistant to water, acids, alkalis, solvents and disinfectants and easy to clean	Yes (bench)	Yes (bench, floor)	Yes (bench, floor)	Yes (bench, floor, ceiling, walls)
10.	Facility equipped for disinfection of effluent from hand-washing sink, showers and drains	No	No	Optional, subject to risk assessment (accident preparedness)	Yes
11.	Observation window or the equivalent provided so that occupants can be seen.	Optional, subject to risk assessment	Optional, subject to risk assessment	Yes	Yes
12.	Autoclave provided	Yes, failing some other adequate decontamination arrangement	Yes, adjoining the activity	Yes, in the laboratory, possibly double ended	Yes, in the laboratory, double ended
13.	Laboratory's own equipment inside the controlled area	No	Optional, subject to risk assessment	Yes	Yes
14.	Microbiological safety cabinet with HEPA filter or corresponding enclosure provided within the working area	No	Yes, for handling infected material if there is a risk of significant aerosol generation or otherwise subject to risk assessment	Yes, safety cabinet class 1 or 2 for handling infected material	Yes, safety cabinet class 3

AFS 2000:5

A		B	C	D	E
Containment and other protective measures		Containment levels			
		Level 1	Level 2	Level 3	Level 4
15.	Alarm system provided to indicate whether technical safety equipments are out of order	No	Yes, for safety cabinet and otherwise subject to risk assessment	Yes	Yes
16.	Reserve power supply provided for technical safety equipments in the laboratory	No	No	Subject to risk assessment	Yes
Working routines and organisation					
17.	Restricted access	No	Yes, access only for persons informed of the risks	Strict, access only for authorised personnel. Locking routines	Strict, access only for authorised personnel. Locking routines
18.	Protective clothing used within the working area and removed when leaving it	Generally	Suitable protective clothing	Full protective clothing, change of footwear and use of shower when necessary	Complete change of protective clothing and footwear, shower before exit
19.	Gloves used	No	Subject to risk assessment	Yes	Yes
20.	Secure GMM storage	Subject to risk assessment	So that no-one is inadvertently exposed and no unauthorised person can gain access to the material	So that no-one is inadvertently exposed and no unauthorised person can gain access to the material. Storage primarily in the controlled area.	So that no-one is inadvertently exposed and no unauthorised person can gain access to the material. Storage in the controlled area.
21.	Routines exist for the prevention of exposure and for dealing with spillage, accidents and incidents	Yes	Yes, including written instructions	Yes, including written instructions	Yes, including written instructions
22.	Specific measures to control aerosol dissemination	Yes, subject to risk assessment	Yes, minimised	Yes, prevented	Yes, prevented

AFS 2000:5

A		B	C	D	E
Containment and other protective measures		Containment levels			
		Level 1	Level 2	Level 3	Level 4
23.	Used material containing GMMs is decontaminated before being washed, re-used, discarded (waste included)	Yes	Yes	Yes, before leaving the laboratory	Yes, before leaving the laboratory
24.	Effective pest control (e.g. for rodents and insects)	Optional, subject to risk assessment	Yes	Yes	Yes

AFS 2000:5

Table 1b

Containment and other protective measures, over and above those indicated in Table 1a, when working with animals deliberately infected with GMMs

A Containment and other protective measures		B Containment levels			
		C Level 1	D Level 2	E Level 3	F Level 4
Facilities and equipment					
25.	Isolator or other HEPA-filtered containment provided	No	Optional, subject to risk assessment	For airborne infection or otherwise subject to risk assessment	Yes
26.	Animal facilities separated by lockable doors	Optional, subject to risk assessment	Yes	Yes	Yes
27.	Measures taken to limit the possibility of the animals escaping from the controlled area	Yes	Yes	Yes	Yes
28.	Material and equipment designed for easy cleaning and decontamination	Optional, subject to risk assessment	Yes	Yes	Yes
29.	Surfaces easy to clean, over and above the requirements of Table 1 a, item 9	Optional, subject to risk assessment		Walls	
Working routines and organisation					
30.	Incineration of animal cadavers	Recommended	Yes	Yes	Yes, incinerator on the spot
31.	Disposable clothing used, changed every time	No	Optional, subject to risk assessment	Yes	Yes, complete change
32.	Bedding and waste decontaminated	Optional, subject to risk assessment	Yes	Yes	Yes

Table 1 c

Containment and other protective measures, over and above those indicated in Table 1a, when working with plants deliberately infected with GMMs

A Containment and other protective measures		B Containment levels			
		C Level 1	D Level 2	E Level 3	F Level 4
Facilities and equipment					
33.	Greenhouse/ growth room: structure with walls, a roof and a floor intended for growing plants in a controlled and protected environment	Optional, subject to risk assessment	Yes	Yes	Yes
34.	Permanent structure with continuous water-proofed covering, designed to prevent entry of surface-water run-off and having lockable doors	No	Yes	Yes	Yes
35.	Entry to greenhouse/ growth room through airlock only	No	Optional, subject to risk assessment	Yes	Yes
36.	Control of contaminated run-off water	Optional, subject to risk assessment	Water run-off minimised where transmission of GMMs can occur through the ground	Water run-off prevented	Water run-off prevented
37.	Procedures for transfer of living material between different places, e.g. greenhouse and laboratory	Minimised dissemination of GMMs	Minimised dissemination of GMMs	Prevent dissemination of GMMs	Prevent dissemination of GMMs
38.	Effective pest control (e.g. for rodents and insects)	Yes	Yes	Yes	Yes

AFS 2000:5

Table 2

Containment and other protective measures for large-scale processes

A Containment and other protective measures		B C D E Containment levels			
		Level 1	Level 2	Level 3	Level 4
Facilities and equipment					
39.	Viable organisms handled in a system which separates the process from the environment (closed system)	Yes	Yes	Yes	Yes
40.	Closed systems located within a controlled area.	Optional, subject to risk assessment	Yes	Yes	Yes
41.	Access to the controlled area through airlock only	No	Optional, subject to risk assessment	Yes	Yes
42.	The controlled area has specific ventilation to minimise air contamination.	Optional, subject to risk assessment	Optional, subject to risk assessment	Optional, subject to risk assessment	Yes
43.	Extract and input air from the controlled area HEPA-filtered	No	Optional, subject to risk assessment	Yes, for extract air, subject to risk assessment for input air	Yes
44.	Controlled area maintained at an air pressure negative to the immediate surroundings	No	Optional, subject to risk assessment	Optional, subject to risk assessment	Yes
45.	Controlled area sealable to permit fumigation	No	Optional, subject to risk assessment	Optional, subject to risk assessment	Yes
46.	Surfaces resistant to water, acids, alkalies, solvents and disinfectants and easy to clean	Yes, bench if any	Yes, bench, if any, and floor	Yes, bench, if any, and floor	Yes, bench, floor, ceiling and walls

AFS 2000:5

A		B	C	D	E
Containment and other protective measures		Containment levels			
		Level 1	Level 2	Level 3	Level 4
47.	The controlled area is designed so that spillage and the entire contents of the closed system can be contained and decontaminated in the event of an accident	Optional, subject to risk assessment	Yes	Yes	Yes
48.	Exhaust gas from closed systems is handled in such a way that emissions:	Do not harm health or the environment	Are minimised	Are prevented	Are prevented
49.	Seals are designed so that release:	Does not harm health or the environment	Is minimised	Is prevented	Is prevented
50.	Alarm system provided to indicate whether technical safety equipments are out of order	No	Optional, subject to risk assessment	Yes	Yes
51.	Reserve power supply provided for technical safety equipments on the premises	No	Optional, subject to risk assessment	Optional, subject to risk assessment	Yes
52.	Biohazard sign posted	No	Yes	Yes	Yes
53.	Hand-washing facilities provided	Yes	Yes, preferably with hands-free control and hand disinfection	Yes, with hands-free control and hand disinfection	Yes, with hands-free control and hand disinfection
54.	Shower provided within the controlled area	No	No	Optional, subject to risk assessment	Yes
Working routines and organisation					
55.	Restricted access	No	Yes, access only for persons informed of the risks	Strict, access only for authorised personnel. Locking routines	Strict, access only for authorised personnel. Locking routines
56.	Special protective clothing used	Yes	Yes	Yes	Yes, complete change
57.	Personnel use shower before exit from the controlled area	No	No	Optional, subject to risk assessment	Yes

AFS 2000:5

A		B	C	D	E
Containment and other protective measures		Containment levels			
		Level 1	Level 2	Level 3	Level 4
58.	Inactivation of GMMs in contaminated material and waste including those in process effluent before final discharge	Yes, using methods decided after risk assessment	Yes, decontamination by validated inactivation methods	Yes, decontamination by validated inactivation methods	Yes, decontamination by validated inactivation methods
59.	Sample collection, addition of material to a closed system and transfer of viable organisms to another closed system are performed in such a way that release:	Does not cause harm to health or the environment	Is minimised	Is prevented	Is prevented
60.	Decontamination of bulk culture fluids before removal from the closed system for further handling	Subject to risk assessment of other containment measures applied	Yes, decontamination by validated inactivation methods	Yes, decontamination by validated inactivation methods	Yes, decontamination by validated inactivation methods
61.	Effluence from hand-washing sinks, showers etc collected and inactivated before being released.	No	No	Optional, subject to risk assessment	Yes

Information to be provided in notification of F activity as referred to in Sections 15 and 23 of the Genetically Modified Organisms (Contained Use) Ordinance (SFS 2000:271)

1. The name, address and (where relevant) corporate registration number of the user.
2. Description of the allocation of tasks as referred to in Section 4 of the Internal Control (Users) Ordinance (SFS 1998:901) and of how this relates to the allocation of tasks under the Provisions of the National Board of Occupational Safety and Health on Internal Control of the Working Environment (AFS 1996:6).
3. Names of the persons in charge of the activity, including those responsible for supervision and safety, and information on the training and qualifications of these persons.
4. Information on biosafety committees, if such exist, or on any other advisory competence to which the user has access as provided in Section 3.
5. The address and identifying designation of the premises.
6. Information on the extent of the premises, with identifying designations of the rooms.
7. Description of the nature of the activity.
8. Approximate culture volumes to be used.
9. Summary of the assessment, referred to in Section 3, of the risks which the activity entails to health and the environment, together with one example of documentation of the assessment, as referred to in Section 5, for a GMM use included in the activity.
10. Description of containment and other protective measures. Indication of applicable table and containment level as per App. 3, together with any deviations from the same as regards individual containment and other protective measures.
11. Approximate number of persons to be employed in the activity.
12. Description of waste management.

Information to be provided in notification of L activity and of new use within previously notified L activity as referred to in Sections 15 and 25 of the Genetically Modified Organisms (Contained Use) Ordinance (SFS 2000:271)

General information about the activity

1. The name, address and (where relevant) corporate registration number of the user.
2. Description of the allocation of tasks as referred to in Section 4 of the Internal Control (Users) Ordinance (SFS 1998:901) and of how this relates to the allocation of tasks under the Provisions of the National Board of Occupational Safety and Health on Internal Control of the Working Environment (AFS 1996:6).
3. Information on biosafety committees, if such exist, or on any other advisory competence to which the user has access as provided in Section 3.
4. The address and identifying designation of the premises.

Specific information about each individual use within the L activity

5. Information about the part of the premises to be used, with identifying designations of rooms and a drawing or sketch.
6. Names of the persons in charge of the activity, including those responsible for supervision and safety, and information on the training and qualifications of these persons.
7. Description of the nature of the activity.
8. Information about the biological material, including the identity and characteristics of the GMMs used, together with components relevant to the risk assessment referred to in App. 1.
9. Description of the purpose of the contained use, including the expected results.
10. Description of specific procedures or conditions with a possible bearing on risk.
11. Description of the maximum culture volume to be handled at any one time and of the mode of cultivation.
12. Summary of the assessment of risks to health and the environment, as referred to in Section 3.
13. Information about the persons taking part in the risk assessment (e.g. a biosafety committee) and any advice given by them.
14. Description of containment and other protective measures. Indication of applicable table and containment level as per App. 3, together with any deviations from the same as regards individual containment and other protective measures.
15. Handling and safety instructions drawn up for the work.
16. Description of the waste which will be generated, its treatment, final form and destination.
17. Approximate number of persons to be employed in the activity.

Information to be provided in permit application for R activity and of new use within R activity for which permit previously has been issued as referred to in Sections 15 and 26 of the Genetically Modified Organisms (Contained Use) Ordinance (SFS 2000:271)

General information about the activity

1. The name, address and (where relevant) corporate registration number of the user.
2. Description of the allocation of tasks as referred to in Section 4 of the Internal Control (Users) Ordinance (SFS 1998:901) and of how this relates to the allocation of tasks under the Provisions of the National Board of Occupational Safety and Health on Internal Control of the Working Environment (AFS 1996:6).
3. Information on biosafety committees, if such exist, or on any other advisory competence to which the user has access as provided in Section 3.
4. The address and identifying designation of the premises.

Specific information about each individual use within the R activity

5. Information about the part of the premises to be used, with identifying designations of rooms and a drawing or sketch.
6. Names of the persons in charge of the activity, including those responsible for supervision and safety, and information on the training and qualifications of these persons.
7. Description of the nature of the activity.
8. Information about the biological material, including the identity and characteristics of the GMMs used, together with components relevant to the risk assessment referred to in App. 1.
9. Description of the purpose of the contained use, including the expected results.
10. Description of specific procedures or conditions with a possible bearing on risk.
11. Description of the maximum culture volume to be handled at any one time and of the mode of cultivation.
12. Summary of the assessment of risks to health and the environment, as referred to in Section 3.
13. Information about the persons taking part in the risk assessment (e.g. a biosafety committee) and any advice given by them.
14. Description of containment and other protective measures. Indication of applicable table and containment level as per App. 3, together with any deviations from the same as regards individual containment and other protective measures.
15. Handling and safety instructions drawn up for the work.
16. Description of the waste which will be generated, its treatment, final form and destination.
17. Description of routines for verifying the continuing effectiveness of the containment measures as referred to in Section 10.
18. Approximate number of persons to be employed in the activity.

AFS 2000:5

19. Information about medical preventive measures and controls.
20. Information about accident prevention and contingency plan as referred to in Section 18:
 - (a) Risk sources and circumstances in which accidents may occur,
 - (b) conceivable consequences of an accident for health and the environment and the specific dangers which the location of the installation may entail,
 - (c) the preventive measures applied, e.g. safety equipment, alarm system and containment methods and procedures,
 - (d) description of the information provided to the employees, and
 - (e) an assurance that the competent authorities charged with rescue measures have been informed of the contingency plan.
21. Time for which a permit is requested.

General Recommendations of the Swedish National Board of Occupational Safety and Health on the implementation of the Provisions on Contained Use of Genetically Modified Micro-Organisms

The following General Recommendations are issued by the National Board of Occupational Safety and Health on the implementation of its Provisions (AFS 2000:5) on Contained Use of Genetically Modified Micro-Organisms (GMMs).

Background

General Recommendations have a different legal status from Provisions. They are not mandatory. Instead they serve to elucidate the meaning of the Provisions (e.g. by explaining suitable ways of meeting the requirement, giving examples of practical solutions and procedures) and to provide recommendations, background information and references.

Council Directive 90/219/EEC on the contained use of genetically modified micro-organisms has been amended through Council Directive 98/81/EC. The amendments amount to a re-writing of virtually every article of Directive 90/219/EEC. The system of classification has been altered, partly through the introduction of containment and other protective measures at four levels, which accords better with the rules applying to unmodified micro-organisms. Cf. the Provisions of the National Board of Occupational Safety and Health on **Biological Agents**. At the same time a holistic view has been introduced whereby the entire activity is factored into risk assessment and classification, i.e. not just the organism but also what is done with it.

The amendments introduced in Sweden by reason of Directive 98/81/EC are found in the Environmental Code and its appurtenant Ordinances and also in these Provisions.

Under Section 13 and Appendix 1, point F, of the Supervision (Environmental Code) Ordinance (SFS 1998:900), the National Board of Occupational Safety and Health is centrally responsible for the direction of supervision and is also in charge of operative supervision of contained use of genetically modified micro-organisms. Given the definition of supervisory authority in Section 2 of the Genetically Modified Organisms (Contained Use) Ordinance (SFS 2000:271), the Swedish Work Environment Authority is the supervisory authority for contained use of genetically modified micro-organisms since 1st January 2001. This supervisory responsibility applies with reference to human health and the environment.

Guidance on individual sections

Guidance on Section 1

Use of genetically modified organisms in Sweden is regulated by the Environmental Code (1998:808). Accordingly, the Code and other rules issued by authority of it are applicable, where relevant, to contained use of genetically modified micro-organisms. Chap. 13 of the Environmental Code lays down rules for genetically modified organisms, but other parts of the Code also contain rules with a direct bearing on the contained use

AFS 2000:5

of genetically modified micro-organisms, e.g. the general rules of care set forth in Chap. 2.

Rules issued by authority of the Environmental Code include, for example, Genetically Modified Organisms (Contained Use) Ordinance (SFS 2000:271) and the Internal Control (Users) Ordinance (SFS 1998:901).

Section 3 of Ordinance (SFS 2000:271) indicates certain kinds of activity to which the stipulations of Chap. 13 of the Environmental Code concerning contained use shall not apply. The exception only concerns the stipulations expressly mentioned. These include, for example, the administrative stipulations, such as those concerning notification and permits. Obviously, an assessment has to be made in order to establish whether the criteria for the exception, as referred to in Section 3 of the Ordinance, are satisfied. GMMs excluded from the stipulations on contained use, on condition that they cannot entail negative effects on human health or the environment, include organisms produced by mutagenesis, the reference here being to mutagenesis by traditional chemical and physical methods occurring prior to the breakthrough of recombinant DNA technology. Activities may not be excluded from the rules if they involve the use of recombinant nucleic acid molecules or genetically modified organisms produced by methods other than those indicated in points 1-5 of Section 3, paragraph one, of the Genetically Modified Organisms (Contained Use) Ordinance (SFS 2000:271).

The exceptions under Section 3 of the Genetically Modified Organisms (Contained Use) Ordinance (SFS 2000:271) do not apply to the stipulations of Chap. 13 of the Environmental Code concerning deliberate release into the environment. Instead special exceptions apply to such activities. So long as there is no permit or exception for deliberate release, therefore, use must be contained. Other rules applying to these activities include, for example, various rules issued by the National Board of Occupational Safety and Health concerning microbiological work environment hazards.

Nor does the exception apply, for example, to the requirement of investigation laid down in Chap. 13, Section 8 or the General Rules of Care in the Environmental Code as applied to contained use of GMMs.

In addition to the Provisions on contained use of GMMs based on the Environmental Code, there are Provisions based on other legislation, e.g. The Work Environment Act. Provisions of this kind are not subject to the exceptions in Ordinance (SFS 2000:271). The Provisions of the National Board of Occupational Safety and Health on **Biological Agents** apply to all biological agents (micro-organisms, cell cultures and human endoparasites), whether genetically modified or not. The Provisions of the National Board of Occupational Safety and Health on **contained use of genetically modified micro-organisms** include requirements for the working environment which agree with those in the Board's Provisions on **Biological Agents**, but there are also requirements concerning protection of the environment generally. The two sets of Provisions differ regarding the administrative requirements of notification, permission and supply of information. The work environment Provisions, e.g. the Provisions of the National Board of Occupational Safety and Health on **Biological Agents**, also include further requirements specific to the working environment.

For teaching in schools it may be an advantage to use methods and GMMs which are excluded from certain stipulations, because laboratory exercises can then be performed without extensive risk assessment or notification procedures.

Criteria of safe GMMs which are deemed safe for human health and the environment and therefore come within the scope of far-reaching exceptions to the stipulations on contained use of GMMs will be adopted by the Council of Ministers not later than 5th December 2000. GMMs which satisfy the criteria and can be considered for exception will be examined by a committee procedure within the EU. When a decision is taken concerning excluded GMMs, the Swedish Work Environment Authority will compile a list of them as provided in Section 4 of Ordinance (SFS 2000:271).

Guidance on Section 2

Chap. 13, Section 5 of the Act to amend the Environmental Code (SFS 2000:119) defines contained use as an activity in which organisms are genetically modified or in which such genetically modified organisms are cultured, stored, transported, destroyed, disposed of or used in any way, and for which specific containment measures are used to limit their contact with the general population and the environment. Section 10 of Genetically Modified Organisms (Contained Use) Ordinance (SFS 2000:271) provides that a physical barrier or a combination of physical and other barriers shall be used to limit the contact of organisms with the general population and the environment.

The definition of GMM

Ordinance (SFS 2000:271) defines a genetically modified micro-organism as "a micro-organism in which the genetic material has been altered in a way that does not occur naturally by mating and/or natural recombination." A micro-organism is defined as "any microbiological entity, cellular or non-cellular, capable of replication or of transferring genetic material, including viruses, viroids, animal and plant cells in culture."

Micro-organism, thus defined, is a **legal term** indicating the scope of regulation. The definition does not agree with that customarily used for scientific purposes. GMM is a term indicating what is regulated by these Provisions. The scope of GMM in this sense has a counterpart in Directive 98/81/EC on the contained use of genetically modified micro-organisms and in CEN standards for biotechnology.

Micro-biological units capable of replication can be instanced with bacteria, including actinomycetes and rickettsias and blue-green bacteria, microfungi, such as yeast and mould and micro-algae and protozoas. Lower replicating units, capable of replicating only with the aid of a host organism, e.g. viruses and viroids, are also included, but so too are infectious nucleic acids.

Cells from superior organisms such as humans, animals and plants can be cultivated as cell cultures, in which case they are micro-biological units capable of becoming GMMs when genetically modified, e.g. with the aid of viral vectors or if the cells come from genetically modified plants or animals. If, on the other hand, a cell culture from a plant, for example, is developed into a genetically modified plant, it is no longer a GMM. Contained use of genetically modified organisms (GMOs) other than GMMs is governed by rules issued by the Swedish Board of Agriculture and the National Board of Fisheries.

Examples of techniques considered, respectively, to result and (normally) not result in GMMs are given in App. A to these Recommendations.

AFS 2000:5

Definition of recipient organism

Sometimes it is impossible to identify the donor and recipient organisms respectively, as for example in the fusion of cells from different original organisms. Original organisms of this kind are sometimes also termed parental organisms. In these Provisions the expression "recipient organism" is consistently used for such cases.

Definition of vector

Vectors, e.g. viral vectors and plasmids, can transfer genetic material and thus constitute GMMs as defined, while at the same time being vectors. Even if a viral vector has been made incapable of replication, it may have the actual task of transmitting genetic material, in which case it remains a GMM.

In other contexts, "vector" can mean some other kind of carrier, e.g. an insect capable of transferring infection from a reservoir to a recipient, such as a human being. Vectors of this kind are not referred to here.

Definition of decontamination

Inactivation and decontamination of GMMs can mean treatment which renders them incapable of replication or of transferring genetic material. Autoclaving and treatment with chemical agents are examples of decontamination.

Definition of primary containment measures

Many of the containment and other protective measures in App. 3 can be regarded as primary containment measures. In the first instance they constitute protection for the personnel working in the activity.

In Ordinance (SFS 2000:271), a containment or other protective measure is defined as a containment measure or other precaution taken in order to prevent, impede or counteract harmful effects of the activity on human health or the environment. This can, for example, mean measures to prevent employees, the general public, plants, animals or the environment generally being exposed to GMMs.

Containment or other protective measures can, for example, relate to the design of premises and equipment and also to routines, organisation and the use of personal protective equipment. Containment and other protective measures afford protection with differing margins of safety at different levels and are applied according to risk assessment and the type of activity. See App. 3 and Recommendations.

Definition of secondary containment measures

Sometimes a GMM may be harmless to humans but constitute a risk, for example, to animals or plants in the surrounding environment. Certain of the primary containment and protective measures may then be unnecessary while secondary containment and protective measures, such as filtered extract air ventilation, effluent processing and an airlock, for example, may be important.

Guidance on Section 3

Chap.13, Section 8 of the Environmental Code (1998:808) requires a contained use and intentional release of genetically modified organisms to be preceded by an investigation. This shall be capable of forming the basis of a satisfactory assessment of the harm which the organisms are capable of causing to health and the environment. The investigation shall be conducted in accordance with science and proven experience. App.1 shows that the risk assessment concerns the organism, what is done with it and in what environment. In other words, the assessment relates to the activity in its entirety.

The persons carrying out and examining a risk assessment should between them have sufficient competence to be able to understand the risks to both health and the environment which could possibly occur as a consequence of the proposed use. This also involves being able to judge the likelihood of the activity being capable of having negative consequences for health and the environment and the gravity of those consequences in such an event.

If the contained use implies use of an organism having unknown characteristics, a thoroughly considered risk assessment is needed, especially if there may be potential risks involved to health and the environment. The risk assessment can be made more summary if direct comparisons are possible with similar uses, especially in the case of biological systems of which there is extensive experience.

In a major organisation, such as a company or a university for example, aggregate advisory competence in matters of risk assessment can appropriately be achieved by forming a biosafety committee. Failing a biosafety committee, other bodies possessing sufficient knowledge and experience should be consulted in cases of uncertainty.

Biosafety committees should be comprehensively recruited among experts in different fields, so as

- (a) To be able to understand the risks to health or the environment which might possibly arise as a consequence of the proposed use and uncertainty in the assessment of these risks, and
- (b) To discuss to a suitable extent, the results of risk assessment in such a way that the committee's advice truly results from a joint decision and not the standpoint of an individual person.

It is the user who is ultimately responsible for the risk assessment and the consequences of the contained use of GMMs, even when advice has been obtained concerning risk assessment and the activity.

The rules on prior assessment and official examination of activities involving GMMs serve a specific purpose in that genetically modified micro-organisms often have different characteristics from those occurring naturally. The risks which may be associated with naturally occurring organisms are often known, unlike those associated with GMMs.

See also the Guidance on App. 1.

AFS 2000:5

Guidance on Section 4

Categories of activity are primarily administrative categories which decide when stipulations on notification and permits apply. Stipulations of this kind are contained in Sections 15 and 23-26 of Ordinance (SFS 2000:271). Stipulations concerning the information to be provided in connection with such notification and applications for permits are contained in Sections 19-21 and Apps. 4-6 of the Board's Provisions.

The criteria of activity classification are set forth in App. 2. They are based on the containment and other protective measures in App. 3 which are needed in order for the activity not to cause harm to health or the environment. Under Section 4, the containment level is also based on the containment and other protective measures identified as necessary in the risk assessment process described in App. 1.

It is important to note that if one or more containment or other protective measures are needed from a higher containment level or table, the containment level and activity category are deemed to pertain to the higher category or containment level. It is possible, however, to adapt the containment and other protective measures to the risks of the individual case if it is a specified activity which does not agree with the templates represented by a certain activity category or containment level. See also Section 7 and Guidance on the same.

At present The Swedish Work Environment Authority is the supervisory authority for contained use of GMMs, under the Supervision (Environmental Code) Ordinance (SFS 1998:900) and can, if there are grounds for doing so, resolve if the activity belongs to a different containment level from that which would have followed from the containment and other protective measures chosen.

Guidance on Section 5

The risk assessment forms the basis for the choice of containment and other protective measures. Factors to be taken into account and the risk assessment procedure as referred to in Section 3 are described in App. 1.

The documentation of the risk assessment should be logically coherent, e.g. with a clear description of the supportive data, an assessment of the risks (possibly with a discussion of the same) and a conclusion giving a concise description of the risks which may be associated with the GMM use in question and of the foundations of this assessment. It is the holistic picture which is assessed, i.e. the characteristics of the organisms, facilities, culture equipment, the methods which will be used, the surrounding environment and other circumstances which may affect the risk associated with the contained use. See further App. 1 and Guidance on the same.

The extent to which the risk assessment needs to be documented depends on what is previously known about the type of GMM which will be used. If a GMM is identical with or very similar to GMMs which are commonly used and have previously been a subject of risk assessment, a brief account to this effect may suffice. Often, though, the assessment has to be supplemented with information concerning deviations in the particular case, with an indication of how this alters the risk or, alternatively, why the risk is unaffected.

As work proceeds there is cause for vigilance concerning the limits within which changes are made, so that a continuous assessment can be made as to whether the original risk assessment remains valid. The risk may be affected, for example, by a change of

organisms, materials or method. It is important that the notes needed in order to show that review and updating of the assessments have taken place should be kept in such a way that it is possible, for example, to trace the genetic modifications which have been made, their results and any unexpected findings. It is especially important to keep careful notes when using GMMs which entail great risks, since usually there are more factors influencing the risk than is the case with less hazardous organisms.

Application of good laboratory practice (GLP) can lead to a working routine which affords good reproducibility. It can also be a starting point for appropriate record-keeping, which can be supplemented with special notes for comparison with the original risk assessment in the event of changes in the biological material or working method compared with the conditions dictating the terms of the original risk assessment.

In the event of changes of material, method, equipment and procedure or in the event of new knowledge emerging of matters which can create different pre-conditions from those on which the original risk assessment was based, a note should be made as to whether, and if so in what way, the new conditions are expected to affect the risk.

Section 21 of the Genetically Modified Organisms (Contained Use) Ordinance (SFS 2000:271) contains stipulations on the duty of notifying the Supervisory Authority at the earliest possible opportunity of changes which can have a substantial bearing on the risks associated with the activity.

Even if the activity has not changed since notification was effected, new scientific findings or the user's own discoveries may give cause for a change of risk assessment compared with that presented earlier. Changed conditions of this kind are also notifiable to the supervisory authority, under Section 21 of the Ordinance. At present The Swedish Work Environment Authority is the supervisory authority for contained use of GMMs, under the Supervision (Environmental Code) Ordinance (SFS 1998:900).

Information concerning changed conditions may also need to be supplemented with a new notification or permit application. This, of course, is always the case if, as a result of the change, the activity is judged to belong to a different activity category than that originally notified, but also if it implies a new use as defined in Section 2 of the Genetically Modified Organisms (Contained Use) Ordinance (SFS 2000:271).

Guidance on Section 6

It is important to have a strategy which takes account, not only of suitable containment and other protective measures but also of the sequence in which they should be chosen. If, for example, a GMM is chosen which involves less risk, certain other containment and protective measures may become unnecessary.

Sometimes measures may need to be taken from more than one level on the "staircase".

- (a) In large-scale production, it is primarily non-pathogenic GMMs that should be used. In vaccine production this is not always possible, but the risks can often be reduced by using attenuated strains. Genetic engineering provides many opportunities for reducing risks, e.g. by expressing only minor parts of pathogenic organisms.

Low mobilisability in vectors, other marker genes than those giving resistance to antibiotics which are needed for the treatment of disease, and inability to replicate

AFS 2000:5

are examples of characteristics which can sometimes be chosen to reduce the risks.

Chap. 13 Section 10 of the Environmental Code stipulates ethical considerations. This can mean that a balance is struck between the scientific value and public benefit of using a certain GMM and, on the other hand, the risks to human health and the environment.

- (b) A good working routine, e.g. good microbiological practice, is essential in order to reduce risks and counteract exposure to GMMs. See App. 3A. Contaminants consisting of GMMs can occur, for example, when use is made of aerosol-generating equipment such as a centrifuge or agitator. If contaminants occur, steps can be taken to prevent their diffusion, e.g. by immediately wiping up spillage or by using a safety cabinet for operation entailing a risk of the formation of aerosols or splashing.
- (c) Taking containment and other protective measures at source can, for example, mean using a safety cabinet or other process ventilation instead of allowing general ventilation to deal with air contaminants. It can also mean inactivating waste at the earliest possible stage.
- (d) It is important to delimit activities involving major risks from those involving less risk. Activities at different containment levels are normally conducted on different premises. See Guidance on App. 3, Table 1a, Line 1.C.
- (e) Chap. 2, Section 7 of the Work Environment Act stipulates the use of personal protective equipment when other measures are insufficient. In other words, the use of personal protective equipment instead of other containment and protective measures is not acceptable.

Guidance on Section 7

If one or more containment or other protective measures are needed at a higher containment level, this means that the activity belongs to the higher activity level. If so, all applicable containment and other protective measures from the higher containment level are assumed to be relevant. If, following a risk assessment, it is concluded that not all containment and other protective measures at the higher containment level are needed, then, subject to approval by the supervisory authority, a combination of containment and other protective measures can be used, both from different containment levels and from Tables 1 and 2. In certain cases, if there is cause for doing so from the viewpoint of risk, the supervisory authority can decide that protective measures other than those chosen by the user shall be complied. At present The Swedish Work Environment Authority is the supervisory authority for contained use of GMMs, under the Supervision (Environmental Code) Ordinance (SFS 1998:900).

Guidance on Section 8

Cleaning and decontamination are facilitated by surfaces being smooth and leak-proof and free from nooks and crannies. Flooring should also be selected and managed so as to minimise the risk of slipping. On premises used for microbiological activity, it is important that disinfectants and other chemicals used should not be capable of damaging the surface materials.

Guidance on Section 9

It is very important for safety equipment to be checked systematically. Checks should take place annually or more frequently if necessary. Safety cabinets should be inspected in accordance with standard procedure, e.g. the R³ Nordic code or some other standard.

Checks of unwarranted occurrences of GMMs may need to be carried out in or around the installation, to check the effectiveness of the primary or secondary containment measures. Checks may also need to be carried out in connection with malfunctions or accidents entailing accidental release, or in order to check the effect of decontamination. A check of this kind can also form part of the employer's **internal control of the working environment**.

The supervisory authority may come to request control measures, e.g. as a condition for permits, or in other cases where they are judged necessary. At present The Swedish Work Environment Authority is the supervisory authority for contained use of GMMs, under the Supervision (Environmental Code) Ordinance (SFS 1998:900).

It is important that the persons carrying out measurements should have sufficient competence for the task. It is appropriate to comply with the applicable portions of the standards existing for workplace air and biotechnology.

The Internal Control (Users) Ordinance (SFS 1998:901) contains rules applying to activities for which permits and notification are required, e.g. under Chap.13 (Genetic Engineering) of the Environmental Code. Internal control means among other things that there shall be routines for continuously verifying that equipment for operation and control is kept in good condition and that inconveniences to human health and the environment are prevented. The Ordinance also requires this to be documented.

Guidance on Section 10

Information concerning access restrictions for activities at containment levels 3 and 4 can, for example, mean a text saying that only persons having permission to occupy the facility are entitled to admission, and possibly also giving the names of the persons having access. Particulars of the names and phone numbers of persons to be contacted in the event of accidents, failures and suchlike are important for facilities where activities at containment levels 3 and 4 are conducted. Sometimes it may be necessary to indicate access restrictions for activities at containment level 2, e.g. if vaccination is required.

If a particular type of personal protective equipment needs to be used on the premises, it is appropriate for this to be indicated by means of a supplementary sign.

Guidance on Section 11

It is essential that material containing GMMs should be marked in a way affording adequate information about the risks associated with the contents. This is especially important if such material is handled by persons who cannot be expected to know the risks, as for example in waste handling, laundry and the washing of infected material.

If there is a sign at the entrance to a facility or, for example, on a thermostat or refrigerating device, the content of the sign, e.g. an indication of the containment level can be deemed common knowledge. This means that individual containers present in these spaces do not normally need to be marked with such information. Information

AFS 2000:5

about contents, however, is one instance of particulars needing to be supplied on containers since data of this kind are not normally included in the sign.

Material handled under the supervision of persons who are acquainted with the contents, e.g. test tubes with dilution series, does not normally have to be marked with a warning.

Guidance on Section 12

The nature of the work and the hazards of the GMMs handled decide the extent of decontamination which is needed.

Suitable agents and methods of decontamination need to be available. Heat treatment is the method of first preference where possible. When choosing a chemical treatment method, one needs to consider the effect of the agent on the GMMs used, and also the harmful effects of the agent on health in the event of inhalation, skin contact, etc. Sometimes spraying can be the most effective method, e.g. for cleaning animal facilities, but this also augments the risk of diffusion. If spraying is judged necessary, measures need to be taken to prevent diffusions. Respiratory protective equipment can be needed as a last resort. The choice of decontamination agent and method is best decided in consultation with experts in the field, e.g. hospital hygienic, clinical microbiological or suchlike expertise.

It is important that GMM spillage should be securely collected without delay. Cultivation of GMMs in large quantities calls for special devices and routines so as to be able to collect and inactivate the volumes of spillage which may be involved.

GMM-contaminated equipment needs to be decontaminated in a suitable way before washing, re-use, discarding or suchlike. Autoclaving or possibly, use of an effective flush/washing up disinfectant is to be recommended rather than chemical treatment, because organic material can reduce the effect of chemical treatment to such an extent that some GMMs will survive. What is more, chemical agents can constitute a health hazard in themselves.

It is important that decontamination should precede repair and maintenance of equipment which may be GMM-contaminated, e.g. centrifuges and cultivation equipment. A certificate of this having been done should accompany the equipment.

Guidance on Section 13

The handling or management of waste includes among other things packing, moving, storage and processing. It is important that packaging should be so leak-proof and durable that GMMs will not spread. It is also important that packaging should be handled without breaking. The GMM content of waste can be regarded as GMM contaminants. Section 6 requires it to be inactivated at source as far as possible. After the waste has been decontaminated it need not be handled with any special consideration for risks caused by GMMs to the health and environment. On the other hand, there may be other risks associated with the waste which have to be taken into consideration.

Specific requirements for the handling of waste at different containment levels are set forth in App. 3. The Provisions of the National Board of Occupational Safety and Health on **Hazardous Waste** include among other things infected waste.

The Provisions and General Recommendations of the National Board of Health and Welfare on Infected Medical Waste (SOSFS 1999:27) includes certain stipulations on infected waste. There are international rules on the transport of dangerous goods. Different rules apply to different kinds of transport, but they are all similar and based on a common classification devised within the United Nations. Under this classification, GMMs capable of causing infections in humans and animals are assigned to class 6.2. Other GMMs, together with other genetically modified organisms than micro-organisms, are assigned to class 9. There are Swedish equivalents to the international rules on the transport of dangerous goods, e.g. ADR-S, issued by the Swedish Rescue Services Agency. In cases where different Provisions do not make the same requirements, it is the strictest Provisions that apply.

Guidance on Section 14

See App. 3 for specifications at various containment levels. Procedures containing a risk of GMMs entering the mouth include, for example, oral pipetting, smoking, use of wet snuff, consumption of food and drink, storage of foodstuffs and application of cosmetics on premises where activities occur which entail the contained used of GMMs. Good personal hygiene also means not putting contaminated objects in one's pocket.

Only gentle agents must be used for decontamination of the skin. Certain alcohols, in a suitable concentration can, by means of glycerol additives, reduce the risk of desiccation or other effects on the skin.

It is important that hand-washing facilities should be available within the shortest possible distance. To avoid the spread of infection, a facility of this kind can be designed in such a way that the hands do not have to touch the taps and could be washed in running water. It is advisable to use liquid soap and disinfectant in dispensers designed in such a way that these agents cannot enter the eyes, an occurrence which is frequently reported as a work injury. Disposable towels should be available.

An eye-wash facility and a emergency shower may be needed in certain cases.

Guidance on Section 15

It is essential to change contaminated protective clothing. It is also important that protective clothing should be laundered separately from private clothing and never in private homes. Removing protective clothing and other protective equipment when leaving the workplace means, for example, that these items are not worn when visiting personnel facilities or other premises where no work is done with GMMs.

Working clothes can sometimes serve as protective clothing, but if so they should be appropriate for the purpose, e.g. long-sleeved and washable at temperatures exceeding 80°C. Working clothes can also be supplemented when necessary with special protective garments for certain operations. Work is in progress within CEN, the European Committee for Standardisation, on devising standards for footwear and protective clothing for protection against micro-organisms. These standards had not been finalised at the time of writing (Spring 2000).

Scratches and eczema on the hands, barely visible to the naked eye, can provide a means of entry for infectious substances and augment the risk of ill-health. It is important, therefore that protective gloves should be selected according to the nature of the work involved. The Provisions of the National Board of Occupational Safety and

AFS 2000:5

Health on Use of Personal Protective Equipment require the employer to analyse and evaluate the risks and to judge the necessary characteristics of protective equipment for the current working situation. When disposing of cullets or sharp waste, for example, it is important that the gloves worn should be stout enough. If the protective gloves are also expected to afford protection against chemical substances, it is important to make sure that they are really intended to do so.

When choosing gloves, attention should also be paid to the risk of allergy and hypersensitivity which can be entailed by the material they are made of. Latex allergy, i.e. allergy to natural rubber latex, is not all that uncommon and can produce serious symptoms, at worst in the form of anaphylactic shock, a life-threatening state. The rising frequency of latex allergy observable in recent years among medical personnel can be counteracted by the person in charge of the activity ensuring that routines exist to indicate when gloves of natural rubber latex need to be used. The powder in itself can carry the allergenic proteins and evoke reaction on the part of persons with latex allergy working in the same room.

Protective gloves can also cause other forms of hypersensitivity. Most commonly they cause irritative eczema due to the hand being enclosed in the glove or perhaps because of the powder which the glove contains. In addition, contact allergy may occur due to the chemicals added in the manufacturing process. This makes it even more important to have routines for the use of gloves at work. Inner gloves of cotton, the selection of a non-latex glove material or a material with a low content of soluble natural rubber proteins and powder-free gloves are examples of possible ways of reducing the risks.

Other personal protective equipment includes a face shield for protection from splashing, and respiratory protective equipment when dangerous concentrations of GMMs are suspected, e.g. in connection with plant malfunction.

Respiratory protective equipment can consist of a full or half face mask with an interchangeable particle filter or of a filtered half-mask (short-term mask). Equipments are available with different separating efficiencies for different purposes. A class P2 particle filter (class FFP2 for filtered half-mask) normally affords adequate protection against relatively large micro-organisms such as mould spores. For smaller units such as a virus, a class P3 particle filter is needed (class FFP3 for filtered half-mask). In situations which can entail considerable risks due to inhalation of GMMs, a class THP2 or THP3 filter protection, fitted with a fan and including a helmet or hood may be needed. Filter protective equipment fitted with fans may also be needed for reasons of comfort, instead of filter masks. It is important to remember that a mask is not the same thing as a respiratory protective device and, consequently, affords no protection against airborne agents.

Guidance on Section 16

If exposure is at the lowest practical level, only a limited circle of persons need to be informed. Often, however, washing, cleaning, caretaking and service personnel are affected. The co-ordinating responsibility imposed by the Work Environment Act means that information about risks and their avoidance should be supplied to all undertakings or the equivalent carrying out work which can entail exposure to GMMs at the workplace.

The containment and other protective measures stipulated in App. 3 can serve as guidance for the compilation of handling and safety instructions. Handbooks like the

WHO Laboratory Biosafety Manual and experience from workplaces resembling one's own can also furnish guidance for the compilation of handling and safety instructions. Clinical trials protocols may also contain descriptions of methods on which instructions of this kind can be based.

It is important, however, that local conditions and the assessment of risks at the individual workplace should form the basis of the instructions addressed to the personnel. It is also vitally important for handling and safety instructions to be appropriately co-ordinated with methods descriptions and procedures included in any quality assurance systems.

Important components of handling and safety instructions include, for example:

- working methods,
- disinfection and cleaning routines,
- use of equipment,
- use of personal protective equipment,
- maintenance and inspection of equipment,
- waste management and
- measures to remedy unwanted occurrences.

If anything unplanned occurs, it is extremely important to have gone over what is to be done in such situations, so that time will not have to be spent working out what to do when it has already occurred. Drill provides useful information on the true feasibility of the measures planned. Experience has shown that exercises of this kind often give cause for revising the instructions.

Written safety and handling instructions can serve many important purposes, among them the following:

- When drawing up the instructions, it becomes necessary to think through the work planned with GMMs step by step, evaluating the hazards of the different operations and selecting appropriate protective measures. This way there will be less likelihood of unforeseen occurrences.
- Misunderstandings can be avoided by combining verbal briefings with written instructions. With written instructions one can go back and check in the event of uncertainty, as well as making sure that vital aspects have not been overlooked. This is an advantage, for example, for the introduction of new employees.
- Routines can be maintained for long periods. Many laboratories today have quality management systems which regulate activities in detail so as to ensure that the results of the work done will be of acceptable quality. Similarly, written instructions taking into account the hazards of the work are also a form of quality assurance to prevent any harm being done to human health and the environment.

Safety and handling instructions for work can include a fairly detailed description of the procedure for working with GMMs. Other information which should be included concerns suitable ways of protecting oneself and what to do in the event of unwanted occurrences (e.g. spillage or cuts). Detailed instructions can very well be combined with itemised notices or suchlike for particular operations, e.g. air lock routines, unpacking of specimens, handling of items to be washed or safety cabinet work.

AFS 2000:5

Different instructions can be needed for different personnel categories. It is important that washing, cleaning and other service personnel should not be forgotten. Special instructions may also need to be issued to security staff, for example.

Instructions may need to be given in different languages, so that persons not proficient in Swedish may be able to understand them.

Sometimes written handling and safety instructions may also be necessary for F activities, e.g. if an activity entails a complicated organisation or a mixture of operations.

Guidance on Section 17

Interaction between supervisory staff and other employees is important with a view to bringing about improvements once a safety problem has been observed. Those who are directly affected often possess the kind of experience of the problem which makes a solution easier to find. In addition, discussion of this kind improves vigilance, which in turn usually reduces the number of incidents.

It is important to document not only reported cases of ill-health and accidents, but incidents as well. Documentation makes things visible and often inspires remedial action. It is a good instrument for ascertaining whether measures for the avoidance of repetitions have had the intended effect. Documentation can also form a basis of the annual report which the employer is required to submit under the Provisions of the National Board of Occupational Safety and Health **on Internal Control of the Working Environment**.

Rules concerning notification to the Labour Inspectorate by Employers are contained in Section 2 of the Work Environment Ordinance.

Section 2a of the Work Environment Ordinance contains rules on the duty of physicians to supply certain information.

The Communicable Diseases Act (SFS 1988:1472) and the Communicable Diseases Ordinance (SFS 1989:301) contain rules on the duty of a person infected or suspected of being infected with a communicable disease to undergo medical examination.

Special stipulations concerning a contingency plan and measures to be taken in the event of major accidents capable of causing serious danger to the environment or to human beings in or outside the installation are found in Sections 30 and 31 of Ordinance (SFS 2000:271) and in Section 18 of these Provisions.

Guidance on Section 18

At present the Swedish Work Environment Authority is the supervisory authority for contained use of GMMs, under the Supervision (Environmental Code) Ordinance (SFS 1998:900). Under Section 30 of the Genetically Modified Organisms (Contained Use) Ordinance (SFS 2000:271), the supervisory authority, acting within the scope of its supervision, may issue Provisions on the duty of the user to draw up a contingency plan (response plan). Section 31 of the same Ordinance contains stipulations, for example, on information to the competent authorities and to other parties possibly affected by an accident.

Section 2 of the Rescue Services Act lays down that rescue services shall rescue and protect persons, property and the environment in connection with accidents or imminent

danger of accidents. It is the rescue director who decides whether a response is to be regarded as a rescue service in the statutory sense. To facilitate the location, inactivation or disposal of organisms of this type, contingency plans are needed indicating the risks which can occur in different situations and the action to be taken together with other authorities and organisations. The task of the rescue services include alerting, where necessary, all other parties who may be affected and, if necessary, issuing VMA ("Important Public Announcement") notices.

Guidance on Sections 19-21

The stipulations indicating which activities are subject to permit and notification, respectively, are contained in Sections 23-26 of Genetically Modified Organisms (Contained Use) Ordinance (SFS 2000:271). At present the Swedish Work Environment Authority is the supervisory authority for contained use of GMMs, under the Supervision (Environmental Code) Ordinance (SFS 1998:900), and is thus the authority to which notification and permit applications have to be addressed. App. 2 contains criteria for the classification of F activities, L activities and R activities. Apps. 4-6 indicate the information to be provided in connection with notification of F and L activity and when applying for a permit for R activity. App. B to the Recommendations gives a conspectus of the administrative requirements applying to different kinds of activity.

Guidance on Section 22

The system of charges implies that a charge is made only for time directly relating to the processing of the matter concerned. Charges do not cover travel expenses or the cost of general questions of genetic engineering. Handling time does not include travelling time. In the case of routine matters containing the information needed for administrative processing, the basic charge probably covers the cost of handling in the normal run of things. For matters requiring a handling time in excess of four hours, an hourly charge is made over and above the basic charge. Handling times can be shortened and the charge thus reduced by furnishing complete documents and thoroughly worked out documentation of risk assessment.

Guidance on the Appendices to the Provisions

Recommendations with reference to App. 1, concerning risk assessment

The risk assessment includes an assessment of the biological material, e.g. the recipient organism, and also of what is to be done with the organism and what may constitute a danger to health and the general environment in the event of GMMs being released beyond the primary and secondary containments.

Usually some form of risk assessment is made, consciously or otherwise, by the person who is to perform a task. The documentation required under Section 5 and the procedure as described in App. 1 can help to make the assessment more systematic and to heighten the level of awareness concerning various factors with a bearing on risk.

Assessment of the biological material and GMMs

The investigation of vectors, inserts etc may need to be quite detailed. Interrelationships between different components have to be elucidated, e.g. if virulence factors, antibiotic resistance genes or genes capable of producing other harmful effects are easily

AFS 2000:5

transferable to other micro-organisms or if a GMM is capable of replication and colonisation.

It is common for an organism with known characteristics to be modified so as to become a GMM. In the risk assessment of such an organism, one needs to consider whether the modification could lead to new risks or imply an unaltered or reduced risk. If the original organism is pathogenic, there may be cause to judge whether, and if so in what way, the change affects its pathogenicity. In the risk assessment, special attention should be paid to the diffusion capacity of organisms in the event of their being inadvertently released from the containment. Under Chap. 13, Section 12 of the Environmental Code (1998:808) and the Supervision (Environmental Code) Ordinance (SFS 1998:900), GMMs may not be deliberately released without permission from the National Chemicals Inspectorate unless there is an exception from the stipulations on deliberate release of genetically modified organisms.

Viral vectors for genetic therapy are very often clear examples of GMMs made up of components from several different organisms. They may contain genes from different viruses and, moreover, genes from humans, for example. When assessing the risk posed by such an organism, it is important to factor in the characteristics of the different components separately and in combination, together with possible occurrences when the vector is introduced in various host organisms, e.g. different kinds of cell culture, laboratory animals or humans.

It is advisable to prepare a concise description of the risks which, according to the risk assessment, can occur as a result of the contained use and of the measures which will be taken to prevent or avert these risks. This documentation can also be used to inform those working directly with the GMM concerned, and other persons in the immediate vicinity, of the risks involved.

App. 1 to the Provisions on **Biological Agents** gives criteria for the different safety classes applied to the classification of human pathogens. The Recommendations accompanying those Provisions also contain guidance on classification, with a list of Biological Agents in safety classes 2, 3 and 4.

Chap. 14, Section 8 of the Environmental Code contains stipulations to the effect that a party professionally manufacturing, importing to Sweden or supplying a chemical product or biotechnical organism shall provide the information necessary for the protection of human health or the environment (**product information**). In the Provisions of the National Chemicals Inspectorate on Chemical Products and Biotechnical Organisms (KIFS 1998:8), this obligation is specified through rules on investigation reports for chemical products and on the duty of a supplier to furnish product data sheets. No equivalent exists as yet for biotechnical organisms. A supplier may, for example, be ATCC or some other party supplying organisms from commercial collections, but he may also be a researcher who has produced a certain GMM. In the case of products and organisms for which the legislation does not furnish detailed rules, the supplier himself must devise a suitable means of providing information.

The user decides whether the information obtained from the supplier is sufficient for an assessment of the organism. It may be necessary to obtain supplementary information or to carry out investigations of one's own.

AFS 2000:5

In certain cases it is not practically feasible to have a good knowledge of the characteristics of an organism, especially if it constitutes a new structure. In cases of this kind it is important to consider carefully the nature of the worst case eventuality and to adapt containment and other protective measures accordingly.

The activity and its surroundings as a basis for assessing the need of containment and other protective measures.

Several different factors may need to be included in the overall assessment made in order to identify the containment and other protective measures needed. The nature of the activity has to decide which of the tables in App. 3b contains appropriate containment and other protective measures.

In order to be able to predict the risks and assess the containment and other protective measures needed for the protection of health and the environment, it is important to be closely familiar with the handling operation and to have an adequate knowledge of the organisms occurring. The purpose of the activity can often furnish useful guidance on the risk factors needing to be taken into account.

A detailed risk assessment is not usually needed for each individual procedure in laboratory work at lower containment levels, where the effects of normal laboratory procedures on exposure are well known. More detailed assessments may, on the other hand, be needed in connection with special circumstances which may possibly impact on the risk level, e.g. the use of relatively large volumes or the harvesting of continuous culture with centrifuges capable of causing aerosols. Agitators for mixing solutions may also generate aerosols. There can be special risks associated with working with animals, such as that of pricking oneself on syringe needles or sustaining bites from infected animals.

Highly concentrated cultures can entail an elevated risk in the event of exposure to GMMs. The risks can increase considerably as work proceeds, in connection with operations whereby the concentration of GMMs increases as a result of growth or concentration steps further downstream in the process. Concentration affects the likelihood of inadvertent release having harmful consequences.

Activities can be considered large-scale on various grounds, e.g. the handling of large volumes of culture medium with GMMs in individual operations, or the handling of smaller volumes with such frequency that a large total volume is handled within a short space of time. Large-scale activities can entail greater likelihood of exposure, in terms both of the number of people and the proportion of the environment exposed, if containment and other protective measures prove inadequate.

The scale affects the extent to which containment and other protective measures from Table 1 or 2 in App. 3B are applicable to the activity concerned.

If an activity is not harmful to human health, the emphasis of the containment and other protective measures can be put on secondary containment. It is important, however, to bear in mind that containment and other protective measures intended above for the protection of personnel may also be needed to protect the environment, e.g. to prevent personnel inadvertently carrying GMMs out of the area.

AFS 2000:5

Recommendations with reference to App. 2, concerning F,L or R classification of activities

The activity category is a purely administrative classification. It is closely connected with the level of containment, i.e. the maximum level for any of the containment and other protective measures that are needed. Category R, for which permits are required, comprises the activities with the highest risks.

For activities in which more than 10 litres of culture fluid are handled at once, it is especially important that the scale of activity be included in the assessment. This can, for example, result in certain containment and other protective measures at containment level 2 in App. 3, Table 2 needing to be applied. If so, then in accordance with App. 2, the activity shall be classified as an R activity unless otherwise decided by the supervisory authority following presentation of a risk assessment. At present The Swedish Work Environment Authority is the supervisory authority for contained use of GMMs, under the Supervision (Environmental Code) Ordinance (SFS 1998:900).

The category of activity, however, does not entirely decide which containment and other protective measures are to be applied. For one thing, category R can include activities ranging all the way from containment level 2, medium scale, to containment levels 3 and 4, irrespective of scale, added to which, the containment and other protective measures ultimately applied can in certain cases be selected from different levels and tables, subject to permission from the supervisory authority. The containment or other protective measures needed for activities at containment levels 3 and 4 can, in particular cases, differ considerably, but even so these are still R activities. At present The Swedish Work Environment Authority is the supervisory authority for contained use of GMMs, under the Supervision (Environmental Code) Ordinance (SFS 1998:900).

The permit requirements for contained use of GMMs are in principle on a level with the permit requirements indicated in the Provisions of the National Board of Occupational Safety and Health on **Biological Agents**. In the work environment context, those Provisions apply to both genetically modified and unmodified micro-organisms. The handling of such permit applications under the two sets of legislation can normally be co-ordinated.

Recommendations with reference to App. 3A concerning good microbiological practice

Good microbiological practice is the foundation of safe working with micro-organisms. The WHO Laboratory Biosafety Manual describes the basics of laboratory work. Much of this can also be applied to other activity entailing exposure to micro-organisms.

When handling infected material, it is important to avoid wherever possible the use of syringes and sharp objects, because these always imply a particular risk. Whenever such items are used, it is particularly important that they be handled in a safe manner. Many accidents have occurred due to a protective cover being replaced on the syringe with both hands after use, whereupon the syringe has missed the cover or penetrated the cover and struck the worker's hand. There are technical aids for avoiding this situation, e.g. syringes with protective devices and waste bins with syringe removers.

Safety gloves have been shown capable of reducing the amount of blood transmitted through inadvertent pricking with a syringe. It is also possible to investigate whether

there are gloves of a quality affording better protection from penetration by syringe needles and against cuts. Sometimes this can mean using double gloves.

When inoculating laboratory animals, it is vital to use safety gloves affording a certain measure of protection against bites, and to avoid using unprotected syringes. The risk of cuts and punctured skin can also be reduced by sedating the animals beforehand.

Guidance on App. 3B, concerning containment and other protective measures at different containment levels

It is important to keep an open mind when selecting containment and other protective measures so as to effectively avert the risks which have been identified. If containment or other protective measures are needed from different containment levels or tables, then, under Section 4 it is the higher level or table which decides the containment level and category of activity. Even if less strict protective measures are justifiable in individual cases, it is important to remember that no chain is stronger than its weakest link. Very often, besides, it is both simpler and less expensive to have uniform routines and containment measures in an activity. Protective measures from different containment levels and tables can, under Section 7, be combined by permission of the supervisory authority. At present The Swedish Work Environment Authority is the supervisory authority for contained use of GMMs, under the Supervision (Environmental Code) Ordinance (SFS 1998:900).

The rider "subject to risk assessment" occurs at several points in the Tables. The reason why, in these cases, it is impossible to give an unambiguous answer as to whether the protective measure referred to is needed, is that activities at the same containment level can still pose different risks to their surroundings. Accordingly, there can be differences in the protective measures needed. At containment level 1, for example, it may be the differing capacities of the organisms to cause hyper-sensitivity which decides whether a certain containment or other protection measure needs to be taken. At containment level 2, activities can occur which involve everything from relatively harmless organisms to relatively dangerous pathogens.

The containment class 3 organisms which, in accordance with the illustrative classification list in the Provisions of National Board of Occupational Safety and Health on **Biological Agents** are marked 3** do not normally constitute an airborne infection hazard, and certain protective measures can then be excluded. They can, however, be transmitted through splashing or aerosols, and this normally means that specific containment or other protective measures are needed for operations entailing a risk of splashing or aerosol formation. At containment level 3 and especially containment level 4, where very dangerous micro-organisms are used, additional containment and other protective measures, over and above those given in Tables 1 and 2 may prove necessary. In the processing of permit applications, the containment and other protective measures needed are decided with reference to each individual case.

In connection with **clinical trials** using GMMs, laboratory activity usually takes place for making up the GMM preparations concerned and sometimes for examining specimens from patients. Containment and other protective measures as indicated in Table 1a are normally applied to this kind of handling. In the event of testing on laboratory animals, containment and other protective measures as per Table 1b are also applied. If patients are being treated with GMMs for clinical trials, the containment and other protective measures needed have to be decided with reference to each individual case.

AFS 2000:5

Containment and other protective measures as per App. 3 may then furnish guidance but they need to be modified according to these specific situations. If the containment and other protective measures are insufficient to meet the criteria for contained use of GMMs, permission must be obtained for deliberate release. Permits of this kind are issued by the National Chemicals Inspectorate. For clinical trials, permits are also needed from the Medical Products Agency, which among other things assesses matters of patient safety and is also ultimately responsible for the examination of a medicinal product with a view to its placement on the market.

Table 1 is divided into three parts:

- (a) Containment and other protective measures in connection with laboratory activity,
- (b) Containment and other protective measures over and above those indicated in Table 1a for work with animals deliberately infected with GMMs, and
- (c) Containment and other protective measures, over and above those indicated in Table 1a for work with plants deliberately infected with GMMs.

When using animals, it is therefore not sufficient to consult just Table 1b: Table 1a is the basis of the containment and other protective measures to be considered, also where activities with animals are involved. Table 2 sets forth containment and other protective measures for large-scale processes.

Recommendations and Guidance on the protective measures in the tables are given by reference to the co-ordinates of each square. Thus the Guidance on Table 1.4 is divided into general Guidance on 4.A explaining the concept of the HEPA-filter, and Guidance for 4.E, explaining the meaning of the requirement of containment level 4. Numbering is continuous from Table 1 to Table 2 with the result that Table 2 starts with 39A.

Guidance on Table 1a concerning containment and other protective measures for laboratory activity

For medium-scale activities in which less than 500 litres of culture are handled at any one time, it may sometimes be appropriate to use a combination of containment and other protective measures as per Tables 1 and 2, subject to permission from the supervisory authority. At present The Swedish Work Environment Authority is the supervisory authority for contained use of GMMs, under the Supervision (Environmental Code) Ordinance (SFS 1998:900).

1.C

Separation normally means the laboratory being physically separated from other activities by doors and walls. If a mixture of activities occurs in one and the same space, separation can mean activities at, say, containment levels 1 and 2 being separate in time or all activities taking place at level 2, even when, normally, protective measures at containment level 1 would only be needed. In this way one can avoid inadvertently working with too low a level of containment.

3.C, D, E

Note that, under Section 10, supplementary information may be needed over and above the symbol.

4.A

A HEPA "high efficiency particulate air" filter is highly efficient for the separation of particles used, for example, for filtering air to and from spaces where GMMs are used. It is important to have routines for functional testing and replacement of these filters. There are various filter classes. See classification as per Swedish Standard SS-EN 1822-1, High-Efficiency Air Filters (HEPA and ULPA) – Part 1: Classification, functional testing, marking.

4.E

As regards additional air handling requirements, the measures needing to be taken can be decided in the individual case, on the basis of the risk assessment, e.g. with regard to the characteristics of the viruses used.

5.C, D

Negative pressure in the facility is not required for classes 2 and 3** (no airborne infection). Care should be taken, however, to ensure that the premises are not under positive pressure, and a neutral pressure should be aimed for.

7.B, C

If there are no special devices for the avoidance of touching the taps, instructions need to be provided concerning other ways of preventing the hands from coming into direct contact with the taps. For example, disposable towels can be used and discarded after being used once.

7.C, D, E

Devices facilitating hands-free operation include, for example, photo-relay operation and foot-pedal or elbow-controlled taps. From the viewpoint of easy cleaning, photo-relay control is preferable to mechanical control.

9.B-E

The word "bench" refers to the worktop normally used. This can, for example, take the form of an open bench or a safety cabinet.

12.C

Autoclaving of GMMs used at containment level 2 should not take place in an autoclave too far away from the activities in which the organisms are used. Normally this means the autoclave being located in the same building or complex of buildings.

If GMMs need to be moved over considerable distances within a building, it is appropriate to have distinct routines ensuring that the organisms will continue to be enclosed until the autoclaving is concluded. This can, for example, include the use of special transport vessels, distinctly marked and the issue of instructions to washing personnel and others concerned.

It is important that infected material should not be left in corridors or suchlike spaces but transferred to the autoclave as soon as it leaves the controlled area.

AFS 2000:5

13.C

If, for example, analytical equipment is shared between activities at different containment levels, it is important that a risk assessment be made concerning safety requirements for this operation.

20.A

It is important that GMMs used at a higher containment level should be stored quite separately from material at a lower containment level and be clearly marked as indicated in Section 11.

20.D

Normally, safe storage at containment level 3 means the organism being present within the controlled area. In special circumstances, storage can occur elsewhere, provided adequate safety can be guaranteed. If, for example, storage takes place in a special low-temperature freezer which is also used for the storage of micro-organisms for other projects or suchlike, special safety measures are needed. Safety can, for example, be maintained by means of a lock, restriction of the group of persons allowed to use the freezer and the position of the material in a separate space in the freezer. It is important to mark the freezer or the space occupied by the material, to have routines for keeping things in good order and to mark the storage vessels used for the organisms, using an unambiguous marking system with which everyone having access to the freezer is familiar.

21.A

Reference is particularly made to Section 12 on the subject of cleaning and decontamination, Section 16, for requirements concerning instruction in order for work to proceed safely, and to Section 18, concerning the preparation of a contingency plan. See also the Guidance on these various sections.

22.B

GMM aerosols can always present a risk, for example, of hyper sensitivity. Fungal spores spread easily, for example, with air currents.

22.C

Aerosol diffusion can be minimised by a working procedure which counteracts the formation of aerosols. In cases where aerosol formation cannot be avoided, it is important to decide which measures are needed to prevent aerosols from spreading. If they cannot be prevented from spreading, then a safety cabinet is needed, for example, and safety cups must be used for centrifuging.

23.A

Section 6 lays down that GMM-contaminated matter must be treated as near to its source as possible. It is therefore best for decontamination of GMMs to take place as early as possible. Release of GMMs which have not been decontaminated does not come within the definition of contained use and is therefore subject to the granting of permission for

deliberate release as referred to in Chap. 13 of the Environmental Code, regardless of whether or not the GMMs are judged harmless to health and the environment.

Guidance on Table 1b on containment and other protective measures, over and above those indicated in Table 1a, for work with animals deliberately infected with GMMs

27.A

Various measures may be needed, depending on the type of animals used. Stipulations on the use of genetically modified animals are found in the Provisions issued by the Swedish Board of Agriculture (SJFS 1995:33) on the Use of Genetically Modified Animals. The National Board of Fisheries has issued Stipulations on genetically modified aquatic organisms.

30.A

It is important that animal cadavers should be incinerated in an incineration plant with a sufficiently high combustion temperature. Facilities for the incineration of ordinary contaminated waste are not always suitable.

Guidance on Table 1c, concerning containment and other protective measures, other than those indicated in Table 1a, for work with plants deliberately infected with GMMs

35.A

Provisions on genetically modified plants are issued by the Swedish Board of Agriculture.

Guidance on Table 2, concerning containment and other protective measures for large-scale processes

This Table is adapted to large-scale processes, e.g. those in which more than 500 litres of culture medium are in use at any one time, but it may also need to be applied to medium-scale processes. Note that in large-scale activity laboratory activity is normally also included, e.g. for the upgrading of inoculation material, taking of samples etc. The laboratory side is then subject to the requirement of containment and other protective measures as set forth in Table 1.

39.A

The degree of containment is decided on the basis of the risk assessment. For a certain activity at containment level 1, this could mean the processed culture not being allowed to escape unprocessed into the sewerage system but the culture vessel not needing to be hermetically sealed. In another instance the risk assessment may show a stricter containment to be necessary. Requirements concerning the design of seals, vents, bleed devices etc become more stringent with a higher containment level and are decided in connection with the processing of permit applications.

40.A

AFS 2000:5

The controlled area is taken to include all the process facilities, laboratories, storage spaces etc where GMMs are used and which are located within a strict demarcation.

46.B-E

The word "bench" refers to the worktop normally used. This can, for example, take the form of an open bench or a safety cabinet.

51.A

When presenting a contingency plan and accident prevention arrangements, the user may need to indicate whether there are special reasons why a reserve power supply is not necessary.

52.A

Cf. the Guidance on Table 1.7

59.D-E

Escapes can be prevented, for example, by HEPA filtration or decontamination, using a proven method.

60.A

The reference here is to downstream processing, e.g. upgrading and purification of substances for as long as GMMs can remain, and the extent to which the entire chain of handling operations is kept within a closed system.

Guidance on Apps. 4-6, concerning information to be provided in connection with notification and permit application

Also note the specific recommendations for each Appendix

Stipulations indicating when different kinds of activity and use are notifiable and when they are subject to the grant of a permit are contained in the Genetically Modified Organisms (Contained Use) Ordinance (SFS 2000:271). An activity can involve several different uses. In the case of F activity, the activity is notified for the first time and new uses are permitted within this activity without the supervisory authority being notified so long as the activity does not deviate from the description which has been submitted. All individual uses in L activity are notifiable. Uses in R activity are subject to the grant of a permit. At present The Swedish Work Environment Authority is the supervisory authority for contained use of GMMs, under the Supervision (Environmental Code) Ordinance (SFS 1998:900). In the Genetically Modified Organisms (Contained Use) Ordinance (SFS 2000:271), a new use is defined as a contained use of genetically modified organisms in a previously notified activity, added to which, compared with the notified activity, the use differs in a not insignificant manner with regard to the genetically modified organisms used or with regard to the method whereby the organisms are used or produced.

AFS 2000:5

The user can be a legal or natural person, e.g. a company, university, county council or private individual conducting the activity in his or its own name.

Persons supervising work and safety may, among other things have the task of ensuring that routines for record-keeping, risk assessment and choice of containment and other protective measures are complied with, and that the necessary notifications and applications are filed. It is appropriate to indicate the person or persons tasked with ensuring that the Internal Control (Users) Ordinance (SFS 1998:901) is complied with at different levels within the activity.

The organisation can vary, depending on the activity conducted. In certain cases one and the same person may have tasks relating to the entire activity, while in others several persons may have been allotted tasks relating to the safety of different parts of the activity. If, for example, an F activity involves several research groups in different parts of an installation, it is appropriate that the information provided should make clear who is in charge of which part of the activity.

The information to be provided concerning training and qualifications can include a brief account of the training and experience of the persons concerned, insofar as it is relevant to the activity.

An installation may comprise one or more rooms in one or more buildings within a limited area. An installation cannot normally consist of rooms in buildings in different parts of a town or city with great distances between them. It is suitable to identify the installation so that an outsider can easily find the way there, e.g. by giving, in addition to the street address, the building number, storey, room number or some other identifying designation where necessary.

Under Section 5 of the Environmental Code, "contained use" refers to an activity in which someone modifies organisms genetically or cultivates, stores, transports, destroys, disposes of or, in any other way, uses such genetically modified organisms, and where specific containment measures are used to limit the contact of these organisms with the general public and the environment.

The broad definition of "contained use" means that, in addition to premises where GMMs are cultivated and modified, the definition also includes spaces for the storage and destruction of GMMs, e.g. freezers, cold stores and rooms for waste and autoclaving. If GMMs are used to produce proteins, working facilities for the upgrading and purification of proteins ("downstream processing") are also included, so long as GMMs are used. Plant and animal facilities are also installations for contained use if the plants or animals in them are infected or otherwise treated with GMMs. For clinical trials involving the use of GMMs, hospital wards (e.g. single rooms and toilets with flush disinfectors) and treatment rooms can be included in the installation for contained use of GMMs, as well as the premises used for making up the preparation.

The description of the nature of the activity can be made to indicate the type of activity to which the notification refers, e.g. laboratory work, animal work, industrial production, clinical testing, diagnosis or research.

The description of containment and other protective measures presented together with notification and application for permit needs at least to include the measures selected according to the relevant Table and containment level as per App. 3. If it is found that not

AFS 2000:5

all containment and other protective measures are necessary according to the containment level indicated, reasons need to be given on which the authority can base its own standpoint. When describing containment and other protective measures, it is appropriate to indicate the rooms in the installation where the measures referred to are applied, e.g. if not all parts of the installation have access to the same equipment.

The approximate number of persons can be stated as size categories, e.g. fewer than 5, 5-10, 10-30 or more than 30. For activities involving major risks, it is appropriate for the number of persons exposed to be stated more exactly.

Guidance on App. 4

The example of documentation of an assessment as per Section 5, for one GMM use included in the activity, required under point 9, can serve as an object of comparison for the assessments which have to be made for all contained use of GMMs within the activity. It must be possible for the assessments to be presented on request, as provided in Section 5.

Guidance on App. 5

If the activity has been notified previously, reference to information in the previous notification can be made in connection with the notification of a new use, if it is clearly apparent what that information is.

The information provided, as per point 8 concerning the biological material, needs to be extensive enough to serve as a basis for assessments of whether the risk assessment is realistic and whether the containment and other protective measures chosen are acceptable. It is also important for the biological material to be described well enough to eliminate any uncertainty as to what the notification or the permit application refers to.

Guidance on App. 6

If a permit for the activity has been granted previously, then, when applying for a permit for a new use, reference can be made to information supplied previously, if this is easily identifiable.

For category R activity, a closer description of facilities and safety equipment is normally required than for F and L activities.

The information provided, as per point 8 concerning the biological material, needs to be extensive enough to serve as a basis for assessments of whether the risk assessment is realistic and whether the containment and other protective measures chosen are acceptable. It is also important for the biological material to be described well enough to eliminate any uncertainty as to what the notification or the permit application refers to.

Permits are normally valid for 5 years under Chap. 13, Section 17 of the Environmental Code (1998:808), unless otherwise indicated in the award of a permit.

A permit for activity, as referred to in the Provisions of the National Board of Occupational Safety and Health on **Biological Agents**, is needed in most cases for the GMMs which can occur in R activity. Permit applications under the two sets of Provisions can be processed simultaneously. Most of the information needed is common to both sets of

AFS 2000:5

Provisions. The user as referred to in the Provisions on Contained Use of GMMs, and the employer as referred to in the Provisions of the National Board of Occupational Safety and Health on **Biological Agents** may, for example, be one and the same legal person. A permit application under the Provisions of the National Board of Occupational Safety and Health on **Biological Agents** needs to be supplemented with a statement by the safety delegate. For Recommendations concerning the safety delegate's statement, see the Guidance on Section 18 of the Provisions of the National Board of Occupational Safety and Health on **Biological Agents**.

Appendix A

Guidance on interpreting the definition of GMMs in Section 2

1. Examples of techniques deemed capable of resulting in GMMs

Techniques of genetic modification referred to in the definition of GMMs include:

- (a) Recombinant nucleic acid techniques involving the formation of new combinations of genetic material by the insertion of nucleic acid molecules produced by whatever means outside an organism, into any virus, bacterial plasmid or other vector system and their incorporation into a host organism in which they do not naturally occur but in which they are capable of continued propagation.
- (b) Techniques involving the direct introduction into a micro-organism of heritable genetic material prepared outside the micro-organism including micro-injection, macro-injection and micro-encapsulation.
- (c) Cell fusion or hybridisation techniques where live cells with new combinations of heritable genetic material are formed through the fusion of two or more cells by means of methods that do not occur naturally.

2. Examples of techniques not normally considered to result in GMMs

Techniques not normally considered to result in GMMs, on condition that they do not involve the use of recombinant-nucleic acid molecules or GMMs (see Part A) are as follows:

- (a) *in vitro* fertilisation;
- (b) natural processes such as: conjugation, transduction, transformation;
- (c) polyploidy induction.

Remarks

The term "transformation" is also used in a wider sense in genetic engineering, but the reference in point 2.(b) is to the kind of transformation which can occur naturally, e.g. uptake by competent bacteria of natural nucleic acid from their surroundings.

Section 3 of the Genetically Modified Organisms (Contained Use) Ordinance (SFS 2000:271) gives examples of techniques and methods which can be included in the definition of GMM but to which the specified stipulations of the Environmental Code and the Ordinance are not to apply; see also the Guidance on Section 1.

Appendix B

Summary of administrative routines for activity involving contained use of GMMs, together with a comparison with the rules applying to Biological Agents

Containment level and scale	GMMs	Administrative measure (1)	Biological Agents	Administrative measure (1)
Containment level 1, For GMMs see App. 2	F activity	Notification. The activity may not commence less than 45 days after full notification has been effected (2), (3).	Use of biological agents in safety class 1.	
Containment level 1, For GMMs see App. 2	New use in previously notified F activity.	(3)	Use of biological agents in safety class 1.	
Containment level 2, Small scale, For GMMs see App. 2	L activity	Notification. The activity may not commence less than 45 days after full notification has been effected (2), (3).	Use of biological agents in safety class 2, less than 500 litres of culture medium.	Notification to Labour Inspectorate.
Containment level 2, Small scale, For GMMs see App. 2	New use in previously notified L activity.	The new use may commence as soon as full notification has been effected (2), (3).	Use of biological agents in safety class 2, less than 500 litres of culture medium.	
Containment level 2, Large scale, Containment level 3, Containment level 4 For GMMs see App. 2	R activity	Permit not more than 90 days after a complete application has been received (2), (3).	Use of biological agents in safety class 2, more than 500 litres of culture medium. Use of biological agents in safety classes 3 and 4.	Permit.
Containment level 2, Large scale, Containment level 3, Containment level 4 For GMMs see App. 2	New use in an R activity for which a permit has already been granted.	Permit not more than 45 days after a complete application has been received (2), (3).	Use of biological agents in safety class 2, more than 500 litres of culture medium. Use of biological agents in safety classes 3 and 4.	Permit.

AFS 2000:5

- (1) Unless otherwise indicated, the Swedish Work Environment Authority is at present the authority which receives notifications and grants permits.
- (2) The times indicated apply failing any decision to the contrary by the supervisory authority. Shorter times can apply in certain cases. Certain restrictions may be prompted by the content of a notification.
- (3) For all GMM activity, risk assessments have to be documented and the authority informed of changes in particulars previously furnished.

Information from the Swedish Work Environment Authority

Other relevant rules

Current rules

Acts, Ordinances and Provisions being subject to revision or replacement by other statutes, it is important to keep oneself updated concerning the instruments in force. When revised, Acts and Ordinances often retain their reference number in the Swedish Statute Code (SFS). The Work Environment Act, for example, is assigned SFS number 1977:1160, despite having been revised many times since 1977. To find the text of the current (consolidated) Act or Ordinance, one can, for example, visit the "Debatt och Beslut/Rixlex" (www.riksdagen.se/debatt) on the Internet and look up the full text of the latest version of the latest Acts or Ordinances in which one is interested.

To keep abreast of the rules issued by the Swedish Work Environment Authority, it is advisable, for example, to regularly visit the Board's web site (www.av.se) on the Internet and, under "Arbetsmiljoregler, AFS", check which rules are at present applicable to the activity concerned. Particulars of the statutes in force and available to order can also be obtained from the publication service at: Publikationsservice, Box 1300, S-171 25 SOLNA, fax +46-(0)8-735 85 55, tel. +46-(0)8-730 97 00.

Please note that documents on the Internet are liable to contain errors and that it is the printed text that is legally valid.

Acts and Ordinances

The Environmental Code (SFS 1998:808)
The Genetically Modified Organisms, contained use, Ordinance (SFS 2000:271)
The Genetically Modified Organisms, deliberate release, Ordinance (SFS 2002:1086)
Managements self check Ordinance (SFS 1998:901)
The Supervision (Environmental Code) Ordinance (SFS 1998:900)
The Work Environment Act, with amendments (SFS 1977:1160)
(*The Work Environment Act, in consolidated form and with commentaries, is published regularly by the Swedish Work Environment Authority*)
The Work Environment Ordinance, with amendments (SFS 1977:1166)
The Rescue Services Act (SFS 1986:1102)

Provisions issued by the National Board of Occupational Safety and Health and Swedish Work Environment Authority

Use of Personal Protective Equipment (AFS 2001:3)
Work with Laboratory Animals (AFS 1990:11)
Ergonomics for the Prevention of Musculoskeletal Disorders (AFS 1998:1)
Biological Agents (AFS 1997:12)
Solitary Work (AFS 1982:3)
First Aid and Crisis Support (AFS 1999:7)
Gas Cylinders (AFS 2001:4)
Pregnant and Breast-Feeding Employees (AFS 1994:32)
Occupational Exposure Limit Values and Measures against Air Contaminants (AFS 2000:3)

AFS 2000:5

Systematic Work Environment Management (AFS 2001:1), replacing provisions on Internal Control of the Working Environment (AFS 1996:6)
 Chemical Hazards in the Working Environment (AFS 2000:4)
 Chemical Laboratory Work (AFS 1997:10)
 Manual Handling (AFS 2000:1)
 Minors at Work (AFS 1996:1)
 Hazardous Waste (AFS 1989:2)
 Protection against Bloodborne Infections (AFS 1986:23)
 Work involving Infection Risks (AFS 1991:2)
 Pressure-retaining Devices (AFS 1999:4)
 Pressure Vessels (AFS 1999:6)
 Safety Signs and Warning Signals at Workplaces (AFS 1997:11)
 Workplace Design (AFS 2000:42)

Supervisory Authorities for activities with genetically modified organisms

Authority	Contained Use	Deliberate Release	Placement on the Market
The Swedish Work Environment Authority	Micro-organisms	—	—
The National Board of Fisheries	Aquatic organisms	Aquatic organisms	Aquatic organisms
The National Board of Forestry	—	Forest trees for timber production	Forest trees for timber production
The National Chemicals Inspectorate	—	Micro-organisms, nematodes, arachnids and insects	Micro-organisms, nematodes, arachnids and insects
The Medical Products Agency	—	Medicinal products	Medicinal products
The Swedish Board of Agriculture	Other organisms	Other organisms	Other organisms
The National Food Administration	—	—	Foodstuffs

Provisions relating to genetic engineering

Organism	Contained Use	Deliberate Release	Placement on the Market
Micro-organisms	AFS 2000:5	KIFS 1998:8	KIFS 1998:8
Aquatic organisms	FIFS 1995:10	FIFS 1995:10	FIFS 1995:10
Forest trees for timber production	SJVFS 1999:123	SKFS 1996:1	SKFS 1996:1
Nematodes, arachnids and insects	SJVFA 1995:33, 2000:17	KIFS 1998:8	KIFS 1998:8
Medicinal products	AFS 2000:5	Soon being issued	The Medicinal

AFS 2000:5

Organism	Contained Use	Deliberate Release	Placement on the Market
	(micro-organisms)		Products Act (1992:859) LVFS 1995:8
Other organisms	SJVFS 1999:123 SJVFS 1995:33, 2000:17	SJVFS 1999:124 SJVFS 1995:33, 2000:17	SJVFS 1999:122 SJVFS 1995:33, 2000:17
Foodstuffs	—	—	SLVFS 1995:3

Provisions issued by the National Board of Health and Welfare

Handling infections waste from health care service (in Swedish) Hantering av smittförande avfall från hälso- och sjukvården (SOSFS 1999:27)

Other relevant literature

(all in Swedish)

Nordiska R3-föreningens norm för säkerhetsbänkar, Nordiska R3-föreningen (compendium, in Swedish)

Personlig skyddsutrustning, Arbetarskyddsstyrelsen 1999, order ref. no. H 227 (book, in Swedish)

Desinfektion på arbetsplatsen – hantering, risker och regler, Arbetarskyddsstyrelsen 1999, order ref. no. H338 (book, in Swedish)

Laboratory biosafety manual, second edition, World Health Organization, Geneva 1993 ISBN 92 4 154450 3 (book)

Standards

European standards exist for biotechnology, e.g. SS-EN 12740 Biotechnology – Laboratories for research, development and analysis - Guidance for handling, inactivating and testing of waste. Standards work continues and further standards are pending. It is not certain that these standards are always framed so as to comply with the stipulations existing under Swedish legislation. In the event of a standard procedure not complying with the rules of Swedish legislation, it is the national rules which apply.