Ordinance on Safety Levels and Safety Measures for Genetic Engineering Work in Genetic Engineering Plants (Genetic Engineering Safety Ordinance - GenTSV)

GenTSV

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quote:

"Genetic Engineering Safety Ordinance of 12 August 2019 (BGBl. I p. 1235)".

Replaces V 2121-60-1-4 v. 24.10.1990 I 2340 (GenTSV)

Footnote

(+++ Text reference from: 1.3.2021 +++)
(+++ For application cf. § 12 para. 3, § 15 para. 3, § 16 para. 3,
§ 18 para. 6 in conjunction with para. 1 and § 26 para. 4 sentence 6 in conjunction with
sentences 1 and 2 +++)

The Ordinance was enacted as Article 1 of the Ordinance of 12 August 2019 I
1235 by the Federal Government after consultation of the Central Commission
for Biological Safety and with the consent of the Bundesrat. Pursuant to Art.
4 para. 1 sentence 1 of this V, it shall enter into force on 1.3.2021.

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Section 1
General provisions

§ 1 Scope of application

This Ordinance regulates safety requirements for genetic engineering work in genetic engineering facilities, including activities in the hazardous area. The regulations in Sections 4, 5 and 6 also apply to releases. Occupational health and safety measures required under other regulations remain unaffected.

§ 2 Security levels and security measures

(1) Genetic engineering work in genetic engineering facilities shall be assigned to the safety levels specified in Section 7(1) of the Genetic Engineering Act in accordance with the provisions of Sections 4 to 12.

(2) For each security level, security measures are specified in §§ 13 to 26 and in the Annexes to this Ordinance. These safety measures represent the requirements for the normal case, but are not an exhaustive list. In individual cases, with regard to the special safety-relevant circumstances of genetic engineering work, the following may apply

1. it may be necessary to lay down certain additional safety measures to protect the legal interests referred to in section 1 number 1 of the Gene Technology Act,
2. certain safety measures may be dispensed with if the protection of the legal interests in accordance with § 1 number 1 of the Gene Technology Act is also ensured without these measures or by other means.

§ 3 Definitions

For the purposes of this Regulation, the following is or are

1. Microorganisms:
   Viruses, viroids, bacteria, fungi, microscopic unicellular or multicellular algae, lichens, other eukaryotic unicellular organisms or microscopic animal multicellular organisms as well as animal and plant cell cultures,
2. Cell culture:
   in vitro cultured cells isolated from multicellular organisms,
3. Plants:
   macroscopic algae, mosses, ferns and seed plants,
4. Animals:
   all macroscopic animal multicellular organisms,
5. highly effective toxins:
   very toxic metabolites which may cause extremely serious acute or chronic damage to health or death as a result of inhalation, ingestion or absorption through the skin; in particular, they are highly potent toxins if the following have been identified with them:
   a) after administration to the stomach of the rat, an LD_{50} at a level of up to 50 mg/kg body weight,
   b) after application to the skin of the rat or rabbit, an LD_{50} at a level of up to 200 mg/kg body weight,
   c) after ingestion via the respiratory tract of the rat, an LC_{50}
      aa) at a level of up to 0.5 mg/l air per 4 hours of airborne solid particles as dust or of liquid droplets as mist,
      bb) at a level of up to 2 mg/l air per 4 hours, of vapours of the gaseous phase originating from the liquid or solid phase, or
      cc) at a rate of up to 500 parts per million in volume per 4 hours of gases,

6. Inactivation:
Destruction of the ability of organisms to reproduce and infect, including their ability to transfer genetic material, and destruction of their toxic effects, as well as destruction of other dangerous effects of organisms,

7. Disinfection:
Reduction of the number of organisms capable of reproduction or infectious organisms to the extent that they do not cause any harmful effects and in particular do not pose any risk of infection,

8. Sterilisation; Sterilisation:

   a) Sterilisation is the killing of all organisms capable of reproduction or infectious organisms, including their permanent forms, and destruction of their dangerous effects,

   b) Sterilisation is an intervention to remove the ability of animals to reproduce,

9. Laboratory area:
Area in which genetically modified organisms are usually produced or in which genetically modified organisms are handled experimentally in typical laboratory equipment,

10. Production area:
Area in which

    a) genetically modified organisms are usually propagated in standardised processes or substances are obtained with their help, or

    b) genetically modified organisms are produced by way of exception,

    whereby the handling of the genetically modified organisms takes place in mostly closed apparatus,

11. Animal rooms:
Buildings or separate areas within a building with livestock rooms and associated functional and operating rooms.

Section 2
Basics and implementation of the safety rating

§ 4 Principles of risk assessment and safety classification of genetic engineering work

The risk assessment and the assignment of genetic engineering operations to the safety levels according to Section 7 (1) of the Gene Technology Act shall be carried out taking into account the risk assessment of the organisms according to Sections 5 and
6 and the envisaged biological safety measures according to §§ 7 and 8 on the basis of an overall assessment of the following points:

1. Identification of all properties relevant to safety

   a) of the recipient or the source organism,

   b) of the transferred genetic material,

   c) of the vector, if used,

   d) of the donor organism, if a donor organism is used during the procedure,

   e) of the genetically modified organism resulting from the activity,

2. Characteristics of the activity,

3. Severity and probability of a risk to the legal interests specified in § 1 number 1 of the Genetic Engineering Act.

§ 5 Risk assessment of organisms

(1) The hazard potential of the donor and recipient or parental organism as well as the genetically modified organism results from the assignment of the organisms to four groups, the risk groups 1 to 4. The assignment to a risk group is based on the determination of the hazard potential of the organism, namely

1. for donor, recipient and parental organisms, using the general risk assessment criteria set out in point 1 of Appendix 1; and
2. for genetically modified organisms using the general criteria for risk assessment set out in Annex 1, point 2,

insofar as these criteria are relevant in the individual case.

(2) If the genome of a donor organism of risk groups 2 to 4 or if subgenomic nucleic acid segments which determine the hazard potential of the donor organism are to be transferred into the recipient organism, or if such transfers cannot be excluded, the hazard potential of the donor organism shall be fully included in the risk assessment of the genetically modified organism. If other subgenomic nucleic acid segments are to be transferred, their hazard potential may be assessed lower than that of the donor organism; in this context, particular consideration shall be given to:

1. the information content of the nucleic acid segment to be transferred, in particular the type of encoded information or regulatory sequence,
2. the degree of purity and characterisation of the nucleic acid from the donor organism,
3. the risk, especially to employees, from gene products of the donor organism, such as toxins.

If subgenomic nucleic acid segments are transferred that code for highly effective toxins, it must be taken into account when assigning them to the risk groups that the hazard potential of the genetically modified organism may increase compared to the donor organism.

(3) If the genome or subgenomic nucleic acid segments of a donor organism are modified during transfer into a recipient organism in such a way that recombinant proteins are produced with new characteristics arise which may be expected to endanger the legal interests specified in § 1 of the Genetic Engineering Act, it must be taken into account when assigning the organism to the risk groups that the hazard potential of the genetically modified organism may increase compared to that of the donor organism.

(4) Paragraphs 2 and 3 shall apply mutatis mutandis to nucleic acid segments that cannot be assigned to a donor organism.

(5) The hazard potential of the recipient organism shall be fully included in the risk assessment. If vectors are used, an overall assessment of the vector-recipient system shall be carried out.

§ 6 Publication of the list of risk-assessed donor and recipient organisms

The Federal Ministry of Food and Agriculture regularly publishes a list in the Federal Gazette, after consulting the Central Commission for Biosafety, which contains both the classification of microorganisms according to the applicable EU occupational health and safety legislation as well as assigning donor and recipient organisms to risk groups according to the general criteria pursuant to Section 5(1).

§ 7 Biological safety measures

(1) If biological safety measures are applied to genetic engineering work in accordance with Paragraphs 2 to 6 and with § 8, a lower hazard potential than that determined in accordance with § 5 may be taken as a basis.

(2) Biosafety measures, except for the measures in paragraph 4, shall consist of the use of recognised vectors and recipient organisms. They shall be taken into account in the overall assessment pursuant to § 4.

(3) Recognised biological safety measures are the use of eukaryotic cells, observing the usual safety precautions for cell cultures, in conjunction with vectors such as defective SV40 virus, defective adenovirus, defective bovine papillomavirus or non-viral replicons, each of which fulfils the requirements of § 8(2). The prerequisite is that the eukaryotic cells do not regenerate into an organism either spontaneously or during the intended genetic engineering work and that they do not contain any contamination of microorganisms and exogenous viruses. Until the expiry of 31 December 2021, the recognised biological safety measures shall be the vector-receptor systems listed in Annex II

Section A, indents 1 to 3 of the Genetic Engineering Safety Ordinance in the version published on 14 March 1995 (BGBl. I p. 297).

(4) Biosafety measures to prevent the effective spread of plants and their associated organisms used in genetic engineering operations are as follows:

1. the prevention of the effective dispersal of plant pollen or seeds, in particular through
   a) Removal of reproductive organs, use of male-sterile varieties or termination of the experiment and harvesting of the plant material before the reproductive stage is reached,
   b) Ensure that the test plants flower at a time of year when no other plant with which cross-pollination could occur is flowering within the normal pollen range of the test plant, or
   c) Ensure that no other plant grows within the known pollen range of the test plant with which cross-pollination would be possible,
2. the prevention of the effective spread of micro-organisms beyond the area of the greenhouse, in particular through
   a) Ensure that there is no organism within the entire radius in which effective airborne dispersal of a micro-organism is possible that could serve as a host and thus contribute to the transmission of the micro-organism,
   b) Conduct the experiment at a time of year when the plants being considered as hosts are either not growing or not susceptible to successful infection,
   c) Use of microorganisms,
      aa) which contain genetic defects that minimise the chances of survival of the micro-organisms outside the facility, or
      bb) where it is otherwise ensured that an accidental release could only have a very low probability of successfully infecting organisms outside the experimental facility,
3. the prevention of the effective spread of arthropods and other small animals, in particular through
   a) Use of flightless, barely flightless or sterile arthropods,
   b) Use of immobile or sterile strains of other small animals,
   c) Conduct the experiment at a time of year when survival of escaped organisms is very unlikely,
   d) Use of arthropods or other small animals that depend for their survival or reproduction on such plants that do not occur in the environment accessible to them.

Biological safety measures, such as sterilisation, are also possible to prevent the effective spread of other animals used in genetic engineering work.

(5) The Central Commission for Biological Safety may

1. recognise new vector-receptor systems pursuant to paragraph 1 and § 8 or new security measures pursuant to paragraph 4 as a biological security measure when giving their opinion in the course of the notification, application or approval procedure, or
2. confirm the continued existence of already recognised biological security measures in accordance with paragraph 3 sentence 3.

(6) The Federal Office of Consumer Protection and Food Safety shall publish in the Federal Gazette the biological safety measures which have been newly recognised or continue to be recognised by the Central Biosafety Commission, unless the operator on whose notification, application or licence application the recognition is based objects to the publication. An objection in accordance with sentence 1 shall prevent the notice temporarily for a period of three years from the date of filing of the objection. The Federal Office of Consumer Protection and Food Safety publishes a compilation of the recognised biological safety measures on the website of the Central Biosafety Commission.

Footnote

(+++ § 7 par. 1: For application cf. § 12 par. 3 +++)

§ 8 Recipient organisms and vectors as part of a biological safety measure

(1) The use of a recipient organism may be recognised as part of a biosafety measure when

1. a scientific description and a taxonomic classification of the recipient organism are available,
2. the propagation of the recipient organism is only possible under conditions which are rarely or not encountered outside genetic engineering facilities, or if it is possible to control the spread of the recipient organism outside genetic engineering facilities by appropriate measures,
3. the recipient organism has no properties that cause disease in humans, animals or plants and no properties that are harmful to the environment, and
4. the recipient organism engages in little horizontal gene exchange with other species.

(2) The use of a vector may be recognised as part of a biosecurity measure if

1. there is sufficient characterisation of the vector's genome,
2. there is limited host specificity of the vector, and
3. for a vector for
   a) bacteria or fungi have no transfer system of their own, a low cotransfer rate and low mobilisability, or
   b) eukaryotic cells on a viral basis, no independent infectivity and little transfer by endogenous helper viruses is to be expected.

§ 9 Principle of safety classification

In accordance with their hazard potential, genetic engineering operations are classified into the four safety levels of Section 7, paragraph 1 of the Genetic Engineering Act, taking into account the state of the art in science, in accordance with Sections 4, 5 and 6 and in accordance with Sections 10 to 12.

§ 10 Safety classification of genetic engineering work with microorganisms

(1) Genetic engineering work with microorganisms shall be assigned to safety level 1 if

1. the recipient organisms are microorganisms of risk group 1 according to § 5 paragraph 1 sentence 1 and do not release microorganisms of a higher risk group,
2. vectors and other nucleic acids introduced into the recipient organism are characterised in such a way that the genetically modified microorganisms, following a preliminary risk assessment in accordance with § 5 paragraph 1 sentence 2 do not exceed the hazard potential of microorganisms of risk group 1, and
3. the genetically modified microorganisms do not release genetically modified microorganisms of a higher risk group.

(2) Genetic engineering work with microorganisms shall be assigned to safety level 2 if

1. the recipient organisms are microorganisms of risk group 1 or 2 according to § 5 paragraph 1 sentence 1 and do not release microorganisms of risk group 3 or 4,
2. vectors and other nucleic acids introduced into the recipient organisms are characterised such that the genetically modified microorganisms do not exceed the hazard potential of risk group 2 organisms according to a preliminary risk assessment pursuant to Section 5 (1) sentence 2, and

3. the genetically modified microorganisms do not release genetically modified microorganisms of a higher risk group.

(3) Genetic engineering work with microorganisms shall be assigned to safety level 3 if

1. the recipient organisms are microorganisms of risk groups 1, 2 or 3 according to § 5 paragraph 1 sentence 1 and do not release microorganisms of risk group 4,
2. vectors and other nucleic acids introduced into the recipient organisms are characterised such that the genetically modified microorganisms do not exceed the hazard potential of microorganisms of risk group 3 according to a preliminary risk assessment pursuant to Section 5 (1) sentence 2, and
3. the genetically modified microorganisms do not release genetically modified microorganisms of risk group 4.

(4) Genetic engineering work with microorganisms shall be assigned to safety level 4 if it is associated with a high risk to human health or the environment or if there are reasonable grounds to suspect that it is associated with such a risk. This includes in particular genetic engineering work with viruses of risk group 4 or genetic engineering work with defective viruses of risk group 4 in the presence of helper viruses.

(5) Genetic engineering work with microorganisms aimed at producing genetic elements that drive their own propagation in populations of sexually reproducing organisms must generally be assigned to safety level 3. As part of the licensing procedure, the authority may assign the work to another safety level on the basis of the risk assessment. The competent authority shall obtain an opinion from the Central Commission for Biological Safety with recommendations on the specific safety measures required for such work.

§ 11 Safety classification of genetic engineering work with animals and plants

(1) Genetic engineering work with animals and plants shall be assigned to safety level 1 if

1. the recipient organisms are animals or plants from which no harmful effects on the legal interests according to § 1 number 1 of the Genetic Engineering Act are to be expected,
2. vectors and other nucleic acids introduced into the recipient organisms are characterised such that the genetically modified organisms do not exceed the hazard potential of risk group 1 organisms according to a preliminary risk assessment pursuant to Section 5 (1) sentence 2,
3. viral vectors are not horizontally transmissible and
4. the genetically modified organisms do not release genetically modified microorganisms of a higher risk group.

(2) Genetic engineering work with animals and plants shall be assigned to safety level 2 if

1. the recipient organisms are animals or plants from which at most a low risk for the legal interests according to § 1 number 1 of the Genetic Engineering Act is to be expected,
2. vectors and other nucleic acids introduced into the recipient organisms are characterised such that the genetically modified organisms do not exceed the hazard potential of risk group 2 organisms according to a preliminary risk assessment pursuant to Section 5 (1) sentence 2, and
3. the genetically modified organisms do not release genetically modified microorganisms of a higher risk group.

(3) Genetic engineering work with animals and plants shall be assigned to safety level 3 if

1. the recipient organisms are animals or plants from which at most a moderate risk to the legal interests according to § 1 number 1 of the Genetic Engineering Act is to be expected,
2. vectors and other nucleic acids introduced into the recipient organisms are characterised such that the genetically modified organisms do not exceed the hazard potential of risk group 3 organisms according to a preliminary risk assessment pursuant to Section 5 (1) sentence 2, and

3. the genetically modified organisms do not release genetically modified microorganisms of risk group 4.

(4) Genetic engineering work with animals and plants shall be assigned to safety level 4 if it is associated with a high risk to human health or to the environment or if there are reasonable grounds for suspecting that it is associated with such a risk.

(5) If genetically modified microorganisms are transferred to animals or plants during genetic engineering work, the hazard potential of the genetically modified microorganisms must be taken into account in the safety classification of the genetic engineering work.

(6) Genetic engineering work with animals or plants aimed at producing genetic elements that drive their own propagation in populations of sexually reproducing organisms must generally be assigned to safety level 3. As part of the authorisation procedure, the authority may assign the work to another safety level on the basis of the risk assessment. The competent authority shall obtain an opinion from the Central Commission for Biological Safety with recommendations on the specific safety measures required for such work.

§ 12 Genetic engineering work for the production of highly effective toxins

(1) Genetic engineering work aimed at producing highly potent toxins shall be assigned to safety level 3.

(2) The Central Biosafety Commission makes recommendations on the necessary technical and biological safety measures that take into account the mode of action of these toxins.

(3) § 7 paragraph 1 shall apply.

Section 3 Security measures

§ 13 General duty to protect, occupational health and safety

(1) The operator who has genetic engineering work carried out must identify and assess possible hazards and determine the necessary safety measures in order to protect the legal assets specified in Section 1 No. 1 of the Genetic Engineering Act and to protect the employees. The assessment of the hazards must contain information in accordance with Section 10, paragraph 2, sentence 2, numbers 4 and 5 of the Gene Technology Act.

(2) The operator of a genetic engineering facility shall take the necessary measures in accordance with the provisions of this Ordinance, including its Annexes, and the precautionary measures required in accordance with the state of the art in science and technology, in order to protect the legal interests specified in Section 1 No. 1 of the Genetic Engineering Act and to keep exposure of employees and the environment to the genetically modified organism as low as possible. In particular, the general recommendations of the Central Commission on Biological Safety shall be observed and, for the protection of workers, the safety standards determined by the Committee on Biological Agents or the Maternity Protection Committee and adopted by the Federal Ministry of Labour and Social Affairs or the Federal Ministry for Family Affairs, Senior Citizens, Women and Youth in the Joint Commission on Biological Agents shall be observed.
The rules and findings published in the Ministerial Gazette shall be taken into account. These rules and findings do not have to be taken into account if equivalent protective measures are taken; this must be demonstrated in individual cases at the request of the competent authority.

(3) Measures to avert immediate danger must be taken by the operator without delay.

(4) In case of imminent danger, the competent authority may also issue orders against supervisors and other employees in accordance with Section 26 of the Gene Technology Act.

(5) In the case of genetic engineering work of safety levels 2 to 4 in accordance with Section 7(1) numbers 2 to 4 of the Genetic Engineering Act in the production area, the operator shall examine whether genetic engineering work can be carried out with a lower health risk for the employees than that which he is considering. If the operator can reasonably be expected to carry out this other genetic engineering work, he shall only carry out this work.

(6) The operator must determine which measures are to be taken to avert hazards before commencing genetic engineering work.

Footnote

(+++ § 13 para. 1 sentence 1: For application cf. § 18 para. 6 in conjunction with para. 1 +++)

§ 14 Safety measures for laboratory and production areas

(1) Genetic engineering work of safety levels 1 to 4 according to Section 7, paragraph 1, sentence 1 of the Genetic Engineering Act in the laboratory and in the production area may only be carried out in compliance with the safety measures specified in Appendix 2.

(2) The safety measures according to Annex 2 Part A for the laboratory area can also be applied for laboratory-typical work in the production area, the safety measures according to Annex 2 Part B for the production area can also be applied for production-typical work in the laboratory area.

(3) As a rule, the structural, technical, organisational and personal safety measures according to Annex 2 shall be designed in such a way that the personal protective equipment of workers is only required as a supplement to the other safety measures.

(4) If genetic engineering work with plants or animals is carried out in laboratory or production areas, the safety measures of Annex 3 for greenhouses or Annex 4 for animal rooms shall also apply accordingly and depending on the safety level of the genetic engineering work.

Footnote

(+++ § 14 par. 3: For application cf. § 15 par. 3 and § 16 par. 3 +++)

§ 15 Security measures for greenhouses

(1) If plants are grown in greenhouses which have been produced by genetic engineering work or which are used in genetic engineering work, the safety measures specified in Annex 3 shall apply to genetic engineering work of safety levels 1 to 4 in accordance with the first sentence of Section 7(1) of the Genetic Engineering Act. These shall also apply accordingly to climate chambers.

(2) If work with genetically modified microorganisms is carried out in greenhouses, the safety measures in Annex 2 for the laboratory area shall also apply accordingly and depending on the safety level of the genetic engineering work.

(3) § Section 14(3) shall apply mutatis mutandis.

§ 16 Safety measures for animal rooms

(1) If animals are kept in animal rooms which have been created by genetic engineering work or which are used in genetic engineering work, or if these animals are handled, the safety measures specified in Annex 4 must be observed in the case of genetic engineering work of safety levels 1 to 4 in accordance with Section 7, paragraph 1, sentence 1 of the Genetic Engineering Act.

(2) If work with genetically modified microorganisms is carried out in animal rooms, the safety measures of Annex 2 for the laboratory area shall also apply accordingly and depending on the safety level of the genetic engineering work.

(3) § Section 14(3) shall apply mutatis mutandis.

§ 17 General occupational safety measures

(1) Employees may only be assigned to genetic engineering work if they are sufficiently qualified and instructed.

(2) The operator shall, in particular on the basis of the risk assessment and the hazard assessment pursuant to Section 5 of the Occupational Health and Safety Act, prepare operating instructions for the employees prior to the commencement of genetic engineering work in which the hazards identified and assessed in accordance with Section 13 (1) are

The operating instructions must describe the risks of genetic engineering work for human health and the environment and specify the necessary safety measures and rules of conduct. The operating instructions

1. shall be written in a clear form and in a language understandable to the employees and shall be posted in a suitable place in the workplace,
2. must be immediately available,
3. shall be reviewed as necessary, but at least every two years, and updated if required,
4. shall contain instructions on what to do in the event of danger and on first aid; and
5. must contain information on possible immunisation and post-exposure prophylaxis measures.

(3) The operator must draw up a hygiene plan for working with genetically modified organisms, which contains a brief overview of the hygiene measures to be observed, for example with time specifications and with regard to the agent and the application method.

(4) Employees who are assigned genetic engineering work must be instructed by the project manager on the basis of the operating instructions with regard to the possible hazards and the necessary safety measures. The instructions must be given orally in safety levels 2, 3 or 4, or orally or by means of electronic communication with success control in safety level 1 and in each case in relation to the workplace before the first employment and thereafter at least once a year. The content and time of the instructions must be recorded in writing and signed by the persons instructed.
to confirm. Women shall additionally be instructed about possible hazards that may exist during pregnancy or breastfeeding. In the case of genetic engineering work at safety level 2, 3 or 4, the instruction must be given before any safety-relevant change is made to this work. The content and time of this instruction shall be recorded in writing and confirmed by the signatures of the persons instructed. The project manager may delegate the obligation under sentences 1 to 6 to suitable employees.

(5) For work processes where experience has shown that there is an increased risk of accidents or particularly serious consequences of accidents, work instructions with safety-relevant instructions must be available at the workplace in order to prevent occupational accidents.

(6) The operator shall regularly check the functionality and effectiveness of the safety-relevant devices or equipment such as, in particular, the autoclaves and safety cabinets in accordance with the state of the art in science and technology. The result and date of the effectiveness test shall be documented.

§ 18 Occupational safety during inspection, maintenance and modification of installations, apparatus and equipment

(1) Inspection, maintenance, cleaning, modification or demolition work in or on installations, apparatus or facilities in which genetic engineering work of safety level 2, 3 or 4 has been carried out may only be carried out if written permission has been obtained from the operator, the project manager or the person directly responsible for the operation of the installation, apparatus or facility, or his superior.

(2) The prerequisites for work in accordance with paragraph 1 are that the necessary safety measures have been taken and that the employees have been instructed in relation to the workplace.

(3) Before carrying out inspection, maintenance, cleaning, modification or demolition work, the installations, apparatus and equipment must be disinfected. If this is not sufficiently possible, the inspection, maintenance, cleaning, modification or demolition work may only be carried out using technical protective measures or suitable personal protective equipment. In this context, personal protective equipment is subordinate to technical protective measures.

(4) Paragraphs 1 and 2 shall apply mutatis mutandis to the testing, maintenance and repair of contaminated equipment.

(5) For regular work within the meaning of paragraphs 1 and 3, a corresponding permanent permit may be granted; if a permanent permit is granted, the employees shall be instructed at least once a year.

(6) Section 13, paragraph 1, sentence 1 and Section 20 shall apply mutatis mutandis to the activities under paragraph 1.

§ 19 Adaptation of occupational safety measures and monitoring of the work area

(1) If the state of the art in safety technology of a work process has developed further and if the safety technology has proven itself and occupational safety has increased considerably as a result, the operator shall adapt the work process that does not comply with the state of the art in safety technology to this further development within a reasonable period of time.

(2) If the occurrence of genetically modified organisms in a concentration which poses or could pose a risk to human health cannot be excluded according to the state of the art in science and technology, the working area shall be monitored by appropriate measures.

§ 20 Occupational health preventive measures

(1) The operator shall provide appropriate occupational health care for employees who carry out genetic engineering work with organisms that may pose a risk to human health.
to take preventive measures. These include the regulations and measures specified in section 14(2) of the Biological Substances Ordinance of 15 July 2013 (Federal Law Gazette I p. 2514), as amended by Article 146 of the Act of 29 March 2017 (Federal Law Gazette I p. 626), and the regulations and measures specified in the Ordinance on Occupational Health Precautions of 18 December 2008 (Federal Law Gazette I p. 2768), as last amended by Article 3(1) of the Ordinance of 15 November 2016 (Federal Law Gazette I p. 2549).

(1a) The operator shall coordinate the implementation of appropriate occupational health preventive measures with employers of contractors.

(2) The Federal Ministry of Labour and Social Affairs may, after consulting the Central Commission for Biological Safety, use the rules and findings determined by the Committee on Occupational Health for the purpose of
The Federal Ministry of Education and Research shall publish the recommendations on occupational health precautions for genetic engineering work in the Joint Ministerial Gazette.

Footnote

(+++ § 20: For application cf. § 18 par. 6 in conjunction with par. 1 +++)

§ 21 Informing employees

(1) The operator shall inform the employees concerned and, if there is a works council or staff council, the latter as well as the company doctor of the following:

1. about the risks associated with the genetic engineering work and the safety measures to be taken, and
2. on the reasons for the choice of protective equipment and the conditions under which it is to be used, where the operator is required to provide protective equipment.

(2) In the event of operational disruptions, the employees concerned and the works or staff council shall be informed.
In urgent cases, the operator shall immediately inform the employees concerned and the works council or staff council of measures taken. Sentence 1 shall also apply in the event that, following the inspection of a workplace, measures are taken which are necessary on the basis of findings from occupational health precautions.

(3) The works council or staff council as well as the works doctor shall have the right to propose to the operator additional protective measures to prevent damage to health in individual cases which go beyond the measures provided for in this Ordinance.

(4) Information and participation obligations under other legal provisions shall remain unaffected.

(5) Information and participation obligations vis-à-vis the works council or staff council as well as vis-à-vis the employees exist only insofar as the persons concerned are employees within the meaning of the Works Constitution Act or the Staff Representation Acts.

§ 22 General requirements for waste water and waste treatment

Waste water and liquid and solid waste from genetic engineering facilities are harmless with regard to the hazards

posed by genetically modified organisms according to the state of the art in science and technology.

to be disposed of. Requirements for waste water and waste disposal to be made according to other regulations remain unaffected.

§ 23 Waste water and waste treatment during genetic engineering work of safety levels 1 and 2

(1) The operator shall ensure that waste water and liquid and solid waste from installations in which genetic engineering work of safety level 1 or 2 is carried out in accordance with section 7, paragraph 1, sentence 1, number 1 or 2 of the Genetic Engineering Act is pretreated in such a way that the substances contained therein are
genetically modified organisms are inactivated to such an extent that hazards to the legal interests specified in § 1 number 1 of the Gene Technology Act are not to be expected. The requirements for the Pre-treatment according to sentence 1 shall be deemed to be fulfilled if it is demonstrated by means of inactivation kinetics that the inactivation period corresponds at least to the value at which no ability to multiply and, if applicable, no infectivity of the genetically modified organism is observed any longer.

(2) Wastewater and waste treatment methods that can be considered are in particular:

1. Inactivation of the genetically modified organism by physical processes, such as exposure to specific temperature and pressure conditions during specific residence times, or
2. Inactivation of the genetically modified organism by chemical methods by exposure to appropriate chemicals under specific temperature, residence time and concentration conditions, if the nature of the waste or waste water does not permit a physical inactivation method according to Number 1.

§ 24 Disposal of waste water and waste without pre-treatment in genetic engineering operations of safety levels 1 and 2

(1) By way of derogation from § 23, the following waste water and the following liquid and solid waste may be disposed of without special pre-treatment:

1. Shower and hand washing water as well as comparable waste water from facilities in which genetic engineering work of safety level 1 or 2 is carried out according to § 7 paragraph 1 sentence 1 number 1 or 2 of the Genetic Engineering Act,
2. liquid and solid waste from installations in which genetic engineering operations of safety levels 1 or 2 are carried out in accordance with section 7, paragraph 1, sentence 1, number 1 or 2 of the Genetic Engineering Act, if the waste has not arisen in direct connection with genetic engineering operations and is therefore not potentially contaminated with genetically modified organisms, and
3. liquid and solid waste originating from installations in which only genetic engineering operations of safety level 1 are carried out and which has arisen in direct connection with these genetic engineering operations, if
   a) for the production of the genetically modified microorganisms
      aa) such strains are used as recipient organisms of risk group 1 which fulfil the conditions of § 8 paragraph 1,
      bb) the vectors fulfil the conditions of § 8 paragraph 2 and
      cc) the imported nucleic acids are not expected to have any harmful effects on the legal interests specified in Section 1 No. 1 of the Genetic Engineering Act

      or
   b) the waste is contaminated to such a low level that harmful effects on the legal interests specified in § 1 number 1 of the Gene Technology Act are not to be expected.

(2) For waste water, except for shower and hand washing water, paragraph 1, sentence 1, numbers 2 and 3 shall apply accordingly.

§ 25 Inactivation of genetically modified organisms prior to waste water or waste disposal

(1) Inactivation of genetically modified organisms pursuant to section 23 subsection (1) sentence 2 in conjunction with subsection (2) number 1 shall normally be deemed to have occurred if the waste water or waste is autoclaved at a temperature of 121 degrees Celsius for a period of 20 minutes. In the case of thermostable organisms, permanent forms of organisms or organisms containing a thermostable substance with a hazard potential

it may be necessary to increase the temperature to 134 degrees Celsius during autoclaving or to extend the exposure time. When autoclaving genetically modified micro-organisms in special matrices, such as in animal cadavers, it must be ensured that the temperatures and exposure times listed in sentences 1 and 2 are achieved in all layers. In the cases listed in sentences 2 and 3, the effectiveness of the intended inactivation shall be demonstrated prior to its use.

(2) On application, the competent authority may also approve physical processes other than autoclaving. The competent authority may, on application, approve chemical inactivation processes if it is ensured that they are environmentally sound and that the requirements of § 23 are met. In particular, there must be no indications that the inactivation substances used may have harmful effects on a downstream waste water treatment facility, on water bodies or on the waste disposed of after inactivation.

(3) The operator shall demonstrate the effectiveness of the alternative procedure referred to in paragraph 2 to the competent authority in an appropriate manner, for example by submitting inactivation kinetics.

Footnote

(+++ § 25 par. 3: For application cf. § 26 par. 4 sentence 6 in conjunction with sentences 1 and 2 +++)

§ 26 Waste water and waste treatment during genetic engineering work of safety levels 3 and 4

(1) The operator shall ensure that the following wastes and effluents are sterilised by autoclaving at a temperature of 121 degrees Celsius for a period of 20 minutes in the facility where they were generated:

1. liquid and solid waste from facilities in which genetic engineering work of safety level 3 is carried out in accordance with section 7, paragraph 1, sentence 1, number 3 of the Genetic Engineering Act,
2. liquid and solid waste and waste water from installations in which genetic engineering work of safety level 4 is carried out in accordance with section 7(1) sentence 2 number 4 of the Genetic Engineering Act.

In the case of thermostable organisms, permanent forms of organisms or organisms which form a thermostable substance with a hazard potential, it may be necessary to increase the temperature to 134 degrees Celsius or to extend the exposure time during autoclaving in accordance with sentence 1. When autoclaving genetically modified microorganisms in special matrices, such as in animal cadavers, it must be ensured that the temperatures and exposure times specified in sentences 1 and 2 are achieved in all layers. In the cases listed in sentences 2 and 3, the effectiveness of the intended sterilisation must be demonstrated before it is used.

(2) Compliance with the temperature and duration of sterilisation shall be recorded by self-recording devices. The operator shall ensure that the devices for checking the temperature and duration are designed in such a way that, in the event of non-compliance with the requirements, the release of organisms is prevented.
is excluded. The operator must check the sterilisation success by means of a functional check of the autoclave. Cooling systems must be designed in such a way that contamination of the cooling water with genetically modified organisms is excluded.

(3) In its statement on the safety classification of a genetic engineering work of safety level 3 and on the necessary safety measures, the Central Commission for Biological Safety also gives an indication of the necessity of waste water treatment.

(4) By way of derogation from paragraph 1, the competent authority may, on application, also approve other physical processes for sterilisation. If sterilisation by physical methods is not possible, the competent authority may, on application, also approve other methods such as chemical sterilisation methods. These must be environmentally compatible. In particular, there must be no evidence that
the substances used have harmful effects on a downstream waste water treatment plant, on water bodies or on the waste disposed of after sterilisation. Homogeneous distribution of chemicals in waste water or waste shall be ensured and operating data, such as the chemical dose used, shall be recorded. Section 25(3) shall apply mutatis mutandis to the procedures pursuant to sentences 1 and 2.

(5) If equipment or parts of equipment or waste from installations in which genetic engineering operations of safety levels 3 and 4 are carried out in accordance with Section 7(1), first sentence, numbers 3 and 4 of the Genetic Engineering Act cannot be sterilised in the genetic engineering installation because of their size, they shall be used for the

sterilisation in secure, tightly closed, appropriately labelled and externally disinfected containers to another genetic engineering facility that meets the necessary requirements for sterilisation.

Section 4
Project Manager

§ 27 Responsibilities of the project manager

(1) The project leader shall carry out the direct planning, management or supervision of the genetic engineering work or release. He is responsible

1. for the observance of the protection regulations of §§ 13 to 26 as well as the infection control, animal health, animal welfare, species protection and plant protection regulations,
2. for the genetic engineering work not to be started until
   a) a notification has been made in accordance with § 8 paragraph 2 sentence 1 or § 9 paragraph 2 sentence 1 of the Gene Technology Act and § 12 paragraph 5a sentence 2 of the Gene Technology Act does not conflict with this,
   b) the time limit under Section 8(2) in conjunction with Section 12(5) of the Gene Technology Act has expired or the consent under Section 12(5) of the Gene Technology Act has been granted, or
   c) the authorisation is enforceable under section 8(1), second sentence, (2), (3) or (4) or under section 9(2), second sentence, (3) or (4) of the Gene Technology Act,
3. for the release not to be commenced until the authorisation under section 14(1)(1) of the Genetic Engineering Act is enforceable,
4. for the implementation of official requirements and orders,
5. for the sufficient qualification and instruction of the employees,
6. for the implementation of instructions for employees in accordance with section 17(4), for the implementation of occupational health precautions and for the logging of accidents,
7. for informing the Biosafety Officer or the Biosafety Committee in detail about the genetic engineering work and the precautions required under sections 13 to 26 or about the release,
8. to ensure that, in the event of danger to the legal interests specified in § 1 number 1 of the Genetic Engineering Act, appropriate measures are taken without delay to avert this danger,
9. for immediately notifying the operator of any occurrence which does not correspond to the expected course of the genetic engineering work or the release and which gives rise to the suspicion of a risk to the people involved in the genetic engineering work or the release.
   § 1 number 1 of the Genetic Engineering Act,
10. ensure that a competent person is regularly present and generally available during releases.

(2) If a genetic engineering work, a genetic engineering facility or a release is jointly assigned to several project leaders, the responsibilities of the individual project leaders must be clearly defined.

§ 28 Expertise of the project manager

(1) Only a person who has the required expertise may be appointed as project leader. The project leader must have demonstrable knowledge, in particular in classical and molecular genetics and practical experience in handling microorganisms, plants or animals and the necessary knowledge of safety measures and occupational health and safety in genetic engineering work. The provisions of infection control, animal health, animal welfare, species protection and plant protection law shall remain unaffected.

(2) The expertise required in accordance with paragraph 1 shall be demonstrated by

1. the completion of a university degree in natural sciences, medicine or veterinary medicine with a Master's degree, a diploma or a state examination or by a completed doctorate in these fields,
2. at least three years' experience in the field of genetic engineering, in particular in microbiology, cell biology, virology or molecular biology, and, if the project management sought relates to

genetic engineering work at safety level 3 or 4, at least two years' experience at safety level 2, 3 or 4, and

3. the certificate of attendance of a further training event recognised by the competent Land authority at which the knowledge pursuant to paragraph 5 is imparted.

If genetic engineering work is to be carried out in the production area, the required expertise may be demonstrated by the following instead of by the requirements specified in sentence 1, numbers 1 and 2

1. the completion of a university degree in engineering and
2. at least three years of work in the field of bioprocess engineering.

If releases of plants are to be carried out, the required expertise may, as a rule, be demonstrated by the following instead of by the requirements specified in sentence 1, numbers 1 and 2

1. a degree in biological or agricultural sciences from a university, and
2. at least three years of work in a plant breeding company or in a scientific institution in plant protection, plant cultivation or plant breeding.

If the project leader is only to be responsible for certain specified genetic engineering work, the competent authority may, by way of derogation from paragraph 2, sentence 1, numbers 1 and 2, limit the proof of the required expertise.

(3) The knowledge imparted in the further training pursuant to sub-section 2 sentence 1 number 3 must be updated at least every five years by renewed participation in a recognised further training event. Notwithstanding sentence 1, the knowledge imparted in the further training pursuant to sub-section 2 sentence 1 number 3 may be updated in another suitable manner in individual cases. The updating must be suitable to ensure a level of knowledge that corresponds to the knowledge imparted in a recognised training event pursuant to sub-section 5. Evidence of the updating shall be submitted to the competent authority. The competent authority shall decide on the recognition of the update.

(4) The competent authority may also recognise the completion of another initial, further or continuing training course as proof of the required expertise in accordance with paragraph 2, sentence 1, numbers 1 and 2, sentence 2 or sentence 3 if the teaching of the knowledge and skills required in accordance with paragraph 1 has been the subject of this initial, further or continuing training course and, taking into account the genetic engineering work to be carried out, it is to be regarded as equivalent to the requirements specified in paragraph 2, sentence 1, numbers 1 and 2, sentence 2 or sentence 3.

(5) The further training course pursuant to paragraph 2 sentence 1 number 3 must cover the essentials of the following topics:

1. Hazard potentials of organisms during genetic engineering work in genetic engineering facilities with special consideration of microbiology and during releases,
2. Safety measures for genetic engineering laboratory areas, production areas, greenhouses, animal rooms and releases; and
3. Legislation on safety measures for genetic engineering laboratory areas, production areas, greenhouses, animal rooms and releases and on occupational health and safety.

The competent authority may recognise suitable events as training events within the meaning of sentence 1.

(6) Where a project manager is employed by a third party, the competent authority may, upon request, allow the operator to appoint that project manager by way of a written agreement with the operator, the operator and the third party. A prerequisite for this is that

1. the Project Manager undertakes vis-à-vis the Operator in the Agreement to perform the tasks pursuant to § 27 and to follow the instructions of the Operator to that extent, and
2. it is to be expected that the project manager so appointed will properly perform the tasks specified in § 27.

Section 5
Biological Safety Officer

§ 29 Appointment of a Biosafety Officer

(1) After consulting the works council or staff council, the operator shall appoint in writing one or, if necessary with regard to the type or scope of the genetic engineering work or the releases for the protection of the legal interests specified in Section 1 No. 1 of the Genetic Engineering Act, several biological safety officers. If several authorised representatives for biological safety are appointed, they shall form these a Biosafety Committee. The tasks of each individual Biosafety Officer shall be specified.

(2) The competent authority may, upon application, permit the operator to appoint one or more non-operating biosafety representatives if this ensures the proper fulfilment of the tasks specified in Article 31.

§ 30 Expertise of the Biosafety Officer

Only a person who has the required expertise may be appointed as the Biological Safety Officer. The requirements for the necessary expertise and the proof thereof shall be based on the provision of § 28 applicable to the project manager.

§ 31 Tasks of the Biosafety Officer

(1) The Biosafety Officer is authorised and obliged to,

1. supervise the fulfilment of the project manager's tasks related to the safety of genetic engineering operations or releases, in particular by regularly inspecting the genetic engineering facility or release sites, by notifying the operator and the project manager of any deficiencies found and by verifying that these deficiencies have been rectified,
2. advise the operator, the works council or staff council at their request and the persons responsible in each case
   a) in the risk assessment pursuant to Section 6 (1) of the Gene Technology Act,
   b) in the planning and execution of genetic engineering work and the maintenance of facilities in which genetically modified organisms are handled,
   c) in the procurement of facilities and operating resources and in the introduction of procedures for the use of genetically modified organisms,
   d) in the selection and testing of personal protective equipment and
   e) before the commissioning of facilities and equipment and before the introduction of procedures for the use of genetically modified organisms.

(2) The Biosafety Officer shall submit an annual written report to the operator on the measures taken and intended under paragraph 1.

§ 32 Obligations of the operator towards the Biosafety Officer

(1) The operator shall support the Biosafety Officer in the fulfilment of his tasks and, in particular, provide him with auxiliary staff as well as rooms, facilities, equipment and working materials to the extent necessary for the fulfilment of his tasks.

(2) The operator shall enable the biosafety officer to receive the further training necessary for the fulfilment of his tasks, taking into account operational concerns, at the operator's expense.

(3) The biosafety officer appointed as an employee of the operator shall not be disadvantaged because of the performance of the tasks assigned to him.

(4) Before procuring equipment and resources that may be significant for the safety of genetic engineering work in genetic engineering facilities, the operator shall obtain an opinion from the Biosafety Officer. The opinion must be obtained in good time so that it can be adequately taken into account in the decision on procurement. It shall be submitted to the body deciding on the procurement.

(5) The operator shall ensure that the Biosafety Officer can directly present his proposals or concerns arising in the course of his performance of duties pursuant to Section 31 to the decision-making body if he has not been able to reach an agreement with the project manager and the Biosafety Officer considers a decision by this body to be necessary due to the particular importance of the matter.

Section 6
Administrative offences

§ 33 Administrative offences

A regulatory offence within the meaning of section 38(1) number 12 of the Genetic Engineering Act shall be committed by any person who intentionally or negligently

1. contrary to § 14 paragraph 1 in conjunction with Annex 2 Part A Section III letter a number 2 sentence 2 or 3, number 3, 7, 9 sentence 1, number 11 sentence 1, 2 or 3, number 14, Section III letter b
Point 20, Section IV(a)(1) fifth sentence, points (2), (3), (5), (6) first, second, fourth or fifth sentence, points (7), (8), (11), (12), (13) or Section IV(b)(17) or Part B, Section II(a)(7), Section III(a)(2) second or third sentence, point (7), (9) first sentence, number 12, 13 first sentence, number 14, 16 or 18, section III(b)(21), section IV(a)(1) seventh sentence, number 2, 3, 5, 9, 10, 12 first sentence, number 14, 15 first or third sentence or number 18 or section IV(b)(17) carries out genetic engineering work,
2. transports a genetically modified organism or waste specified therein in contravention of section 15 subsection (1) first sentence in conjunction with Annex 3 section II letter b number 4 first sentence, section III letter b number 3 first sentence or section IV letter b number 4 first sentence,
3. connects a greenhouse contrary to § 15 paragraph 1 sentence 1 in conjunction with Annex 3 Section IV letter a number 11 sentence 2,
4. transports a genetically modified organism or waste specified therein in contravention of section 16 subsection (1) in conjunction with Annex 4 section II letter b number 16 sentence 1, section III letter b number 5 sentence 1 or section IV letter b number 5 sentence 1,
5. recirculates contaminated exhaust air in contravention of section 16(1) in conjunction with Annex 4, section III(a)(8), third sentence, or section IV(a)(14),
6. connects an animal room contrary to § 16 paragraph 1 in conjunction with Annex 4 Section IV letter a number 9 sentence 2,
7. contrary to § 17 Paragraph 2 Sentence 1, fails to draw up an operating instruction or fails to do so in good time,
8. contrary to section 17(4), first or second sentence, fails to instruct an employee correctly, fully, in the prescribed manner or in good time,
9. contrary to section 23(1), first sentence, fails to ensure that waste water or waste is pre-treated,
10. contrary to the first sentence of section 26(1), fails to ensure that waste or waste water referred to therein is sterilised,
11. contrary to the second sentence of section 26(2), fails to ensure that a device is designed in the manner specified therein, or
12. contrary to § 29 Paragraph 1 Sentence 1, fails to appoint a Biosafety Officer or fails to do so in good time.

Annex 1 (to § 5 paragraph 1)
General criteria for risk assessment

(Source: Federal Law Gazette I 2019, 1248 - 1250)

General criteria for risk assessment of organisms in genetic engineering work, where relevant:

1. Information on donor and recipient organisms or parental organisms

a) Name and designation

b) Degree of relationship

c) Origin

d) Information on reproductive cycles (sexual/asexual) of the source organism or the recipient organism, if applicable.

e) Information on previous genetic modifications

f) Stability of the recipient organism in relation to the relevant genetic characteristics

g) Pathogenicity of the organism for defence-healthy humans or animals

h) smallest infectious dose

i) Toxicity to the environment and toxicity and allergenicity to humans

j) Resilience of the organism: survival of the organism or maintenance of the ability of microorganisms to multiply and infect under relevant conditions.

k) Colonisation capacity

l) Host range

m) Type of transmission, e.g. by

- direct or indirect contact with the injured or uninjured skin or mucous membrane
- Aerosols or dust via the respiratory tract
- Water or food via the digestive tract
- Bite, sting or injection as well as via the germ line in animal vectors
- diaplacental transfer

n) Possibility of transmission of pathogens through the organism

o) Availability of therapeutics and/or vaccines and/or other effective methods for the prevention and treatment of human diseases

p) Type and properties of the vectors contained in the organisms:

- Sequence
- Mobilisability
- Host specificity
- Presence of relevant genes, e.g. resistance genes

q) Adventitious agents that could mobilise genetic material inserted into the organism.

r) Other potentially significant physiological characteristics

s) Stability of characteristics according to letter r

t) epidemiological situation:

- Occurrence and spread of the organism
- Role of living vectors and reservoirs of organisms
- Extent of natural resistance in humans and animals to the organism
- Degree of acquired immunity in humans and animals (e.g. through silent celebration and vaccination).
- Presence or non-presence of a suitable host animal
- Resistance in plants (natural or through breeding)
- Occurrence or non-occurrence and distribution of a suitable host plant for the organism.

u) Significant involvement of the organism in environmental processes (e.g. nitrogen fixation or pH regulation).

v) Presence of suitable conditions for colonisation of the environment by the organism.

w) Interaction with and effects on other organisms in the environment (including likely competitive or symbiotic properties).

x) Ability to form survival structures (e.g. seeds, spores or sclerotia) and their means of dispersal.

2. Information about the genetically modified organism

2.1 Description of the genetic modification

a) Description of the genetic modification, including the method of introduction of the vector or insert into the recipient organism or the method used to achieve the genetic modification in question.

b) Origin of the genetic material, identity of the donor organism(s) and characteristics, if applicable.

c) Previous genetic modification of the insert

d) Function of the genetic modification in question and/or the new nucleic acid

e) Type and origin of the vector

f) Structure and amount of a vector and/or a nucleic acid of the donor organism, if the vector and/or the nucleic acid still remain in the final structure of the modified organism

g) Stability of the organism in relation to the genetically modified characteristics

h) Frequency of mobilisation of the inserted vector and/or ability of the vector to transfer genetic information

i) Level of expression of the genetically introduced material; measurement method and degree of sensitivity

j) Location of inserted genetic material (indication of possible activation/deactivation of host genes by the insertion).

k) Activity of the protein brought to expression

2.2 Health considerations

a) toxic or allergenic effects of the genetically modified organisms and/or their metabolites

b) Product risks

c) Comparison of the pathogenicity of the genetically modified organism with that of the donor or recipient organism or, if applicable, the parental organism.

d) Colonisation capacity

e) in the case of pathogenicity of the genetically modified organism for people who are immune healthy:

- diseases caused and mechanism of disease-causing properties including invasiveness and virulence
- Transferability
- Infection dose
- Host range, possible change of host range
- Possible change in the route of infection or tissue specificity.
- Possibility of survival outside the human host
- Presence of vectors or means of dissemination
- biological stability
- Patterns of antibiotic resistance
- Allergenicity
- Toxicity
- Availability of appropriate therapies and prophylactic measures

2.3 Environmental considerations

a) Factors influencing the survival, reproduction and dissemination of the genetically modified organisms in the environment

b) available techniques for the detection, identification and monitoring of the genetically modified organisms

c) available techniques to detect the transfer of the genetically introduced material to other organisms

d) known and predicted habitats of the genetically modified organism

e) Description of the ecosystems to which the organism could be inadvertently disseminated

f) Expected mechanism and outcome of the interaction between the genetically modified organism and the organisms or micro-organisms that could be contaminated in the event of release into the environment.

g) known or predictable effects on plants and animals, such as disease-causing properties, infection, toxigenicity, virulence, vector of disease-causing properties, allergenicity, altered patterns of antibiotic resistance, altered tropism,
Colonisation

h) Known or predictable involvement in biogeochemical processes

i) Availability of methods to decontaminate the area in the event of a release of genetically modified organisms into the environment.

Annex 2 (to § 14)
Safety measures for laboratory and production areas

(Source: Federal Law Gazette I 2019, 1251 - 1268)

A. Safety measures for the laboratory area

Pursuant to Section 14(4), if work with genetically modified plants or animals is carried out in laboratory areas, the requirements of Annex 3 for greenhouses or Annex 4 for animal rooms of the corresponding safety level shall be observed accordingly in addition to the requirements of this Annex.

I. Safety level 1

a. Structural and technical safety measures

1. The work shall be carried out in delimited and sufficiently large rooms. Depending on the activity, sufficient working space shall be provided for each employee.
2. Work surfaces and surfaces adjacent to work surfaces, in particular wall surfaces, floors and the furniture, should be easy to clean and must be resistant to the substances used and to cleaning agents and disinfectants.
3. A washbasin with a handwash dispenser and a disposable towel dispenser and, if necessary, a disinfectant dispenser should be provided in the work area.
4. Laboratory doors should open in the direction of escape and have viewing windows for reasons of personal protection.
5. An autoclave or equivalent device for inactivation or sterilisation must be available within the premises of the site.

b. Organisational security measures

1. The genetic engineering facility shall be designated as a safety level 1 genetic engineering work area.
2. Windows and doors should be closed during the work.
3. The rooms should be kept tidy and clean. Only the equipment and materials that are actually needed should be on the work tables. Supplies of working materials should only be stored in rooms or cupboards provided for this purpose.

4. Pipetting aids are to be used.
5. Cannulas and pointed or sharp objects should only be used when absolutely necessary. Used needles and used pointed or sharp objects should be collected and disposed of in puncture-proof and tightly closable waste containers. Cannulas must not be put back into their sheaths.
6. During all work, care must be taken to avoid aerosol formation as far as possible. When working with genetically modified organisms of risk group 1 with sensitising or toxic effects, appropriate measures must be taken to minimise exposure of workers. Here it may be
For example, the avoidance of spore-forming development phases in fungi, the use of a microbiological safety cabinet or the use of respiratory protection.
7. The identity and purity of the organisms used must be checked regularly if this is necessary for assessing the hazard potential of the organisms. The time intervals of the verification shall depend on the possible hazard potential.
8. The storage of genetically modified organisms must be carried out appropriately.
9. Genetically modified organisms and waste containing genetically modified organisms should only be transported to other genetic engineering facilities in the building or on the premises in tightly closed containers that are protected against breakage, can be disinfected and are labelled accordingly. The containers must be disinfected regularly from the outside and whenever they are contaminated.
10. Where appropriate, ensure safe storage of contaminated laboratory equipment and materials.
11. Infestation with vermin and vectors of genetically modified organisms (for example with rodents and arthropods) shall be prevented; vermin and vectors shall be controlled in an appropriate manner, if necessary.
12. After finishing the activity and before leaving the work area, hands must be disinfected if necessary and carefully cleaned and cared for according to the skin protection plan.
13. In case of injuries, first aid measures must be initiated immediately. The project manager must be informed and, if necessary, medical assistance must be sought. If there is a possibility that genetically modified organisms have been ingested or if an infection with genetically modified organisms seems possible, the project leader and, if necessary, the attending physician must be informed.
14. If necessary, for example if protective and hygienic measures are suspected to be inadequate, the work area must be checked for the presence of viable organisms used in genetic engineering work.
15. Effective disinfectants and specific disinfection procedures must be available for the case of leakage of genetically modified organisms, as well as any necessary aids such as absorbent material.
16. The operating instructions, the hygiene plan and the skin protection plan must be posted in suitable places in the genetic engineering facility or must otherwise be readily available.
17. Food, beverages and cosmetics must not be stored in workrooms.
18. Eating, drinking, smoking or putting on make-up is not allowed in workrooms.
19. Areas shall be provided for workers to eat and drink without compromising their health.

c. Protective clothing, personal protective equipment and related safety measures

1. Laboratory coats or comparable protective clothing and, if necessary, suitable personal protective equipment (e.g. protective gloves, protective goggles if necessary) must be worn in the genetic engineering facility.
2. Protective clothing used must be stored separately from street clothing. Street clothes, bags, etc. must not be stored in the work area.

II. Safety level 2

a. Structural and technical safety measures

1. The work shall be carried out in delimited and sufficiently large rooms. Depending on the activity, sufficient working space shall be provided for each employee.
2. Laboratory doors should open in the direction of escape and have viewing windows for reasons of personal protection.
3. Surfaces in the workrooms (for example work surfaces, walls, floors and surfaces of the furniture) must be easy to clean and resistant to the substances used as well as to cleaning agents and disinfectants. The work surfaces, adjacent wall surfaces and the floor as well as the wall-floor connection must be liquid-tight.
4. A washbasin, a disinfectant dispenser, a handwash dispenser and a disposable towel dispenser must be available for disinfecting and cleaning hands. These shall be easily accessible and preferably located near the laboratory door. The fittings of the washbasin as well as the disinfectant dispenser and the hand-wash dispenser shall be operable without touching the hand. Facilities for rinsing the eyes shall be available.
5. Work areas should be free of floor drains. Drainage basins in work areas should be provided with an upstand.
6. During work where aerosols may be generated, it must be ensured that these do not enter the work area. The following measures are particularly suitable for this purpose:

   aa) Carrying out work in a microbiological safety cabinet or

   bb) Use of devices and equipment that do not release aerosols, such as centrifuges with aerosol-tight rotors or rotor inserts.

   The exhaust air from the device referred to in sentence 2, double letter aa must be passed through a high-efficiency particulate air filter or be rendered sterile by another tested method. If technical or organisational measures are not sufficient or not applicable, suitable protective equipment must be used in accordance with letter c number 1 be worn.
7. An autoclave or equivalent inactivation or sterilisation equipment with sufficient capacity must be present in the genetic engineering facility or available within the same building.
8. Contaminated process exhaust air must be cleaned by suitable processes such as filtering or thermal post-treatment before it is released into the work area. This also applies, for example, to exhaust air from autoclaves, pumps or bioreactors.

b. Organisational security measures

1. The genetic engineering facility shall be marked as a genetic engineering work area of safety level 2 and additionally with the warning sign "Biohazard".
2. Apart from those involved in the work, only persons authorised by the project manager or by third parties authorised by the project manager have access to the laboratory. This must be indicated by suitable labelling at the access points.
3. Windows and doors must be closed during the work.
4. The rooms should be kept tidy and clean. Only the equipment and materials that are actually needed should be on the work tables. Stocks of

Working materials should only be stored in rooms or cupboards provided for this purpose.

5. Pipetting aids are to be used.
6. Cannulas and pointed or sharp objects should only be used when absolutely necessary. Used needles and used pointed or sharp objects should be collected and disposed of in puncture-proof and tightly closable waste containers. Cannulas must not be put back into their sheaths.
7. Work with genetically modified microorganisms of risk group 2 shall be carried out in such a way that exposure of workers is avoided as far as possible.
8. The identity and purity of the organisms used must be checked regularly if this is necessary for assessing the hazard potential of the organisms. The time intervals of the verification shall depend on the possible hazard potential.
9. Genetically modified organisms must be stored safely in tightly sealed containers.
10. Genetically modified organisms and waste containing genetically modified organisms may only be transported in tightly closed containers that are protected against breakage, can be disinfected and are labelled accordingly. The containers shall be disinfected regularly from the outside and whenever they become contaminated.
11. Where appropriate, ensure safe storage of contaminated laboratory equipment and materials.
12. Infestation with vermin and vectors of genetically modified organisms (for example with rodents and arthropods) shall be prevented; vermin and vectors shall be controlled in an appropriate manner.
13. Before testing, maintenance, cleaning, modification or demolition work is carried out on equipment or facilities that may be contaminated, disinfection of such equipment or facilities must be carried out or arranged for by laboratory personnel.
14. All work surfaces must be disinfected after completion of the activities.
15. After finishing the activity and before leaving the work area, hands must be disinfected, carefully cleaned and cared for according to the skin protection plan.
16. In case of injuries, first aid measures must be initiated immediately. The project manager must be informed and, if necessary, medical assistance must be sought. If there is a possibility that genetically modified organisms have been ingested or if an infection with genetically modified organisms seems possible, the project leader and, if necessary, the attending physician must be informed.
17. If necessary, for example if protective and hygienic measures are suspected to be inadequate, the work area must be checked for the presence of viable organisms used in genetic engineering work.
18. Effective disinfectants and specific disinfection procedures, as well as any necessary aids such as absorbent material, must be available in the event of the escape of genetically modified organisms. A contaminated area (for example, after spillage of organisms) must be closed and disinfected immediately.
19. The operating instructions, the hygiene plan and the skin protection plan must be posted in suitable places in the genetic engineering facility or must otherwise be readily available.
20. Food, beverages and cosmetics must not be stored in workrooms.
21. Eating, drinking, smoking or putting on make-up is not allowed in workrooms.
22. Areas shall be provided for workers to eat and drink without compromising their health.

c. Protective clothing, personal protective equipment and related safety measures

1. In the genetic engineering facility, laboratory coats or comparable protective clothing and, depending on the activity, any suitable personal protective equipment required must be worn.
protective equipment (for example protective gloves, safety goggles, mouth and nose protection or respiratory protection with particle filtering effect) must be worn. The protective clothing and, if necessary, the personal protective equipment are to be provided by the operator. Cleaning of the protective clothing is to be carried out by the operator. Protective clothing and protective equipment must not be worn outside the genetic engineering facility.
2. Separate storage facilities must be provided for protective and street clothing. Street clothes, bags, etc. must not be stored in the work area.

III. Safety level 3

a. Structural and technical safety measures

1. Work must be carried out in enclosed (shielded) and sufficiently large rooms. Depending on the activity, sufficient working space must be ensured for each employee. Technical measures shall prevent unintentional or unauthorised entry into the area.
2. As a rule, an airlock is to be installed through which the laboratory can be entered and exited. The airlock shall be equipped with doors that are locked against each other during intended operation. The outer door must be self-closing. The airlock must contain a hand disinfection device with a disinfectant dispenser. As a rule, in the
The fittings of the wash basin as well as the disinfectant and hand towel dispensers must be operated without touching the hand. The fittings of the washbasin as well as the disinfectant dispenser and the hand-wash dispenser must be operable without touching them by hand. If necessary, a shower must be provided. In justified individual cases, a sluice may be dispensed with.
3. The laboratory area as well as the contaminated part of the ventilation and air-conditioning system up to and including the first high-efficiency particulate air filter stage must be sealable for the purpose of fumigation.
4. Windows must not be openable.
5. Laboratory doors should open in the direction of escape and have viewing windows for reasons of personal protection.
6. Waste water generated in the work area must generally be sterilised as follows: Collection in collection containers and thermal sterilisation or central waste water sterilisation.
No waste water to be sterilised may be produced in the sluice when operated as intended and in compliance with the organisational safety measures.
7. Suitable equipment must be available for communication from the laboratory and the airlock.
8. All surfaces (for example, work surfaces, walls, floors, ceilings and furniture surfaces) must be easy to clean and resistant to the substances used and to cleaning agents and disinfectants. The work surfaces, adjacent wall surfaces and the floor as well as the wall-floor connection must be liquid-tight. As a rule, the floor shall be designed with a cove in a tub function.
9. Disinfectant dispensers that can be operated without touching hands must be available for disinfecting hands. These must be easily accessible and preferably located near the laboratory door. If a washbasin is provided, the taps of the washbasin and the hand-wash dispensers must be operable without touching the hands. Facilities for rinsing the eyes must be available.
10. Working areas should be free of floor drains.

11. If work is done with pathogenic organisms for which airborne transmission cannot be ruled out, the laboratory must be kept under constant negative pressure and the exhaust air must be passed through high-efficiency particulate air filters. The existing negative pressure must be easily verifiable from the outside and also from the inside by the laboratory users and monitored by an alarm device with visual and acoustic signals. The recirculation of contaminated exhaust air into working areas is not permissible. The filter of the ventilation and air-conditioning system must be able to be checked on site in its installed state to see whether it is functioning properly.
12. An emergency power supply shall be installed for safety-relevant equipment such as ventilation systems including ventilation systems, microbiological safety cabinets and emergency call and monitoring equipment. Safety lighting shall be provided so that work can be safely terminated and the work area safely evacuated in the event of a power failure.
13. Work with organisms that may generate aerosols must always be carried out in microbiological safety cabinets or in a comparable facility in terms of personal protection. Non-aerosol-tight equipment must be used in a microbiological safety cabinet or, in the case of large equipment, in an equivalent physical safety device. It must be ensured that the protective properties of the respective safety device are not impaired. Contaminated process exhaust air must be cleaned by suitable processes such as filtering or thermal post-treatment before it is released into the work area. This also applies, for example, to exhaust air from autoclaves, pumps or bioreactors.
14. An autoclave or an equivalent device for sterilisation with sufficient capacity must be available in the laboratory area of the genetic engineering facility.

b. Organisational security measures

1. The genetic engineering facility shall be marked as a genetic engineering work area of safety level 3 and additionally with the warning sign "Biohazard".
2. Access to the genetic engineering facility shall be restricted to those persons whose presence is required to carry out the work and who are authorised to enter. This must be indicated by suitable labelling at the entrances. The project manager is responsible for determining the persons authorised to enter.
3. (omitted)
4. A person may only work alone in the genetic engineering facility if there is an emergency call system that can be operated from inside. It must be possible for the emergency call signal to be triggered voluntarily and automatically.
5. Each laboratory should have its own laboratory equipment.
6. The rooms should be kept tidy and clean. Only the equipment and materials that are actually needed should be on the work tables. Supplies of working materials should only be stored in rooms or cupboards provided for this purpose.
7. Pipetting aids are to be used.
8. Cannulas and pointed or sharp objects should only be used when absolutely necessary. Used needles and used pointed or sharp objects should be collected and disposed of in puncture-proof and tightly closable waste containers. Cannulas must not be put back into their sheaths.
9. The identity and purity of the organisms used must be checked regularly if this is necessary for assessing the hazard potential of the organisms. The time intervals of the verification shall depend on the possible hazard potential.
10. Genetically modified organisms must be stored safely in tightly sealed containers.
11. Work with genetically modified micro-organisms should be carried out in such a way that exposure of workers is avoided as far as possible.

12. Infestation with vermin and vectors of genetically modified organisms (for example with rodents and arthropods) shall be prevented; vermin and vectors shall be controlled in an appropriate manner.
13. Genetically modified organisms and waste containing genetically modified organisms may only be transported in tightly closed, break-proof, disinfectable and appropriately labelled containers. The containers must be regularly disinfected from the outside and must also be disinfected whenever they are contaminated from the outside.
14. Safe storage of contaminated laboratory equipment and materials shall be provided.
15. Before testing, cleaning, repair and modification work is carried out on equipment or facilities that may be contaminated, disinfection of such equipment or facilities must be carried out or arranged for by laboratory personnel.
16. All work surfaces must be disinfected after completion of the activities.
17. After finishing the activity and before leaving the work area, hands must be disinfected, carefully cleaned and cared for according to the skin protection plan.
18. In case of injuries, first aid measures must be initiated immediately. The project manager must be informed and, if necessary, medical assistance must be sought. If there is a possibility that genetically modified organisms have been ingested or if an infection with genetically modified organisms seems possible, the project leader and, if necessary, the attending physician must be informed.
19. If necessary, for example if protective and hygienic measures are suspected to be inadequate, the work area must be checked for the presence of viable organisms used in genetic engineering work.
20. If filters, for example of ventilation and air-conditioning systems or microbiological safety cabinets, are replaced, they must either be installed at the installation site inactivated by fumigation or packed in an airtight container for later sterilisation by an exchange system provided by the device, so that infection of the maintenance personnel and other persons can be excluded.
21. Effective disinfectants and specific disinfection procedures, as well as any necessary aids such as absorbent material, must be available in the event of the escape of genetically modified organisms. A contaminated area (for example, after spillage of organisms) must be closed and disinfected immediately.
22. The operating instructions, the hygiene plan and the skin protection plan must be posted in suitable places in the genetic engineering facility or must otherwise be readily available.
23. Food, beverages and cosmetics may not be stored in work rooms and the airlock.
24. It is not permitted to eat, drink, smoke or put on make-up in work rooms and the airlock.
25. Areas shall be provided for workers to eat and drink without compromising their health.

c. Protective clothing, personal protective equipment and related safety measures

1. In the airlock, suitable protective clothing closed at the front of the torso as well as personal protective equipment (protective gloves and, depending on the activity, further protective equipment such as mouth and nose protection (contact protection), eye protection, respiratory protection with particle filtering effect) must be put on and taken off again after the activity is finished. The protective clothing must be labelled and include closed shoes to be put on according to the activity. The protective clothing and personal protective equipment shall be provided by the operator and sterilised and cleaned or disposed of by the operator after use.

Protective clothing and equipment must not be worn outside the genetic engineering facility.

2. Protective clothing must be stored separately from street clothing. Suitable storage facilities shall be provided for this purpose.

IV. Safety level 4

a. Structural and technical safety measures

1. The laboratory must either be an independent building or, as part of a building, be clearly separated from the generally accessible circulation areas by a corridor or anteroom. The laboratory should have no windows and must have sufficiently large rooms. If windows are present, they must be tight and shatterproof and must not be able to be opened. Technical measures must be taken to prevent any unintentional or unauthorised entry into the laboratory. All doors
of the laboratory must be self-closing. Doors should open in the direction of escape and have viewing windows for reasons of personal protection. Preferably, there should be sight lines from the laboratory to the outside, the material of which is leak-proof and unbreakable. It must only be possible to enter the laboratory via a four-chamber airlock.

2. The airlock must be appropriately pressurised against the working spaces to prevent the escape of air from the insulated part of the laboratory. The airlock must be structured as follows:

   – Outer lock chamber for removing street clothes and putting on undergarments,
   – Personal shower with space for removing undergarments,
   – Suit room for putting on and taking off the full protective suits and
   – inner lock chamber with the chemical shower for disinfecting the full protective suits.

   When used as intended, the doors of the airlock shall be locked against each other. A means shall be provided for the insertion of large-scale equipment or furnishings.

3. Walls, ceilings and floors of the laboratory must be sealed to the outside. All penetrations of supply and disposal lines must be sealed. The floor shall be constructed with a cove in a trough function.

4. All surfaces (for example, work surfaces, walls, floors, ceilings and furniture surfaces) must be easy to clean and resistant to the substances used and to cleaning agents and disinfectants.

5. The laboratory must be ventilated by its own ventilation system, which must be redundant. This system must be designed in such a way that a controlled negative pressure is constantly maintained in the laboratory with respect to the outside world. The negative pressure must increase from the chambers of the airlock to the work room. The negative pressure actually present in the last stage must be easily controllable and verifiable from the inside as well as from the outside. Unacceptable pressure changes must be indicated by a visual and acoustic alarm. It must be possible for the valves of the ventilation and air-conditioning system to reach a safe state even when de-energised.
   Supply and exhaust air must be coupled in such a way that, in the event of fan failure, the air cannot escape uncontrolled from the laboratory under any circumstances.
   The exhaust air from the laboratory must leave the building in such a way that it cannot endanger the environment. Supply and exhaust air from the laboratory must each be passed through two successive high-efficiency particulate air filters. The filters are
   be arranged in such a way that they can be checked on site in their installed state to see whether they are functioning properly. It must be possible to mechanically seal the supply and exhaust air ducts behind the filters so that the filters can be changed without danger.

The supply and exhaust air ducts and the laboratory itself must be gas-tight and suitable for fumigation.

6. The laboratory must be equipped with a pass-through autoclave of sufficient capacity. The condensed water from the autoclave must be sterilised before it enters the general waste water line. Through a suitable arrangement of valves and by venting valves secured by high-efficiency particulate filters, these sterilisation units are to be protected against malfunction. Through a automatic interlock, it must be ensured that the door can only be opened after the sterilisation cycle in the airlock has been completed. An immersion tank or gassable pass-through with interlocking doors shall be provided for the entry and exit of equipment and heat-sensitive material.
7. Waste water generated in the work area must be sterilised as follows: Collection in collection containers and autoclaving or central waste water sterilisation.
8. Supply and disposal lines must be secured against contamination with organisms that may be caused by the backflow of media (for example, for gases, secure with high-efficiency particulate air filters or for liquids, secure with non-return valves). The laboratory must not be connected to a general vacuum system.
9. Work that may generate aerosols must always be carried out in microbiological safety cabinets or in a comparable facility in terms of personal protection. Non-aerosol-tight equipment must be used in a microbiological safety cabinet or, in the case of large equipment, in an equivalent physical safety device. It must be ensured that the protective properties of the respective safety device are not impaired.
10. Centrifuges in which organisms are centrifuged that may only be operated under the conditions of safety level 4 may only be used in microbiological safety cabinets or must be converted accordingly. If this is not possible, the centrifuge rotors must always be opened in the microbiological safety cabinet. It must be ensured that the protective properties of the microbiological safety cabinet are not impaired.
11. The recirculation of contaminated exhaust air into working areas is not permitted.
12. There must be a continuous communication possibility (for example radio connection) from the laboratory.
13. An emergency power supply shall be installed for safety-relevant equipment such as ventilation systems including ventilation systems, emergency call and monitoring equipment, microbiological safety workbenches and the breathing air supply for the externally ventilated full protective suits. Safety lighting shall be provided so that work can be safely terminated and the work area safely evacuated in the event of a power failure.
14. When planning safety-relevant technical systems, such as ventilation and air-conditioning systems, waste water treatment systems or autoclaves, the procedure for malfunctions and maintenance must also be taken into account as a matter of principle. The ventilation and air-conditioning system must be designed in such a way that it is possible to change the filter without violating the safety standard, since otherwise the safety level 4 laboratory would have to be shut down and disinfected before the filter is changed. In the case of larger genetic engineering facilities, it is advisable to divide the ventilation and air-conditioning system in such a way that partial operation is possible in the event of a malfunction or during maintenance work.

b. Organisational security measures

1. The genetic engineering facility shall be marked as a genetic engineering work area of safety level 4 and additionally with the warning sign "Biohazard".
2. Access to the laboratory shall be restricted to those persons whose presence is required to carry out the work and who are authorised to enter. This shall be

by means of suitable labelling at the entrances. The project manager is responsible for determining the persons authorised to enter.

3. (omitted)
4. The rooms should be kept tidy and clean. Only the equipment and materials that are actually needed should be on the work tables. Supplies of working materials should only be stored in rooms or cupboards provided for this purpose.
5. No person shall ever work alone in the laboratory unless there is continuous visual and voice communication (for example, camera and radio communication) and sufficient personnel are available on site in case of an emergency.
6. Each laboratory must have its own laboratory equipment.
7. Pipetting aids are to be used.
8. Cannulas and pointed or sharp objects should only be used when absolutely necessary. Used needles and used pointed or sharp objects should be collected and disposed of in puncture-proof and tightly closable waste containers. Cannulas must not be put back into their sheaths.
9. The identity and purity of the organisms used must be checked regularly if this is necessary for assessing the hazard potential of the organisms. The time intervals of the verification shall depend on the possible hazard potential.
10. Genetically modified organisms must be stored safely in tightly sealed containers.
11. Infestation with vermin and vectors of genetically modified organisms (for example with rodents and arthropods) shall be prevented; vermin and vectors shall be controlled in an appropriate manner.
12. Genetically modified organisms and waste containing genetically modified organisms may only be transported in tightly closed, break-proof, disinfectable and appropriately labelled containers. The containers must be regularly disinfected from the outside and must also be disinfected whenever they are contaminated from the outside.
13. Safe storage of contaminated laboratory equipment and materials shall be provided.
14. Before testing, cleaning, repair and modification work is carried out on equipment or facilities that may be contaminated, disinfection of such equipment or facilities must be carried out or arranged for by laboratory personnel.
15. All work surfaces must be disinfected after completion of the activities.
16. In case of injuries, first aid measures must be initiated immediately. The project manager must be informed and, if necessary, medical assistance must be sought. If there is a possibility that genetically modified organisms have been ingested or if an infection with genetically modified organisms seems possible, the project leader and, if necessary, the attending physician must be informed.
17. If filters, for example of ventilation systems or microbiological safety cabinets, are replaced, they must be inactivated at the place of installation by fumigation and, for the purpose of subsequent sterilisation in the genetic engineering facility, packed in an airtight container by an exchange system provided by the equipment, so that infection of the maintenance personnel and other persons can be excluded.
18. If necessary, for example if protective and hygienic measures are suspected to be inadequate, the work area must be checked for the presence of viable organisms used in genetic engineering work.
19. Effective disinfectants and specific disinfection procedures, as well as any necessary aids such as absorbent material, must be available in the event of the escape of genetically modified organisms. A contaminated area

(for example after spillage of organisms) must be blocked and disinfected immediately.

20. The operating instructions, the hygiene plan and the skin protection plan must be posted in suitable places in the genetic engineering facility or must otherwise be readily available.
21. Food, beverages and cosmetics must not be stored in work rooms and in the airlock.
22. It is not permitted to eat, drink, smoke or put on make-up in work rooms or in the airlock.
23. Areas shall be provided for workers to eat and drink without compromising their health.

c. Protective clothing, personal protective equipment and related safety measures

1. Employees must be protected by a fully ventilated protective suit when working in a safety level 4 laboratory, whereby the breathing air supply must be provided by a self-sufficient air supply. The full protective suit must be provided by the operator and meet the following criteria:
   - Mechanical properties: abrasion-resistant, tear-resistant and made of air-impermeable material,
   - chemical properties: resistant to the disinfectant used in the disinfectant shower and to the chemicals used in the work.

   The full protective suit should preferably have boots welded on. To protect the hands, two pairs of suitable gloves must be worn on top of each other, with at least the outer glove being tightly fastened to the sleeve cuffs of the protective suit.
   Before entering the work area, all clothing as well as watches and jewellery shall be removed to the outer lock chamber and light undergarments shall be worn for put on the full protective suits. The protective suit is put on in the suit room and the laboratory is entered through the inner lock chamber without the disinfection shower is actuated. After leaving the inner lock chamber, it is subjected to a short shower cycle with decontaminant and a short water phase. After completion of the work, a shower cycle is carried out in the disinfection shower, by which the full protective suit is decontaminated. After a final rinse with water, the full protective suit is put away in the suit room and remains there.
   The undergarments are taken off in the personal shower and a hygiene shower is taken if needed.
2. Suitable storage facilities must be provided for other street clothing outside the genetic engineering facility.

B. Safety measures for the production area

I. Safety level 1

a. Structural and technical safety measures

1. The work is to be carried out in demarcated and sufficiently large rooms.
2. Work surfaces and surfaces adjacent to work surfaces, in particular wall surfaces, floors and fixtures, should be easy to clean and must be resistant to the substances used and to cleaning agents and disinfectants.
3. A washbasin with a handwash dispenser and a disposable towel dispenser and, if necessary, a disinfectant dispenser should be provided in the work area.
4. Doors of the production area should open in the direction of escape and have viewing windows for reasons of personal protection.

5. Sufficient inactivation capacity must be available within the site's premises.
6. Depending on their characteristics, viable microorganisms including cell cultures must be enclosed in a system that separates the process from the environment (fermenter).
7. Within the framework of the rules of good microbiological technology, the avoidance of aerosols is of particular importance. In order to prevent larger quantities of genetically modified organisms from escaping from technical equipment via the exhaust air, the following measures can be taken, for example:
   - Filling of the fermenters up to max. 80 % and/or
   - Monitoring of foam formation by sensors and continuous or controlled addition of antifoaming agents and/or
   - Installation of washing and separation devices, such as demisters or centrifugal separators.

   Aerosol formation during sampling, harvesting, addition of material to a fermenter or transfer of material to another fermenter shall be controlled.
8. Stuffing boxes are sufficient for shaft sealing.
9. If pre-treatment of waste water or waste is required, the working area shall be designed in such a way that uncontrolled escape of the genetically modified organisms is prevented, in particular by means of collecting devices whose volumes are based at least on the largest individual volume in each case.

b. Organisational security measures

1. The genetic engineering facility shall be designated as a safety level 1 genetic engineering work area.
2. Windows and doors should be closed during the work.
3. The rooms should be kept tidy and clean. Only the equipment and materials that are actually needed should be on the work tables.
4. During all work, care must be taken to avoid aerosol formation as far as possible. When working with genetically modified organisms of risk group 1 with sensitising or toxic effects, appropriate measures must be taken to minimise exposure of workers. Here it may be
   For example, the avoidance of spore-forming development phases in fungi, the use of a microbiological safety cabinet or the use of respiratory protection.
5. If necessary, apply specific measures to adequately ventilate the work area to minimise air contamination.
6. If necessary, inactivate large amounts of culture liquid before removing it from the fermenter.
7. The identity and purity of the organisms used must be checked regularly if this is necessary for assessing the hazard potential of the organisms. The time intervals of the verification shall depend on the possible hazard potential.
8. The storage of genetically modified organisms must be carried out appropriately.
9. Genetically modified organisms and waste containing genetically modified organisms shall only be transported to other genetic engineering facilities in the building or on the premises in tightly closed containers that are protected against breakage, can be disinfected and are labelled accordingly. The containers must be disinfected regularly from the outside and whenever they are contaminated.

10. Where appropriate, ensure safe storage of contaminated equipment and materials.
11. Infestation with vermin and vectors of genetically modified organisms (for example with rodents and arthropods) shall be prevented; vermin and vectors shall be controlled in an appropriate manner, if necessary.
12. After finishing the activity and before leaving the work area, hands must be disinfected if necessary and carefully cleaned and cared for according to the skin protection plan.
13. In case of injuries, first aid measures must be initiated immediately. The project manager must be informed and, if necessary, medical assistance must be sought. If there is a possibility that genetically modified organisms have been ingested or if an infection with genetically modified organisms seems possible, the project leader and, if necessary, the attending physician must be informed.
14. If necessary, for example if protective and hygienic measures are suspected to be inadequate, the work area shall be checked for the presence of viable organisms used in the application.
15. Effective disinfectants and specific disinfection procedures must be available for the case of leakage of genetically modified organisms, as well as any necessary aids such as absorbent material.
16. The operating instructions, the hygiene plan and the skin protection plan must be posted in suitable places in the genetic engineering facility or must otherwise be readily available.
17. Foodstuffs, luxury foodstuffs and cosmetics must not be stored in production rooms.
18. No eating, drinking, smoking or putting on make-up is allowed in production rooms.
19. Areas shall be provided for workers to eat and drink without compromising their health.

c. Protective clothing, personal protective equipment and related safety measures

1. In production rooms of the genetic engineering facility, protective gowns or comparable protective clothing and, if necessary, suitable personal protective equipment (e.g. protective gloves, protective goggles if necessary) must be worn.
2. Protective clothing used must be stored separately from street clothing. Street clothes, bags, etc. must not be stored in the work area.

II. Safety level 2

a. Structural and technical safety measures

1. The work is to be carried out in demarcated and sufficiently large rooms.
2. Doors of the production area should open in the direction of escape and have viewing windows for reasons of personal protection.
3. Surfaces in the workrooms (for example work surfaces, walls, floors and surfaces of the inventory) must be easy to clean and resistant to the substances used as well as to cleaning agents and disinfectants. The work surfaces, adjacent wall surfaces and the floor as well as the wall-floor connection must be liquid-tight.
4. For disinfection and cleaning of hands, a wash basin, a disinfectant dispenser, a handwashing liquid dispenser and a
Disposable towel dispensers must be available. These shall be easily accessible and preferably located near the door of the production area. The fittings of the washbasin as well as the disinfectant dispenser and the handwashing detergent dispenser

should be operable without touching them by hand. Facilities for rinsing the eyes must be available.

5. The working area should be free of floor drains. Drain basins in work areas should be provided with an upstand.

6. Viable microorganisms, including cell cultures, must be enclosed in a system that separates the process from the environment (for example, fermenter). Closed lines shall be used for inoculation and transfer operations.

7. The working area shall be designed in such a way that uncontrolled escape of the genetically modified organisms is prevented by means of collecting devices whose volumes are oriented at least to the largest individual volume in each case.

8. During work where aerosols may be generated, it must be ensured that these do not enter the work area. The following measures are particularly suitable for this purpose:

   aa) Carrying out work in a microbiological safety cabinet or

   bb) Use of devices and equipment that do not release aerosols, such as centrifuges with aerosol-tight rotors or rotor inserts.

   The exhaust air from the device referred to in sentence 2, double letter aa must be passed through a high-efficiency particulate air filter or be sterilised by another tested method. If technical or organisational measures are not sufficient or not applicable, suitable protective equipment must be worn in accordance with letter c number 1.

9. The technical equipment must be designed in such a way that aerosol formation and leaks are avoided.
   To ensure that no aerosols enter the work area, the following measures are particularly suitable:

   aa) when using centrifuges and separators:

   - Operating the centrifuge in fume cupboards with exhaust air filters or in safety cabinets,
   - Use of dense centrifuges (for example, continuously operated in-line units),
   - Use of a rotor with a tightly closing lid, use of unbreakable and closed centrifuge inserts or containers, or
   - Placing non-breakable centrifuge tubes in closed and breakable inserts,

   bb) when using homogenisers:

   - special design features such as sealing the lid with an O-ring, suitable materials for bowl and lid,
   - Operation and in particular opening of the equipment in fume cupboards or safety cabinets or
   - Use of continuously operated in-line units.

   These measures shall be applied mutatis mutandis to the operation of equipment which serves to achieve a comparable objective and which must therefore be subject to the same requirements.

10. Seals must be such that the unintentional escape of genetically modified organisms is minimised. For example, the following seals are suitable for shaft penetrations:

    - single-acting mechanical seal,
    - Stuffing box with steam or disinfectant barrier.

11. If necessary, the fermenters and other facilities where viable microorganisms of risk group 2 are handled shall be located within a controlled area.
12. If necessary, the controlled area must be sealable to allow fumigation.
13. Sufficient inactivation capacity must be available in the genetic engineering facility or within the same building.
14. Contaminated process exhaust air must be cleaned by suitable processes such as filtering or thermal post-treatment before it is released into the work area. This also applies, for example, to exhaust air from autoclaves, pumps or bioreactors.

b. Organisational security measures

1. The genetic engineering facility shall be marked as a genetic engineering work area of safety level 2 and additionally with the warning sign "Biohazard".
2. Apart from those involved in the work, only persons authorised by the project manager or by third parties authorised by him shall have access to the production area. This must be indicated by suitable labelling at the access points.
3. Windows and doors must be closed during the work.
4. The rooms should be kept tidy and clean. Only the equipment and materials that are actually needed should be on the work tables.
5. Work with genetically modified microorganisms of risk group 2 shall be carried out in such a way that exposure of workers is avoided as far as possible.
6. Equipment used for sampling must be disinfected after each sampling procedure. The formation of aerosols shall be avoided during sampling.
7. Genetically modified organisms shall be inactivated by validated methods or further processed in closed equipment before harvesting. The following are possible processing devices:
   - Separators and decanters in closed design,
   - Filter systems (closed),
   - encapsulated rotary vacuum filter,
   - Chamber filter press.
8. Before opening technical equipment in which genetically modified organisms have been handled, the contaminated parts must be disinfected.
9. If necessary, inactivate large amounts of culture liquid before removing it from the fermenter.
10. The identity and purity of the organisms used must be checked regularly if this is necessary for assessing the hazard potential of the organisms. The time intervals of the verification shall depend on the possible hazard potential.
11. Genetically modified organisms must be stored safely in tightly sealed containers.
12. Genetically modified organisms and waste containing genetically modified organisms may only be transported in tightly closed containers which are protected against breakage, can be disinfected and are labelled accordingly, or via closed, if necessary double-walled pipes (if necessary with leakage detection). The containers must be disinfected regularly from the outside and whenever contamination occurs.
13. Where appropriate, ensure safe storage of contaminated equipment and materials.

14. Infestation with vermin and vectors of genetically modified organisms (for example with rodents and arthropods) shall be prevented; vermin and vectors shall be controlled in an appropriate manner.
15. Before inspection, cleaning, repair and modification work is carried out on equipment or facilities that may be contaminated, disinfection of such equipment or facilities must be carried out or arranged for by the staff of the production area.
16. All work surfaces must be disinfected after completion of the activities.
17. After finishing the activity and before leaving the work area, hands must be disinfected, carefully cleaned and cared for according to the skin protection plan.
18. In case of injuries, first aid measures must be initiated immediately. The project manager must be informed and, if necessary, medical assistance must be sought. If there is a possibility that genetically modified organisms have been ingested or if an infection with genetically modified organisms seems possible, the project leader and, if necessary, the attending physician must be informed.
19. If necessary, for example if protective and hygienic measures are suspected to be inadequate, the work area shall be checked for the presence of viable organisms used in the application.
20. Effective disinfectants and specific disinfection procedures, as well as any necessary aids such as absorbent material, must be available in case of leakage of genetically modified organisms. A contaminated area (for example, after spillage of organisms) must be closed and disinfected immediately.
21. The operating instructions, the hygiene plan and the skin protection plan must be posted in suitable places in the facility or must otherwise be readily available.
22. Foodstuffs, luxury foodstuffs and cosmetics must not be stored in production rooms.
23. No eating, drinking, smoking or putting on make-up is allowed in production rooms.
24. Areas shall be provided for workers to eat and drink without compromising their health.

c. Protective clothing, personal protective equipment and related safety measures

1. In the genetic engineering plant, protective gowns or comparable protective clothing and, depending on the activity, suitable personal protective equipment may be required.
   protective equipment (for example protective gloves, safety goggles, mouth and nose protection or respiratory protection with particle filtering effect) must be worn. The protective clothing and, if necessary, the personal protective equipment are to be provided by the operator. Cleaning of the protective clothing is to be carried out by the operator. Protective clothing and protective equipment must not be worn outside the genetic engineering facility.
2. Separate storage facilities must be provided for protective and street clothing. Street clothes, bags, etc. must not be stored in the work area.

III. Safety level 3

a. Structural and technical safety measures

1. Work must be carried out in demarcated and sufficiently large areas. Technical measures shall prevent unintentional or unauthorised entry into the area.
2. As a rule, an airlock is to be installed through which the production area can be entered and exited. The airlock shall be equipped with doors that are locked against each other during intended operation. The outer door must be self-closing. The sluice must be equipped with a hand disinfection device with

disinfectants. As a rule, a hand-washing basin with a hand-washing agent dispenser and a disposable towel dispenser must be installed in the sluice. The fittings of the washbasin as well as the disinfectant dispenser and the hand-wash dispenser must be operable without touching them by hand. If necessary, a shower must be provided. In justified individual cases, a sluice may be dispensed with.

3. The controlled area as well as the contaminated part of the ventilation system up to and including the first high-efficiency particulate air filter stage shall be sealable for the purpose of fumigation, if necessary.
4. Windows must not be openable.
5. Doors of the production area should open in the direction of escape and have viewing windows for reasons of personal protection.
6. Waste water generated in the work area must generally be sterilised as follows: Collection in collection containers and thermal sterilisation or central waste water sterilisation.
   No waste water to be sterilised may be produced in the sluice when operated as intended and in compliance with the organisational safety measures.
7. Suitable equipment must be available for communication from the production area and the airlock.
8. All surfaces (for example, work surfaces, walls, floors, ceilings and inventory surfaces) must be liquid-tight, easy to clean and resistant to the substances used as well as to cleaning agents and disinfectants. As a rule, the floor is to be executed with a cove in a tub function.
9. Disinfectant dispensers that can be operated without touching hands must be available for disinfecting hands. These must be easily accessible and preferably located near the door of the production area. If a washbasin is provided, the fittings of the washbasin and the hand-wash dispensers must be operable without touching the hands. Facilities for rinsing the eyes must be available.
10. Viable microorganisms, including cell cultures, must be enclosed in a system that separates the process from the environment (e.g. fermenter). Apparatus shall be designed as closed systems in accordance with the state of the art in science and technology. Closed lines shall be used for inoculation and transfer operations.
11. All facilities in which viable microorganisms of risk group 2 or 3 are handled (for example fermenters, centrifuges) must be located within a controlled area.
12. Seals must be designed to prevent the unintentional escape of genetically modified organisms.
13. Contaminated process exhaust air must either be discharged via a suitable filter system, for example with high-performance HEPA filters, or must be sterilised by heating. This applies, for example, to the exhaust air from fermenters, autoclaves, pumps or apparatus for further processing of microorganisms.
14. The working area shall be designed in such a way that an uncontrolled escape of the genetically modified organisms is prevented by collecting devices whose volumes are oriented at least to the largest individual volume in each case.
15. The working area must be free of floor drains.
16. If pathogenic organisms are handled for which transmission through the air cannot be ruled out, the production area must be kept under constant negative pressure and the exhaust air must be passed through high-performance particulate air filters. The existing negative pressure must be easily verifiable from the outside and also from the inside by the users of the production area and must be controlled by a
    be monitored by an alarm device with visual and acoustic signal. The recirculation of contaminated exhaust air into working areas is not permitted. The filter of the ventilation system

The system must be able to be checked on site in its installed state to ensure that it is functioning properly.

17. An emergency power supply shall be installed for safety-relevant equipment such as ventilation systems including ventilation systems, microbiological safety cabinets and emergency call and monitoring equipment. Safety lighting shall be provided so that work can be safely terminated and the work area safely evacuated in the event of a power failure.

18. Sufficient sterilisation capacity must be available in the genetic engineering facility.

b. Organisational security measures

1. The genetic engineering facility shall be marked as a genetic engineering work area of safety level 3 and additionally with the warning sign "Biohazard".

2. Access to the work area is only permitted to authorised persons who have been instructed in the safety requirements. This must be indicated by suitable labelling at the access points. The project manager is responsible for determining the persons authorised to enter.

3. (omitted)

4. A person may only work alone in the genetic engineering facility if there is an emergency call system that can be operated from inside. It must be possible for the emergency call signal to be triggered voluntarily and automatically.

5. Each production area should have its own equipment.

6. Before opening technical equipment in which genetically modified organisms have been handled, the contaminated parts must be disinfected.

7. Equipment used for sampling shall be disinfected after each sampling procedure. Sampling shall be carried out avoiding the formation of aerosols.

8. The rooms should be kept tidy and clean. Only the equipment and materials that are actually needed should be on the work tables.

9. The identity and purity of the organisms used must be checked regularly if this is necessary for assessing the hazard potential of the organisms. The time intervals of the verification shall depend on the possible hazard potential.

10. Work with genetically modified micro-organisms should be carried out in such a way that exposure of workers is avoided as far as possible.

11. Genetically modified organisms shall be stored in tightly sealed containers and in a safe place.

12. Infestation with vermin and vectors of genetically modified organisms (for example with rodents and arthropods) shall be prevented; vermin and vectors shall be controlled in an appropriate manner.

13. Genetically modified organisms and waste containing genetically modified organisms may only be transported on-site in tightly closed containers that are protected against breakage, can be disinfected and are labelled accordingly, or via closed, double-walled pipes with leakage detection.
be disinfected. The containers must be disinfected regularly from the outside, and they must also be disinfected in case of contamination from the outside.

14. Safe storage of contaminated equipment and materials shall be provided.

15. Large quantities of culture liquid shall be sterilised by validated procedures before being removed from the fermenter. Before harvesting, the genetically modified organisms shall be sterilised or further processed in closed apparatus.

16. Before inspection, cleaning, repair and modification work is carried out on possibly contaminated equipment or facilities, the disinfection of such equipment or facilities must be carried out or arranged for by the staff of the production area.
17. All work surfaces must be disinfected after completion of the activities.
18. After finishing the activity and before leaving the work area, hands must be disinfected, washed carefully and cared for according to the skin protection plan.
19. In case of injuries, first aid measures must be initiated immediately. The project manager must be informed and, if necessary, medical assistance must be sought. If there is a possibility that genetically modified organisms have been ingested or if an infection with genetically modified organisms seems possible, the project leader and, if necessary, the attending physician must be informed.
20. If necessary, for example if protective and hygienic measures are suspected to be inadequate, the work area must be checked for the presence of viable organisms used in genetic engineering work.
21. If filters, for example of ventilation and air-conditioning systems or microbiological safety cabinets, are replaced, they must either be installed at the installation site inactivated by fumigation or packed in an airtight container for later sterilisation by an exchange system provided by the device, so that infection of the maintenance personnel and other persons can be excluded.
22. Effective disinfectants and specific disinfection procedures, as well as any necessary aids such as absorbent material, must be available in the event of the escape of genetically modified organisms. A contaminated area (for example, after spillage of organisms) must be closed and disinfected immediately.
23. The operating instructions, the hygiene plan and the skin protection plan must be posted in suitable places in the genetic engineering facility or must otherwise be readily available.
24. Foodstuffs, luxury foodstuffs and cosmetics must not be stored in production rooms and the airlock.
25. It is not permitted to eat, drink, smoke or put on make-up in the production rooms and the airlock.
26. Areas shall be provided for workers to eat and drink without compromising their health.

c. Protective clothing, personal protective equipment and related safety measures

1. In the airlock, suitable protective clothing closed at the front of the torso as well as personal protective equipment (protective gloves and, depending on the activity, further protective equipment such as mouth and nose protection (contact protection), eye protection, respiratory protection with particle filtering effect) must be put on and taken off again after the activity is finished. The protective clothing must be labelled and include closed shoes to be put on according to the activity. Protective clothing and personal protective equipment shall be provided by the operator and sterilised and cleaned or disposed of by the operator after use. Protective clothing and protective equipment must not be worn outside the genetic engineering facility.
2. Protective clothing must be stored separately from street clothing. Suitable storage facilities shall be provided for this purpose.

IV. Safety level 4

a. Structural and technical safety measures

1. The production area must either be an independent building or, as part of a building, clearly separated from the generally accessible areas by a corridor or anteroom.

traffic areas must be separated. The production area should have no windows and must have sufficiently large rooms. If windows are present, they must be tight and unbreakable and must not be able to be opened. Technical measures must be taken to prevent any unintentional or unauthorised entry into the production area. All doors of the production area must be self-closing, should swing open in the direction of escape and have viewing windows for reasons of personal protection. Preferably, viewing windows should
to the outside, the material of which is leak-proof and unbreakable. Entry to the production rooms must only be possible via a four-chamber airlock.

2. The airlock must be appropriately pressurised against the production areas to prevent air from escaping from the isolated part of the production area. The airlock must be structured as follows:

   – Outer lock chamber for removing street clothes and putting on undergarments,
   – Personal shower with space for removing undergarments,
   – Suit room for putting on and taking off the full protective suits and
   – inner lock chamber with the chemical shower for disinfecting the full protective suits.

   When used as intended, the doors of the airlock shall be locked against each other. A means shall be provided for the insertion of large-scale equipment or furnishings.

3. Walls, ceilings and floors of the production area must be sealed to the outside. All penetrations of supply and disposal lines must be sealed. The floor must be constructed with a cove in a trough function.

4. All surfaces (for example, work surfaces, walls, floors, ceilings and inventory surfaces) must be easy to clean and resistant to the substances used and to cleaning agents and disinfectants.

5. The production area must be ventilated by its own ventilation system, which must be redundant. This system must be designed in such a way that a controlled negative pressure is constantly maintained in the production area with respect to the outside world. The negative pressure shall be maintained from the chambers of the airlock to to the working space increase in each case. The negative pressure actually present in the last stage must be easily controllable and verifiable from the inside as well as from the outside. Unacceptable pressure changes must be indicated by a visual and acoustic alarm. It must be possible for the valves of the ventilation and air-conditioning system to reach a safe state even when de-energised.
   Supply and exhaust air must be coupled in such a way that, in the event of fan failure, the air cannot escape in an uncontrolled manner under any circumstances. The exhaust air from the production area must leave the building in such a way that it cannot endanger the environment. Supply air and exhaust air from the production area must each be routed through two successive high-efficiency particulate air filters. The filters must be arranged so that they
   can be checked on site in installed condition to see whether they are functioning properly. It must be possible to mechanically seal the supply and exhaust air lines behind the filters in order to enable the filters to be changed without danger.
   The supply and exhaust air ducts and the production area itself must be gas-tight and suitable for fumigation.

6. Supply and disposal lines must be secured against contamination with organisms that may be caused by the backflow of media (for example, for gases, secure with high-efficiency particulate air filters or for liquids, secure with non-return valves).
   The production area must not be connected to a general vacuum system.

7. Viable microorganisms, including cell cultures, must be enclosed in a system that separates the process from the environment (for example, fermenter). All containers and apparatus must be designed according to the state of the art in science.

and technology as closed systems. Closed lines must be used for inoculation and transfer operations.

8. All facilities where viable microorganisms of risk groups 2 to 4 are handled must be located within a controlled area.

9. Waste water generated in the work area must be sterilised as follows: Collection in collection containers and thermal sterilisation or central waste water sterilisation. The genetic engineering facility must be designed in such a way that the entire volume of waste water from fermenters and drains can be collected and sterilised.

10. Seals must be designed in such a way that the unintentional escape of genetically modified organisms is reliably prevented.

11. Centrifuges in which organisms are centrifuged that may only be operated under the conditions of safety level 4 may only be used in microbiological safety cabinets or must be modified accordingly. If this is not possible, the centrifuge rotors must always be opened in the microbiological safety cabinet. It must be ensured that the protective properties of the microbiological safety cabinet are not impaired.

12. Contaminated process exhaust air must either be discharged via a suitable filter system, for example with high-performance HEPA filters, or must be sterilised by heating. This applies, for example, to the exhaust air from fermenters, autoclaves, pumps or equipment for further processing of microorganisms.

13. The recirculation of contaminated exhaust air into working areas is not permitted.

14. There must be a continuous communication facility (for example, radio link) from the production area.

15. Safety circuits must be provided for the entire work area to prevent the escape of genetically modified organisms even in the event of a power failure. These can be, for example:

    – Forced switching of valves to the safe state,
    – Check valves on supply lines,
    – Emergency power supply.

    Safety lighting shall be provided so that work can be safely terminated and the work area safely exited in the event of a power failure.

16. An emergency power supply shall be installed for safety-relevant equipment such as ventilation systems, including ventilation system, microbiological safety cabinets, emergency call and monitoring equipment and the breathing air supply of the forced-ventilated full protective suits.

17. Areas where aerosols can form must be spatially separated. The exhaust air from the extractors must be routed through double high-efficiency particulate air filters or work must be carried out in microbiological safety cabinets.

18. The genetic engineering facility must have sufficient sterilisation capacity.

19. An immersion tank or fumigatable pass-through with interlocking doors shall be provided for the entry and exit of equipment and heat-sensitive material.

20. Closed systems are to be used for sampling. The sampling vessel must be protected in particular from mechanical damage.

21. When planning safety-relevant technical systems such as ventilation and air-conditioning systems, waste water treatment systems or autoclaves, the procedure for malfunctions and maintenance must also be taken into account as a matter of principle. The ventilation and air-conditioning system must be designed in such a way that a filter change is possible without violating the safety standard, as the production area of safety level 4 would otherwise have to be shut down and disinfected before the filter change. At
    For larger genetic engineering systems, it is advisable to install the ventilation system in such a way that it is

that partial operation is possible in the event of a malfunction or during maintenance work.

b. Organisational security measures

1. The genetic engineering facility shall be marked as a genetic engineering work area of safety level 4 and additionally with the warning sign "Biohazard".
2. Access to the production area shall be restricted to those persons whose presence is required to carry out the work and who are authorised to enter. This shall be indicated by suitable marking at the entrances. The project manager is responsible for determining the persons authorised to enter.
3. (omitted)
4. The rooms should be kept tidy and clean. Only the equipment and materials that are actually needed should be on the work tables.
5. No person shall ever work alone in the production area unless there is continuous visual and voice communication (for example camera and radio communication) and sufficient personnel are available on site in case of an emergency.
6. Each production area must have its own equipment.
7. The identity and purity of the organisms used must be checked regularly if this is necessary for assessing the hazard potential of the organisms. The time intervals of the verification shall depend on the possible hazard potential.
8. Genetically modified organisms must be stored safely in tightly sealed containers.
9. Infestation with vermin and vectors of genetically modified organisms (for example with rodents and arthropods) shall be prevented; vermin and vectors shall be controlled in an appropriate manner.
10. Genetically modified organisms and waste containing genetically modified organisms may only be transported internally in tightly closed containers which are protected against breakage, can be disinfected and are labelled accordingly, or via closed, double-walled pipes with leakage detection. The containers must be regularly disinfected from the outside, and they must also be disinfected from the outside whenever they are contaminated.
11. Safe storage of contaminated equipment and materials shall be provided.
12. Before inspection, cleaning, repair and modification work on contaminated equipment or facilities, disinfection of such equipment or facilities must be carried out or arranged for by the staff of the production area.
13. All work surfaces must be disinfected after completion of the activities.
14. Large quantities of culture liquid must be sterilised before being removed from the fermenter. Before harvesting, the genetically modified organisms shall be sterilised or further processed in closed and disinfectable equipment.
15. Equipment used for sampling shall be disinfected after each sampling operation.
16. In case of injuries, first aid measures must be initiated immediately. The project manager must be informed and, if necessary, medical assistance must be sought. If there is a possibility that genetically modified organisms have been ingested or if an infection with genetically modified organisms seems possible, the project leader and, if necessary, the attending physician must be informed.
17. If filters, for example of ventilation systems or microbiological safety cabinets, are replaced, they must be inactivated at the place of installation by fumigation and, for the purpose of subsequent sterilisation in the genetic engineering facility, packed in an airtight container by an exchange system provided by the equipment.

so that infection of the maintenance staff and other persons can be excluded.

18. Before opening technical equipment in which genetically modified organisms have been handled, the contaminated parts must be disinfected.
19. If necessary, for example if protective and hygienic measures are suspected to be inadequate, the work area must be checked for the presence of viable organisms used in genetic engineering work.
20. Effective disinfectants and specific disinfection procedures, as well as any necessary aids such as absorbent material, must be available in the event of the escape of genetically modified organisms. A contaminated area (for example, after spillage of organisms) must be closed and disinfected immediately.
21. The operating instructions, the hygiene plan and the skin protection plan must be posted in suitable places in the genetic engineering facility or must otherwise be readily available.
22. Foodstuffs, luxury foodstuffs and cosmetics must not be stored in production rooms and the airlock.
23. It is not permitted to eat, drink, smoke or put on make-up in production rooms and the airlock.
24. Areas shall be provided for workers to eat and drink without compromising their health.

c. Protective clothing, personal protective equipment and related safety measures

1. Employees must be protected by a fully ventilated protective suit when working in a safety level 4 production area, whereby the
breathing air supply must be provided by a self-sufficient air supply. The self-contained full protective suit must be provided by the operator and meet the following criteria:
   - Mechanical properties: abrasion-resistant, tear-resistant and made of air-impermeable material,
   - Chemical properties: resistant to the disinfectant used in the disinfectant shower.

   The full protective suit should preferably have boots welded on. To protect the hands, two pairs of suitable gloves must be worn on top of each other, with at least the outer glove being tightly fastened to the sleeve cuffs of the protective suit.
   Before entering the work area, all clothing, watches and jewellery shall be removed to the outer lock chamber and light undergarments for the full protective suits shall be put on. The protective suit shall be put on in the suit room and
   the production area is entered through the inner lock chamber without operating the disinfection shower. After leaving the inner lock chamber, it is subjected to a short shower cycle with decontaminant and a short water phase. After completion of the work, a shower cycle is carried out in the disinfection shower, by which the full protective suit is decontaminated. After a final rinse with water, the full protective suit is put away in the suit room and remains there.
   The undergarments are taken off in the personal shower and a hygiene shower is taken if needed.
2. Suitable storage facilities must be provided for other street clothing outside the genetic engineering facility.

Annex 3 (to § 15)
Security measures for greenhouses

(Source: Federal Law Gazette I 2019, 1269 - 1275)

Pursuant to § 15, paragraph 1, sentence 2, the safety measures for greenhouses shall be observed accordingly for climate chambers. Pursuant to Section 15(2), if work with genetically modified microorganisms is carried out in greenhouses, the requirements of Annex 2 for the laboratory area for the corresponding safety levels shall be observed accordingly in addition to the requirements of this Annex.

I. Safety level 1

a. Structural and technical safety measures

1. The floor of the greenhouse can be made of gravel or other greenhouse-typical material. Straw beds are also suitable. However, at least the walkways should be paved (e.g. concrete). It should be possible to collect run-off water if it may contain genetically modified organisms.
2. The windows and other openings of the greenhouse may be opened for ventilation purposes and in principle do not require any special protective device to keep out or exclude pollen, micro-organisms or small flying animals (for example arthropods or birds). If the discharge of genetically modified organisms is possible to such an extent that it may endanger the objects of protection, safety measures must be taken against the discharge of genetically modified organisms or
against the intrusion of animals that can spread genetically modified organisms. These can be, for example, nets to prevent the spread of flyable seeds or against birds or insects.
3. There shall be an easily accessible washing facility for cleaning hands with a handwash dispenser and, if necessary, a disposable towel dispenser and a disinfectant dispenser.

b. Organisational security measures

1. The genetic engineering facility shall be designated as a safety level 1 genetic engineering work area.
2. Plants used in genetic engineering experiments shall be rendered incapable of reproduction by suitable methods, in particular by cutting off the reproductive organs, before they are harmlessly disposed of outside the greenhouse but on the operator's surrounding premises. Generative or reproductive parts of the plants shall be inactivated within the greenhouse or in another genetic engineering facility within the premises of the site.
3. A suitable programme, adapted to the experimental plants, shall be established for the successful control of plant diseases, weeds, arthropods and rodents.
4. The discharge of genetically modified organisms from the greenhouse shall be reduced to the lowest possible level by appropriate measures.
5. In case of injuries, first aid measures must be initiated immediately. The project manager must be informed and, if necessary, medical assistance must be sought. If there is a possibility that genetically modified organisms have been ingested or if an infection with genetically modified organisms seems possible, the project leader and, if necessary, the attending physician must be informed.
6. The operating instructions, the hygiene plan and the skin protection plan must be posted in suitable places in the facility or must otherwise be readily available.
7. Plants must be easily identifiable, in particular with regard to their genetic modification or with regard to the assigned genetic work.
8. Food, beverages and cosmetics must not be stored in workrooms.
9. Eating, drinking, smoking or putting on make-up is not allowed in workrooms.
10. Areas shall be provided for workers to eat and drink without compromising their health.

c. Protective clothing, personal protective equipment and related safety measures

1. Suitable, i.e. activity-related, protective clothing must be worn in the greenhouse. Protective clothing should not be worn outside the greenhouse in order to prevent the possibility of the release of genetically modified organisms through clothing.
2. Used protective clothing must be stored separately from street clothes. Street clothes, bags or similar must not be stored in the work area.

II. Safety level 2

a. Structural and technical safety measures

1. The greenhouse must be a solid structure with a continuous waterproof and weatherproof covering (for example, resistant to hail). It should be level so that no surface water can penetrate and have self-closing, lockable doors. The floor in the greenhouse must be easy to clean, impervious to liquids and resistant to the substances, cleaning agents and disinfectants used. Run-off water must be reduced to the lowest possible level, if a transfer of genetically modified organisms can take place via the soil. Run-off water that contains or could contain genetically modified organisms shall be collected and inactivated. Provided that the spread of genetically modified organisms via the soil can be ruled out, the floor of the greenhouse may consist of gravel or other greenhouse-typical material. However, at least the walkways should be paved (e.g. concrete).
2. The discharge of genetically modified plants, including pollen or seeds, into the open air through windows, doors and other openings of the greenhouse shall be prevented by appropriate structural or technical measures. Windows and other openings of the greenhouse may only be opened for ventilation purposes if they are equipped with devices to protect against birds and arthropods. Special protective devices to ward off pollen or micro-organisms from outside are generally not required. If blow-out fans are used, the ingress of arthropods shall be kept to a minimum. Air dampers and fans are to be designed in such a way that they only open when the fan is started up.
3. Doors should swing open in the direction of escape.
4. A washbasin, a disinfectant dispenser, a handwash dispenser and a disposable towel dispenser must be provided for disinfecting and cleaning hands. These shall be easily accessible and preferably located near the access area. The fittings of the washbasin as well as the disinfectant dispenser and the hand-wash dispenser shall be operable without touching the hand. Facilities for rinsing the eyes shall be provided.
5. An autoclave or equivalent device for inactivation or sterilisation with sufficient capacity must be available in the genetic engineering facility or, in exceptional cases, in the building in which the genetic engineering facility is located.
6. If necessary, filters must be provided in the exhaust air system of the climate chambers.

b. Organisational security measures

1. The genetic engineering facility shall be marked as a genetic engineering work area of safety level 2 and additionally with the warning sign "Biohazard".
2. If necessary, access to the greenhouse shall be via a separate room with two lockable doors in front of it. Apart from the persons involved in the experiments, only persons authorised by the project manager or by third parties authorised by the project manager have access to the greenhouse. This must be indicated by suitable labelling at the entrances.
3. Work equipment that has been in direct contact with genetically modified organisms must be disinfected or autoclaved before cleaning if genetically modified organisms could have been transmitted during this contact.
4. Genetically modified organisms and waste containing genetically modified organisms may only be placed in tightly closed, protected against breakage, disinfectable and

be transported in appropriately labelled containers. The containers must be disinfected regularly from the outside and whenever they are contaminated.

5. A suitable programme, adapted to the experimental plants, shall be established for the successful control of plant diseases, weeds, arthropods and rodents.
6. The discharge of genetically modified organisms from the greenhouse shall be reduced to the lowest possible level by appropriate measures. In particular, the measures pursuant to Article 7(4) shall be taken into account.
7. In case of injuries, first aid measures must be initiated immediately. The project manager must be informed and, if necessary, medical assistance must be sought. If there is a possibility that genetically modified organisms have been ingested or if an infection with genetically modified organisms seems possible, the project leader and, if necessary, the attending physician must be informed.
8. After finishing the activity and before leaving the work area, hands must be disinfected, carefully cleaned and cared for according to the skin protection plan.
9. The operating instructions, the hygiene plan and the skin protection plan must be posted in suitable places in the facility or must otherwise be readily available.
10. Plants must be easily identifiable, in particular with regard to their genetic modification or with regard to the assigned genetic work.
11. Food, beverages and cosmetics must not be stored in workrooms.
12. Eating, drinking, smoking or putting on make-up is not allowed in workrooms.
13. Areas shall be provided for workers to eat and drink without compromising their health.

c. Protective clothing, personal protective equipment and related safety measures

1. Suitable activity-related protective clothing and suitable personal protective equipment must be worn in the greenhouse. The protective clothing and personal protective equipment shall be provided by the operator. Cleaning of the protective clothing is to be carried out by the operator. Protective clothing and protective equipment must not be worn outside the genetic engineering facility.
2. Separate storage facilities must be provided for protective and street clothing. Street clothes, bags, etc. must not be stored in the work area.

III. Safety level 3

a. Structural and technical safety measures

1. The greenhouse must be a solid, self-contained building with a continuous roof and waterproof and weatherproof covering (for example, resistant to hail). It must be separated from the freely accessible areas. The building should be level so that no surface water can penetrate and have self-closing, lockable doors. Controlled access to the greenhouse must be ensured by suitable technical measures. The floor of the greenhouse shall be made of water-impermeable material with provisions for the collection and sterilisation of waste water. This is not necessary if the experimental plants are cultivated in closed systems where collection and sterilisation of the waste water is possible.
2. As a rule, an airlock is to be installed through which the greenhouse can be entered and exited. The airlock shall be equipped with doors that are locked against each other when used as intended. The outer door must be self-closing. The
The first airlock must contain a hand disinfection device with a disinfectant dispenser. As a rule, a hand-washing basin with a hand-washing agent dispenser and a disposable towel dispenser must be installed in the sluice. The fittings of the washbasin as well as
the disinfectant and handwash dispensers must be operable without touching the hands. If necessary, a shower must be installed. In justified individual cases, an airlock may be dispensed with.

3. Windows and other openings to the outside must be closed and sealed. Shatterproof glass shall be used.
4. Doors should swing open in the direction of escape.
5. Waste water generated in the work area must generally be sterilised as follows: Collection in collection containers and thermal sterilisation or central waste water sterilisation.
No waste water to be sterilised may be produced in the sluice when operated as intended and in compliance with the organisational safety measures.
6. The greenhouse installation shall be surrounded by a security fence or protected by an equivalent security system.
7. All surfaces (for example, work surfaces, walls, floors, ceilings and inventory surfaces) must be easy to clean and resistant to the substances used as well as to cleaning agents and disinfectants. The floor shall normally be constructed with coving in a tub function. All penetrations in the structures and surfaces, such as pipe and power lines, shall be sealed.
8. Vacuum lines shall be secured by high efficiency HEPA filters or equivalent filters and closures for liquid disinfectants.
9. A separate ventilation and exhaust system must be provided. The system shall provide for the pressure differences and air flow direction necessary to ensure air supply from outside into the greenhouse.
10. When working with pathogenic organisms for which transmission through the air cannot be ruled out, the following shall apply with regard to negative pressure control and the
The requirements of Annex 2, Part A, shall be met by the ventilation system. If pathogenic organisms are handled for which airborne transmission cannot be ruled out, the exhaust air from the greenhouse shall be routed to the outside through high-efficiency particulate air filters. Ventilation fans shall be equipped with backflow dampers that close when the ventilation fan is switched off. The aeration fans shall be operated in such a way as to ensure an inward air flow.
11. A washbasin, a disinfectant dispenser, a handwash dispenser and a disposable towel dispenser must be provided for disinfecting and cleaning hands. These shall be easily accessible and preferably located near the access area. The fittings of the washbasin as well as the disinfectant dispenser and the hand-wash dispenser shall be operable without touching the hand. Facilities for rinsing the eyes shall be provided.
12. An autoclave or an equivalent device for sterilisation with sufficient capacity must be available in the greenhouse.
13. If climate chambers are used, their exhaust air must be filtered by means of high-efficiency particulate filters.
14. Suitable equipment must be available for communication from the greenhouse and the airlock.

b. Organisational security measures

1. The genetic engineering facility shall be marked as a genetic engineering work area of safety level 3 and additionally with the warning sign "Biohazard".
2. It must be ensured that only authorised persons can enter the greenhouse. Furthermore, access must be restricted to those persons whose presence is required to carry out the work. This must be indicated by suitable labelling. The project manager is responsible for determining the persons authorised to enter.

2a. Doors must be closed during the work.

3. Genetically modified organisms and waste containing genetically modified organisms may only be disposed of in tightly closed, disinfectable containers that are protected against breakage.
and appropriately labelled containers. The containers must be disinfected regularly from the outside, and they must also be disinfected from the outside whenever they are contaminated.

4. Work equipment that has been in direct contact with genetically modified organisms must be disinfected or autoclaved before cleaning if genetically modified organisms could have been transmitted during this contact.
5. A suitable programme, adapted to the experimental plants, shall be established for the successful control of plant diseases, weeds, arthropods and rodents.
6. Plants infected with airborne organisms shall be kept, if possible, in devices (climatic chambers, climatic cabinets, etc.) which prevent the release of these organisms into the ambient air and their transmission to other plants.
7. The discharge of genetically modified plants from the greenhouse shall also be reduced to the lowest possible level by organisational measures. In this context, the measures pursuant to Article 7(4) shall be taken into account.
8. Plants must be easily identifiable, in particular with regard to their genetic modification or with regard to the assigned genetic work.
9. If filters, for example of ventilation systems, are replaced, they must either be inactivated at the place of installation by fumigation or packed directly in an airtight container for later sterilisation by a replacement system provided by the unit, so that there is no risk to maintenance personnel and other persons.
10. A person may only work alone in the genetic engineering facility if there is an emergency call system that can be operated from inside. It must be possible for the emergency call signal to be triggered voluntarily and automatically.
11. Before testing, cleaning, repair and modification work is carried out on equipment or facilities that may be contaminated, the disinfection of this equipment and facilities must be carried out or arranged for by the personnel of the genetic engineering facility.
12. In case of injuries, first aid measures must be initiated immediately. The project manager must be informed and, if necessary, medical assistance must be sought. If there is a possibility that genetically modified organisms have been ingested or if an infection with genetically modified organisms seems possible, the project leader and, if necessary, the attending physician must be informed.
13. After finishing the activity and before leaving the work area, hands must be disinfected, carefully cleaned and cared for according to the skin protection plan.
14. The operating instructions, the hygiene plan and the skin protection plan must be posted in suitable places in the facility or must otherwise be readily available.
15. Food, beverages and cosmetics must not be stored in work rooms and the airlock.
16. It is not permitted to eat, drink, smoke or put on make-up in work rooms and the airlock.
17. Areas shall be provided for workers to eat and drink without compromising their health.

c. Protective clothing, personal protective equipment and related safety measures

1. In the airlock, suitable activity-related protective clothing closed at the front of the torso as well as personal protective equipment (protective gloves and, depending on the activity, further protective equipment such as mouth and nose protection, if necessary) must be worn.
(contact protection), eye protection, respiratory protection with particle filtering effect) and must be taken off again after the end of the activity. The protective clothing must be labelled and include closed shoes to be put on according to the activity. The protective clothing and personal protective equipment shall be provided by the operator and sterilised and cleaned or disposed of by the operator after use.
Protective clothing and equipment must not be worn outside the genetic engineering facility.
2. Protective clothing must be stored separately from street clothing. Suitable storage facilities shall be provided for this purpose.

IV. Safety level 4

a. Structural and technical safety measures

1. The greenhouse must be a permanent structure and consist of either a separate building or a clearly defined and isolated zone within a building. It must be located in such a way that no surface water can penetrate and have self-closing, lockable doors. Controlled access to the greenhouse must be ensured by appropriate technical measures. Entry to the greenhouse must only be possible via a four-chamber airlock.
2. Windows and other openings to the outside must be closed and sealed. Shatterproof glass shall be used. Preferably, there shall be lines of sight from the work area to the outside that allow observation of the work from the outside.
3. Doors should swing open in the direction of escape.
4. The greenhouse shall be surrounded by a security fence or protected by an equivalent security system.
5. The floor of the greenhouse shall be made of waterproof material with provisions for the collection and sterilisation of waste water.
6. The walls, floor and ceiling of the greenhouse must be constructed in such a way that they form a gas-impermeable inner enclosure which allows fumigation and provides security against arthropods. All openings shall be made gas-tight. The glass surfaces shall in principle have the same break resistance and fire resistance as the surrounding walls.
7. All surfaces (for example, work surfaces, walls, floors, ceilings and inventory surfaces) must be easy to clean and resistant to the substances used as well as to cleaning agents and disinfectants. The floor shall generally be executed with coving in a tub function. All penetrations in the structures and surfaces, such as pipe and power lines, shall be sealed.
8. The airlock must be appropriately pressurised against the working spaces to prevent air from escaping from the insulated part of the greenhouse. The airlock must be structured as follows:
   - Outer lock chamber for removing street clothes and putting on undergarments,
   - Personal shower with space for removing undergarments,
   - Suit room for putting on and taking off the full protective suits and
   - inner lock chamber with the chemical shower for disinfecting the full protective suits.

   When used as intended, the doors of the airlock shall be locked against each other. A means shall be provided for the insertion of large-scale equipment or furnishings.
9. The greenhouse must be ventilated by its own ventilation system, which must be redundant. The system must be designed in such a way that a controlled negative pressure is maintained in the greenhouse at all times with respect to the outside world. The
   Negative pressure must increase from the chambers of the airlock to the working area. The actually existing negative pressure must be easily controllable and verifiable from the inside as well as from the outside. Unacceptable pressure changes must be indicated by a visual and acoustic alarm. The valves of the ventilation and air-conditioning system must be able to reach a safe state even when de-energised.
   Supply and exhaust air must be coupled in such a way that, in the event of fan failure, the air cannot escape uncontrolled from the greenhouse under any circumstances.
   The exhaust air from the greenhouse must leave the building in such a way that it cannot endanger the environment. Supply air and exhaust air from the greenhouse must each pass through two successive high-efficiency particulate air filters. The filters must be arranged in such a way that they can be checked on site in their installed state to see whether they are functioning properly. Supply and exhaust air pipes must be mechanically tightly sealable behind the filters to enable the filters to be changed without danger.

The supply and exhaust air ducts and the greenhouse itself must be gas-tight and suitable for fumigation.

10. The ventilation fans shall be equipped with backflow dampers that close when the ventilation fan is switched off. The ventilation fans shall be operated in such a way as to ensure an inward air flow.

11. Supply and disposal lines must be secured against contamination with organisms that may be caused by the backflow of media (for example, in the case of gases, secure with high-efficiency particulate air filters or, in the case of liquids, secure with non-return valves). The greenhouse must not be connected to a general vacuum system. Vacuum lines must be secured by high-efficiency particulate air filters or by equivalent filters and closures for liquid disinfectants.

12. The greenhouse must be equipped with a pass-through autoclave. An automatic interlock must ensure that the door can only be opened after the sterilisation cycle has been completed. The condensed water from the autoclave must be sterilised before it enters the general waste water pipe. These sterilisation units must be protected against malfunction by a suitable arrangement of valves and by vent valves secured with high-efficiency particulate air filters. An immersion tank or gassable pass-through with interlocking doors shall be provided for the entry and exit of equipment and heat-sensitive material.

13. There must be a continuous means of communication (for example, radio link) from the greenhouse.

14. For safety-relevant equipment such as ventilation systems including ventilation system, An emergency power supply must be installed for emergency call and monitoring equipment. Safety lighting shall be provided so that work can be safely terminated and the work area safely evacuated in the event of a power failure.

15. If climate chambers are used, their exhaust air must be filtered by means of high-efficiency particulate filters.

16. When planning safety-relevant technical systems, such as ventilation systems, waste water treatment systems and autoclaves, the procedure for malfunctions and maintenance must also be taken into account. The ventilation and air-conditioning system must be designed in such a way that it is possible to change the filter without violating the safety standard, since the greenhouse of safety level 4 would otherwise have to be shut down and disinfected before the filter is changed. In the case of larger systems, it is expedient to, subdivide the ventilation and air-conditioning system in such a way that partial operation is possible in the event of a malfunction or during maintenance work.

b. Organisational security measures

1. The genetic engineering facility shall be marked as a genetic engineering work area of safety level 4 and additionally with the warning sign "Biohazard".

2. It must be ensured that only authorised persons can enter the greenhouse. Furthermore, access must be restricted to those persons whose presence is required to carry out the work. This must be indicated by suitable labelling. The project manager is responsible for determining the persons authorised to enter.

3. (omitted)

4. Genetically modified organisms and waste containing genetically modified organisms may only be transported in tightly closed containers that are protected against breakage, can be disinfected and are labelled accordingly. The containers shall be disinfected regularly and in the event of any external contamination.

5. Work equipment that has been in direct contact with genetically modified organisms must be disinfected or autoclaved before cleaning if genetically modified organisms could have been transmitted during this contact.

6. A suitable programme, adapted to the experimental plants, shall be established for the successful control of plant diseases, weeds, arthropods and rodents.

7. A record of the material brought into or out of the greenhouse shall be kept by the project leader or a third party authorised by the project leader. Experimental organisms to be moved into or out of the greenhouse in a viable or intact state shall be placed in an unbreakable, sealed primary container and then enclosed in a disinfected, sealed transport container.
8. Plants infected with airborne organisms shall be kept, if possible, in devices (climatic chambers, climatic cabinets, etc.) which prevent the release of these organisms into the ambient air and their transmission to other plants.
9. It must be ensured that there is no discharge of genetically modified plants and their biological material from the greenhouse.
10. Arthropods and other macro-organisms used in connection with genetic engineering operations which require physical containment of this safety level shall be placed in appropriate containers. Where required by the genetically modified organism, the tests shall be carried out in the containers holding the motile macro-organisms to which the genetically modified organism is applied.
11. Waste water generated in the work area must be sterilised as follows: Collection in collection containers and autoclaving or central waste water sterilisation.
12. Plants must be easily identifiable, in particular with regard to their genetic modification or with regard to the assigned genetic work.
13. No person shall ever work alone in the greenhouse unless there is continuous visual and voice communication (for example, camera and radio communication) and sufficient personnel are available on site in case of an emergency.
14. If filters, for example of ventilation systems, are replaced, they must be inactivated at the place of installation by fumigation and, for the purpose of later sterilisation in the system, packed directly into an airtight container by an exchange system provided by the unit, so that there is no risk to the maintenance personnel and other persons.
15. Before testing, cleaning, repair and modification work is carried out on equipment or facilities that may be contaminated, the disinfection of such equipment or facilities must be carried out or arranged for by the personnel of the genetic engineering facility.
16. In the event of an emergency, all reasonable measures shall be taken to prevent the escape of replicable biological material from the genetic engineering facility.
17. In case of injuries, first aid measures must be initiated immediately. The project manager must be informed and, if necessary, medical assistance must be sought. If there is a possibility that genetically modified organisms have been ingested or if an infection with genetically modified organisms seems possible, the project leader and, if necessary, the attending physician must be informed.
18. The operating instructions, the hygiene plan and the skin protection plan must be posted in suitable places in the plant or must otherwise be readily available.
19. Food, beverages and cosmetics must not be stored in work rooms and the airlock.
20. It is not permitted to eat, drink, smoke or put on make-up in work rooms and the airlock.
21. Areas shall be provided for workers to eat and drink without compromising their health.

c. Protective clothing, personal protective equipment and related safety measures

1. Employees must be protected by a fully ventilated protective suit when working in a greenhouse of safety level 4, whereby the breathing air supply must be provided by a self-sufficient air supply. The full protective suit must be provided by the operator and meet the following criteria:
   - Mechanical properties: abrasion-resistant, tear-resistant and air-impermeable material,

– Chemical properties: resistant to the disinfectant used in the disinfectant shower and to the chemicals used in the work.

The full protective suit should preferably have boots welded on.
Two pairs of suitable gloves must be worn on top of each other to protect the hands, with at least the outer glove being tightly fastened to the sleeve cuffs of the protective suit.
Before entering the work area, all clothing as well as watches and jewellery are to be removed in the room in front of the shower and light undergarments for the full protective suits are to be put on. The protective suit is put on in the suit room. The greenhouse is entered through the inner airlock chamber without operating the disinfection shower. After leaving the inner lock chamber, it is subjected to a short shower cycle with decontaminant and a short water phase. After completion of the work, a shower cycle is carried out in the disinfection shower, by which the full protective suit is decontaminated. After a final rinse with water, the full protective suit is placed in the
suit room and remains there. The undergarments are taken off in the personal shower and a hygiene shower is taken if needed.

2. Suitable storage facilities must be provided for other street clothing outside the genetic engineering facility.

Appendix 4 (to § 16) Safety measures for animal rooms

(Source: Federal Law Gazette I 2019, 1276 - 1285)

Pursuant to Section 16(2), if work with genetically modified microorganisms is carried out in animal rooms, the requirements of Annex 2 for the laboratory area shall be observed accordingly in addition to the requirements of this Annex.

I. Safety level 1

a. Structural and technical safety measures

1. If necessary, screening of the animal rooms shall be carried out.
2. Animal rooms must be easy to clean and disinfect. Depending on the activity, sufficient working space must be ensured for each employee.
3. Animal rooms must be lockable and escape-proof for the animals housed and must be designed in such a way as to prevent the spread of any viable developmental stages of the animals into the environment.
4. Animal rooms must be adequately ventilated depending on the occupancy density.
5. There should be an easily accessible washing facility for cleaning hands with handwash, disinfectant and disposable towel dispensers.

b. Organisational security measures

1. The animal rooms shall be designated as a genetic engineering work area of safety level 1.
2. Access to animal rooms shall be restricted to authorised persons.
3. Animals shall be housed in animal cages, stalls, containers or other facilities suitable for the species.
4. If there is no risk of horizontal transfer of the transferred gene in transgenic animals, they may also be kept outside in a securely fenced area or otherwise confined. Appropriate measures shall be taken to counteract the risk of theft or escape. The animals shall be monitored in such a way that any escape can be detected immediately.
5. Animal rooms should be kept tidy and clean. Only the equipment and materials that are actually needed should be placed in the animal rooms.
6. Pipetting aids are to be used.

7. Cannulas and pointed or sharp objects should only be used when absolutely necessary. Used needles and used pointed or sharp objects should be collected and disposed of in puncture-proof and tightly closable waste containers. Cannulas must not be put back into their sheaths.
8. During all work, care must be taken to avoid aerosol formation as far as possible.
9. Measures shall be taken to prevent reproduction of the animals unless reproduction is part of the experiment.
10. All animals must be easily identifiable, in particular with regard to their genetic modification or the assigned genetic work.
11. Staff shall be trained in the handling of the animals. The project manager and, where appropriate, those responsible for handling animals must ensure that all those who come into contact with the animals and waste material are familiar with the local rules and know any precautions that may be required.
12. In the event of the escape of genetically modified microorganisms, effective disinfectants and specific disinfection procedures must be available, as well as any necessary aids such as absorbent material.
13. Hands must be disinfected immediately if contamination is suspected. After finishing work and before leaving the work area, hands must be disinfected if necessary and carefully cleaned and cared for according to the skin protection plan.
14. In case of injuries, first aid measures must be initiated immediately. The project manager must be informed and, if necessary, medical assistance must be sought. If there is a possibility that genetically modified organisms have been ingested or if an infection with genetically modified organisms seems possible, the project leader and, if necessary, the attending physician must be informed.
15. An intrusion of wild forms of the corresponding animal species into the animal rooms must be excluded.
16. Infestation with vermin and vectors of genetically modified organisms (e.g. rodents, arthropods) shall be prevented; if necessary, vermin and vectors shall be controlled in an appropriate manner.
17. Animal cages and other facilities shall be cleaned after use.
18. Material intended for inactivation, sterilisation or incineration and used animal cages and other equipment shall be transported in such a way as to minimise contamination of the environment.
19. The operating instructions, the hygiene plan and the skin protection plan must be posted in suitable places in the facility or must otherwise be readily available.
20. Foodstuffs, luxury foodstuffs and cosmetics must not be stored in animal rooms.
21. No eating, drinking, smoking or putting on make-up is allowed in animal rooms.
22. Areas shall be provided for workers to eat and drink without compromising their health.

c. Protective clothing, personal protective equipment and related safety measures

1. Suitable protective clothing and footwear shall be provided by the operator. The protective clothing and footwear provided by the operator shall be worn. Before leaving the animal rooms, protective clothing and footwear shall be cleaned or removed.
2. Used protective clothing must be stored separately from street clothes. Street clothes, bags, etc. must not be stored in the work area.

II. Safety level 2

a. Structural and technical safety measures

1. Animal rooms shall be separate buildings or clearly demarcated or screened and physically separated areas within buildings.

2. All animals shall be kept in enclosed and lockable premises (animal holding rooms or similar) to exclude the risk of theft or accidental release. Technical measures shall be taken to ensure that only authorised persons can enter the animal rooms.
3. Animal rooms must be easy to clean and resistant to the substances used as well as to cleaning agents and disinfectants. Depending on the activity, sufficient working space must be provided for each employee.
4. Animal rooms must be lockable and escape-proof for the animals housed and must be designed in such a way as to prevent the spread of any viable developmental stages of the animals into the environment.
5. Doors of the animal rooms should open in the direction of escape.
6. A washbasin, a disinfectant dispenser, a handwash dispenser and a disposable towel dispenser shall be provided for disinfecting and cleaning hands. These are easily accessible and should be placed near the door. The fittings of the washbasin as well as the disinfectant and handwash dispensers shall be operable without touching the hands.
7. Animal rooms must be adequately ventilated depending on the occupancy density.
8. During work where aerosols may be generated, it must be ensured that these do not enter the work area. The following measures are particularly suitable for this purpose:

   aa) Carrying out the work in a microbiological safety cabinet or in a cage changing station, or

   bb) Use of devices and equipment that do not release aerosols, such as centrifuges with aerosol-tight rotors or rotor inserts.

   The exhaust air from the devices referred to in sentence 2, double letter aa must be passed through a high-efficiency particulate air filter or be rendered sterile by another tested method. If technical or organisational measures are not sufficient or not applicable, suitable protective equipment must be worn in accordance with letter c number 1.
9. Where necessary, filters shall be provided on isolators (transparent containers in which small animals are kept inside or outside a cage) or for the exhaust air of isolated rooms.
10. Contaminated process exhaust air must be cleaned by suitable processes such as filtering or thermal post-treatment before it is released into the work area. This also applies, for example, to exhaust air from insulators, from cages with infected animals or from autoclaves.
11. Facilities shall be available to immobilise infected animals or animals to be infected in such a way that they can be handled safely. A
    Safety lighting shall be provided for workplaces with particular hazards so that in the event of a power failure work can be safely terminated, animals can be adequately housed and the work area can be safely exited.
12. An autoclave or equivalent inactivation or sterilisation equipment with sufficient capacity must be present in the animal rooms or available within the same building.

b. Organisational security measures

1. The animal rooms shall be marked as a genetic engineering work area of safety level 2. The premises shall additionally be marked with the warning sign "Biohazard".
2. Apart from those involved in the genetic engineering work, only persons authorised by the project manager or by third parties authorised by the project manager have access to the animal rooms. This must be indicated by suitable labelling at the entrances.
3. Windows and doors must be closed during the work.
4. No other animals should be kept in animal rooms where infected animals are housed, unless cross-contamination is not possible, such as in the case of

Use of special insulating housing systems. The doors shall be marked with an indication of the type of genetic engineering work.

5. Animals shall be housed in animal cages, stalls, containers or other facilities suitable for the species. Animals infected with airborne micro-organisms shall, as a general rule, be kept in cages or isolators which prevent the release of these organisms into the indoor air and prevent cage-to-cage transmission.
6. Animal rooms should be kept tidy and clean. Only the equipment and materials that are actually needed should be placed in the animal rooms.
7. Pipetting aids are to be used.
8. Cannulas and pointed or sharp objects should only be used if absolutely necessary. If use is essential, additional protective measures should be taken where possible, such as the use of puncture and cut resistant gloves or cannulas with safety mechanisms. Used cannulae and used pointed or sharp objects shall be collected and disposed of in puncture-resistant and tightly closable waste containers. Cannulas must not be put back into their sheaths.
9. Measures shall be taken to prevent reproduction of the animals unless reproduction is part of the experiment.
10. All animals must be easily identifiable, in particular with regard to their genetic modification or the assigned genetic work.
11. Staff shall be trained in the handling of the animals. The project manager and, where appropriate, those responsible for handling animals must ensure that all those who come into contact with the animals and waste material are familiar with the local rules and know any precautions that may be required.
12. An intrusion of wild forms of the corresponding animal species into the animal rooms must be excluded.
13. Infestation with vermin and vectors of genetically modified organisms (e.g. rodents, arthropods) shall be prevented; vermin and vectors shall be controlled in an appropriate manner.
14. Material intended for inactivation or sterilisation and used animal cages and other equipment shall be transported in such a way as to minimise contamination of the environment.
15. Infected animals must always be transported within the farm in their cages.
16. Genetically modified organisms and waste containing genetically modified organisms may only be transported in tightly closed, break-proof, disinfectable and appropriately labelled containers. The containers shall be disinfected regularly from the outside and whenever they become contaminated.
17. The animal rooms shall be disinfected and cleaned regularly. If floor drains are present in animal rooms, these drains shall be designed in such a way that they are escape-proof for the housed animals.
18. Effective disinfectants and specific disinfection procedures, as well as any necessary aids such as absorbent material, must be available in the event of the escape of genetically modified microorganisms. A contaminated area (for example, after spillage of organisms) must be closed and disinfected immediately.
19. All work surfaces must be disinfected after completion of the activity.
20. Hands must be disinfected immediately if contamination is suspected. In addition, hands must be disinfected, carefully cleaned and cared for according to the skin protection plan after finishing the activity and before leaving the work area.
21. Work equipment or facilities that have been in direct contact with genetically modified organisms must be autoclaved or disinfected before testing, cleaning, maintenance or repair if genetically modified organisms could have been transmitted during this contact.

22. Animal cages and other equipment shall be disinfected or autoclaved and cleaned after use.
23. In case of injuries, first aid measures must be initiated immediately. The project manager must be informed and, if necessary, medical assistance must be sought. If there is a possibility that genetically modified organisms have been ingested or if an infection with genetically modified organisms seems possible, the project leader and, if necessary, the attending physician must be informed.
24. The operating instructions, the hygiene plan and the skin protection plan must be posted in suitable places in the facility or must otherwise be readily available.
25. Foodstuffs, luxury foodstuffs and cosmetics must not be stored in animal rooms.
26. No eating, drinking, smoking or putting on make-up is allowed in animal rooms.
27. Areas shall be provided for workers to eat and drink without compromising their health.

c. Protective clothing, personal protective equipment and related safety measures

1. In the animal rooms, suitable personal protective clothing including footwear and, depending on the activity, suitable personal protective equipment that may be required (for example, protective gloves, protective goggles, mouth and nose protection or respiratory protection with a particle-filtering effect) must be worn. The protective clothing and, if necessary, the personal protective equipment shall be provided by the operator. The cleaning of the
Protective clothing is to be carried out by the operator. Protective clothing and protective equipment must not be worn outside the genetic engineering facility.
2. Separate storage facilities must be provided for protective and street clothing. Street clothes, bags, etc. must not be stored in the work area.

III. Safety level 3

a. Structural and technical safety measures

1. Animal rooms shall be a separate building or a clearly demarcated or screened and physically separated area within a building. Technical measures shall prevent unintentional or unauthorised entry into the area.
2. All animals shall be kept in enclosed and lockable premises (animal holding rooms or similar) to eliminate the risk of theft or accidental release.
3. Animal rooms must be easy to clean and resistant to the substances used as well as to cleaning agents and disinfectants. Depending on the activity, a sufficiently large working area must be ensured for each employee.
4. Animal rooms must be lockable and escape-proof for the animals housed and must be designed in such a way as to prevent the spread of any viable developmental stages of the animals into the environment.
5. Windows must not be openable.
6. The doors of the animal rooms should open in the direction of escape.
7. As a rule, an airlock shall be installed in the animal rooms through which the animal rooms can be entered and exited. The sluice shall be equipped with doors which are locked against each other during normal operation. The outer door shall be self-closing. The airlock must contain a hand disinfection device with a disinfectant dispenser. As a rule, a hand-washing basin with a hand-washing agent dispenser and a disposable towel dispenser must be installed in the sluice.
The fittings of the washbasin as well as the disinfectant dispenser and the handwash dispenser must be operable without touching them by hand. If necessary, a shower must be installed. In justified individual cases, a sluice may be dispensed with.
8. If pathogenic organisms are handled for which transmission through the air cannot be ruled out, the animal rooms must be kept under constant negative pressure.
and the exhaust air must be led through high-efficiency particulate air filters. The existing negative pressure must be easily compensated from the outside and, by the users of the animal rooms, also from the inside.

be verifiable and monitored by an alarm device with visual and acoustic signal. The recirculation of contaminated exhaust air into working areas is not permitted. The filter of the ventilation and air-conditioning system must be able to be checked on site in its installed state to see whether it is functioning adequately.

9. The animal rooms must be sufficiently ventilated depending on the occupancy density.

10. There must be an emergency power supply for safety-relevant equipment (for example, ventilation system, isolator, microbiological safety cabinets, individually ventilated cages).

11. An autoclave or equivalent device for sterilisation with sufficient capacity must be available in the animal rooms of the genetic engineering facility.

12. Waste water generated in the work area must generally be sterilised as follows: Collection in collection containers and thermal sterilisation or central waste water sterilisation.
No waste water to be sterilised may be produced in the sluice when operated as intended and in compliance with the organisational safety measures.

13. Surfaces in the animal rooms (for example, work surfaces, walls, floors, ceilings and surfaces of the inventory) must be impervious to liquids, easy to clean and resistant to the substances used as well as to cleaning agents and disinfectants. As a rule, the floor shall be constructed with a cove in a tub function.

14. Disinfectant dispensers that can be operated without touching hands must be available in the animal rooms for disinfecting and cleaning hands. These shall be easily accessible and preferably near the door. If there is a washbasin, the fittings of the washbasin as well as the handwashing detergent dispenser must be without
be operable by hand. Facilities for rinsing the eyes must be available.

15. When working where aerosols may be generated, it must be ensured that these do not enter the work area. The following measures are particularly suitable for this purpose:

    aa) Carrying out the work in a microbiological safety cabinet or in a cage changing station, or

    bb) Use of devices and equipment that do not release aerosols, such as centrifuges with aerosol-tight rotors or rotor inserts.

    The exhaust air from the devices referred to in sentence 2, double letter aa must be passed through a high-efficiency particulate air filter or be rendered sterile by another tested method. If technical or organisational measures are not sufficient or not applicable, suitable protective equipment must be worn in accordance with letter c number 1.

16. Filters must be fitted on isolators or for the exhaust air of isolated rooms.

17. Facilities shall be available to immobilise infected animals or animals to be infected in such a way that they can be handled safely. A
Safety lighting shall be provided for workplaces with particular hazards so that work can be safely terminated in the event of a power failure, adequate shelter can be provided for animals and the work area can be safely exited.

18. Suitable equipment must be available for communication from animal rooms and, if necessary, from the sluice.

19. Contaminated process exhaust air must be cleaned by suitable processes such as filtering or thermal post-treatment before it is released into the work area. This also applies, for example, to exhaust air from insulators, from cages with infected animals or from autoclaves.

b. Organisational security measures

1. The animal rooms shall be marked as a genetic engineering work area of safety level 3. The premises shall additionally be marked with the warning sign "Biohazard".

2. Access to the animal rooms shall be restricted to those persons whose presence is necessary for the performance of the genetic engineering work and who are authorised to enter. This shall be indicated by suitable marking at the entrances. The project leader is responsible for determining the persons authorised to enter. A person may

work alone in the animal room only if the handling of the laboratory animals can be safely controlled alone and if an emergency call system to be operated from inside is available. It must be possible to trigger the emergency call signal automatically.

3. (omitted)

4. No other animals shall be kept in animal rooms where infected animals are housed, unless cross-contamination is not possible, such as when special isolated housing systems are used. Doors shall be marked with a notice indicating the nature of the genetic work.

5. Genetically modified organisms and waste containing genetically modified organisms may only be transported in tightly closed containers that are protected against breakage, can be disinfected and are labelled accordingly. The containers must be disinfected regularly and in the event of any external contamination.

6. Animals shall be housed in animal cages, stalls, containers or other facilities suitable for the species. Animals infected with airborne micro-organisms shall be kept in cages or isolators which prevent the release of these organisms into the indoor air and prevent cage-to-cage transmission. Filters shall be provided on isolators and for the exhaust air from isolators.

7. The following must be observed when disposing of animal carcasses and material:

   aa) Animal carcasses and material shall be sterilised before disposal. Sterilisation shall be carried out by autoclaving or other suitable means (e.g. alkaline hydrolysis). It must be ensured that the core layers of the animal carcass and the animal material are also covered.

   bb) If sterilisation in the animal room is not possible, transport must be carried out in tightly closed containers which are protected against breakage, can be disinfected and are labelled accordingly. The containers must be disinfected regularly and whenever they are contaminated from the outside.

8. If filters, for example of ventilation systems or microbiological safety cabinets, are replaced, they must either be inactivated at the place of installation by fumigation or packed in an airtight container for later sterilisation by an exchange system provided by the equipment, so that infection of the maintenance personnel and other persons can be excluded.

9. Each animal room must have its own equipment.

10. Pipetting aids are to be used.

11. Cannulas and pointed or sharp objects should only be used if absolutely necessary. If use is essential, additional protective measures such as the use of puncture and cut resistant gloves or cannulas with safety mechanisms shall be taken where possible. Used cannulae and used pointed or sharp objects shall be collected and disposed of in puncture-proof and tightly closable waste containers. Cannulas must not be put back into their sheaths.

12. Measures shall be taken to prevent reproduction of the animals unless reproduction is part of the experiment.

13. All animals must be easily identifiable, in particular with regard to their genetic modification or the assigned genetic work.

14. Staff shall be trained in the handling of the animals. The project manager and, if applicable, the persons responsible for handling animals must ensure that all persons who come into contact with the animals and waste material are familiar with the local rules and know all the necessary precautions.

15. An intrusion of wild forms of the corresponding animal species into the animal rooms must be excluded.

16. Infestation with vermin and vectors of genetically modified organisms (for example rodents and arthropods) shall be prevented; vermin and vectors shall be controlled in an appropriate manner.

17. Infected animals must always be transported in their cages within the farm.
18. Hands must be disinfected immediately if contamination is suspected. After finishing the activity and before leaving the work area, hands must be disinfected, carefully cleaned and cared for according to the skin protection plan.
19. The animal rooms must be disinfected and cleaned regularly.
20. Effective disinfectants and specific disinfection procedures, as well as any necessary aids such as absorbent material, must be available in the event of the escape of genetically modified microorganisms. A contaminated area (for example, after spillage of organisms) must be closed and disinfected immediately.
21. All work surfaces must be disinfected after completion of the activity.
22. Work equipment or facilities that have been in direct contact with genetically modified organisms must be autoclaved or disinfected before testing, cleaning, maintenance or repair if genetically modified organisms could have been transmitted during this contact.
23. Animal cages and other equipment shall be disinfected or autoclaved and cleaned after use.
24. In case of injuries, first aid measures must be initiated immediately. The project manager must be informed and, if necessary, medical assistance must be sought. If there is a possibility that genetically modified organisms have been ingested or if an infection with genetically modified organisms seems possible, the project leader and, if necessary, the attending physician must be informed.
25. The operating instructions, the hygiene plan and the skin protection plan must be posted in suitable places in the plant or must otherwise be readily available.
26. Food, beverages and cosmetics may not be stored in the animal rooms and the airlock.
27. It is not allowed to eat, drink, smoke or put on make-up in the animal rooms and the sluice.
28. Areas shall be provided for workers to eat and drink without compromising their health.

c. Protective clothing, personal protective equipment and related safety measures

1. In the airlock, suitable protective clothing closed at the front of the torso as well as personal protective equipment (protective gloves and, depending on the activity, further protective equipment such as mouth and nose protection (contact protection), eye protection, respiratory protection with particle filtering effect) must be put on and taken off again after the activity is finished. The protective clothing must be labelled and include closed shoes to be put on according to the activity. The protective clothing and personal protective equipment shall be provided by the operator and sterilised and cleaned or disposed of by the operator after use.
2. Protective clothing must be stored separately from street clothing. Suitable storage facilities shall be provided for this purpose.

IV. Safety level 4

a. Structural and technical safety measures

1. The animal rooms must either be an independent building or, as part of a building, clearly separated from the generally accessible circulation areas by a corridor or anteroom. Animal rooms shall have no windows and shall have sufficiently large rooms. If windows are present, they shall be tight and shatterproof and shall not be openable. Technical measures must be taken to prevent any unintentional or unauthorised entry into the animal rooms. All doors in the area shall be self-closing. They shall swing open in the direction of escape. Entry into the animal rooms shall only be possible via a four-chambered airlock.

2. The airlock must be provided with an appropriate pressure grading to prevent the escape of air from the respective animal compartments. The airlock must be structured as follows:

   – Outer lock chamber for removing street clothes and putting on undergarments,
   – Personal shower with space for removing undergarments,
   – Suit room for putting on and taking off the full protective suits and
   – inner lock chamber with the chemical shower for disinfecting the full protective suits.

   When used as intended, the doors of the airlock shall be locked against each other. A means shall be provided for the insertion of large-scale equipment or furnishings.

3. Walls, ceilings and floors of the animal rooms must be sealed to the outside. All penetrations of supply and disposal pipes must be sealed. The floor shall be constructed with a cove in a trough function.

4. All animals shall be kept in enclosed and lockable premises (animal holding rooms or similar) to eliminate the risk of theft or accidental release.

5. All surfaces of the animal rooms (for example work surfaces, walls, floors, ceilings and surfaces of the inventory) must be easy to clean and resistant to the substances used as well as to cleaning agents and disinfectants.

6. The animal rooms must be ventilated by their own ventilation system, which must be redundant. The system must be designed in such a way that a controlled negative pressure is constantly maintained in the animal room with respect to the outside world. The negative pressure must increase from the chambers of the entrance sluice to the work rooms and animal housing rooms. The actual negative pressure must be easily controllable and verifiable from the inside as well as from the outside. Unacceptable pressure changes must be indicated by a visual and acoustic alarm. The valves of the ventilation and air-conditioning system must be de-energised to a safe position. condition. Supply and exhaust air must be coupled in such a way that, in the event of fan failure, the air cannot escape in an uncontrolled manner under any circumstances.
   The exhaust air from the animal rooms must leave the building in such a way that it cannot endanger the environment. Supply air and exhaust air from the animal rooms shall each pass through two successive high-efficiency particulate air filters. The filters shall be arranged in such a way that they can be checked on site in their installed condition to ensure that they are functioning properly. It must be possible to close the supply and exhaust air pipes behind the filters mechanically and tightly so that the filters can be changed without danger.
   The supply and exhaust air ducts and the animal rooms themselves must be gas-tight and suitable for fumigation. The animal rooms must be sufficiently ventilated depending on the occupancy density.

7. The genetic engineering facility must be equipped with a pass-through autoclave with sufficient capacity. The condensed water from the autoclave must be sterilised before it enters the general waste water line. Through a suitable arrangement of valves and by venting valves secured by high-efficiency particulate filters, these sterilisation units shall be protected against malfunction. An automatically acting interlock shall ensure that the door can only be opened after the sterilisation cycle in the airlock has been completed. An immersion tank or a gasable pass-through with interlocking doors shall be provided for the entry and exit of equipment and heat-sensitive material.

8. Waste water generated in the animal rooms shall be sterilised as follows:
   Collection in collection containers and autoclaving or central waste water sterilisation.

9. Supply and disposal lines must be secured against contamination with organisms that could be caused by the backflow of media (for example, in the case of gases: Secure with high-efficiency particulate air filters or, in the case of liquids, secure with non-return valves). The animal rooms must not be connected to a general vacuum system.

10. Animal rooms shall be escape-proof for the housed animals and shall be designed in such a way as to prevent the spread of any viable developmental stages of the animals into the environment.

11. When working with animals where aerosols may be generated, it must be ensured that these do not enter the working area. The following measures are particularly suitable for this purpose:

    aa) Carrying out the work in a microbiological safety cabinet or in a cage changing station, or

    bb) Use of devices and equipment that do not release aerosols, such as centrifuges with aerosol-tight rotors or rotor inserts.

    The exhaust air from the devices referred to in sentence 2, double letter aa must be passed through a high-efficiency particulate air filter or be sterilised by another tested method.

12. Facilities shall be available to immobilise infected animals or animals to be infected in such a way that they can be handled safely.

13. Centrifuges in which organisms are centrifuged that may only be worked with under the conditions of safety level 4 may only be operated in a microbiological safety cabinet or must be converted accordingly. If this is not possible, the centrifuge rotors must always be opened in the microbiological safety cabinet. It must be ensured that the protective properties of the microbiological safety cabinet are not impaired.

14. The recirculation of contaminated exhaust air into the animal rooms is not permitted.

15. Filters on insulators are to be provided.

16. There must be a continuous communication link from the animal rooms and from the sluice (for example radio link).

17. An emergency power supply shall be installed for safety-relevant equipment such as ventilation systems including ventilation systems, emergency call and monitoring equipment, microbiological safety workbenches and the breathing air supply for the forced-ventilated full protective suits. Safety lighting shall be provided so that, in the event of a power failure, work can be safely terminated, animals can be adequately housed and the work area can be safely exited.

18. When planning safety-relevant technical systems such as ventilation systems, waste water treatment systems and autoclaves, the procedure for malfunctions and maintenance must also be taken into account as a matter of principle. The ventilation and air-conditioning system must be designed in such a way that a filter change is possible without violating the safety standard, as otherwise the animal rooms would have to be shut down and disinfected before the filter change. In the case of larger systems, it is advisable to have the air handling unit
to be divided in such a way that partial operation is possible in the event of a malfunction or during maintenance work.

b. Organisational security measures

1. The animal rooms shall be marked as a genetic engineering work area of safety level 4. The premises shall additionally be marked with the warning sign "Biohazard".

2. Access shall be restricted to those persons whose presence in the animal room is necessary to carry out the genetic engineering work and who are authorised to enter. This must be indicated by suitable labelling at the entrances. The project manager is responsible for determining the persons authorised to enter. The presence of persons shall be documented.

3. No person shall ever work alone in the animal room unless there is continuous visual and voice communication (for example, camera and radio communication) and sufficient staff are available on site in case of an emergency.

4. No other animals should be kept in animal rooms in which infected animals are housed, unless cross-contamination is not possible, such as

when special insulated housing systems are used. The doors shall be marked with an appropriate indication of the type of genetic engineering work.

5. Genetically modified organisms and waste containing genetically modified organisms may only be transported in tightly closed containers that are protected against breakage, can be disinfected and are labelled accordingly. The containers shall be disinfected regularly and in the event of any external contamination.
6. If genetically modified organisms or biological material contaminated with genetically modified organisms are to be discharged from the animal rooms in a viable or intact state for further examination, they shall be packed in tightly closed containers that are protected against breakage, can be disinfected and are labelled accordingly. The containers shall be disinfected from the outside (e.g. immersion in disinfectant, fumigation). The container must be placed in an unbreakable second container which is also tightly closed.
7. All other materials must be sterilised or disinfected by an equivalent treatment before removal from the animal rooms.
8. Work equipment or facilities that have been in direct contact with genetically modified organisms must be autoclaved or disinfected before testing, cleaning, maintenance or repair if genetically modified organisms could have been transmitted during this contact.
9. Animals shall be housed in animal cages, stalls, containers or other facilities suitable for the species.
10. Animal carcasses and animal material shall be sterilised within the facility before disposal. Sterilisation shall be carried out by autoclaving or by other suitable means (e.g. alkaline hydrolysis). It must be ensured that the core layers of the animal carcass and the animal material are also covered.
11. If filters, for example of ventilation systems or of microbiological safety cabinets, are replaced, they must be inactivated at the place of installation by fumigation and, for the purpose of later sterilisation on site, packed in an airtight container by an exchange system provided by the equipment, so that infection of the maintenance personnel and other persons can be excluded.
12. Pipetting aids are to be used.
13. Cannulas and pointed or sharp objects should only be used if absolutely necessary. If use is essential, additional protective measures such as the use of puncture and cut resistant gloves or cannulas with safety mechanisms shall be taken where possible. Used cannulae and used pointed or sharp objects shall be collected and disposed of in puncture-proof and tightly closable waste containers. Cannulas must not be put back into their sheaths.
14. Measures shall be taken to prevent reproduction of the animals unless reproduction is part of the experiment.
15. All animals must be easily identifiable, in particular with regard to their genetic modification or the assigned genetic work.
16. Staff shall be trained in the handling of the animals. The project manager responsible for handling animals must ensure that all persons who come into contact with the animals and waste material are familiar with the local rules and know all the necessary precautions.
17. An intrusion of wild forms of the corresponding animal species into the animal rooms must be excluded.
18. Infestation with vermin and vectors of genetically modified organisms (for example rodents and arthropods) shall be prevented; vermin and vectors shall be controlled in an appropriate manner.
19. Infected animals must always be transported within the farm in their cages.
20. In the event of the escape of genetically modified microorganisms, effective disinfectants and specific disinfection procedures, as well as any necessary

aids such as absorbent material are available. A contaminated area (for example, after spillage of organisms) must be closed and disinfected immediately.

21. The animal rooms must be disinfected and cleaned regularly.
22. Work surfaces as well as animal cages and other equipment must be disinfected or autoclaved and, if necessary, cleaned after the end of the activity.
23. The materials, objects and animals required in the animal rooms shall be introduced into the animal room via sluices, fumigation chambers or pass-through autoclaves with facilities for disinfection. The airlock shall be disinfected before and after entry.
24. Each animal room must have its own equipment.
25. Safe storage of contaminated equipment and materials shall be provided.
26. If necessary, for example if protective and hygienic measures are suspected to be inadequate, the work area must be checked for the presence of viable organisms used in genetic engineering work.
27. In the event of an emergency, all reasonable measures shall be taken to prevent the escape of animals and the escape of reproducible biological material from the animal room.
28. In case of injuries, first aid measures must be initiated immediately. The project manager must be informed and, if necessary, medical assistance must be sought. If there is a possibility that genetically modified organisms have been ingested or if an infection with genetically modified organisms seems possible, the project leader and, if necessary, the attending physician must be informed.
29. The operating instructions, the hygiene plan and the skin protection plan must be posted in suitable places in the facility or must otherwise be readily available.
30. Food, beverages and cosmetics may not be stored in the animal rooms and the airlock.
31. It is not allowed to eat, drink, smoke or put on make-up in the animal rooms and the sluice.
32. Areas shall be provided for workers to eat and drink without compromising their health.

c. Protective clothing, personal protective equipment and related safety measures

1. Employees must be protected by a fully ventilated protective suit when working in animal rooms of safety level 4, whereby the breathing air supply must be provided by a self-sufficient air supply. The full protective suit must be provided by the operator and meet the following criteria:
   - Mechanical properties: abrasion-resistant, tear-resistant and made of air-impermeable material,
   - chemical properties: resistant to the disinfectant used in the disinfectant shower and to the chemicals used in the work,

   The full protective suit should preferably have boots welded on.
   Two pairs of suitable gloves must be worn on top of each other to protect the hands, with at least the outer glove being tightly fastened to the sleeve cuffs of the protective suit. Before entering the work area, all clothing as well as watches and jewellery are to be removed in the room in front of the shower and light undergarments for the full protective suits are to be put on. The protective suit is put on in the suit room and the animal room is entered through the inner sluice chamber without operating the disinfection shower. After leaving the inner sluice chamber, it is subjected to a short shower cycle with decontaminant and a short water phase. After completion of the work, a shower cycle is carried out in the disinfection shower, by which the full protective suit is decontaminated. After a final rinse with water, the full protective suit is placed in the suit room and remains there. The undergarments are taken off in the personal shower and a hygiene shower is taken if needed.

2. Suitable storage facilities must be provided for other street clothing outside the genetic engineering facility.