Ministry of Social Affairs and Health, Finland

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No. 1053/2005

Decree of the Ministry of Social Affairs and Health on principles of risk assessment of the contained use of genetically modified micro-organisms, on classification of the contained use, and on containment and other protective measures

Issued in Helsinki on 13 December 2005

Section 1

Minimum requirements for risk assessment

The operator shall observe in the risk assessment of the contained use of genetically modified organisms at least what is laid down in sections 2 – 11.

Section 2

General principles of risk assessment

(1) The risk assessment shall identify the potentially harmful effects of a genetically modified micro-organism that are due to a genetic alteration or alterations in the earlier properties of the recipient organism. The following are considered as potentially harmful effects of a genetically modified micro-organism:
1) disease to humans, including allergenic or toxic effects;
2) disease to animals or plants;
3) deleterious effects due to the impossibility of treating a disease or providing an effective prophylaxis;
4) deleterious effects due to establishment or dissemination in the environment; and
5) deleterious effects due to the natural transfer of inserted genetic material to other organisms.

(2) The risk assessment shall be based on:
1) the identification of all potentially harmful effects, in particular such as are associated with:
a) the recipient micro-organism;
b) the genetic material originating from the donor organism inserted;
c) the vector;
d) the donor micro-organism if the donor micro-organism is used during the operation, and
e) the resulting genetically modified micro-organism;
2) the characteristics of the activity;
3) the severity of the potentially harmful effects; and
4) the likelihood of the potentially harmful effects being realised.

Section 3

The stages of risk assessment

(1) The risk assessment consists of two stages at which:
1) at stage 1, at first the potentially harmful effects of the genetically modified micro-organism are identified and the initial classification (classes 1 – 4) of the contained use of the genetically modified micro-organism is determined taking into account the severity of the potentially harmful effects; thereafter the likelihood of the harmful effects resulting from exposure of humans and the environment is assessed taking into account the nature and scale of the activity, and the containment measures according to the initial classification are chosen; and
2) at stage 2, at first the final classification of the contained use and the containment measures required by it are determined, and thereafter the final classification and the appropriateness of the final containment measures is reviewed by repeating stage 1.

(2) Provisions on stage 1 are laid down in sections 4 – 9 and provisions on stage 2 in sections 10 and 11.

Section 4

Identification of harmful properties

(1) When identifying the potentially harmful properties of the genetically modified micro-organism, the following shall be taken into account in regard to the recipient organism, as necessary:
1) the nature of pathogenicity and virulence, and infectivity, allergenicity, toxicity and vectors for disease transmission;
2) the nature of indigenous vectors and adventitious agents if these vectors or agents can mobilise the inserted genetic material, and the frequency of mobilisation;
3) the nature and stability of disabling mutations;
4) prior genetic modifications;
5) the host range;
6) the significant physiological properties that can change in the final genetically modified micro-organism, and their stability on case-by-case basis;
7) natural habitat and geographical distribution;
8) significant involvement in environmental processes such as nitrogen fixation or pH regulation;
9) interaction with other organisms in the environment and its effects on them, including its likely competitive properties and pathogenic and symbiotic properties; and
10) the ability to form structures enhancing survival, such as spores or sclerotia.

(2) When identifying the potentially harmful effects of the genetically modified micro-organism, the following considerations shall be taken into account in regard to the donor organism, if it is question of a fusion experiment and if the properties of the insert are not carefully defined:
1) the nature of pathogenicity and virulence, and infectivity, toxicity and vectors for disease transmission;
2) the following factors associated with the nature of the indigenous vectors of the donor organism:
a) sequence;
b) mobilisation frequency and specificity; and
c) the presence of genes which confer resistance to antimicrobial agents, including antibiotics;
3) the host range; and
4) other significant physiological properties.

(3) When identifying the potentially harmful properties of the genetically modified micro-organism, the following shall be taken into account in regard to the insert, as necessary:
1) the identity of the insert and its function;
2) the level of expression of the inserted genetic material;
3) the source of genetic material, the identity of the donor organisms and their characteristics on case-by-case basis;
4) potential prior genetic modifications; and
5) the location of the inserted genetic material taking into account that the insertion may activate or deactivate the genes of the recipient organism.

(4) When identifying the potentially harmful properties of the genetically modified micro-organism, the following shall be taken into account in regard to the vector, as necessary:
1) the nature and source of the vector;
2) the structure and amount of the nucleic acid from the vector and donor organism that remains in the final construction of the genetically modified micro-organism; and
3) the mobilisation frequency and capability of the inserted vector for transfer of genetic material if the vector remains in the final genetically modified micro-organism.

(5) When identifying the potentially harmful properties of the resulting genetically modified micro-organism, the following shall be taken into account, as necessary:
1) the following considerations related to human health:
    a) the foreseeable toxic and allergenic effects of the genetically modified micro-organism and its metabolites;
    b) comparison of the pathogenicity of the genetically modified micro-organism to the pathogenicity of the recipient or parental organism; and
    c) foreseeable colonisation potential;
2) the following considerations related to human health, if the micro-organism concerned is pathogenic to immunocompetent people;
    a) diseases caused by the micro-organism and the disease transmission mechanism, including invasiveness and virulence;
    b) the infective dose;
    c) possible alteration of the route of infection or tissue-specificity;
    d) survivability outside of human host;
    e) biological stability;
    f) antibiotic resistance patterns;
    g) allergenicity;
    h) toxicity; and
    i) availability of appropriate methods of treatment and prophylaxis; and
3) the following environmental considerations:
    a) the ecosystems to which the micro-organism can unintentionally be disseminated from the contained use;
    b) the foreseeable survivability, multiplication and dissemination of the genetically modified micro-organism in the ecosystems concerned;
    c) the predicted result from interaction of the genetically modified micro-organism with such organisms or micro-organisms that may be exposed to the genetically modified micro-organism that has been unintentionally disseminated into the environment;
    d) known or predicted effects on plants and animals, such as pathogenicity, toxicity, allergenicity, vector for a pathogene, altered antibiotic resistance pattern, altered tropism or host specificity and colonisation; and

e) known or predicted involvement in biogeochemical processes.

Section 5

Initial classification of the genetically modified micro-organism

(1) For the initial classification of the genetically modified micro-organism it is necessary to identify the risks that are possibly related to the recipient and donor organism, and to the vector and insert. In the identification it is possible to use the general requirements for the properties of class 1 laid down in paragraph 3 and the up-to-date national and international classification systems, such as the Decision of the Ministry of Social Affairs and Health 229/1998. The containment and protective measures described in Tables 1 – 4 of the Annex to this Decree can be used as a point of comparison when deciding if the control of the identified harmful effects requires more stringent containment and other protective measures.

(2) The risk of harmful effects related to the properties of genetically modified micro-organisms is evaluated by taking into account the severity and all biological properties of each effect, such as disabling mutations that reduce the likelihood of the effect. The severity and likelihood of harmful effects shall be evaluated separately so that the estimate of the severity of consequences will not be based on how likely a harmful effect will manifest itself in a certain case. The estimated severity of effects shall be taken into account in the initial classification of the genetically modified micro-organism, and it shall also be seen to it that the severity of the harmful effects on human health and on the environment has been taken into account in all respects.

(3) Under section 13 of the Gene Technology Act (377/1995) as genetically modified micro-organisms suitable to be included in class 1 are in general considered only those with the following characteristics:
1) the recipient or parental organism is not likely to cause disease to humans or to animals or plants in the environment likely to be exposed;
2) the nature of the vector and insert is such that they do not endow the genetically modified micro-organism with a phenotype likely to cause disease to humans or to animals or plants in the environment likely to be exposed or cause deleterious effects in the environment; and
3) the genetically modified micro-organism is not likely to cause disease to humans or to animals or plants in the environment likely to be exposed, and is not likely to cause deleterious effects in the environment.

Section 6

Principles of evaluating the likelihood of harmful effects

When evaluating the likelihood of harmful effects it is essential to pay attention to which extent and how people and the environment are exposed to the genetically modified micro-organism. The likelihood of people or the environment being exposed to the genetically modified organism depends on the activity involving exposure to it and on the containment measures undertaken in connection with the work involving exposure. The special characteristics of the activity shall be taken into account in the final classification and choice of the containment measures. The nature and scale of the activity must be taken into account when evaluating the likelihood of exposure of people and the environment. Furthermore, the nature and scale of the activity affect the choice of the risk management methods. In particular the waste and effluents management shall be taken into account in the assessment.

Section 7

The nature of the planned use in evaluation of the likelihood of harmful effects

(1) When evaluating the likelihood of harmful effects it shall be taken into account that the nature of the planned activities affects the size of the risk and the application of such protective measures by which the risk associated with the genetically modified micro-organism becomes sufficiently small. The nature of the activities partly also determines which of the Tables 1 – 4 in the Annex to this Decree contains the most suitable containment and other protective measures.

(2) In laboratory activities in which the effects of standardised laboratory methods on exposure are generally known, it probably is not necessary to evaluate in detail the risks associated with each method, unless a very dangerous organism is used. A detailed consideration may however be necessary when it is question of methods other than routine methods or such methods that may considerably affect the risk level, such as methods in which aerosols are generated.

Section 8

Concentrations and the scale of activity in evaluation of the likelihood of harmful effects

When evaluating the likelihood of harmful effects it shall be taken into account that dense cultures can expose to high concentrations of genetically modified organisms in particular when it is question of downstream processing measures. In addition, the scale of the measures or frequent repetition of the process must be taken into account. In that case it must be taken into account that failure of the containment measures in an extensive activity may increase the likelihood of exposure. The scale of the activity also partly determines which of the Tables in the Annex to this Decree contains the most suitable containment and other protective measures.

Section 9

Culture conditions in evaluation of the likelihood of harmful effects

(1) When evaluating the likelihood of harmful effects attention shall be paid to the reliability of the growth vessels and other equipment used in culture and to the possibility of failures in the operation, if the failure of equipment may lead to a major exposure of humans and the environment to dangerous genetically modified organisms. If unintentional releases are foreseeable, it may be necessary to increase the containment measures. The standard methods used, such as centrifugation and sonication, also considerably affect the effectiveness of the containment measures.

(2) In addition to the physical containment measures, biological and chemical measures may constitute a considerable part of the required containment measures and affect the likelihood of occurrence of harmful effects. As biological containment measures can be used, among others, such auxotrophic mutants that require specific growth factors to be supplied to grow. Among others, disinfectant solutions can be used as chemical containment measures in drainage systems.

(3) The following factors shall be taken into account on case-by-case basis when evaluating how the properties of the recipient environment affect the likelihood of harmful effects and thus also the risk level and choice of containment measures:
1) the environment potentially exposed; in most cases the environment that will potentially be exposed is limited to the work environment or the environment immediately surrounding the

establishment, but it may be necessary to take into account exposure of a wider environment; the scale of environmental exposure can be affected by the nature and scale of the activity, but at the same time it is necessary to take into account all the modes by which genetically modified organisms can be disseminated to the environment, including physical modes of transfer such as local drains, watercourses, waste treatment and air movement, as well as biological vectors such as insects and other animals;
2) presence of susceptible species;
3) a possibility that the genetically modified micro-organism is capable of surviving and persisting in the environment; and
4) effects on physico-chemical properties; apart from the direct harmful effects of the genetically modified micro-organism also the indirect harmful effects that are due to significant changes in the physico-chemical properties of the soil or water and ecological balance of the environment must be taken into account.

Section 10

Determination of the final classification of the genetically modified micro-organism and of the final containment measures

(1) The final classification of the genetically modified micro-organism and the final containment measures can be determined when the severity and likelihood of all potentially harmful effects and the adequacy of the containment and other protective measures according to the initial classification have been evaluated. In that context, it shall be reviewed whether the initial classification is appropriate taking into account the nature of the proposed activity and measures.

(2) A comparison of the initial classification and related containment measures with the final classification and related containment measures can give rise to three results:
1) the initial classification has not adequately taken into account all harmful effects, and therefore the containment measures initially chosen at stage 1 would not be sufficient and they should be supplemented by other containment measures, and the classification of the activity must possibly be revised;
2) the initial classification is correct and the related containment measures are sufficient to prevent or minimise the harmful effects on human health and the environment; or
3) in the initial classification the risk associated with the activity was estimated too high, and therefore a lower risk level and containment measures corresponding to that must be chosen.

Section 11

Confirmation of the final containment measures

(1) Once the final classification and the final containment measures have been determined, it has to be reassessed to which extent humans and the environment can be exposed to harmful effects. In this way it is ensured that the likelihood of the harmful effects is so low that it can be accepted taking into account the nature and scale of the activity and the proposed containment measures. When this has been done, the risk assessment has been completed.

(2) The risk assessment shall be reviewed later on if the nature or scale of the activity changes significantly, and if there is reason to suspect in the light of new scientific and technical knowledge that the assessment is no more appropriate. Any alteration to the containment measures shall be

applied without delay so as to ensure an adequate level of protection for human health and the environment.

Section 12

General principles of operation

For the handling of genetically modified micro-organisms the principles of good microbiological practice and the following principles of good occupational safety and hygiene shall apply:
1) to keep the workplace and environmental exposure to any genetically modified micro-organism to the lowest level possible;
2) to exercise engineering control measures at the place of work and to supplement them with appropriate protective clothing and equipment when necessary;
3) to test adequately and maintain control measures and equipment;
4) to test, when necessary, the presence of viable organisms outside the primary physical containment;
5) to provide appropriate training for personnel;
6) to set up working groups for biological safety, if required;
7) to formulate and implement local codes of practice for the safety of personnel, as required;
8) where appropriate to display biohazard signs;
9) to provide washing and decontamination facilities for personnel;
10) to keep adequate records of operations;
11) to prohibit eating, drinking, smoking, applying cosmetics or the storing of food for human consumption in the work area;
12) to prohibit mouth pipeting;
13) to provide written standard operating procedures where appropriate to ensure safety;
14) to have effective disinfectants and specified disinfection procedures available in case of spillage of genetically modified organisms; and
15) to provide safe storage for contaminated laboratory equipment and materials, when appropriate.

Section 13

Containment and other protective measures corresponding to the containment levels

(1) The tables annexed to this Decree present the usual minimum requirements and measures corresponding to each containment level as follows:
1) Table 1 presents the minimum requirements for laboratory activities;
2) Table 2 presents additions to and modifications of Table 1 for glasshouse or growth-room activities involving genetically modified organisms;
3) Table 3 presents additions to and modifications of Table 1 for activities with animals involving genetically modified organisms; and
4) Table 4 presents the minimum requirements for activities other than laboratory activities.

(2) In some particular cases, it may be necessary to apply a combination of measures, from both Table 1 and Table 4 to achieve a particular containment level.

(3) In some cases the Board for Gene Technology may grant an operator permission not to apply a requirement under a particular containment level or a permission to combine requirements from two different levels.

(4) In the Tables “optional” means that the operator may apply these measures on case-by-case basis taking into account the result from the risk assessment referred to in section 8 of the Gene Technology Act.

Section 14

Entry into force

(1) This Decree enters into force on 1 January 2006.

(2) This Decree repeals the Decree of the Ministry of Social Affairs and Health on principles of risk assessment of the contained use of genetically modified micro-organisms and on containment and other protective measures of 31 May 2000 (492/2000).

Council Directive 98/81/EC (31998L0081); ECOJ No. L 330, 5.12.1998, p. 13

Table 1

Containment and other protective measures

	Specifications	Containment levels			
		1	2	3	4
1	Laboratory suite: isolation ([1])	Not required	Not required	Required	Required
2	Laboratory: sealable for fumigation	Not required	Not required	Required	Required
Equipment					
3	Surfaces resistant to water, acids, alkalis, solvents, disinfectants and decontamination agents, and easy to clean	Required (bench)	Required (bench)	Required (bench, floor)	Required (bench, floor, ceiling, walls)
4	Entry to lab via airlock ([2])	Not required	Not required	Optional	Required
5	Negative pressure relative to the pressure of the immediate environment	Not required	Not required	Required except for ([3])	Required
6	Extract and input air from the laboratory should be HEPA ([4])-filtered	Not required	Not required	Required (HEPA - extract air except for ([3]))	Required (HEPA - input and extract air ([5]))
7	Microbiological safety post	Not required	Optional	Required	Required
8	Autoclave	On site	In the building	En suite ([6])	In lab = double-ended
System of work					
9	Restricted access	Not required	Required	Required	Required
10	Biohazard sign on the door	Not required	Required	Required	Required
11	Specific measures to control aerosol dissemination	Not required	Required minimise	Required prevent	Required prevent
12	Shower	Not required	Not required	Optional	Required

[1] Isolation = the laboratory is separated from other areas in the same building or is in a separate building.
[2] Airlock = entry must be through an airlock which is a chamber isolated from the laboratory. The clean side of the airlock must be separated from the restricted side by changing or showering facilities and preferably by interlocking doors.
[3] Activities where transmission does not occur via airborne route.
[4] HEPA = High efficiency particulate air.
[5] Where viruses which are not retained by HEPA filters are used, extra requirements will be necessary for extract air.
[6] With validated procedures, allowing the safe transfer of material into an autoclave outside the lab, and providing an equivalent level of protection.

13	Protective clothing	Suitable protective clothing	Suitable protective clothing	Suitable protective clothing and (optional) footwear	Complete change of clothing and footwear before entry and exit
14	Gloves	Not required	Optional	Required	Required
15	Efficient vector control (e.g. for rodents and insects)	Optional	Required	Required	Required

Waste

16	Inactivation of GMMs in effluent from hand-washing sinks or drains and showers or similar effluents	Not required	Not required	Optional	Required
17	Inactivation of GMMs in contaminated material and waste	Optional	Required	Required	Required

Other measures

18	Laboratory to contain its own equipment	Not required	Not required	Optional	Required
19	An observation window or alternative is to be present so that occupants can be seen	Optional	Optional	Optional	Required

Table 2

Containment and other protective measures for glasshouses and growth-rooms

The terms ‘glasshouse’ and ‘growth-room’ refer to a structure with walls, a roof and a floor designed and used principally for growing plants in a controlled and protected environment.

All provisions of Table 1 shall apply with the following additions/modifications:

	Specifications	Containment levels			
		1	2	3	4
Building					
1	Glasshouse: permanent structure ([7])	Not required	Required	Required	Required
2	Entry is via a separate room with two interlocking doors	Not required	Optional	Optional	Required
3	Control of contaminated run-off water	Optional	Minimise ([8]) run-off	Prevent run-off	Prevent run-off
System of work					
4	Measures to control undesired species such as insects, rodents, arthropods	Required	Required	Required	Required
5	Procedures for transfer of living material between the glasshouse/ growthroom, protective structure and laboratory shall control dissemination of GMMs	Minimise dissemination	Minimise dissemination	Prevent dissemination	Prevent dissemination

[7] The glasshouse shall consist of a permanent structure with a continuous waterproof covering, located on a site graded to prevent entry of surface-water run-off, and with self-closing lockable doors.
[8] Where transmission can occur through the ground.

Table 3

Containment and other protective measures for activities in animal units

All provisions of Table 1 shall apply with the following additions/modifications:

	Specifications	Containment levels			
		1	2	3	4
Facilities					
1	Isolation of animal unit ([9])	Optional	Required	Required	Required
2	Animal facilities separated by lockable doors	Optional	Required	Required	Required
3	Animal facilities ([10]) designed to facilitate decontamination (waterproof and easily washable material (cages, etc.))	Optional	Optional	Required	Required
4	Floor and/or walls easily washable	Optional	Required (floor)	Required (floor and walls)	Required (floor and walls)
5	Animals kept in appropriate containment facilities such as cages, pens or tanks	Optional	Optional	Optional	Optional
6	Filters on isolators or isolated room ([11])	Not required	Optional	Required	Required

[9] Animal unit: a building or separate area within a building containing facilities and other areas such as changing rooms, showers, autoclaves, food storage areas, etc.

[10] Animal facility: a facility normally used to house stock or experimental animals or one which is used for the performance of minor surgical procedures.

[11] Isolators: transparent boxes where small animals are contained within or outside a cage; for large animals, isolated rooms may be more appropriate.

Table 4

Containment and other protective measures for other activities

	Specifications	Containment levels			
		1	2	3	4
General					
1	Viable micro-organisms should be contained in a system which separates the process from the environment (closed system)	Optional	Required	Required	Required
2	Control of exhaust gases from the closed system	Not required	Required, minimise dissemination	Required, prevent dissemination	Required, prevent dissemination
3	Control of aerosols during sample collection, addition of material to a closed system or transfer of material to another closed system	Optional	Required, minimise dissemination	Required, prevent dissemination	Required, prevent dissemination
4	Inactivation of bulk culture fluids before removal from the closed system	Optional	Required, by validated means	Required, by validated means	Required, by validated means
5	Seals should be designed so as to minimise or prevent release	No specific requirement	Minimise dissemination	Prevent dissemination	Prevent dissemination
6	The controlled area should be designed to contain spillage of the entire contents of the closed system	Optional	Optional	Required	Required
7	The controlled area should be sealable to permit fumigation	Not required	Optional	Optional	Required
Equipment					
8	Entry via airlock	Not required	Not required	Optional	Required
9	Surfaces resistant to water, acids, alkalis, solvents, disinfectants and decontamination agents, and easy to clean	Required (bench, if any)	Required (bench, if any)	Required (bench, if any, floor)	Required (bench, floor, ceiling, walls)
10	Specific measures to adequately ventilate the controlled area in order to minimise air contamination	Optional	Optional	Optional	Required

11	The controlled area should be maintained at an air pressure negative to the immediate surroundings	Not required	Not required	Optional	Required
12	Extract and input air from the controlled area should be HEPA filtered	Not required	Not required	Required (extract air, optional for input air)	Required (input and extract air)

System of work

13	Closed systems should be located within a controlled area	Not required	Optional	Required	Required
14	Access should be restricted to nominated personnel only	Not required	Required	Required	Required
15	Biohazard signs should be posted	Not required	Required	Required	Required
16	Personnel should shower before leaving the controlled area	Not required	Not required	Optional	Required
17	Personnel should wear protective clothing	Required (work clothing)	Required (work clothing)	Required	Complete change before exit and entry

Waste

18	Inactivation of GMMs in effluent from hand-washing sinks and showers or similar effluents	Not required	Not required	Optional	Required
19	Inactivation of GMMs in contaminated material and waste, including those in process effluent before final discharge	Optional	Required, by validated means	Required, by validated means	Required, by validated means