

Statutory order on transport and import of genetically modified organisms¹⁾

In pursuance of Sections 10(2), 13(1) and (2), 14(2), 20(2), 27(1) and (2), 36(4) and (5) of Act no 356 of 6 June 1991 concerning the environment and genetic engineering the following provisions are laid down:

Part 1

Scope

Article 1(1). This order concerns:

- 1) Import and transport of genetically modified organisms intended for research, large-scale experiments, production, test release, teaching, display and other types of dissemination of information (see Section 10 of the act).
- 2) Notification of the National Forest and Nature Agency in connection with the marketing in Denmark of genetically modified organisms for which approval has been granted in a another member state in the European Community (see Section 14 of the act).
 - (2) Genetically modified organisms are plants, animals, microorganisms including cell cultures and viruses, in which the genetic material has been altered in a way that does not occur naturally (see Annex 1).
 - (3) Reproductive genetically modified plants are genetically modified plants in a phase of life where sexual or asexual propagation takes place.
 - (4) Activities involving genetically modified microorganisms, including cell cultures and viruses, are classified in four classes (see Annex 2).

Article 2(1). Transport of genetically modified organisms may be carried out without approval in pursuance of Section 10 of the act and without meeting the requirements laid down in Part 2 of this statutory order if the transport takes place within:

- 1) laboratories and large-scale plants approved or classified in accordance with the Ministry of Labour's statutory order on genetic engineering and working environment, provided that the transport exclusively takes place within the approved or classified area; or
- 2) production plants covered by approval granted in pursuance of Section 8 of the act if the transport concerns organisms approved or registered for production at the plant, provided that the transport exclusively takes place within the plant.
 - (2) The provisions of the statutory order concerning transport, including the provisions concerning approval, packaging and labelling, shall also apply in cases where rules concerning the transport of genetically modified organisms have been laid down in other legislation or in pursuance of other legislation, including rules concerning the transport of hazardous goods.

¹⁾ Bekendtgørelsen indeholder bestemmelser, der gennemfører Rådets Direktiv nr. 90/220/EØF om udsætning i miljøet af genetisk modificerede organismer EF-Tidende 1990 L 117, s. 15 og Direktiv nr. 98/81/EF af 26. oktober 1998 om ændring af direktiv 90/219/EØF om indesluttet anvendelse af genetisk modificerede mikroorganismer, EF-Tidende 1998 L 330, s. 13.

Part 2

Exemptions from approval for transport and import

Article 3. Prior to the initiation of transport or import activities, the sender must carry out a risk assessment. In the case of transport or import of genetically modified microorganisms the risk assessment shall be carried out in compliance with Annex 3 and Annex 5, according to which the activity will be classified. A concrete assessment of the activity shall be carried out in relation to genetically modified plants and animals.

Article 4(1). Transport and import of genetically modified microorganisms and of genetically modified plants and genetically modified animals in class 1, class 2 and class 3 may be carried out without prior approval in pursuance of Section 10 of the act, provided that the provisions in paragraph (2) hereof and in Articles 5-10 concerning packaging, labelling, etc of the organism in question are observed.

(2) The sender shall keep the risk assessment until transport and import have been completed.

Article 5. Each packaging unit shall be labelled in Danish or English in such a way that it clearly appears that the unit contains genetically modified organisms. In addition the type of organisms as well as the name and address of the sender must be clearly indicated on the packaging unit. In the case of microorganisms, the microorganism class shall be stated.

Article 6. The following requirements concerning packaging and transport containers shall be met in relation to genetically modified microorganisms which are used for class 1 or class 2 activities:

- 1) The container shall be tight, closed and unbreakable,
- 2) The container shall be able to resist pressure, shocks, etc and to prevent release of the contents.

Article 7. The following requirements concerning packaging and transport container shall be met in relation to genetically modified microorganisms which are used for class 3 activities:

- 1) Both an inner and an outer container shall be used.
- 2) Both the inner and the outer container shall be impermeable to liquids.
- 3) Liquid-absorbing material shall be placed between the inner and the outer container. This material shall be able to absorb the quantity of liquid inside the inner container. If more than one inner container are placed in the same outer container, each inner container shall be wrapped in material that can absorb shocks and liquids.
- 4) The outer container shall be tight, closed, unbreakable and able to absorb pressure and shocks, etc and it must prevent release of the contents.

Article 8(1). The following requirements concerning packaging and transport containers shall be met in relation to genetically modified plants or parts of plants:

- 1) The packaging shall be tight and closed.
- 2) The packaging shall be able to resist pressure, shocks, etc and must prevent release of the contents.

(2) Both an inner and an outer packaging which comply with the requirements stated in paragraph (1) hereof shall always be used in relation to reproductive genetically modified plants or parts of plants and in relation to genetically modified seeds and pollen.

Article 9. The following requirements concerning packaging shall be met in relation to genetically modified animals:

- 1) The packaging shall be a cage or a container from which the animals cannot escape.

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2) The cage or container shall be unbreakable.

Article 10. If transport and import include microorganisms in class 2 or class 3, reproducing genetically modified plants or parts of plants, genetically modified seeds or pollen, or genetically modified animals, the consignment shall be accompanied by instructions in Danish or English specifying procedures to be followed in the event of an accident.

Part 3

Approval of transport and import

Article 11. If transport or import includes microorganisms used in class 4 activities, or if the transport or import does not meet the requirements concerning labelling, packaging, etc laid down in Article 4(2) and Articles 5-10 hereof, prior approval shall be obtained in accordance with the provisions of this part of the order.

Article 12. Decisions concerning approval of transport and import of genetically modified organisms shall be made by the National Forest and Nature Agency.

Article 13. Applications for approval shall be in writing and shall include all information necessary for the processing of the applications, including:

- 1) the name and address of the person in charge of transport and import;
- 2) information about transport route and transport mode;
- 3) information about the time of transport and import;
- 4) a description of donor, recipient or possible parental organisms, a description of the genetically modified organisms, and information about the impact of the organisms on public health and the environment (see Annex 4);
- 5) the volume to be imported and transported;
- 6) an assessment of environmental risks and health risks associated with transport and import (see Annex 3 and Annex 5);
- 7) the properties of the packaging and the layout of the labelling;
- 8) safety measures that will be taken; and
- 9) emergency response plans in the event of accidents.

Article 14(1). The National Forest and Nature Agency may require additional information to any extent deemed necessary for the processing of the application and may also carry out a public hearing concerning aspects of the planned transport or import.

(2) The National Forest and Nature Agency may fix a deadline for the submission of additional information and may also state that the application will lapse if the information is not submitted on or before the deadline date.

Article 15(1). Approvals shall include an explanation and an assessment of the information included in the application, including the overall factors on which the decision has been based. In addition, approvals shall contain the conditions on which transport and import may take place (see Section 16 of the act).

(2) If necessary conditions may be laid down concerning an emergency response plan in the event of accidents. Such a plan shall always be prepared in relation to transport of microorganisms for use in class 4 activities.

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Article 16. The approval or a copy of the approval shall accompany the consignment during transport. If an emergency response plan has been requested, this plan or a copy of the plan shall accompany the consignment during transport.

Part 4

Charges

Article 17. A charge shall be paid for the processing of applications. The charge will be fixed in accordance with the provisions of the statutory order on charges in relation to the Environment and Genetic Engineering Act in force at any time.

Part 5

General precautions in relation to transport and import

Article 18(1). Persons who requisition genetically modified microorganisms shall inform the sender of the requirements applying to packaging, labelling, etc.

(2) Senders of genetically modified organisms shall ensure:

- 1) that the consignment meets the requirements laid down in Part 2 hereof or the conditions stipulated in the approval granted in pursuance of the provisions of Part 3; and
- 2) that the carrier of genetically modified organisms is aware of the precautions to be taken in the event of an accident.

Article 19(1). Persons who transport or import genetically modified organisms shall immediately notify the county council in the county where an accident has occurred and shall also notify the Medical Health Officer of accidents which have resulted in or may result in spillage of genetically modified organisms.

(2) If an accident happens in the City of Copenhagen, the city council or the local health officer shall be notified. If an accident happens in Frederiksberg Municipality, the municipal council and the Medical Health Officer shall be notified.

(3) Notifications shall contain information about:

- 1) particular circumstances relating to the accident;
- 2) the identity and quantities of the genetically modified organism(s) spilled;
- 3) all details necessary to assess the impact of the accident on public health and the environment; and
- 4) the measures taken to prevent negative consequences of the accident in an effective manner.

(4) Notification shall not imply any limitation in the duty of the person in charge to try to prevent any consequences of the accident, and shall not imply any exemption from the obligation to restore former conditions to the greatest possible extent.

Part 6

Marketing

Article 20(1). When genetically modified organisms approved for marketing in another member state in the European Community is to be marketed in Denmark (see Section 9(3) of the act), the holder of the approval or the importer shall notify the National Forest and Nature Agency (see Section 14(1) of the act).

(2) Notifications shall be in writing. If the marketing approval contains conditions to this effect, the notification shall include information about:

- 1) the labelling accompanying the product; and
- 2) product packaging.

Article 21. The National Forest and Nature Agency shall check that the information contained in the notification submitted in pursuance of Article 20 hereof complies with the provisions on labelling and packaging contained in the marketing approval, and the Agency may issue orders to ensure that this is the case.

Part 7

Supervision and complaints

Article 22(1). The National Forest and Nature Agency shall supervise:

- 1) that the provisions in Part 2 and Part 3 of this statutory order are observed; and
 - 2) that conditions laid down in approvals issued in pursuance of the provisions of Part 3 hereof are observed.
- (2) The provisions of Part 3 and Part 4 of the act shall otherwise apply to supervision and enforcement.

Article 23(1). It shall not be possible to file complaints with any other administrative authority concerning decisions made by the National Forest and Nature Agency in pursuance of Article 21 hereof.

(2) Complaints concerning decisions made by the National Forest and Nature Agency in pursuance of Article 12 hereof may be lodged with the minister for environment and energy in accordance with the provisions in Part 5 of the act.

Part 8

Penalties, entry into force and transitional provisions

Article 24(1). Unless a higher penalty applies under other legislation, a fine will be imposed on persons who:

- 1) do not comply with Article 2, Articles 5-10 and Article 18 hereof;
- 2) fail to obtain prior approval as stated in Article 11 hereof;
- 3) ignore conditions relating to an approval;
- 4) fail to submit notification in accordance with the provisions of Articles 19 and 20 hereof;
- 5) fail to comply with orders issued in pursuance of the provisions of Article 21 hereof; or
- 6) fail to comply with orders stating that illegal matters must be rectified.

(2) The penalty may increase to simple detention or imprisonment for a period of up to two years if the circumstances stated in Section 36(2) of the Environment and Genetic Engineering Act apply.

(3) Companies and others may incur criminal liability under Part 5 of the Danish Criminal Code.

Article 25(1). This statutory order shall enter into force on 5 June 2000.

(2) On the same date, statutory order no 732 of 5 November 1991 concerning transport and import of genetically modified organisms shall be repealed.

(3) Decisions made in pursuance of the statutory order mentioned in paragraph (2) hereof shall remain valid until the expiry of the period stated or until a new decision is made in pursuance of the provisions of this statutory order. Non-compliance with decisions made in pursuance of the statutory order mentioned in paragraph (2) hereof shall be punished in accordance with the provisions previously in force.

(4) Pending cases concerning approval which have not been finally processed by the date on which this order enters into force shall be finally processed in accordance with the provisions of this statutory order.

Scope of application of the statutory order

An organism is any microbiological entity, cellular or non-cellular, capable of replication or of transferring genetic material, including viruses and viroids and animal and plant cells in culture.

A genetically modified organism is an organism in which the genetic material has been altered in a way that does not occur naturally by mating and/or natural recombination.

Within the terms of this definition, genetic modification occurs at least through the use of:

- 1) Recombinant DNA-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
- 2) Techniques involving the direct introduction into a micro-organism of heritable material prepared outside the micro-organism including micro-injection, macro-injection and micro-encapsulation;
- 3) Cell fusion (including protoplast 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.

The following techniques are not considered to result in genetic modification, on condition that that they do not involve the use of recombinant DNA molecules or GMOs:

- 1) *in vitro* fertilisation;
- 2) conjugation, transduction, transformation or any other natural process;
- 3) polyploidy induction.

The Statutory order does not apply to organisms produced by application of the following techniques for genetic modification on the condition that they do not involve the use of GMOs as recipient or parental organisms:

- 1) mutagenesis;
- 2) cell fusion (including protoplast fusion) of prokaryotic species that exchange genetic material by known physiological processes.
- 3) cell fusion (including protoplast fusion) of cells of any eukaryotic species, including production of hybridomas and plant cell fusions.

Criteria for classification of genetically modified microorganisms in relation to transport and import

Class 1: Activities of no or negligible risk.

Class 2: Activities of low risk.

Class 3: Activities of moderate risk.

Class 4: Activities of high risk.

Principles governing risk assessment of genetically modified microorganisms

This Annex describes in general terms the elements to be considered and the procedure to be followed to perform the assessment referred to in Article 3.

Guidelines for the carrying out of risk analyses are given in Annex 5.

A. Elements of the assessment mentioned in Article 3

1. The following should be considered potentially harmful effects:
 - disease to humans including allergenic or toxic effects;
 - disease to animals or plants;
 - adverse effects resulting from the inability to treat disease or offer effective prophylaxis;
 - adverse effects resulting from establishment or dissemination in the environment;
 - adverse effects resulting from the natural transfer of inserted genetic material to other organisms.

2. The assessment referred to in Article 3 should be based on the following:
 - (a) identification of any potentially harmful effects, in particular those associated with:
 - (i) the recipient microorganism;
 - (ii) the inserted (donated) genetic material;
 - (iii) the vector;
 - (iv) the donor microorganism (as long as the donor microorganism is used during the operation);
 - (v) the resulting GMM;
 - (a) the characteristics of the activity;
 - (b) the severity of the potentially harmful effects;
 - (c) the likelihood of the potentially harmful effects being realised.

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B. Procedure

2. The first stage in the assessment process should be to identify the harmful properties of the recipient and, where appropriate, the donor microorganism, as well as any harmful properties associated with the vector or inserted material, including any alteration in the recipient's existing properties.
3. In general, only GMMs which show the following characteristics would be considered appropriate for inclusion in class 1:
 - (i) the recipient or parental micro-organism is unlikely to cause disease to humans, animals or plants ⁽¹⁾;
 - (ii) the nature of the vector and the insert is such that they do not endow the GMM with a phenotype likely to cause disease to humans, animals and plants ⁽¹⁾, or likely to cause adverse effects in the environment;
 - (iii) the GMM is unlikely to cause disease to humans, animals or plants ⁽¹⁾ and is unlikely to have adverse effects on the environment.
2. In order to inform this process the person in charge of transport and import may first take into account relevant Community legislation, especially Council Directive 90/679/EEC (²). International and national classification schemes (for example WHO, NIH) and their adaptation to scientific and technological development may also be taken into account.

These schemes concern natural microorganisms and as such are usually based on the ability of microorganisms to cause disease in humans, animals or plants and on the severity and transmissibility of the disease likely to be caused. Council Directive 90/679/EEC classifies microorganisms, as biological agents, into four classes of risk on the basis of potential effects on a healthy human adult.

The classes of risk can be used as guidance to the categorisation of the contained use activities in the four classes, as stated in Annex 2. The person in charge of transport and import may also take classification systems into account which refer to plant and animal pathogens (and which are normally prepared on a national basis). These classification systems give only a preliminary indication of the risk class of an activity and the associated set of containment and control measures.

3. The hazard identification process carried out in accordance with paragraphs 3 to 5 above, should lead to the identification of the level of risk associated with the GMM.
4. Selection of the containment and other protective measures should then be made on the basis of the level of risk associated with the GMMs, including especially consideration of disposal of waste and discharge of waste water, together with the consideration of:

⁽¹⁾ This would only apply to animals and plants in the environment likely to be exposed.

⁽²⁾ OJ L 374, 31.12.1990, p. 1. Directive as last amended by Commission Directive 97/59/EC (OJ L 282, 15.10.1997, p.33)

- (i) the characteristics of the environment likely to be exposed (e.g. whether in the environment likely to be exposed to the GMMs there are known biota which can be adversely affected by the micro-organisms used in the contained use activity);
- (ii) the characteristics of the activity (e.g. its scale; nature);
- (iii) any non-standard operations (e.g. the inoculation of animals with GMMs; equipment likely to generate aerosols).

Consideration of items (i) to (iii) above for the particular activity may increase, reduce or leave unaltered the level of risk associated with the GMM as identified under paragraph 6.

2. The analysis carried out as described above will finally lead to the assignment of the activity to one of the classes described in Annex 2. In case of doubt as to the class which is suitable for the proposed containment, the strictest protective measures shall be applied unless adequate documentation submitted by agreement with the competent authority justifies less strict measures.
3. The final classification of the contained use should be confirmed by reviewing the completed assessment referred to in Article 3.

Information about the genetically modified production organism

Applications shall contain the information listed below. Any omission of information shall be explained.

A. Characteristics of the donor, recipient or (where appropriate) parental organism(s)

- names and designation;
- sources of the organism(s);
- information on reproductive cycles (sexual/asexual) of the parental organism(s) or, where applicable, of the recipient micro-organism;
- history of prior genetic manipulations;
- stability of the parental or of recipient organism in terms of relevant genetic traits;
- nature of pathogenicity and virulence, infectivity, toxicity and vectors of disease transmission;
- nature of indigenous vectors:
 - sequence
 - frequency of mobilisation
 - specificity
 - presence of genes which confer resistance;
- host range;
- other potentially significant physiological traits;
- stability of these traits;
- natural habitat and geographic distribution; climatic characteristics of original habitats;
- significant involvement in environmental processes (such as nitrogen fixation or pH-regulation);
- interaction with, and effects on, other organisms in the environment (including likely competitive or symbiotic properties);
- ability to form survival structures (such as spores or sclerotia).

B. Characteristics of the modified microorganism

- origin of the genetic material involved in the genetic engineering operations and the intended functions of that material;
- description of the modification including the method for introducing the vector-insert into the recipient organism or the method used for achieving the genetic modification involved;
- the function of the genetic manipulation and/or of the new nucleic acid;
- nature and source of the vector;
- structure and amount of any vector and/or donor nucleic acid remaining in the final construction of the modified organism;
- stability of the organism in terms of genetic traits;
- frequency of mobilisation of inserted vector and/or genetic transfer capability;
- rate and level of expression of the new genetic material; method and sensitivity of measurement;
- activity of the expressed protein.

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B. Health considerations

- toxic or allergenic effects of non-viable organisms and/or their metabolic products;
- products hazards;
- comparison of the modified organisms to the donor, recipient or (where appropriate) parental organism regarding pathogenicity;
- capacity for colonisation;
- if the organism is pathogenic to humans who are immunocompetent;
 - a) diseases caused and mechanism of pathogenicity including invasiveness and virulence;
 - b) communicability;
 - c) infective dose;
 - d) host range, possibility of alteration;
 - e) possibility of survival outside of human hosts;
 - f) presence of vectors or means of dissemination;
 - g) biological stability,
 - h) antibiotic-resistance patterns;
 - i) allergenicity;
 - j) availability of appropriate therapies.

B. Environmental considerations

- factors affecting survival, multiplication and dissemination of the modified organism in the environment;
- available techniques for detection, identification and monitoring of the modified organism;
- available techniques for detecting transfer of the new genetic material to other organisms;
- known and predicted habitats of the modified organism;
- description of ecosystems to which the organism could be accidentally disseminated;
- anticipated mechanism and result of interaction between the modified organism and the organisms or microorganisms which might be exposed in case of release into the environment;
- known or predicted effects on plants and animals such as pathogenicity, infectivity, toxicity, virulence, vector or pathogen, allergenicity, colonisation;
- known or predicted involvement in biogeochemical processes;
- availability of methods for decontamination of the area in case of release to the environment.

Guidelines for risk assessment as mentioned in Annex 3

1. INTRODUCTION

The elements of the risk assessment outlined in paragraphs 1 and 2 of Annex 3 require consideration of potentially harmful effects to human health and the environment. Potentially harmful effects are defined as those effects which may give rise to disease, render prophylaxis or treatment ineffective, promote establishment and/or dissemination in the environment which gives rise to harmful effects on organisms or natural populations present or harmful effects arising from gene transfer to other organisms. The assessment requires that the risk of these potentially harmful effects are considered for each activity and allocated to a class as defined in Article 3, taking into account both the nature and scale of operations, to determine the final containment facilities required. The degree of risk arising from contained uses with a genetically modified organism (GMO), and their construction, is determined by consideration of the severity of the potential harmful effects, to human health or the environment, with the possibility of those effects occurring. The risk assessment considers the exposure of humans or the environment to GMOs during the operation of, or possible unintended release from, a contained use facility. The classification level determined by the risk assessment defines the containment requirements for the activities involving GMOs.

1. RISK ASSESSMENT

The full risk assessment process consists of the two procedures outlined below:

1.1 Procedure 1

Identification of potential harmful properties (hazards) of the GMO and allocation of the GMO to an initial class (class 1 – class 4), taking into account the severity of the potential harmful effects.

AND

Assessment of possible harmful effects occurring by consideration of exposure (both human and environmental), taking into account the nature and scale of the work, with containment measures appropriate to the initial class allocated.

1.1 Procedure 2

Determination of final classification and containment measures required for the activity. Confirmation that final classification and containment measures are adequate by revisiting Procedure 1.

1. PROCEDURE 1

1.1 Identification of harmful properties (hazards) of the GMO.

The risk assessment process requires the identification of any potentially harmful properties of the GMO as a result of the genetic modification or any alteration of the recipient organisms' existing properties. Potentially harmful properties associated with the GMO must be determined. This should be done by consideration of the recipient organism, the donor organism, the characteristics and location of the inserted genetic material and any vector. It is important to appreciate that the genetic modification of a microorganism can affect its ability to cause harm to human health and the environment. Genetic modifications can result in a decreased, unchanged or increased ability to cause harm.

1.1 Aspects that should be considered where relevant are:

1.1.1 The recipient organism

- nature of pathogenicity and virulence, infectivity, allergenicity, toxicity and vectors of disease transmission;
- nature of indigenous vectors and adventitious agents, where they could mobilise the inserted genetic material, and the frequency of mobilisation;
- nature and stability of disabling mutations, if any;
- any prior genetic modifications;
- host range (if relevant);
- any significant physiological traits which may be altered in the final GMO and if relevant their stability;
- natural habitat and geographic distribution;
- significant involvement in environmental processes (such as nitrogen fixation or pH regulation);
- interaction with, and effects on, other organisms in the environment (including likely competitive pathogenic or symbiotic properties);
- ability to form survival structures (such as spores or sclerotia).

1.1.1 The donor organism (for fusion experiments or “shotgun” experiments where the insert is not well characterised)

- nature of pathogenicity and virulence, infectivity, toxicity and vectors or disease transmission;
- nature of indigenous vectors:
 - sequence;
 - frequency of mobilisation and specificity;
 - presence of genes which confer resistance to anti-microbials including antibiotics.
- host range;
- other relevant physiological traits.

1.1.1 The insert

- specific identify and function of the insert (genes);
- level of expression of inserted genetic material;
- source of the genetic material, identity of the donor organism(s) and characteristics where appropriate;
- history of prior genetic modifications if appropriate;
- location of inserted genetic material (possibility of insertional activation/deactivation of host genes).

1.1.1 The vector

- nature and source of the vector;
- structure and amount of any vector and/or donor nucleic acid remaining in the final construction of the modified microorganism;
- if present in the final GMO frequency of mobilisation of inserted vector and/or capability of transfer of genetic material.

1.1.1 The resulting GMO

1.1.1.1 Human health considerations

- expected toxic or allergenic affects of the GMO and/or its metabolic products;
- comparison of the modified microorganism to the recipient or (where appropriate) parental organism regarding pathogenicity;
- expected capacity for colonisation;
- if the microorganism is pathogenic to humans who are immunocompetent:
 - diseases caused and mechanism of transmission including invasiveness and virulence;
 - infective dose;
 - possible alteration of route of infection or tissue specificity;
 - possibility of survival outside of human host;
 - biological stability;
 - antibiotic-resistance patterns;
 - allergenicity;
 - toxigenicity;
 - availability of appropriate therapies and prophylactic measures.

1.1.1.1 Environmental considerations

- ecosystems to which the micro-organism could be unintentionally released from the contained use;
- expected survivability, multiplication and extent of dissemination of the modified microorganism in the identified ecosystems;
- anticipated result of interaction between the modified micro-organism and the organisms or microorganisms which might be exposed in case of unintentional release into the environment;
- known or predicted effects on plants and animals such as pathogenicity, toxicity, allergenicity, vector for a pathogen, altered antibiotic-resistance patterns, altered tropism or host specificity, colonisation;

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- known or predicted involvement in biogeochemical processes.

1.1 Initial classification of the GMO

Paragraphs 3 – 5 of Annex 3 indicate that the first stage of the risk assessment process for a GMO is to identify the potential harmful properties of the GMO, to determine an initial classification of the GMO. This is achieved by the identification of hazards associated with the recipient, donor organism, vector and insert where appropriate. This process can be aided by taking into account the general characteristics for class 1 set out in paragraph 4 of Annex 3 and appropriate up to date national and international classification schemes (including Directive 90/679/EEC³ and amendments thereof).

The risk of harm arising from any harmful property of the GMO is obtained by the consideration of the severity of the harm and any biological properties (e.g. disabling mutations) which limit the possibility of harm occurring. The estimation of the severity of the harmful effects is performed independently of the possibility of the harmful effect occurring. The severity of any possible harm is determined by considering what the result could be, not whether it is likely to occur in the particular case. For instance, for a pathogen it would be estimated how serious the disease would be assuming that the susceptible species was infected. The allocation of the GMO to an initial class includes consideration of severity. Classification schemes such as the scheme in Directive 90/679/EEC take severity into account. However many schemes are based only on either human health or environmental considerations. Care must be taken to ensure that the severity of harmful effects on human health and the environment from the GMO have been fully considered.

1.1 Assessment of possibility of harmful effects occurring

The key factor that affects the possibility of a harmful event occurring is the level and nature of exposure of humans or the environment to a particular GMO. Exposure is, in most cases, of primary importance to risk assessment as it will often determine whether a harmful effect could occur. The possibility of humans or the environment being exposed to a GMO depends upon what operations are being carried out (for example the scale of the operations) and the containment measures appropriate to the initial classification as determined in paragraphs 5 and 6 applied to the work.

Paragraph 7 (ii & iii) of Annex 3 requires that the characteristics of the operation be taken into account when the final classification and selection of control measures are made. The nature and scale of the activity need to be considered in order to estimate the possibility of exposure of humans and the environment and will also affect the choice of appropriate risk management procedures.

The characteristics of the operation that could affect the risk assessment and so should be taken into account as appropriate include the actual activities to be undertaken, work practices, scale and containment measures applied.

³ OJ L 374, 31.12.1990, p. 1

The assessment should especially take into account the question of disposal of waste and effluents. Where appropriate, the necessary safety measures should be implemented in order to protect human health and the environment.

1.1.1 Nature of activities to be undertaken

The degree of risk and application of control measures to reduce the risk from the GMO to an appropriate level will be influenced by the nature of the activities to be undertaken, since these will affect human and environmental exposure and hence possibility of harm occurring.

The nature of the activities will also determine the most appropriate containment and control measures to be considered.

In practice, for laboratory scale work where the effect of standard laboratory procedures on exposure are well known, detailed risk assessment of each individual procedure would be unlikely to be required unless a highly hazardous organism was being used. More detailed consideration however may be necessary for non-routine procedures or procedures which might have a significant effect on the degree of risk, for example, procedures which generate aerosols.

1.1.1 Concentration and scale

The density of a culture can lead to a risk of exposure to high concentrations of the GMO, particularly in downstream processing operations. The effects of concentration on the possibility of a harmful event occurring must be considered.

Scale is also a factor that must be taken into account in the risk assessment. Scale may be in terms of the absolute volume of a single operation or the frequent repetition of a process, because both could give rise to an increased possibility of exposure if the containment and control measures failed and thus affect the possibility of a harmful event occurring.

While large scale does not necessarily mean high risk, increased scale may lead to an increased possibility of exposure both in terms of the number of humans and the amount of environmental exposure that might occur in the event of containment failure.

The scale of the work will also influence the most appropriate containment and control measures.

1.1.1 Culture conditions

In many contained use activities, the culture conditions are rigorously contained to protect the work, however, the nature and design of the growth vessels or other culture equipment will also influence the degree of risk to human health and the environment. Highly engineered and sealed

fermentation vessels can significantly reduce exposure and hence risk from a GMO. Consideration of reliability and possible failure rates for such equipment is important where failure could lead to high levels of exposure to harmful GMOs. Where such loss is reasonably foreseeable, additional containment measures may be required. The standard operating procedures of individuals undertaking work with cultured GMOs such as centrifugation or sonication will have a significant impact on the effectiveness of any containment measures employed.

In combination with physical culture conditions that act as containment measures, both biological and chemical measures that are employed to protect the work can also contribute significantly to the containment measures that may be required. Examples of biological containment could well be auxotrophic mutants that require specific growth factors to be supplied to grow. Examples of chemical containment measures could be disinfectant solutions maintained in drainage systems.

Paragraph 7 (i) of Annex 3 requires that the characteristics of the environment likely to be exposed and the severity of the effect be taken into account when assessing the possibility of harmful effects occurring and their severity.

There are a number of aspects to this consideration of the environment that are important, such as the extent and nature of environmental exposure and whether there are biota which can be adversely affected by the particular GMO in the area exposed.

The following factors should be considered, as appropriate, when assessing how the characteristics of the receiving environment will affect the possibility that the potentially harmful effect will be realised and hence the level of risk and selection of control measures.

1.1.1.1 Environmental considerations

The environment likely to be exposed will in most cases probably be limited to the workplace environment and the area immediately surrounding the facility, but depending on the specific characteristics of the contained use and the facility, a wider environment may need to be considered. The extent of the environmental exposure may be influenced by the nature and scale of the activity, but consideration should also be given to all possible modes of transmission into the wider environment. These can include physical modes (such as local drains, watercourses, waste disposal, air movement) and biological vectors (such as movement of infected animals and insects).

1.1.1.1 Presence of susceptible species

The possibility of harm actually occurring will depend on whether there are susceptible species, including humans, animals and plants, in the environment that is likely to be exposed.

1.1.1.1 Whether the environment can support the survival of the GMO

The extent to which the GMO can survive and persist in the environment is a strong consideration in the risk assessment. The possibility of harm occurring will be significantly reduced if a GMO cannot survive in the environment to which it might gain access.

1.1.1.1 Effects on the physical environment

In addition to direct harmful effects of a GMO, indirect harmful effects from significantly altering the physico-chemical properties and/or ecological balance of the soil or water components of the environment must be considered.

1. PROCEDURE 2

1.1 Determination of final classification of containment measures

When all potentially harmful characteristics have been reviewed for their severity and possibility of occurrence, with the effect of the containment and control measures indicated by the initial classification of the recipient considered, the final classification and containment measures for the GMO can be determined. In considering the final classification and containment measures, the initial classification should be revisited to determine if it was correct bearing in mind the activities and characteristics of the operations proposed. A comparison of the initial classification and associated containment measures with the final class and containment requirements can give rise to three results:

- there are harmful effects which are not adequately taken into account in the initial classification, these would not be adequately contained by the provisional containment considered under Procedure 1. This would require the application of additional containment measures and possibly revision of the classification of the activity;
- the initial classification was correct and the attendant containment measures adequately prevent or minimise harm to human health and the environment;
- the initial classification is higher than the activity warrants and accordingly a lower classification with its attendant containment conditions would be appropriate.

1.1 Confirmation of adequacy of final containment measures

Once the proposed final classification and containment conditions have been determined, the level of human and environmental exposure should be reassessed (Procedure 1). This should confirm that the possibility of any harmful effects occurring, taking into account the nature and scale of the work and the proposed containment conditions are acceptably low. When this has been done the risk assessment process has been completed.

If the nature or scale of the work changes significantly or new scientific or technical knowledge becomes available, such that the risk assessment is no longer adequate, the risk assessment must be reviewed in the light of the changes. Any alteration in containment conditions indicated as a result of the review of the risk assessment must be applied forthwith to maintain adequate protection for human health and the environment.

The classification and the containment and control measures identified in the risk assessment as required to adequately contain the GMO during the proposed operations, leads to the classification of the contained use activities into classes 1 to 4.

The classification of the contained use activities for the GMO defines the administration requirements.

If there are any uncertainties in the final classification and containment conditions, it is advisable to contact the National Forest and Nature Agency.