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If a whole or part of a paragraph has been amended, the date of the amending regulation appears in square brackets at the end of the paragraph. If a whole paragraph or sub-paragraph has been deleted, the date of the deletion appears in square brackets beside the deleted paragraph or sub-paragraph.

Republic of Latvia

Cabinet

Regulation No. 784

Adopted 22 September 2008

Procedures for the Contained Use of Genetically Modified Micro-organisms, Issuance of a Permit and Cancelling Thereof

[15 January 2013]

*Issued pursuant to
Section 5, Paragraph one, Clause 1 of the Law on Circulation of Genetically Modified
Organisms*

1. General Provisions

1. This Regulation prescribes:

1.1. the notification procedures for the contained use of genetically modified micro-organisms (hereinafter – the contained use);

1.2. the procedures for the issuance of a permit for contained use and cancelling thereof;

1.3. the duties and rights of supervisory and control authorities;

1.4. the duties, rights and liabilities of science establishments;

1.5. the risk assessment of contained use;

1.6. the safety criteria for genetically modified micro-organisms;

1.7. the general principles for work with genetically modified micro-organisms.

[15 January 2013]

2. This Regulation shall not apply to:

2.1. contained use activities, if the genetically modified micro-organisms utilised therein comply with the safety criteria referred to in Chapter 7 of this Regulation and the referred-to criteria have been published in the Official Journal of the European Communities;

2.2. genetically modified organisms which may deliberately be released in conformity with the laws and regulations regarding deliberate release of genetically modified organisms;

2.3. food and animal feed permitted to be distributed in accordance with European Parliament and Council Regulation (EC) No. 1829/2003 of 22 September 2003 on genetically modified food and feed.

[15 January 2013]

2. Notification Procedures for Contained Use

[15 January 2013]

3. A science establishment prior to the commencement of the contained use shall submit to the State scientific institute “Institute of Food Safety, Animal Health and Environment - “BIOR”” (hereinafter – the Institute) a notification:

3.1. regarding the workplace where it is intended to use contained use for the first time;

3.2. regarding the intended contained use activities.

[15 January 2013]

4. The notification regarding the workplace, where it is intended to employ contained use for the first time, shall include the following information:

4.1. the name of the science establishment, the registration number in the Register of Science Establishments and date, actual and legal address, telephone number and a plan of the laboratory premises;

4.2. the given name, surname of the person responsible for the supervision and safety measures, as well as the professional qualification in the referred to area;

4.3. a description of the intended contained use activities and the purpose of the genetic modification;

4.4. the expected safety class of the contained use;

4.5. if contained use activities complying with the first safety class are intended in the workplace, the following shall be indicated in addition:

4.5.1. a summary of the risk assessment in accordance with Chapter 6 of this Regulation;

4.5.2. information from the supervision and control authorities regarding the management of waste and waste water in accordance with the laws and regulations regarding the management of waste.

[15 January 2013]

5. A science establishment shall commence the contained use activities that comply with the first safety class in accordance with the requirements referred to in Paragraph 26 of this Regulation after it has notified the Institute regarding the workplace.

[15 January 2013]

6. The notification regarding commencement of such contained use activities, which comply with safety class two, shall include the following information:

6.1. the date when the notification regarding the workplace was submitted;

6.2. the given name, surname of the person responsible for the supervision and safety measures, as well as the professional qualification in the referred to area;

6.3. safety class of the intended contained use activity;

6.4. information regarding the containment and safety measures for the intended contained use activity in accordance with the Annex to this Regulation, periodicity of reviewing the containment measures and the efficiency of the examination plan for the referred to measures;

6.5. a copy of the letter certifying that the State Labour Inspection have been sent the initial notification in accordance with the laws and regulations regarding occupational safety requirements when coming in contact with biological substances;

6.6. a declaration regarding the compliance of waste and waste water management plan, registration, processing and elimination of waste and waste water with the laws and regulations regarding the management of waste and the Annex to this Regulation;

6.7. a copy of the permit regarding management of waste in accordance with the laws and regulations regarding waste management (if a permit is required);

6.8. information regarding the utilised recipient, donor micro-organism and, if possible, regarding the vector systems to be utilised;

6.9. the types of genetic materials involved in the genetic modification and their intended functions in the genetically modified micro-organism;

6.10. the methods for determining the properties and identity of the genetically modified micro-organism;

6.11. the purpose and expected results of utilisation of the genetically modified micro-organism;

6.12. the amount of cell cultures that shall be utilised during the contained use activities;

6.13. a summary of the risk assessment in accordance with Chapter 6 of this Regulation;

6.14. information regarding action during emergencies and a list of the owners of territories that may be endangered in the event of a contained use emergency.

[15 January 2013]

7. Contained use activities complying with the second safety class shall be commenced for the first time 45 days from the date when the notification was submitted to the Institute. The referred to activities shall be commenced earlier if the relevant permit has been received from the Institute.

[15 January 2013]

8. A science establishment, after submitting the notification to the Institute regarding the contained use activities which comply with the second safety class, may commence the contained use activities without delay, if in the previous two years it has already submitted the relevant notification regarding contained use activities, which comply with the second safety class, or has received a permit for contained use activities which comply to a higher safety class and has fulfilled all the requirements specified in the permit.

[15 January 2013]

9. The notification regarding commencement of such contained use activities, which comply with safety classes three and four, shall include the following information:

9.1. the date when the notification regarding the workplace was submitted;

9.2. the given name, surname of the person responsible for the supervision and safety measures, as well as the professional qualification in the referred to area;

9.3. safety class of the intended contained use activity;

9.4. information regarding the containment and safety measures for the intended contained use activity in accordance with the Annex to this Regulation, periodicity of reviewing the containment measures and the efficiency of the examination plan for the referred to measures;

9.5. a copy of the letter certifying that the State Labour Inspection have been sent the initial notification in accordance with the laws and regulations regarding occupational safety requirements when coming in contact with biological substances;

9.6. a declaration regarding the compliance of waste and waste water management plan, registration, processing and elimination of waste and waste water with the laws and regulations regarding the management of waste and the Annex to this Regulation;

9.7. a copy of the permit regarding the management of waste in accordance with the laws and regulations regarding waste management;

9.8. information regarding the utilised recipient, donor micro-organism and regarding the vector systems to be utilised;

9.9. the types of genetic materials involved in the genetic modification and their intended functions in the genetically modified micro-organism;

9.10. the methods for determining the properties and identity of the genetically modified micro-organism;

9.11. the purpose and expected results of utilisation of the genetically modified micro-organism;

9.12. the amount of cell cultures that shall be utilised during the contained use activities;

9.13. an evaluation regarding the compliance of the laboratory facilities with the intended contained use activities;

9.14. information regarding preventative action during emergencies, an emergency plan and a list of the owners of territories that may be endangered in the event of a contained use emergency, if:

9.14.1. risks have been identified which are related to the location of the equipment;

9.14.2. precautionary measures shall be applicable (safety devices, alarm systems and containment methods);

9.14.3. appropriate procedures and plans for permanent examinations of the efficiency of containment measures;

9.14.4. the employees have access to information regarding the description of the contained use activity;

9.15. a copy of the risk assessment report in accordance with Chapter 6 of this Regulation.

[15 January 2013]

10. If the science establishment withdraws the notification regarding the contained use, the Institute shall not disclose the information in the notification.

[15 January 2013]

3. Issuance of a Permit for Contained Use

[15 January 2013]

11. The Institute shall issue a permit for contained use activities that comply with the third and fourth safety class not later than within 90 days after the time when the notification referred to in Paragraph 9 of this Regulation has been received from the science establishment.

[15 January 2013]

12. If a science establishment in the previous two years after submission of the notification regarding contained use activities that comply with the third and fourth safety class has submitted a repeated notification regarding contained use activities complying with the referred to safety classes and has fulfilled the requirements referred to in the permit, the Institute shall issue the permit for the contained use activities which comply with the third and fourth safety class not later than within 45 days after receipt of the notification from the science establishment.

[15 January 2013]

13. The time period necessary for the provision of additional information or consultations shall not be included in the time period referred to in Paragraphs 7, 11 and 12 of this Regulation.

[10 February 2015]

14. During the period of informing the public regarding the contained use activities the Institute may extend the time period for issuing the permit by not more than 30 days from the date when the notification regarding the contained use activities was received.

[15 January 2013]

15. The Institute shall not issue a permit, if:

15.1. the science establishment has not provided the additionally requested information;

15.2. the contained use activities cause significant harm to the health of humans and animals or to the environment;

15.3. the science institution in the summary of the risk assessment or notification has knowingly concealed information regarding possible risks or harm to the health of humans and animals or to the environment.

[15 January 2013]

16. The Institute shall cancel a permit, if:

16.1. new scientifically based information has become available that the contained use causes a significant harm to the health of humans and animals or to the environment;

16.2. the specified safety class of the contained use activity and the containment measures or the requirements of the issued permit are no longer adequate in order for the contained use to be safe;

16.3. an emergency has occurred which has caused a significant risk to the health of humans and animals or to the environment;

16.4. the science establishment has ceased to fulfil the requirements specified in the permit.

[15 January 2013]

4. The Duties and Rights of Supervisory and Control Authorities

17. The State Labour Inspection shall inform the Institute regarding detected infringements or non-conformities at a workplace where contained use is carried out.

[15 January 2013]

18. The Institute has the following duties:

18.1. to issue or annul the permit for contained use activities, which comply with the specified safety class;

18.2. to specify such permit requirements for the intended contained use activities, that shall ensure safe contained use of the specific genetically modified micro-organism;

18.3. to review and provide an opinion to the science establishment regarding the compliance of the genetically modified micro-organism with the safety criteria;

18.4. to timely notify the European Commission regarding the compliance of the specified genetically modified micro-organism with the safety criteria;

18.5. to inform society regarding the notified contained use activities and involve it in the process of issuing a permit for contained use;

18.6. to enter the following information into the Register of the Circulation of Genetically Modified Organisms:

18.6.1. the name of the science institution which has notified regarding the contained use or received a permit for contained use;

18.6.2. the safety class of the contained use activity;

18.6.3. a summary of the risk assessment of the permitted contained use activity or activity in the course of the review or a copy of the notification, except for confidential information;

- 18.6.4. the purpose of the contained use activity and the validity term of the issued permit;
- 18.6.5. an emergency plan, if such is necessary for the intended contained use;
- 18.6.6. a list of the owners of the territory, who could possibly be threatened in case of a contained use emergency;
- 18.7. to enter information regarding the decisions taken into the Register of the Circulation of Genetically Modified Organisms not later than seven days after the issuance of a permit for a specified contained use activity;
- 18.8. to assess the information provided by the science establishment regarding accidents and draft an emergency action plan for the intended contained use;
- 18.9. to agree with the science establishment regarding the information for which a contained use status shall be granted in the notification. The status of restricted access information shall not be granted to the following information:
 - 18.9.1. the name of the science establishment, the registration number in the Register of Science Establishments and date, actual and legal address, telephone number;
 - 18.9.2. the properties of the genetically modified micro-organism and the determination method thereof;
 - 18.9.3. the purposes of the contained use activity and the expected results;
 - 18.9.4. the safety class of the contained use activity and the containment measures;
 - 18.9.5. a summary of the risk assessment or a copy of the risk assessment notification.

[15 January 2013]

19. The Institute has the following rights:

- 19.1. to request additional information from the science establishment if during the assessment period uncertainties have arisen or the information supplied is incomplete, in order to perform a risk assessment analysis;
- 19.2. to make changes to the contained use measures determined by a science establishment or other safety measures or to change the specified safety class of the contained use;
- 19.3. to change the requirements of an issued permit.

[15 January 2013]

5. Duties, Rights and Liabilities of Science Establishments

20. A science establishment has the following duties:

- 20.1. to specify the safety class for the intended contained use activity, the containment and safety measures, based on the risk assessment performed in accordance with Chapter 6 of this Regulation;
- 20.2. to ensure containment and safety measures for the contained use, taking into account the containment level granted;
- 20.3. to submit the initial notification to the State Labour Inspection regarding commencement of the contained use activities which comply with the second, third or fourth safety class, in accordance with the laws and regulations regarding occupational safety requirements, when coming into contact with biological substances;
- 20.4. prepare and submit a summary of the risk assessment to the Institute or a copy of the notification regarding the intended contained use;
- 20.5. to apply the general principles for work with genetically modified micro-organisms in accordance with Chapter 8 of this Regulation;

20.6. to implement tried and true principles, when working with micro-biological preparations;

20.7. to regularly review the applied containment and safety measures and submit to the Institute a report regarding the compliance of the containment measures with the activities to be performed:

20.7.1. for the first safety class – not less than once every three years;

20.7.2. for the second safety class – not less than once every two years;

20.7.3. for the third and fourth safety class – not less than once a year;

20.8. apply higher level containment and safety measures if there are any uncertainties regarding the compliance of the contained use with the specified safety class;

20.9. to store the summary of the risk assessment related to the contained use or a copy of the notification and submit information, if requested by the Institute;

20.10. to record the number of animals used during the contained use and notify the Institute thereof;

20.11. to inform the State Labour Inspection in accordance with the laws and regulations regarding the requirements of occupational safety, when coming into contact with biological substances, and without delay review the containment measures, if:

20.11.1. new scientific information has become available regarding the possible harm to the health of humans and animals or the environment;

20.11.2. it is necessary to make changes to the notification submitted in accordance with the requirements referred to in Paragraphs 4, 6 and 9 regarding contained use activities;

20.11.3. the applied containment and safety measures are no longer adequate for the intended contained use activity or the contained use activities do not comply with the safety class specified in the notification;

20.11.4. there is a reason to believe that the risk assessment performed by the science establishment no longer conforms to the latest scientific or technological knowledge;

20.12. to inform the State Labour Inspection in accordance with the laws and regulations regarding the requirements of occupational safety, when coming into contact with biological substances, and the Institute if an emergency has occurred, and provide information regarding the following:

20.12.1. emergency situations;

20.12.2. the identity of the genetically modified micro-organism and its emission amount;

20.12.3. the effect of the genetically modified micro-organism on human and animal health or the environment;

20.12.4. implemented measures;

20.13. to discontinue the contained use, if:

20.13.1. there is a reason to believe that the contained use causes harm to human and animal health and to the environment;

20.13.2. an accident has occurred.

[15 January 2013]

21. A science establishment has the following rights:

21.1. to request the Institute to issue a permit for contained use activities complying with the second, third and fourth safety class;

21.2. to decrease the containment and safety measures, which comply with a specified containment level, if the Institute has indicated the compliance with a lower containment level to ensure harmlessness;

21.3. to request the Institute to review the compliance of the specified genetically modified micro-organism with the harmlessness criteria in accordance with Chapter 7 of this Regulation.

[15 January 2013]

22. A science establishment shall be responsible for harm caused to human and animal health or to the environment by contained use in accordance with the laws and regulations regarding environmental protection.

[15 January 2013]

6. Risk Assessment of Contained Use

[15 January 2013]

23. In order to grant the appropriate safety class to contained use activities and to prescribe the containment and safety measures, taking into account the containment level, for the intended contained use activities and the processes associated with them the science establishment shall perform a risk assessment in accordance with Sub-chapters 6.1 and 6.2 of this Regulation.

[15 January 2013]

24. For contained use activities which comply with the first and second safety class, the risk assessment summary shall describe the potential harm to human and animal health or to the environment by the genetically modified micro-organism and the activities associated with it.

[15 January 2013]

25. Contained use that complies with the activities of the first safety class is determined by assessing the effect of the genetically modified micro-organism on the health of such humans and animals, which do not possess a weakened immune system, and on plants.

[15 January 2013]

26. The genetically modified micro-organisms shall comply with the contained use activities of the first safety class, if:

26.1. recipients or donor micro-organisms do not induce diseases in humans and animals or harm to the environment and their harmlessness is documentarily proved by scientific publications. In order to determine compliance with these harmlessness criteria, the following shall be specified:

26.1.1. capacity of the recipient or donor micro-organism to induce disease in humans and animals or plants, taking into account the environmental conditions in which the recipient or donor micro-organism may find themselves in the future;

26.1.2. the harmlessness of the non-virulent strain in relation to human and animal health or to the environment, if the relevant non-virulent strain is not among the approved pathogenic species. This strain permanently has such a genetic material deficit that determines virulence or has stable mutations;

26.2. the genetic material of the vector or insert does not impart the genetically modified micro-organism with a phenotype which could induce diseases in humans and animals or plants or cause harm to the environment. In order to determine compliance with this criterion, it shall be determined whether the vector and the insert contain genes that express active proteins or transcripts in such an amount and form that could give such a phenotype to the genetically modified micro-organism, which induces diseases in humans and animals or causes harm to the environment. A genetically modified micro-organism vector or insert may be determined to be harmless if it contains sequences that are responsible for a harmful characteristic to specific micro-organisms, but in general the phenotype of the

genetically modified micro-organism does not induce diseases in humans and animals or plants;

26.3. the genetically modified micro-organism that has genetic material inserted or removed does not induce diseases in humans or animals or plants or cause harm to the environment.

[15 January 2013]

27. For contained use activities which comply with the third and fourth safety class, the risk assessment notification shall include an analysis in accordance with Sub-chapters 6.1 and 6.2 of this Regulation.

[15 January 2013]

28. The risk assessment of contained use activities shall be performed in two stages.

[15 January 2013]

6.1. First Stage of Risk Assessment

29. During the first stage the science establishment shall determine and describe all the harmful or potentially harmful characteristics associated with the genetically modified material, as well as indicate the entirety of the harmful properties that have occurred in the recipient micro-organism as a result of the genetic modification. The properties of the material associated with the genetic modification shall be determined to be harmful if they comply with one of the following characteristics:

29.1. are pathogenic to humans, animals or plants or cause allergenic or toxic effects. The determined allergenic or toxic factor effect is assessed in relation to the health of such person and animal which do not have weakened immunity;

29.2. are capable of causing disorders during prophylactic and disease treatment processes;

29.3. cause detrimental effects to the health of humans and animals or to the environment;

29.4. are capable of uncontrolled dissemination in the environment;

29.5. are capable of moving into other micro-organisms or integrating their genetic material during a period of uncontrolled spreading;

29.6. are phenotypically and genetically unstable.

[15 January 2013]

30. In order to determine the harmful or potentially harmful effects of a genetically modified micro-organism to human and animal health or to the environment, the science establishment shall assess the constituent parts making up a genetically modified micro-organism:

30.1. the recipient micro-organism, indicating the following characteristics:

30.1.1. pathogenesis, virulence, ability to infect, allergenicity, toxicity and the disease transfer vectors present within it;

30.1.2. the nature of the vector and adventitious agent;

30.1.3. places where vectors and adventitious agents can mobilise the inserted genetic material and frequency of the mobilisation;

30.1.4. the type of activity for decreasing mutation and its stability, if such exist;

30.1.5. previously performed genetic modifications;

30.1.6. range of donor micro-organisms;

30.1.7. the more significant physiological properties that could be changed in the final genetically modified micro-organism and, where appropriate – their stability;

30.1.8. the natural biotope and geographical distribution;

- 30.1.9. involvement which is significant in environmental processes;
- 30.1.10. interaction with other micro-organisms in the environment and the consequences thereof;
- 30.1.11. ability to develop structures that are essential to preserving life;
- 30.2. the donor micro-organism (if for fusion experiments or experiments where the shotgun method is utilised, the insert has not been adequately described), indicating the following characteristics:
 - 30.2.1. pathogenesis, virulence, ability to infect, allergenicity, toxicity and the disease transfer vectors present within it;
 - 30.2.2. vectors to be utilised, additionally indicating the following:
 - 30.2.2.1. sequences;
 - 30.2.2.2. frequency and specificity of mobilisation;
 - 30.2.3. the presence of such genes which confer resistance to antimicrobial substances, including antibiotics;
 - 30.2.4. range of donor micro-organisms;
 - 30.2.5. other relevant physiological characteristics;
- 30.3. insert, indicating the following characteristics:
 - 30.3.1. identity of the insert, the nucleotide sequence and functions of the insert (gene);
 - 30.3.2. the expression level of the inserted genetic material;
 - 30.3.3. origin of the genetic material, identity of the donor micro-organism and, where appropriate – the characteristics;
 - 30.3.4. the history of the previous genetic modification;
 - 30.3.5. the site of the inserted genetic material on the recipient genome (specifying if the inserted material activates/deactivates the genes of the recipient micro-organism);
- 30.4. vector, indicating the following characteristics:
 - 30.4.1. type of vector, nucleotide sequence and origin;
 - 30.4.2. structure and number of intended vectors, and the residual nucleic acid sequences of the donor micro-organism in the construction of the final genetically modified micro-organism;
 - 30.4.3. frequency of vector mobilisation and ability to transfer genetic material, if a vector has been placed in the final genetically modified micro-organism;
- 30.5. the genetically modified micro-organism, indicating the following characteristics:
 - 30.5.1. in regard to human health:
 - 30.5.1.1. the toxic or allergenic effect of the genetically modified micro-organism and its metabolic products;
 - 30.5.1.2. the pathogenicity of the genetically modified micro-organism in comparison with the recipient and parent micro-organisms;
 - 30.5.1.3. the colonising capacity of the genetically modified micro-organism;
 - 30.5.2. in regard to the genetically modified micro-organism which is a pathogen to persons with a weakened immune system:
 - 30.5.2.1. diseases caused, the mechanisms of distribution and transfer of virulence;
 - 30.5.2.2. the infective dose;
 - 30.5.2.3. possible changes in the route of infection or tissue subjectivity;
 - 30.5.2.4. viability possibilities outside the human micro-organism;
 - 30.5.2.5. the biological stability;
 - 30.5.2.6. the resistance spectrum against antibiotics;

- 30.5.2.7. the allergenicity;
- 30.5.2.8. the toxicity;
- 30.5.2.9. the existence of applicable therapeutic and prophylactic measures;
- 30.5.3. in regard to the environment:
 - 30.5.3.1. ecosystems in which the genetically modified micro-organism might accidentally disseminate outside the contained use;
 - 30.5.3.2. the survival, multiplication and dissemination of the amounts of the genetically modified micro-organism in specified environments;
 - 30.5.3.3. the expected result if the genetically modified micro-organism should be accidentally released out of the containment measures and interacts with other micro-organisms;
 - 30.5.3.4. harmful or potentially harmful effect on plants or animals;
 - 30.5.3.5. known or possible participation in biogeochemical processes.

[15 January 2013]

31. In order to grant the initial safety class to the recipient micro-organism involved in a modification, the science establishment shall determine a risk group to the recipient micro-organism, utilising the biological agent classification specified in the laws and regulations regarding occupational safety requirements, when coming into contact with biological substances, or utilising other recognised international classifiers. In order to determine the initial safety class of the contained activities, the following activities shall be performed:

31.1. describe the determined harmful properties of the genetically modified micro-organism and the other genetic materials associated with it;

31.2. assess the significance of the harm and all the biological properties limiting the probability of harm. The significance of the harmful effect is assessed irrespective of whether the harmful effect is possible. The significance of any potential harmful effect is determined, taking into account, what the consequences thereof might be, not whether this harm could actually occur. The significance of the harmful or probable harmful effect of a genetically modified micro-organism is assessed in relation to human and animal health or the environment;

31.3. determine containment and safety measures that comply with the initial safety class of the contained use activity.

[15 January 2013]

32. In assessing the potential harmful effects of the genetically modified micro-organism, the science establishment shall:

32.1. describe the survival possibilities of the genetically modified micro-organism in the environment;

32.2. describe the indirect harmful effect of the genetically modified micro-organism that may occur from the changed environmental physical-chemical properties and the ecological balance of the plants and the water components;

32.3. indicate the necessity for additional risk management measures, if a harmful or potentially harmful effect by a genetically modified micro-organism on human and animal health or the environment has been determined or expected to such an extent that the determined harmful expression would be decreased to the lowest level;

32.4. indicate the compliance of the containment measures and the granted safety class, taking into account the special characteristics of the contained use activities (actual activities to be performed, work methods, amount and containment measures).

[15 January 2013]

33. In analysing the type of contained use activity, the science establishment shall:

33.1. repeatedly review and adapt the containment and safety measures, taking into account the type of contained use activities. The determined harmful effect on human and animal health or the environment is decreased to the lowest level with the containment and safety measures;

33.2. describe in detail the contained use activities that comply with the third and fourth safety class or such activities which are not part of the everyday routine procedure, or such procedures which might have a serious effect on the risk level.

[15 January 2013]

34. In analysing the concentration and amount of a genetically modified micro-organisms, the science establishment shall:

34.1. describe the effect of the micro-organisms' concentration and ability for a harmful effect to occur due to the density of the relevant culture during the contained use, if activities are performed that are associated with the presence of highly concentrated genetically modified micro-organisms;

34.2. describe the identified potential risks in relation to the amount of the micro-organism to be utilised, which may be the absolute amount for one operation or frequent repetition of the process.

[15 January 2013]

35. In analysing the conditions for growing of the micro-organism cultures, the science establishment shall:

35.1. describe the safety of the vessels and other equipment used in the contained use activities and the risks associated therewith;

35.2. describe the inefficiency criteria of the vessels and other equipment. If a specific equipment has an identified deficiency, provide additional containment measures or a higher containment level to such an extent that human and animal health or the environment shall be protected;

35.3. during cases of standard activity describe the overall effect of the contained use, taking into account the efficiency of the containment measures;

35.4. specify the appropriate biological or chemical containment measures.

[15 January 2013]

36. In analysing the effect of a genetically modified micro-organism on the environment, the science establishment shall:

36.1. specify and describe whether there are organisms in a particular environment that could become subjected to the effect of the genetically modified micro-organism;

36.2. specify those organisms which are sensitive to the effect of contained use;

36.3. specify the amount and type of the effect of the genetically modified micro-organism on the environment;

36.4. describe the part of the environment subject to the effect of the contained use (the part of the environment which is being set apart with containment measures). Taking into account that the effect on the environment is dependent on the type and quantity of the activities, the possible release of the genetically modified micro-organism is indicated that would result in a greater part of the environment being affected.

[15 January 2013]

6.2. Second Stage of Risk Assessment

37. A science establishment, in specifying the final safety class and containment and safety measures, shall:

37.1. indicate the final contained use activity safety class, taking into account the harmful properties determined for all the involved genetic materials during the first stage;

37.2. describe the final containment and safety measures, taking into account the characterisation of the genetically modified micro-organism during the first stage.

[15 January 2013]

38. The science establishment shall prepare an opinion regarding compliance of the containment and safety measures with the contained use activities, indicating that:

38.1. the possible harmful effect has not been sufficiently taken into consideration during the risk assessment of the first stage, consequently the intended containment measures do not contain the harmful expression at its lowest level. In this case additional containment and safety measures shall be applied or a higher containment level shall be prescribed, the need to review the contained use;

38.2. the granted contained use activity safety class is correct, since the applicable contained use measures are sufficient to contain the expression of the determined harm to the lowest level;

38.3. a higher risk class was granted during the risk assessment of the first stage, in comparison with the determined harm, consequently it shall be permissible to decrease the containment level or safety class.

[15 January 2013]

7. Harmlessness Criteria for Genetically Modified Micro-organisms

[15 January 2013]

39. Genetically modified micro-organisms are safe to human and animal health or the environment if they comply with the general and specific harmlessness criteria.

[15 January 2013]

40. Compliance with the general and specific harmlessness criteria shall be proved with documentary evidence.

41. General harmlessness criteria shall be the following:

41.1. identity of the donor micro-organism has been determined, utilising one or more of the following referred to methods in order to verify its authenticity:

41.1.1. morphology;

41.1.2. colouring;

41.1.3. electron microscopy;

41.1.4. serology;

41.1.5. metabolic profiles after their utilisation or degradation;

41.1.6. isoenzyme analyses;

41.1.7. protein and fatty acid profiles;

41.1.8. total amount of guanine and cytosine nucleotides as a percentage;

41.1.9. deoxyribonucleic acid (hereinafter – DNA)/ribonucleic acid (hereinafter – RNA) analyses – taxon-specific DNA and RNA sequence identification;

41.1.10. gene probe analyses;

41.2. a detailed description of the structure of the vector and insert in the new genetically modified micro-organism, as well as a fully specified nucleotide sequence for the vector and insert. In order to avert the expression of harmful properties, the scale of the inserts and vectors shall be limited in such a manner that they would contain the minimum number of necessary genetic elements;

41.3. the recipient, donor micro-organism and the history of genetic modification shall be described in detail, indicating previously published results of analyses and information regarding the safety assessment of the micro-organisms;

41.4. scientifically based proof is given regarding the safety of the genetically modified micro-organism after such modifications which have been performed in order to eliminate harmful or pathogenic characteristics of the recipient or donor micro-organism;

41.5. the taxonomic relationships of the genetic material involved in the genetic modification process have been described, in order to identify potentially harmful properties that are not normally manifested, but as a result of genetic modification may be manifested later on;

41.6. the identity of the eukaryotic cell and tissue culture is verified in accordance with international classifications;

41.7. scientifically based data have been specified regarding the safety of the genetic material utilised for the genetic modification, taxonomic properties, phenotypic and genetic indicators;

41.8. the analytic confirmation of the micro-organism identity, which is referred to in Sub-paragraph 41.1 of this Regulation, has been performed and recorded, if the specific micro-organism has not been sufficiently studied and written up in scientific literature;

41.9. previously published analyses results regarding the safety of the recipient or donor micro-organism in different conditions have been specified;

41.10. the genetic stability of the genetically modified micro-organism has been proved. A genetically modified micro-organism shall be considered genetically stable if the stability of the genetically modified micro-organism is equivalent to the stability of the unmodified micro-organism. A detailed description regarding the stability of the genetic mobilisation is provided, if after the genetic modification a mutation for decreasing activity has been utilised in order to lower the harmful properties of the micro-organism. If genetic instability has been identified for the genetically modified micro-organism, which is not substantial, then the scientifically based proof shall be specified regarding the safety and harmlessness of the genetically modified micro-organism to human and animal health or the environment.

[15 January 2013]

42. Specific harmlessness criteria shall be the following:

42.1. the genetically modified micro-organism is not a pathogen, if:

42.1.1. upon studying scientific literature, pathogenic action of the genetic material on human and animal health or the environment has not been determined. If the genetically modified micro-organism may have a harmful effect on a person with a weakened immune system, then that harmful effect shall be specially examined and attention drawn to it;

42.1.2. scientific information collected over a long period of time is available regarding the safety of the donor micro-organism to human and animal health or to the environment. If analyses have not been performed in regard to the pathogenicity of the micro-organism, then research on the recipient and donor micro-organism shall be ensured. Especially those newly developed genetically modified micro-organisms shall be examined, which substantially differ from the donor micro-organisms;

42.1.3. the origin of the eukaryotic virus and the mechanism for debilitating it has been determined, as well as the stability of the present properties (only deletion mutations shall be utilised in the formation of eukaryotic virus vectors);

42.1.4. a genetic material stability analysis is available both before and after modification. In order to prove the compliance of the specific strain with the harmlessness criteria which belongs to the pathogen species, the following information shall be provided:

- 42.1.4.1. scientifically based data that the strain is not virulent and causes no harmful effects on human and animal health or to the environment;
- 42.1.4.2. the donor micro-organism has such a genetic material deficit which determines virulence or has a stable mutation significantly decreasing virulence. Analyses have been performed (pathogenicity tests, genetic investigation with probes, phage and plasmid determination, mapping of restriction enzymes, sequencing and protein probes) and it is established that the strains are harmless. When the new gene is transferred, a genetic analysis is ensured regarding the reverse gene deletion or mutation risk;
- 42.1.5. the genetically modified micro-organism contains such vectors and inserts which do not have active proteins or transcripts in such an amount that will confer a phenotype to the genetically modified micro-organism, which could cause human or animal diseases or have a harmful effect on the environment;
- 42.1.6. such vectors and inserts have not been utilised in the genetic modification process, the sequences of which in other micro-organisms are responsible for manifestation of harmful traits and confer such a phenotype to the genetically modified micro-organism, which causes human, animal and plant diseases or have a harmful effect on the environment;
- 42.1.7. the phenotypic changes in various donor micro-organisms caused by the vector have been indicated. In such case attention shall be paid to the ability of the vector to give the genetically modified micro-organism virulence or other harmful characteristics;
- 42.2. the genetically modified micro-organism is not toxic, if:
 - 42.2.1. toxic qualities have not been created in the micro-organism after genetic modification;
 - 42.2.2. the genetically modified micro-organism has been analysed and the ability of the insert and vector to transmit or stimulate (not suppress) toxin production has been indicated. Analyses results are presented, which prove the harmlessness of the vector and insert on human and animal health and on the environment;
- 42.3. the genetically modified micro-organism is not an allergen, if:
 - 42.3.1. biological agents are not used in the micro-organism's genetic modification process, which cause an allergy in accordance with the laws and regulations regarding occupational safety requirements, when coming in contact with biological substances;
 - 42.3.2. the genetically modified micro-organism does not contain such genes which could create significant allergens;
- 42.4. the genetically modified micro-organism does not contain adventitious agents which may cause a harmful effect to human and animal health or to the environment. If, after the genetic modification, the recipient and donor strain not containing adventitious agents is used, it is ascertained whether a new adventitious agent has appeared which could be harmful to human and animal health or to the environment. The genetically modified micro-organism does not contain harmful adventitious agents, if:
 - 42.4.1. viruses, mycoplasmas, microscopic spores of bacteria, plants, animal cells or such symbionts which may cause harm are not utilised in the modification process;
 - 42.4.2. the genetic modification process shall only utilise such cell cultures, recipients or parent strains which do not harbour adventitious agents;
 - 42.4.3. after the genetic modification, the submitter can prove that the genetically modified micro-organism does not contain adventitious agents which may cause harmful effect to human and animal health or to the environment;
- 42.5. the genetically modified micro-organism is stable, if:

42.5.1. when transfer occurs, the inserted genetically modified material is safe and it does not possess the capacity to transfer or be transferred more often than the other genes of the recipient or donor micro-organism;

42.5.2. the vector and insert do not contain marker genes that code resistance and may cause threats to the healing process;

42.5.3. the vector which is utilised for cloning (virus, cosmid or other vector derived from a virus) is not a lysogen;

42.5.4. an insert has not been utilised in the genetic modification process, which has a poxirus sequence or other functional transfer characteristics;

42.6. the genetically modified micro-organism is incapable of surviving outside the containment measures. The harmful effect of the genetically modified micro-organism on the surrounding environment shall be assessed, taking into account the following:

42.6.1. its ability to survive outside its habitual conditions. If the genetically modified micro-organism is capable of surviving outside the containment measures, the probable dissemination and method of survival of the genetically modified micro-organism shall be indicated;

42.6.2. development and effect of the genetically modified micro-organism, upon entering the circulation of food and animal feed;

42.6.3. environmental biotic and abiotic factors, insofar as they apply to the ability of a specific genetically modified micro-organism to survive, establish itself and compete in the environment;

42.6.4. the ability of a genetically modified micro-organism not capable of survival outside of the containment measures to transfer or give genetic material to other micro-organisms.

[15 January 2013]

43. Models of the recipient and donor micro-organisms intended for obtaining the genetically modified micro-organism, which could be regarded as complying with the harmlessness criteria, are the following:

43.1. derivatives of bacterial strains, the growth and viability of which is dependent on the assimilation of such nutrients that are not found in a human organism or the environment;

43.2. eukaryotic cell and tissue culture systems, if they comply with the harmlessness criteria specified in this Regulation. They do not contain harmful adventitious agents and non-mobilisable vectors;

43.3. non-pathogenic wild strains which have their own particular specific ecological niches. These strains, upon getting out of containment measures, do not have a harmful effect on the environment or such effect is negligible. The genetic and molecular structure of these micro-organisms has been well researched.

[15 January 2013]

8. General Principles for Work with Genetically Modified Micro-Organisms

[15 January 2013]

44. A science establishment shall have a duty to observe the following general principles for work with genetically modified micro-organisms:

44.1. to ensure the minimum effect of the genetically modified micro-organism on the workplace and the environment;

44.2. to perform control of the presence of the live micro-organism outside the containment measures;

44.3. to provide employees with appropriate protective clothing and individual safety equipment;

44.4. to adapt the relevant containment and safety measures, in order to ensure protection of human health, as well as prevent the escape of genetically modified micro-organisms outside the containment and safety measures;

44.5. to regularly control the compliance of the technical equipment with the contained use activities to be performed;

44.6. to provide regular training of employees regarding occupational safety requirements while working with genetically modified micro-organisms;

44.7. to draft internal occupational safety instructions for work with genetically modified micro-organisms;

44.8. to place hazard signs in workplaces displaying warning regarding the potential biological risks;

44.9. to set up disinfecting and shower rooms;

44.10. to accurately account for and record the activities performed with genetically modified micro-organisms;

44.11. to prohibit the personnel from eating, drinking, smoking, applying cosmetics or storing food at the workplace;

44.12. to ensure the utilisation of automatic or semi-automatic pipettes;

44.13. to draft instructions, protocols or work descriptions for the contained use activities with genetically modified micro-organisms;

44.14. to provide the premises of the contained use with the appropriate disinfectants and develop specific disinfection procedures for preventing local pollution by the genetically modified micro-organisms;

44.15. to not allow laboratory equipment, instruments or materials to cross in the premises.

[15 January 2013]

9. Provision of Information

45. The Institute shall submit the following information to the Ministry of Agriculture and the European Commission:

45.1. once a year – a summary regarding the contained use activities complying with the third and fourth safety class, including a description of the contained use activities, their purpose and information regarding possible risks to human and animal health or the environment;

45.2. once every three years – a notification regarding application and practice of Council Directive 90/219/EEC on the contained use of genetically modified micro-organisms.

[15 January 2013]

46. The Institute shall inform the Ministry of Agriculture and the European Commission regarding the effects of an emergency, indicating the information referred to in Sub-paragraph 20.12 of this Regulation.

[10 February 2015]

47. If, after an emergency, harm has been caused in another European Union Member State, the Institute upon harmonisation with the Ministry of Foreign Affairs shall inform the European Commission of each emergency, providing the information referred to in Sub-paragraph 20.12 of this Regulation.

[10 February 2015]

10. Closing Provisions

[10 February 2015]

48. This Regulation shall come into force on 1 December 2008.

49. Paragraph 9.¹ of this Regulation shall come into force from 1 January 2016.
[10 February 2015]

Informative Reference to European Union Directive

[15 January 2013]

This Regulation contains legal norms arising from Directive 2009/41/EC of the European Parliament and of the Council of 6 May 2009 on the contained use of genetically modified micro-organisms (Recast).

Prime Minister

I. Godmanis

Acting for the Minister for Agriculture – Minister for the Environment

R. Vējonis

Containment and Safety Measures for Contained Use Activities

[15 January 2013]

1. Minimum requirements for equipment when performing work in a laboratory:

No.	Specification	Containment level			
		1	2	3	4
1.1.	Isolation of the laboratory complex ¹	Not mandatory	Not mandatory	Mandatory	Mandatory
1.2.	Closing of the laboratory for disinfection with steam	Not mandatory	Not mandatory	Mandatory	Mandatory
1.3.	Surfaces that are resistant to the effect of water, acids, alkali, solvents, disinfectants and cleaning products and are easy to clean	Mandatory (for a work desk)	Mandatory (for a work desk)	Mandatory (for a work desk, floor)	Mandatory (for work desks, floors, ceilings, walls)
1.4.	Access to the laboratory through air locks ²	Not mandatory	Not mandatory	Optional	Mandatory
1.5.	Reduced pressure in relation to the surrounding environment	Not mandatory	Not mandatory	Mandatory, except appropriate activities ³	Mandatory
1.6.	Air inflow into the laboratory and exhaust through <i>HEPA</i> filters with highly effective protective substances	Not mandatory	Not mandatory	Mandatory when using <i>HEPA</i> ⁴ filters for exhaust air, except appropriate activities ³	Mandatory when using <i>HEPA</i> ⁵ filters for inflow and exhaust air
1.7. Equipment					
1.7.1.	Laminar air flow cabin or special room for work with micro-organisms	Not mandatory	Optional	Mandatory	Mandatory
1.7.2.	An autoclave	In a complex of buildings	In a building	Specially adapted ⁶	In the laboratory – a two-door installation separating the working zones

1.8. Work organisation					
1.8.1.	Restricted access to work premises	Not mandatory	Mandatory	Mandatory	Mandatory
1.8.2.	A sign on the door indicating the biological hazard	Not mandatory	Mandatory	Mandatory	Mandatory
1.8.3.	Special measures for the control of release of aerosols	Not mandatory	Mandatory in order to reduce the release thereof	Mandatory in order to prevent the release thereof	Mandatory in order to prevent the release thereof
1.8.4.	Shower	Not mandatory	Not mandatory	Optional	Mandatory
1.8.5.	Protective clothing	Appropriate protective clothing	Appropriate protective clothing (and protective footwear optional)	Appropriate protective clothing	Complete change of clothing and footwear before entering and leaving thereof
1.8.6.	Gloves	Not mandatory	Optional	Mandatory	Mandatory
1.8.7.	Effective control of disease carriers (for example, rodents and insects)	Optional	Mandatory	Mandatory	Mandatory
1.9. Waste					
1.9.1.	Inactivation of genetically modified micro-organisms in the outlet of washbasins or drainage system, showers and other outlets	Not mandatory	Not mandatory	Optional	Mandatory
1.9.2.	Inactivation of genetically modified micro-organisms in the infected materials and waste	Optional	Mandatory	Mandatory	Mandatory
1.10. Other measures					
1.10.1.	Service laboratory for maintenance of equipment	Not mandatory	Not mandatory	Optional	Mandatory
1.10.2.	An observation window or another possibility to observe employees working in the laboratory	Optional	Optional	Optional	Mandatory
Notes.					
¹ Isolation of the laboratory complex – the laboratory is separated from other premises in the same building or located in a separate building.					
² Air locks – an isolated room through which the laboratory is entered. The clean part of the					

air locks shall be separated from the part of the contained use of genetically modified micro-organisms by a changing room or a shower room separated by lockable doors.

³ Activities preventing the spread of infection in the air.

⁴ *HEPA* (high efficiency particulate air) filters for the purification of air.

⁵ If viruses, which cannot be detained by *HEPA* filters, are utilised, additional requirements shall be determined regarding the exhaust air.

⁶ With a reasoned work regimen and process allowing safe delivery of the material to the autoclave outside the laboratory ensuring the relevant protection level.

2. Additional requirements when performing work with genetically modified micro-organisms in greenhouses (nurseries). The terms “greenhouse” and “nursery” shall designate such structure with walls, roof and floor which is designed and is mainly used for growing plants in the contained and protected environment. All the provisions referred to in Paragraph 1 shall be applied with the following additions:

No.	Specification	Containment level			
		1	2	3	4
2.1. Building					
2.1.1.	Greenhouse – a separate building ¹	Not mandatory	Mandatory	Mandatory	Mandatory
2.2. Equipment					
2.2.1.	Entering through air locks with double doors	Not mandatory	Optional	Optional	Mandatory
2.2.2.	Control of wastewater	Optional	Mandatory, in order to reduce the drainage thereof ²	Mandatory, in order to prevent the drainage	Mandatory, in order to prevent the drainage
2.3. Work organisation					
2.3.1.	Means to prevent the entering of individuals of undesirable species (for example, arthropods or rodents)	Mandatory	Mandatory	Mandatory	Mandatory
2.3.2.	Methods of containment to prevent the release of genetically modified micro-organisms during the transfer of live material from a greenhouse (nursery) to the laboratory	To reduce the release	To reduce the release	To prevent the release	To prevent the release

Notes.

¹ A greenhouse shall be located in a separate building with lockable self-closing doors, a waterproof roof and equipment to prevent the entering of surface waters into the building.

² If the release of genetically modified micro-organisms may occur through the soil.

3. Additional requirements when performing work with animals if genetically modified micro-organisms are utilised. All the provisions referred to in Paragraph 1 shall be applied with the following additions:

No.	Specification	Containment level
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		1	2	3	4
3.1. Equipment					
3.1.1.	Isolation of an animal holding ¹	Optional	Mandatory	Mandatory	Mandatory
3.1.2.	Compartments of the vivarium ² separated by lockable doors	Optional	Mandatory	Mandatory	Mandatory
3.1.3.	Compartments of the vivarium designed to facilitate the cleaning thereof (cages of waterproof and easy to clean material, etc.)	Optional	Optional	Mandatory	Mandatory
3.1.4.	Floor or walls easy to wash	Optional	Mandatory (for the floor)	Mandatory (for the floor and walls)	Mandatory (for the floor and walls)
3.1.5.	Animals are kept in appropriate demarcated areas (for example, in cages, stalls or containers)	Optional	Optional	Optional	Optional
3.1.6.	Filters before isolators or an isolated site ³	Not mandatory	Optional	Mandatory	Mandatory
<p>Notes.</p> <p>¹ Animal holding – a building or a separate area in the building, in which equipment and other premises are located (for example, changing rooms, showers, autoclaves, food storage facilities).</p> <p>² Compartments of the vivarium – premises where animals to be propagated or utilised in experiments are kept, as well as premises utilised for the performance of simple surgical operations.</p> <p>³ Isolators – transparent cabins where small animals are kept in cages or outside thereof; isolated rooms shall be utilised for keeping large animals.</p>					

4. General containment and safety requirements for the activities not referred to in Points 1, 2 and 3 of this Annex:

No.	Specification	Containment level			
		1	2	3	4
4.1.	Revivable micro-organisms placed in a system that ensures separation of the process from the environment (a closed system)	Optional	Mandatory	Mandatory	Mandatory
4.2.	Control of gases isolated from the closed environment	Not mandatory	Mandatory in order to reduce the release of gases	Mandatory in order to prevent the release of gases	Mandatory in order to prevent the release of gases
4.3.	Control of aerosols during the sampling, supplementation of material in the closed system or during the transfer of the material to another closed system	Optional	Mandatory in order to reduce the release of the material	Mandatory in order to prevent the release of the material	Mandatory in order to prevent the release of the material

4.4.	Inactivation of non-fractionated culture fluids before the outlet from the closed system	Optional	Mandatory with substantiated means	Mandatory with substantiated means	Mandatory with substantiated means
4.5.	Isolation materials and equipment which prevent or reduce the release of genetically modified micro-organisms	No special requirements	To reduce the release	To prevent the release	To prevent the release
4.6.	Control zone to recognise non-restricted release of content of the closed system in the environment	Optional	Optional	Mandatory	Mandatory
4.7.	The control zone shall be lockable for the disinfection thereof with steam	Not mandatory	Optional	Optional	Mandatory
4.8. Equipment					
4.8.1.	Entering through air locks	Not mandatory	Not mandatory	Optional	Mandatory
4.8.2.	Easy to clean surfaces resistant to water, acids, alkali, solvents, disinfectants and cleaning products	Mandatory (for work desks if any)	Mandatory (for work desks if any)	Mandatory (for work desks, if any, floors)	Mandatory (for work desks, floors, ceilings, walls)
4.8.3.	Special means for sufficient ventilation of the control zone and for reduction of air pollution	Optional	Optional	Optional	Mandatory
4.8.4.	Air pressure in the control zone reduced in relation to the surrounding environment	Not mandatory	Not mandatory	Optional	Mandatory
4.8.5.	Inlet and exhaust air of the control zone shall flow through a <i>HEPA</i> filter	Not mandatory	Not mandatory	Mandatory (for exhaust air, optional – for inlet air)	Mandatory (for inlet and exhaust air)
4.9. Work organisation					
4.9.1.	Closed systems are located in the control zone	Not mandatory	Optional	Mandatory	Mandatory
4.9.2.	Access shall be permitted only to the specified personnel	Not mandatory	Mandatory	Mandatory	Mandatory
4.9.3.	The personnel shall take a shower before leaving the control zone	Not mandatory	Not mandatory	Optional	Mandatory
4.9.4.	The personnel shall wear protective clothing	Mandatory (work clothes)	Mandatory (work clothes)	Mandatory	Complete changing of clothes before entering and leaving

					thereof
4.10. Waste					
4.10.1.	Inactivation of genetically modified micro-organisms in the outlet of washbasins, showers and other outlets	Not mandatory	Not mandatory	Optional	Mandatory
4.2.10.	Inactivation of genetically modified micro-organisms in the infected material and waste, including the release of closed processes before their input into the drainage system	Optional	Mandatory with substantiated means	Mandatory with substantiated means	Mandatory with substantiated means
Notes. 1. The science establishment, with the permission of the Institute, shall be allowed to adjust the application of safety measures complying with the particular containment level or to combine measures complying with different levels. 2. "Optional" in the tables shall mean that the science establishment is allowed to perform these measures in individual cases according to the risk assessment.					

Acting for the Minister for Agriculture – Minister for the Environment R. Vējonis