Text consolidated by Valsts valodas centrs (State Language Centre) with amending regulations of:

26 May 2014 [shall come into force on 29 May 2014];

27 January 2015 [shall come into force on 30 January 2015];

14 March 2017 [shall come into force on 29 April 2017];

12 March 2019 [shall come into force on 15 March 2019].

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

Republic of Latvia

Cabinet

Regulation No. 1176

Adopted 22 October 2013

**Procedures for the Use of Human Tissues and Cells**

*Issued pursuant to*

*Section 4.1, Paragraph four, Section 12, Paragraph one, Clause 2, and Section 14, Clauses 2 and 3 of the law On the Protection of the Body of Deceased Human Beings and the Use of Human Tissues and Organs in Medicine and Section 5, Paragraph six and Section 17, Paragraph two of the Sexual and Reproductive Health Law*

[*14 March 2017; 12 March 2019*]

**1. General Provisions**

1. The Regulation prescribes:

1.1. the procedures for the issuance of the authorisation to use human tissues and cells (hereinafter – the tissues and cells) and a duplicate thereof (hereinafter – the authorisation) to a medical treatment institution and a higher education institution which implements an accredited medical study programme (hereinafter – the higher education institution), and also for cancelling the authorisation, suspending it and renewing the validity thereof;

1.2. the requirements for the receipt of the authorisation and the conditions for the use of tissues or cells;

1.3. the sample form of the authorisation;

1.4. the procedures for the assessment, supervision, and control of the use of tissues or cells;

1.5. the quality and safety standards for the use of the tissues and cells of a living donor and a deceased human being;

1.6. the procedures for the medical examination of a potential gamete donor;

1.7. the procedures for the use of the tissues and cells of a living human being for medical studies;

1.8. the procedures for obtaining, processing, storing, distributing (also exporting and importing) gametes and for ensuring the traceability of gametes;

1.9. the quality and security requirements for obtaining, processing, storing, distributing (also exporting and importing) gametes and for traceability of gametes.

[*14 March 2017; 12 March 2019*]

2. Terms used in the Regulation:

2.1. allogeneic transplantation – cells or tissues removed from one person and applied to another person;

2.2. processing – operations involved in the preparation, manipulation, preservation, and packaging of tissues or cells intended for human applications;

2.3. tissue – all constituent parts of the human body formed by cells;

2.4. tissue establishment – a medical treatment institution or a unit thereof where certain activities (for example, processing, preservation, storage, distribution) of tissues or cells are undertaken. A tissue establishment may also be responsible for the procurement or testing of the tissues and cells;

2.5. autologous transplantation – cells or tissues removed from and applied in the same person;

2.6. donor – every human source, whether living or deceased, of human cells or tissues;

2.7. gametes – the tissues and cells intended for use in medically assisted insemination;

2.8. procurement – a process by which tissues or cells are made available;

2.9. procurement organisation – a medical treatment institution or a unit thereof which is not a tissue establishment and where the procurement of donor tissues and cells is carried out by specially trained personnel;

2.10. human application – the use of tissues or cells on or in a human recipient and extracorporal applications;

2.11. application organisation – a medical treatment institution or a unit thereof which uses the tissues and cells on or in human beings;

2.12. distribution – transportation and delivery of tissues or cells intended for human applications;

2.13. traceability – the identification of the tissues and cells during any step from procurement, through processing, testing, and storage to distribution to the recipient or disposal, which also implies the ability to identify the donor and the tissue establishment or organisation receiving, processing, or storing the tissues and cells, the recipient in a medical treatment institution and the third party transferring the tissues and cells to the recipient, and also the ability to identify relevant information (data) relating to products (articles) and materials coming into contact with the tissues and cells;

2.14. quarantine – the status of retrieved tissues or cells, or tissues isolated physically or by other effective means, whilst awaiting a decision on their acceptance or rejection;

2.15. preservation – the use of chemical agents, alterations in environmental conditions or other means during processing to prevent or retard biological or physical deterioration of cells or tissues;

2.16. quality system – the organisational structure, defined responsibilities, procedures, processes, and also resources for implementing quality management and includes all activities which contribute to quality, directly or indirectly;

2.17. quality management – the coordinated activities to direct and control the operations of a tissue establishment in the field of quality;

2.18. serious adverse reaction – an unintended response, including a communicable disease, in the donor or in the recipient associated with the procurement or human application of the tissues and cells that is fatal, life-threatening, disabling, incapacitating, or which results in, or prolongs, hospitalisation or morbidity;

2.19. serious adverse event – any untoward occurrence associated with the procurement, testing, processing, storage, and distribution of the tissues and cells that might lead to the transmission of a communicable disease, to death or life-threatening, disabling, or incapacitating conditions for patients or which might result in, or prolong, hospitalisation or morbidity;

2.20. partner donation – the donation of gametes between a man and a woman who declare that they have an intimate physical relationship;

2.21. recipient – the tissue or cell recipient to whom the tissues or cells are transplanted;

2.22. standard operating procedure – written instructions describing the steps in a specific process, including the materials and methods to be used and the expected end product;

2.23. cells – individual human cells or a collection of human cells when not bound by any form of connective tissue;

2.24. direct use – any procedure where cells are donated and used without storage thereof in a tissue establishment;

2.25. third party – a person who on the basis of a contract entered into with a tissue establishment carries out any activities related to the use of the tissues and cells;

2.26. third country – any country other than a Member State of the European Union or the European Economic Area;

2.27. storage – maintaining the product under appropriate controlled conditions until distribution thereof;

2.28. validation (or qualification in the case of equipment or environments) – establishing documented evidence that provides a high degree of assurance that a specific process, standard procedure, piece of equipment, or environment will consistently produce a product meeting its predetermined specifications and quality attributes. A process is validated to ensure effective operation of the system that is based on the intended use of tissues and cells;

2.29. donation – donating human tissues or cells intended for human applications or medical studies;

2.30. pooling – the physical contact or mixing in a single container of the tissues or cells from more than one procurement from the same donor, or from two or more donors;

2.31. emergency – any unforeseen situation in which there is no practical alternative other than to urgently import the tissues and cells from a third country for immediate application to a known recipient or known recipients whose health would be seriously endangered without such an import;

2.32. importing tissue establishment – a medical treatment institution or a unit thereof which has entered into a contract with a third country supplier for the import of the tissues and cells coming from a third country intended for human application;

2.33. one-off import – the import of any specific type of tissues or cells intended for the personal use of an intended recipient or recipients known to the importing tissue establishment and the third country supplier before the importation occurs. Such an import of any specific type of tissues or cells shall normally not occur more than once for any given recipient. Imports from the same third country supplier taking place on a regular or repeated basis shall not be considered to be one-off import;

2.34. third country supplier – a tissue establishment or another body, registered in a third country, which is responsible for the export of the tissues and cells it supplies to an importing tissue establishment. A third country supplier may also carry out one or more of the activities, which take place outside of a European Union Member State or a country of the European Economic Area, of donation, procurement, testing, processing, preservation, storage, or distribution of imported tissues and cells;

2.35. Single European Code (SEC) – the unique identifier applied to the tissues and cells distributed in the European Union Member States or countries of the European Economic Area. The Single European Code consists of two parts, i.e. a donation identification sequence and a product identification sequence;

2.36. donation identification sequence – the first part of the Single European Code consisting of the European Union tissue establishment code and the unique donation number;

2.37. European Union tissue establishment code – the unique identifier for accredited, designated, authorised, or licensed tissue establishments in a European Union Member State or a country of the European Economic Area. The tissue establishment code consists of an ISO country code and the tissue establishment number set out in the European Union Tissue Establishment Compendium;

2.38. unique donation number – the number attributed to a specific donation of tissues and cells in accordance with the system introduced in each European Union Member State or country of the European Economic Area for allocating such numbers;

2.39. product identification sequence – the second part of the Single European Code consisting of the product code, the split number, and the expiry date (the date by which the tissues and cells can be used);

2.40. product code – the identifier for the specific type of the relevant tissues and cells. The product code consists of the product coding system identifier indicating the coding system used by the tissue establishment (“E” for the EUTC, “A” for ISBT128, “B” for Eurocode) and the tissues and cells product number foreseen in the respective coding system for the product type;

2.41. split number – the number which distinguishes and uniquely identifies the tissues and cells having the same unique donation number and the same product code and originating from the same tissue establishment;

2.42. European Union Tissue Establishment Compendium – the register which includes information on all tissue establishments which have obtained the authorisation from a competent authority of a European Union Member State or a country of the European Economic Area;

2.43. European Union Tissue and Cell Product Compendium – the register which includes information on all types of tissues and cells circulating in the European Union Member States or countries of the European Economic Area and their respective product codes allocated in accordance with any of the three permitted coding systems (EUTC, ISBT128, and Eurocode);

2.44. EUTC – the product coding system for the tissues and cells developed by the European Union consisting of a register of all types of the tissues and cells circulating in the European Union Member States or countries of the European Economic Area and their respective product codes;

2.45. released for circulation – distributed for human application or transferred to another tissue establishment, for example, for further processing with or without return;

2.46. within the same medical treatment institution – all steps from procurement of the tissues and cells to human application are carried out under the supervision of the same responsible person, using the same quality management system and traceability system, within the same medical treatment institution or a unit thereof, comprising at least one tissue establishment with valid authorisation and an application organisation which is responsible for the use of the tissues and cells at the same location.

[*14 March 2017*]

3. The Regulation shall not apply to:

3.1. blood and blood components (excluding hematopoietic ancestor cells);

3.2. tissues and cells used as an autologous graft within the same surgical procedure;

3.3. human organs or parts of organs if it is their function to be used for the same purpose as the entire organ in the human body;

3.4. organs, tissues, and cells of animal origin;

3.5. studies where tissues and cells are not intended for use in the human body (for example, *in vitro* studies, *in vivo* studies in animal models);

3.6. tissues and cells used for pathological-anatomical, cytological, and forensic examinations.

4. It shall be permitted to obtain, donate, process, store, preserve, and distribute the tissues and cells for the following purposes:

4.1. for the production and use of medical grafts (including sterile);

4.2. for transplantation;

4.3. for scientific (including clinical) research;

4.4. as a raw material for the manufacture of medicinal products or veterinary medicinal products, including advanced therapy medicinal products;

4.5. for the manufacture of medical devices;

4.6. for study purposes;

4.7. for medical assisted insemination and methods related thereto.

4.1 The requirements laid down in this Regulation for the import of the tissues and cells shall apply to:

4.11. human tissues and cells intended for human application;

4.12. products derived from human tissues and cells intended for human application, provided that the laws and regulations governing the field of pharmaceuticals do not apply to such products.

[*14 March 2017*]

4.2 If human tissues and cells to be imported are intended solely for use as raw materials in manufactured products subject to the application of the laws and regulations governing the field of pharmaceuticals, the requirements of this Regulation shall only apply to donation, procurement, and testing taking place in the third countries, and also in order to help to ensure traceability from donor to recipient and vice versa.

[*14 March 2017*]

5. The use of the tissues and cells, including donation, is anonymous (except in the case of procurement of the tissues and cells from a living human being and intended for transplantation to the same person or to a relative of the donor), voluntary, based on informed consent (acknowledgement) of the donor.

6. Compliance of tissue establishments and procurement organisations with the requirements laid down in this Regulation shall be supervised by the State Agency of Medicines (hereinafter – the Agency).

7. The use of the tissues and cells in medical treatment shall be supervised and controlled by the Health Inspectorate in accordance with the laws and regulations governing the field of medical treatment, epidemiological safety, and pharmaceuticals.

**2. Procedures for the Issuance of the Authorisation and Duplicate Thereof to a Tissue Establishment, and also for the Cancellation of the Authorisation, Suspension and Renewal of the Validity Thereof**

8. A tissue establishment seeking the authorisation shall:

8.1. submit an application to the Agency. The following information shall be indicated in the application:

8.1.1. the name, registration number, legal address of the tissue establishment;

8.1.2. the given name, surname, qualification, practical experience, and contact details of the responsible person;

8.1.3. information on contracts entered into with other medical treatment institutions for the procurement, testing, processing, preservation, storage, and distribution of the tissues or cells, and also contracts on the basis of which it is planned to export and import the tissues and cells (for example, between a tissue establishment and a donor or a recipient (if relating to gametes));

8.2. append the following to the application referred to in Sub-paragraph 8.1 of this Regulation:

8.2.1. the documents on the tissue establishment, including the duties and obligations of the responsible persons;

8.2.2. a description of the quality management system in accordance with Chapter 4 of this Regulation. The description shall include at least the following documents:

8.2.2.1. the standard operating procedures;

8.2.2.2. the personnel training and reference manuals;

8.2.2.3. the guidelines;

8.2.2.4. report sample forms;

8.2.2.5. the procedures for the record-keeping of donors;

8.2.2.6. information on the final destination of the tissues and cells;

8.3. submit to the Agency copies of the contracts entered into with other tissue establishments, procurement organisations, or third parties for the provision of basic services.

8.1 A medical treatment institution shall not be required to obtain the authorisation from the Agency for the procurement of the tissues and cells (including donor selection and laboratory testing) if the medical treatment institution has a contractual relationship with a tissue establishment that holds the authorisation issued by the Agency for the use of the tissues and cells and the abovementioned medical treatment institution is specified in Annex 2 thereto. In such case, the medical treatment institution shall comply with the requirements of this Regulation in respect of the activities to be carried out and the Agency shall assess the operation of the medical treatment institution within the scope of the supervision of the respective tissue establishment.

[*14 March 2017*]

8.2 A medical treatment institution without contractual relationship with a tissue establishment holding the authorisation issued by the Agency and seeking to perform the procurement of the tissues and cells (including donor selection and laboratory testing) shall be considered to be a tissue establishment within the meaning of this Regulation with regard to the activities for which the authorisation is required in accordance with this Regulation.

[*14 March 2017*]

8.3 If a tissue establishment intends, in addition to the core activity, to import the tissues and cells, it shall, after having taken the necessary measures to ensure that the import of the tissues and cells complies with the quality and safety standards laid down in this Regulation and to ensure traceability of the imported tissues and cells from donor to recipient and vice versa, add the following additional information to the application referred to in Paragraph 8 of this Regulation:

8.31. general information on the tissue establishment which, in addition to the core activity, intends to import the tissues and cells:

8.31.1. the name of the tissue establishment (the name of the medical treatment institution);

8.31.2. the actual address for visitors of the tissue establishment;

8.31.3. the legal address of the tissue establishment (if different);

8.31.4. the status of the tissue establishment:

8.31.4.1. indicate whether the tissue establishment has previously obtained the authorisation from the Agency for certain activities with the tissues and cells or whether the tissue establishment is applying to the Agency to obtain the authorisation for the first time;

8.31.4.2. indicate the code in the database of tissue establishments if the tissue establishment has already obtained the authorisation;

8.31.5. the name of the unit submitting the application (if different from the name of the medical treatment institution);

8.31.6. the actual address for visitors of the unit submitting the application;

8.31.7. if the applicant is a branch of a medical treatment institution, the legal address of the branch (if different from the actual address);

8.31.8. the name of the site of reception of import (if different from the name of the medical treatment institution and the name of the unit submitting the application);

8.31.9. the address of the site of reception for visitors;

8.32. information on the person submitting additional information in relation to the import of the tissues and cells:

8.32.1. the given name, surname of the person responsible for the submission of additional information;

8.32.2. telephone number;

8.32.3. e-mail address;

8.33. information on the responsible person of the tissue establishment (if different from the person responsible for the submission of additional information):

8.33.1. the given name, surname;

8.33.2. the telephone number (if different from the telephone number of the person responsible for the submission of additional information to the Agency);

8.33.3. the e-mail address (if different from the e-mail address of the person responsible for the submission of additional information to the Agency);

8.34. the website of the importing tissue establishment (if applicable);

8.35. information on the tissues and cells to be imported:

8.35.1. a list of the types of the tissues and cells to be imported, including a list of specific types of tissues or cells intended for one-off import;

8.35.2. the product name (if applicable, in accordance with the European Union generic list) of all types of the tissues and cells to be imported;

8.35.3. the trade name (if different from the product name) of all types of the tissues and cells to be imported;

8.35.4. the name of the third country supplier for each type of the tissues and cells to be imported;

8.36. information on the location of activities:

8.36.1. a list specifying which of the activities of donation, procurement, testing, processing, preservation, or storage are carried out prior to import by the third country supplier per type of tissue or cell;

8.36.2. a list specifying which of the activities of donation, procurement, testing, processing, preservation, or storage are carried out prior to import by sub-contractors of the third country supplier per type of tissue or cell;

8.36.3. a list of all activities carried out by the importing tissue establishment subsequent to import per type of tissue or cell;

8.36.4. the names of the third countries in which the activities prior to import take place per type of tissue or cell;

8.37. information on third country suppliers:

8.37.1. the name of the supplier(-s) (the name of the performer of economic activity);

8.37.2. the given name, surname of the contact person;

8.37.3. the address for visitors;

8.37.4. the legal address (if different);

8.37.5. the telephone number including international dialling code;

8.37.6. the continuously available emergency telephone number (if different);

8.37.7. the e-mail address.

[*14 March 2017*]

8.4 The following latest information and documents shall be appended to the information referred to in Paragraph 8.3 of this Regulation:

8.41. a copy of the contract entered into with the third country supplier(-s);

8.42. a detailed description of the flow of imported tissues and cells from their procurement to their reception at the importing tissue establishment;

8.43. a copy of the export authorisation certificate of the third country supplier or, if a specific export authorisation certificate is not issued, certification from the relevant third country competent authority or authorities authorising the activities of the third country supplier in the tissues and cells sector, including exports. This documentation shall also include the contact details of the third country competent authority or authorities. In third countries where such documentation is not available, other forms of documentation shall be provided such as reports of audits of the third country supplier.

[*14 March 2017*]

8.5 A tissue establishment which, in addition to the core activity, intends to import the tissues and cells shall make available and, upon request of the Agency, submit to the Agency the following documents on the tissue establishment and the third country supplier:

8.51. documentation relating to the tissue establishment:

8.51.1. a job description of the responsible person and detailed information on qualification and training in accordance with the requirements laid down in this Regulation;

8.51.2. a copy of the primary label, a copy of the repackage label, and documentation on the external package and transportation container;

8.51.3. a list of the latest versions of standard operating procedures relating to the import activities of the tissue establishment, including standard operating procedures on applying the Single European Code, reception and storage of imported tissues and cells at the tissue establishment, management of adverse events and reactions, management of recalls and traceability from donor to recipient;

8.52. documentation relating to the third country supplier or suppliers:

8.52.1. a detailed description of the criteria used for donor identification and evaluation, and also information provided to the donor or donor family, how consent is obtained from the donor or donor family and whether the donation was voluntary and unpaid or not;

8.52.2. detailed information on the testing centre used by third country suppliers and the tests carried out by such centres;

8.52.3. detailed information on the methods used during the processing of the tissues and cells, including details of the validation for the critical processing procedure;

8.52.4. a detailed description of the facilities, critical equipment and materials, and also the criteria used for quality control and control of the environment for each activity carried out by the third country supplier;

8.52.5. detailed information on the conditions for release of the tissues and cells by the third country supplier or suppliers;

8.52.6. information on any sub-contractors used by the third country suppliers (including the name, location, and activity undertaken);

8.52.7. a summary of the most recent inspection of the third country supplier by the third country competent authority or authorities, including the date of the inspection, type of inspection, and main conclusions;

8.52.8. a summary of the most recent audit of the third country supplier carried out by, or on behalf of, the tissue establishment;

8.52.9. any relevant national or international accreditation document.

[*14 March 2017*]

8.6 The documents referred to in Paragraphs 8.4 and 8.5 of this Regulation need not be submitted:

8.61. in the case of one-off import, if tissue establishments which, in addition to the core activity, intend to import the tissues and cells take the necessary measures to ensure the traceability of imported tissues and cells from donor to recipient and vice versa in accordance with the requirements laid down this Regulation, and use them only for the intended recipients;

8.62. if the tissue establishment which, in addition to the core activity, intends to import the tissues and cells has previously submitted the abovementioned documents to the Agency in relation to obtaining the authorisation.

[*14 March 2017*]

9. The Agency shall assess the application referred to in Paragraph 8 of this Regulation and the documents attached thereto or the information and documents referred to in Paragraphs 8.3, 8.4, and 8.5 of this Regulation, determine whether the tissue establishment is registered in the register of medical treatment institutions and whether it meets the mandatory requirements established for medical treatment institutions and units thereof, assess the compliance of the tissue establishment with the requirements laid down in Chapters 3 and 4 of this Regulation in relation to the use of tissues and cells and within one month after receipt of the application shall take the decision on issuance of the authorisation or refusal to issue the authorisation. The Agency shall notify the applicant of the decision on issuance of the authorisation or refusal to issue the authorisation in accordance with the procedures laid down in the Law on Notification.

[*14 March 2017*]

10. If, upon examination of the application referred to in Paragraph 8 of this Regulation and the documents attached thereto or the information and documents referred to in Paragraphs 8.3, 8.4, and 8.5 of this Regulation, the Agency finds that they are incomplete or do not meet the requirements referred to in Chapters 3 and 4 of this Regulation, it shall, within five working days after receipt of the application, request the tissue establishment in writing to clarify the information.

[*14 March 2017*]

11. The tissue establishment shall, within 10 working days after receipt of the request referred to in Paragraph 10 of this Regulation, submit to the Agency documents certifying the elimination of the deficiencies.

12. The Agency shall assess the documents referred to in Paragraph 11 of this Regulation and assess the compliance of the tissue establishment with the requirements referred to in Chapters 3 and 4 of this Regulation in relation to the use of tissues and cells. Within one month after receipt of the documents referred to in Paragraph 8 of this Regulation, the Agency shall take the decision on issuance of the authorisation (Annex 1) or on refusal to issue the authorisation. The Agency shall notify the applicant of the decision on issuance of the authorisation or refusal to issue the authorisation in accordance with the procedures laid down in the Law on Notification.

[*14 March 2017*]

13. For the purposes of taking the decision referred to in Paragraphs 9, 16, and 20 of this Regulation, an official of the Agency has the right to visit the tissue establishment and the tissue establishment has the obligation to ensure access for the official of the Agency to the documents, facilities, and equipment necessary for taking the decision, and also the presence of the responsible person of the tissue establishment during the visit.

14. The Agency shall take the decision on refusal to issue the authorisation if at least one of the following conditions have set in:

14.1. documents submitted by the tissue establishment contain false information;

14.2. the tissue establishment does not comply with and is unable to meet the requirements referred to in Chapters 3 and 4 of this Regulation in relation to the use of the tissues and cells;

14.3. it has become known to the Agency that the medical treatment institution is not registered in the register of medical treatment institutions;

14.4. it has become known to the Agency that the medical treatment institution fails to comply with the mandatory requirements laid down in the laws and regulations for medical treatment institutions and units thereof;

14.5. the tissue establishment has not submitted all the information referred to in Paragraph 8, 8.3, 8.4, or 8.5 of this Regulation within the time limit referred to in Paragraph 11 of this Regulation.

[*14 March 2017*]

15. The Agency shall indicate the following in the authorisation:

15.1. the special operating conditions, including the tissue and cell preparation processes which may be carried out by the tissue establishment in accordance with the requirements referred to in Sub-chapter 3.2 of this Regulation, and also any restrictions on the type of the tissues and cells to be imported or on third country suppliers;

15.2. information on procurement organisations and third parties which carry out activities in accordance with the contracts entered into;

15.3. information on the laboratory which, on the basis of the contract, carries out the laboratory testing of the donor blood or donation samples and which complies with the mandatory requirements laid down in the laws and regulations for medical treatment institutions and units thereof.

[*14 March 2017*]

16. The Agency shall take into account the information on the tissues and cells obtained but not used in the tissue establishment and included in the annual activity report referred to in Paragraph 142 of this Regulation when taking the decision on issuance of the authorisation and indicating in the authorisation that the tissue establishment is entitled to export tissues or cells to third countries or to receive the tissues and cells imported from third countries.

17. If the authorisation is damaged, destroyed, lost, or stolen, the tissue establishment shall inform the Agency in writing thereof within three working days and apply for a duplicate of the authorisation. The Agency shall, within three working days after receipt of the application, take the decision on the issuance of a duplicate of the authorisation and issue a duplicate of the authorisation. The Agency shall notify the applicant of the decision to issue a duplicate of the authorisation in accordance with the procedures laid down in the Law on Notification.

18. The Agency may suspend the authorisation of a tissue establishment if it is established during supervision that the tissue establishment does not comply with the requirements referred to in Chapters 3 and 4 of this Regulation and shall determine a specific time period for the elimination of the established non-compliances.

[*14 March 2017*]

19. In order to renew the validity of a suspended authorisation, the tissue establishment shall submit to the Agency an application for the renewal of the validity of the authorisation and documents certifying the elimination of the deficiencies due to which the validity of the authorisation has been suspended.

20. The Agency shall assess the application referred to in Paragraph 19 of this Regulation and the documents attached thereto, evaluate the compliance of the tissue establishment with the requirements referred to in Chapters 3 and 4 of this Regulation in relation to the use of the tissues and cells and shall, within one month after receipt of the application, take the decision on renewal of the validity of the authorisation if the deficiencies due to which the validity of the authorisation has been suspended have been eliminated or on cancellation of the authorisation if the deficiencies due to which the validity of the authorisation has been suspended have not been eliminated. The Agency shall notify the applicant of the decision in accordance with the procedures laid down in the Law on Notification.

21. The Agency may cancel the authorisation due to at least one of the following reasons:

21.1. the tissue establishment has requested cancellation of the authorisation issued to it;

21.2. the tissue establishment has infringed the quality and safety requirements for the use of the tissues and cells referred to in Chapters 3 and 4 of this Regulation;

21.3. the activity of the tissue establishment endangers the health and safety of the personnel of the tissue establishment, the donor, and the recipient;

21.4. the tissue establishment fails to comply with the conditions for the activity of the use of the tissues and cells referred to in the authorisation;

21.5. the tissue establishment has failed to eliminate the deficiencies due to which the validity of the authorisation has been suspended within the time period referred to in Paragraph 18 of this Regulation;

21.6. it has become known to the Agency that the tissue establishment has been excluded from the register of medical treatment institutions;

21.7. it has become known to the Agency that the tissue establishment fails to comply with the mandatory requirements laid down in the laws and regulations for medical treatment institutions and units thereof;

21.8. the tissue establishment has submitted false information to the Agency.

[*14 March 2017*]

22. The Agency shall notify the decision on cancellation of the authorisation to the tissue establishment in accordance with the procedures laid down in the Law on Notification.

23. In case of substantial changes (for example, change of the responsible person, introduction of a new type of tissues or cells or processing method) in the activities specified in the authorisation, the tissue establishment, including the importing tissue establishment, shall be required to obtain a new authorisation, in particular for activities carried out in third countries which may affect the quality and safety of imported tissues and cells or in relation to third country suppliers. The importing tissue establishment shall also inform the Agency of its decision to discontinue import activities in whole or in part.

[*14 March 2017*]

23.1 If an importing tissue establishment carries out one-off import of tissues or cells from a third country supplier not covered by the existing authorisation, such import shall not be considered a substantial change if the importing tissue establishment is authorised to import the same type of tissues or cells from another third country supplier or suppliers.

[*14 March 2017*]

23.2 The importing tissue establishment shall immediately inform the Agency of the following:

23.21. the suspension of the export of tissues and cells by the third country supplier or the cancellation of the authorisation;

23.22. any other decision taken on the basis of the non-compliance established by the competent authority or authorities of the country in which the third country supplier is located and that could affect the quality and safety of the imported tissues and cells.

[*14 March 2017*]

24. The Agency shall create and maintain information on tissue establishments, including importing tissue establishments, which have obtained the authorisation, including the information referred to in Paragraph 15 of this Regulation, and shall indicate it in the register that is available on the website of the Agency.

[*14 March 2017*]

24.1 The Agency shall indicate the following in the European Union Tissue Establishment Compendium:

24.11. information on the tissue establishment:

24.11.1. the name of the tissue establishment;

24.11.2. national or international code of the tissue establishment;

24.11.3. the name of the medical treatment institution in which the tissue establishment is located (if applicable);

24.11.4. the address of the tissue establishment;

24.11.5. publishable contact details: e-mail address, telephone, and fax;

24.12. information on the authorisation of the tissue establishment:

24.12.1. the name of the competent authority which issued the authorisation to the tissue establishment;

24.12.2. the name of the competent authority which is responsible for the maintenance of the European Union Tissue Establishment Compendium;

24.12.3. the entity which has obtained the authorisation (if applicable);

24.12.4. the tissues and cells for which the tissue establishment has obtained the authorisation;

24.12.5. the actual activities to be undertaken for which the tissue establishment has obtained the authorisation;

24.12.6. the status of the authorisation (the authorisation has been granted, suspended, cancelled, voluntary cessation of activities);

24.12.7. detailed information on any conditions and exceptions which supplement the authorisation (if applicable).

[*14 March 2017*]

25. The decisions taken by the Agency on issuance of the authorisation or refusal to issue the authorisation, and also on suspension of the validity of the authorisation or cancellation thereof may be contested by the tissue establishment in the Ministry of Health in accordance with the procedures laid down in the Administrative Procedure Law.

26. The decision of the Ministry of Health may be appealed to a court in accordance with the procedures laid down in the Administrative Procedure Law.

27. The Agency may authorise the following:

27.1. the direct distribution of specific tissues and cells from where the procurement is carried out (including by import or export) to medical treatment institutions for immediate transplantation to a known recipient, provided that the supplier has obtained the authorisation for such activity from a competent authority and an application has been submitted to the Agency justifying the necessity for such activity;

27.2. the import or export of specific tissues and cells in case of emergency, provided that an application has been submitted to the Agency, accompanied by a decision of the council of the medical treatment institution that, without such transplantation, the life of the recipient is threatened or irreversible health disorders could occur.

[*14 March 2017*]

27.1 The Agency shall take a decision immediately, but no later than within five working days after receipt of the application and documentation referred to in Paragraph 27 of this Regulation, to authorise or not to authorise the direct distribution of specific tissues and cells from where the procurement is carried out (including import or export) for immediate transplantation or the import or export of specific tissues and cells in case of emergency. The Agency shall notify the tissue establishment of the decision in accordance with the procedures laid down in the Law on Notification.

[*14 March 2017*]

**3. Requirements for the Receipt of the Authorisation and Conditions for the Use of Tissues or Cells**

**3.1. Requirements for the Tissue Establishment and Procurement Organisation for the Procurement of the Tissues and Cells**

28. The procurement of the tissues and cells shall take place in tissue establishments or procurement organisations.

29. The tissue establishment and the procurement organisation shall establish and maintain a quality system based on the principles of good practice.

30. The personnel directly involved in activities relating to the procurement, processing, preservation, storage, and distribution of the tissues and cells in a tissue establishment shall be qualified to perform such tasks and shall be provided with the training determined by clinical personnel specialised in the relevant field or a tissue centre authorised to carry out the procurement of the tissues and cells. The competence of the personnel is evaluated in accordance with Paragraph 106 of this Regulation.

31. The tissue establishment and the procurement organisation shall enter into written contracts with the personnel or clinical personnel responsible for:

31.1. the donor selection (unless they are employed by the same tissue establishment or procurement organisation). The contract shall specify the requirements to be followed to assure compliance with the selection criteria for a donor in accordance with Annex 2 to this Regulation;

31.2. the procurement of tissues or cells (unless they are employed by the same tissue establishment or procurement organisation). The contract shall specify the type of the tissues and cells to be procured and the type of test samples, and also information on compliance with standard operating procedures.

32. The tissue establishment shall designate a responsible person who meets the following criteria and has the following qualifications:

32.1. a higher education diploma in the field of medical or biological sciences;

32.2. at least two years of practical experience in the procurement, testing, processing, preservation, storage, or distribution of the tissues and cells.

33. The responsible person shall ensure the fulfilment of the following requirements in the tissue establishment:

33.1. any activities related to the tissues and cells shall be carried out in accordance with this Regulation and other laws and regulations governing the field of health care;

33.2. the information referred to in Paragraph 8 of this Regulation is provided to the Agency;

33.3. the requirements referred to in Sub-chapters 3.1, 3.2, 3.3, 3.5, 3.6, 3.7, and 3.9, Chapters 2, 4, and 7 of this Regulation, and also Annexes 2, 3, and 4 to this Regulation are complied with.

34. The responsible person shall register and investigate any adverse event occurring during the procurement of the tissues and cells which causes or can cause harm to a living donor and shall carry out an analysis to determine the cause of the adverse event.

35. The responsible person shall identify the potential critical conditions or factors that can affect the quality and safety of the tissues and cells or that come into contact with the tissues and cells.

36. The tissue establishment shall inform the Agency of the given name, surname, and contact details of the responsible person. If the responsible person is replaced by another person, either permanently or for a period of more than three months, the tissue establishment shall immediately inform the Agency of that person, indicating his or her given name, surname, and contact details and the date on which the duties of the abovementioned person commence.

37. The tissue establishment and the procurement organisation shall develop and approve standard operating procedures for the activities to be carried out in order to verify:

37.1. the identity of the donor;

37.2. the consent of a living donor or the authorisation or absence of prohibition of a deceased donor, or the absence of prohibition of the next of kin of the deceased donor for the use of tissues and cells;

37.3. evaluation of the selection criteria for donors in accordance with Sub-chapter 3.3 of this Regulation;

37.4. evaluation of laboratory test results of the donor in accordance with Annexes 3 and 4 to this Regulation.

38. The tissue establishment and the procurement organisation shall develop and approve standard operating procedures describing the traceability of standard operating procedures for the procurement, packaging, labelling, and transportation of tissues and cells (from the point of procurement to the point of delivery to the tissue establishment or application organisation) until the use thereof or until laboratory testing of samples (in the case of direct use and distribution of tissues and cells – until use thereof at the medical treatment institution) in accordance with Sub-chapters 3.4 and 3.5 of this Regulation.

39. The procurement of the tissues and cells shall take place in appropriate facilities, following standard operating procedures established by the tissue establishment and the procurement organisation in order to protect, during the procurement of the tissues and cells, those properties of the tissues and cells which are required for their clinical use, and at the same time minimise the risk of microbiological contamination during the process, including the possibility of contamination of the tissues and cells by personnel, by preventing persons who are carriers of infectious disease from participating in the procurement of the tissues and cells, particularly when the tissues and cells cannot subsequently be sterilised.

40. The tissue establishment and the procurement organisation shall carry out the procurement of the tissues and cells from a living donor in an environment that ensures the health, safety, and privacy of the donors.

41. In case of retrieval of thee tissues and cells from a deceased donor, the area of access must be restricted and a local sterile field using sterile drapes must be used. The personnel carrying out the procurement of the tissues or cells must be clothed appropriately for the type of procurement and this will extend to being scrubbed, gowned in sterile clothing, and also wearing sterile gloves, face shields, and protective masks.

42. Standard operating procedures for the procurement must be appropriate for the type of donor and the type of the tissues and cells donated. The tissue establishment and the procurement organisation shall have standard operating procedures in place to protect the safety of living donors.

43. The laboratory tests provided for in Annexes 3 and 4 to this Regulation shall be carried out on the donor in the tissue establishment or procurement organisation by a medical laboratory which meets the mandatory requirements laid down in the laws and regulations for medical treatment institutions and units thereof, or by a laboratory of another European Union Member State which has been assessed as appropriate by the competent authority of the relevant country.

44. All medical devices used in the tissue establishment and the procurement organisation shall be validated, calibrated, and maintained pursuant to the intended purpose of use in accordance with the laws and regulations regarding the procedures for registration, conformity assessment, distribution, operation, and technical supervision of medical devices.

45. The equipment of the tissue establishment and the procurement organisation shall be maintained, serviced, cleaned, sterilised, and disinfected according to the type and intensity of the use thereof and those activities shall be documented. The results of validation, calibration, and technical supervision of medical devices shall be documented in accordance with Chapter 4 of this Regulation.

46. The tissue establishment shall have a clear standard operating procedure for the removal from distribution of donor tissues and cells and grafts derived therefrom that may have caused serious adverse reactions or serious adverse events.

47. The tissue establishment shall develop standard operating procedures for the handling of the tissues and cells that do not comply with the requirements of this Regulation in order to prevent contamination of other tissues or cells, the operating environment, or personnel.

48. The tissue establishment shall have agreements and standard procedures that prescribe the procedures for the transfer of tissues and cells stored by the tissue establishment after termination of the activity thereof to another tissue establishment duly authorised by the Agency.

**3.2. Requirements for the Standard Operating Procedures of a Tissue Establishment for the Tissue and Cell Preparation**

49. The Agency shall examine regularly compliance of all processes and standard operating procedures related to the preparation, processing, storage, release, and distribution of the tissues and cells, and also compliance of the quality management criteria with the requirements laid down in this Sub-chapter.

50. The tissues and cells received at the tissue establishment shall comply with the requirements referred to in Sub-chapter 3.6 of this Regulation.

51. If the tissue establishment is involved in the processing of the tissues and cells, the standard operating procedures of the tissue establishment shall comply with the following criteria:

51.1. the standard operating procedures for critical processing are validated and provide the recipient with clinically effective tissues or cells. This validation may be based on studies performed by the tissue establishment or on research data published in scientific literature, or, for well-established processing procedures, by retrospective evaluation of the clinical results for tissues supplied by the tissue establishment;

51.2. the tissue establishment has confirmed that the validated process can be carried out consistently and efficiently by the tissue establishment personnel;

51.3. the standard operating procedures are documented in accordance with Sub-paragraphs 111.1, 111.2, 111.3, and 111.4 of this Regulation;

51.4. the tissue establishment shall ensure that all processes are carried out in accordance with the standard operating procedures approved by the tissue establishment;

51.5. the microbial inactivation procedure to be applied to tissues or cells is appropriately specified, documented, and validated;

51.6. the process modified during processing is validated and documented before significant changes are made;

51.7. the standard processing procedures undergo regular critical evaluation to ensure that they continue to achieve the intended results;

51.8. the standard operating procedures for utilisation (disposal) of the tissues and cells must prevent the contamination of other donations and products, the processing environment or personnel. These standard operating procedures shall comply with the laws and regulations governing the management of waste generated in a medical treatment institution.

52. If the tissue establishment is involved in the storage and release of the tissues and cells, the standard operating procedures of the tissue establishment shall comply with the following criteria:

52.1. the maximum storage time is specified according to the type of tissue and cell storage, taking into account the possible deterioration of tissue and cell properties within a specific period of time;

52.2. the tissue establishment shall have a system of inventory hold for the tissues and cells which provides for that the tissues and cells may be distributed only in compliance with all the requirements laid down in this Regulation and shall have a standard operating procedure specifying the conditions for the distribution of the tissues and cells;

52.3. a system for the identification of the tissues and cells throughout any phase of processing in the tissue establishment must clearly distinguish released from non-released (quarantined) and discarded tissues and cells;

52.4. records must demonstrate compliance with all appropriate requirements before the release of the tissues and cells. The relevant medical records, processing records, and test results have been verified by authorised persons and the responsible person in accordance with an approved standard operating procedure. If a computerised system is used to release results from the laboratory, the control records shall reflect the person responsible for that release;

52.5. a documented risk assessment approved by the responsible person in accordance with Sub-chapter 3.1 of this Regulation shall be carried out in the tissue establishment to determine the use of all stored tissues and cells following the introduction of any new donor selection or testing criteria or any significantly modified processing step that enhances safety and quality.

53. If the tissue establishment is involved in the distribution of the tissues and cells, the standard operating procedures of the tissue establishment shall comply with the following criteria:

53.1. critical transportation conditions, for example, temperature and time limit must be defined to maintain the required tissue and cell properties;

53.2. the container (package) must be secure, the tissues and cells must be stored in appropriate conditions, all containers and packages must be validated as fit for purpose;

53.3. if distribution of the tissues and cells is carried out by a contracted third party, the tissue establishment must have entered into a written contract defining conditions for the distribution of the tissues and cells (in order to ensure that the required conditions are maintained);

53.4. there must be personnel authorised within the tissue establishment to assess the need for the recall of tissues or cells, and also to initiate and coordinate the necessary actions;

53.5. an effective recall standard operating procedure must be in place in the tissue establishment, including a description of the responsibilities and actions to be taken. This must include a notification to the Agency;

53.6. actions of the tissue establishment must be taken within pre-defined periods of time and must include tracing all relevant tissues and cells and, where necessary, must include trace-back. The purpose of the investigation is to identify any donor who might have contributed to causing the reaction in the recipient and to retrieve the available tissues and cells from that donor, and also to notify recipients of the tissues and cells procured from the same donor in the event that they might have been put at risk;

53.7. the tissue establishment shall develop standard operating procedures for the handling of requests for the tissues and cells. The rules for the allocation of the tissues and cells to certain patients or medical treatment institutions must be documented and made available to these parties upon request;

53.8. the tissue establishment shall establish a system for the handling of returned tissues and cells, including criteria for their acceptance into the inventory, if applicable, and also shall document this.

**3.3. Selection of Tissue and Cell Donors**

54. In assessing the suitability of a tissue and cell donor for the purpose of procurement and use of specific tissues and cells, the physician of the tissue establishment shall take into account the following:

54.1. the selection criteria for donors (except for gamete donors) in accordance with Annex 2 to this Regulation;

54.2. the evaluation of laboratory test results of the donor (except for gamete donors) in accordance with Annex 3 to this Regulation;

54.3. the evaluation of the selection criteria for and laboratory test results of gamete donors in accordance with Annex 4 to this Regulation.

55. In assessing the suitability of each potential tissue and cell donor (except for partner donation of gametes or autologous donors) for the purpose of procurement and use of specific tissues and cells, the physician of the tissue establishment shall take into account the following:

55.1. the information acquired during conversation with the potential donor or a person who has known the donor well (in the case of a deceased donor) and that may be proved by documentary evidence;

55.2. the information acquired during conversation with the family doctor or attending physician of the potential donor and that may be proved by documentary evidence;

55.3. data of the medical history of the potential donor:

55.3.1. anamnesis of life and diseases;

55.3.2. results of physical, clinical, and laboratory tests;

55.4. autopsy results (in the case of a deceased donor);

55.5. the requirement to perform a physical examination of the body (when justified) in order to detect any signs that may be sufficient in themselves to exclude the donor or conditions which must be assessed in the light of the medical and personal history of the donor.

56. The tissue establishment shall keep donor records for each donor in the donor database which shall contain the following information:

56.1. the given name, surname, sex, date of birth, and age of the donor;

56.2. if a mother and child are involved in the donation, the given name, surname, date of birth of the mother and the given name and surname, if known, and date of birth of the child;

56.3. consent:

56.3.1. acknowledgement of the donor that he or she consents to become a tissue or cell donor (for living donors);

56.3.2. information on the will expressed during the lifetime of a deceased donor, indicating the following:

56.3.2.1. whether there is any information in the Population Register prohibiting or authorising the use of the body, tissues, cells, and organs after death;

56.3.2.2. written acknowledgement by the next of kin of the will expressed during the lifetime of a donor to authorise the use of the body, tissues, cells, and organs after death (if such information is not included in the Population Register);

56.4. anamnesis of life and diseases, indicating the following data:

56.4.1. results of health examination or, where necessary, outcome of body examination;

56.4.2. haemodilution formula (where necessary);

56.4.3. clinical and laboratory test results, and also the results of other tests carried out;

56.4.4. if an autopsy was performed, the results thereof must be included in the donor record (for the tissues and cells that cannot be stored for extended periods, a preliminary verbal report of the autopsy must be recorded);

56.4.5. suitability of haematopoietic progenitor cell donor for the chosen recipient;

56.5. acknowledgement by the authorised medical practitioner of the tissue establishment of the consistency of the information contained in the donor records (except for partner donation of gametes or autologous donors).

57. The tissue establishment or application organisation performing the tissue or cell transplantation must have access to the information on the donor in order to confirm the suitability of the donor in case the procurement organisation has limited access to the recipient data in cases of unrelated donations.

58. A unique identifying code shall be allocated to the donor and the donated tissues and cells, during procurement or at the tissue establishment, and shall be entered in a register maintained for the purpose.

59. Prior to procurement of the tissues and cells, the physician of the tissue establishment shall take the following actions:

59.1. if the tissues and cells are to be procured from a living donor, inform the donor in a comprehensible manner of:

59.1.1. the purpose and nature of the procurement of the tissues and cells, the consequences and possible risks of procurement;

59.1.2. the therapeutic purpose and possible benefits of the procurement of the tissues and cells;

59.1.3. the measures for the recording and protection of donor data (donor data confidentiality);

59.1.4. the donor protection measures;

59.1.5. laboratory tests (if applicable) and the right to receive the results of such tests and explanations thereof;

59.1.6. any significant changes (abnormalities) detected in the evaluation and testing procedures which shall be documented;

59.1.7. the necessity to obtain mandatory donor consent and authorisation prior to the procurement of the tissues and cells;

59.2. if the tissues and cells are to be procured from a deceased donor, the following shall be verified:

59.2.1. existence of the authorisation or absence of prohibition of a deceased donor or absence of prohibition of the next of kin of a deceased donor for the use of the tissues and cells in compliance with the requirements laid down in the law On the Protection of the Body of Deceased Human Beings and the Use of Human Tissues and Organs in Medicine;

59.2.2. whether confirmed results of the donor evaluation have been communicated and explained to the next of kin of a deceased donor.

60. The tissue establishment shall ensure that the information referred to in Paragraphs 56 and 59 of this Regulation is true, clearly legible, without corrections, and complete. There shall be documented evidence of donor information.

61. Prior to procurement of the tissues and cells, the authorised person of the tissue establishment shall verify the following:

61.1. existence of a written consent by a living donor and in the case of a deceased donor – existence of the authorisation or absence of prohibition of a deceased donor or absence of prohibition of the next of kin of a deceased donor for the use of the tissues and cells in compliance with the requirements laid down in the law On the Protection of the Body of Deceased Human Beings and the Use of Human Tissues and Organs in Medicine;

61.2. donor identity and a record of how and by whom the donor was identified;

61.3. that the information referred to in Sub-paragraph 64.6 of this Regulation has been recorded in the case of a deceased donor;

61.4. whether the donor (in case of a living donor):

61.4.1. understood the information referred to in Sub-paragraph 59.1 of this Regulation;

61.4.2. used the opportunity to ask questions and received answers;

61.4.3. confirmed that all the information provided to him or her is true.

**3.4. Donation and Procurement of the Tissues and Cells**

62. Allogeneic transplantation of the tissues and cells may be carried out for the benefit of the recipient only if the following conditions are simultaneously fulfilled:

62.1. the tissues and cells are removed for medical or scientific and therapeutic purposes;

62.2. all the removed tissues and cells are donated.

63. Procurement of the tissues and cells shall be authorised only after fulfilment of all requirements laid down on this Regulation and the law On the Protection of the Body of Deceased Human Beings and the Use of Human Tissues and Organs in Medicine in respect of mandatory consent and authorisation.

64. The procurement organisation shall prepare a report to the tissue establishment and the following information shall be included therein:

64.1. the identification (name and address) of the tissue establishment which receives tissues or cells;

64.2. donor identification data (including how and by whom the donor was identified);

64.3. description and identification of procured tissues and cells (including samples for testing);

64.4. identification of the person who is responsible for the procurement (including signature);

64.5. the date, time, where relevant, start and end, location of procurement, technology used, environmental conditions at the procurement facility (where relevant), and also the standard operating procedure used, including any incidents that occurred;

64.6. for deceased donors – date and time of death (if known), conditions under which the cadaver is kept, refrigerated (or not), time of start and end of refrigeration;

64.7. identification (batch) numbers of reagents and preservation solutions.

65. If sperm is procured at home, the procurement organisation must specify and include the following information in the report:

65.1. the tissue establishment (name and address) which receives tissues or cells;

65.2. donor identification;

65.3. the date and time of procurement (if known).

66. Following procurement, the tissues and cells must be packaged in a manner which minimises the risk of contamination and must be stored at temperatures that preserve the properties and biological functions of the tissues and cells. The packaging must also prevent the risk of contamination of the personnel responsible for packaging and transportation of the tissues and cells.

67. In the case of retrieval of the tissues and cells from a deceased donor, the procurement organisation or tissue establishment shall record the place of procurement and the time interval from death of the donor to procurement of the tissues and cells in order to ensure that the required biological and physical properties of the tissues and cells are retained. Once the tissues and cells have been retrieved from a deceased donor body, it must be reconstructed so that it is as similar as possible to its original anatomical appearance. The tissue establishment and the procurement organisation shall ensure the personnel and equipment required for that purpose.

[*27 January 2015*]

**3.5. Labelling and Transportation of Procured Tissues and Cells**

68. At the time of procurement, every package containing the tissues and cells must be labelled.

69. The following information must be provided when labelling the primary tissue or cell container:

69.1. the type of the tissues and cells, the identification number or code of the tissues and cells, and the lot or batch number, if applicable;

69.2. identification of the tissue establishment;

69.3. expiry date;

69.4. in the case of autologous donations, “Paredzēts tikai autologai izmantošanai” [For autologous use only] and “Identificēt donoru (recipientu)” [The donor (recipient) has to be identified];

69.5. in the case of directed donations, the intended recipient (on the label);

69.6. when the tissues and cells are known to be positive for a relevant infectious disease marker, it must be labelled “Bioloģiski bīstams” [Biological hazard];

69.7. the Single European Code as applicable to the tissues and cells being distributed for human application or the donation identification sequence as applicable to the tissues and cells released for circulation, other than distributed for human application.

[*14 March 2017*]

70. The added tissue, cell or blood samples shall be labelled in order to ensure donor identification, and also the date and place of taking the sample shall be specified.

71. The following information must be provided either on the label of the primary container or in accompanying documentation:

71.1. description and, if relevant, dimensions of the tissue or cell product;

71.2. morphology and functional data, if applicable;

71.3. the date of distribution of the tissues or cells;

71.4. results of laboratory tests carried out on the donor;

71.5. storage recommendations;

71.6. instructions for opening the container, package, and any required manipulation or reconstitution;

71.7. expiry dates after opening or manipulation;

71.8. instructions for reporting serious adverse reactions or serious adverse events in accordance with Sub-chapter 3.9 of this Regulation;

71.9. presence of potential harmful residues (for example, antibiotics, ethylene oxide);

71.10. the information referred to in Sub-paragraphs 69.4, 69.5, and 69.7 of this Regulation. If it is not possible to include this information on the primary container label, it must be provided on a separate sheet accompanying the primary container in a manner that ensures that they remain together;

71.11. for imported tissues and cells, the country of procurement and the exporting country (if different from the procurement country).

[*14 March 2017*]

72. The tissues and cells shall be transported in containers suitable for the transportation of biological materials, ensuring the safety and quality of the tissues and cells contained therein, the appropriate temperature regime and avoiding contamination of tissues, cells, and responsible personnel.

73. During transportation the primary container must be placed in a shipping container that must be labelled with at least the following information:

73.1. an indication that the package contains human tissue and cells and an inscription “Rīkoties uzmanīgi” [Handle with care];

73.2. the identification of the tissue establishment from which the package is being transported (address and telephone number), and also a contact person in the event of problems during transportation;

73.3. the identification of the tissue establishment of destination responsible for human application of the tissues and cells or application organisation (address and telephone number), and also the person to be contacted to take delivery of the container;

73.4. the date and time of the start of transportation;

73.5. specifications concerning conditions of transportation relevant to the quality and safety of the tissues and cells;

73.6. in the case of all cellular products, the indication “Neapstarot” [Do not irradiate];

73.7. where living cells are required for the function of the graft (for example, stem cells, gametes), the indication “Neapstarot” [Do not irradiate];

73.8. when a product is known to be positive for a relevant infectious disease marker, the indication “Bioloģiski bīstams” [Biological hazard];

73.9. in the case of autologous donors, the indication “Tikai autologai izmantošanai” [For autologous use only];

73.10. specifications concerning storage conditions (for example, “Nesasaldēt” [No not freeze]);

73.11. safety instructions and method of cooling (when applicable);

73.12. recommended transport conditions (for example, “Glabāt vēsumā” [Keep cool], “Pārvietot vertikāli” [In upright position], etc.).

**3.6. Reception of the Tissues and Cells at the Tissue Establishment**

74. A consignment of the tissues and cells received at the tissue establishment shall be documented, thus ascertaining the compliance thereof with the requirements referred to in Sub-chapters 3.3, 3.4, 3.5, 3.6, 3.7, and 3.9 of this Regulation, including the conditions for transportation, packaging, labelling, accompanying documents and samples, and also shall indicate whether the consignment has been accepted or rejected.

75. The tissue establishment shall ensure that the tissues and cells received are quarantined until the responsible person has verified the accompanying documents and the donations received and has confirmed their compliance with the requirements laid down in this Regulation, and also informed the donor thereof.

76. The tissue establishment shall establish procedures for the verification of each consignment of the tissues and cells, including samples. The tissues and cells which do not comply with the requirements laid down in this Regulation and regarding the donor of which the results of the laboratory tests specified in this Regulation have not been received shall be documented and stored separately from other tissues and cells and shall not be used until fulfilment of the requirements laid down in this Regulation.

77. The tissue establishment shall include the following information in the tissue and cell database (except for gamete donors for whom a partner donation is intended):

77.1. the purpose for which the tissues and cells may be used (therapeutic, scientific);

77.2. consent of the donor (except for deceased donors) and instructions of the donor for disposal of the tissues and cells if not used for the purpose for which consent was obtained;

77.3. conditions in which the procurement of the tissues and cells takes place (including anamnesis of life and diseases of the donor);

77.4. results of physical examinations, clinical and laboratory tests and of other tests, for example, the autopsy report and cause of the death (for deceased donors);

77.5. donor evaluation in accordance with the selection criteria for donors laid down in Annex 2 to this Regulation (in the case of an allogeneic donor);

77.6. possibility of medicinal allergies of the recipient if the tissues and cells are intended for autologous use (if the use of cells is intended).

78. The tissue establishment shall include the following in the information on gametes intended for partner donation and to be registered in the tissue and cell database:

78.1. the purpose for which the tissues and cells may be used (therapeutic, scientific);

78.2. written acknowledgement of the donor consent to the use of the tissues and cells for a specific purpose;

78.3. instructions for disposal of the tissues and cells (if not used for the purpose for which consent was obtained);

78.4. donor identification and characteristics, i.e. type, age, sex of donor, presence of risk factors (in the case of a deceased donor, the cause of death);

78.5. partner identification;

78.6. place of procurement of the tissues and cells;

78.7. the tissues and cells obtained, their characteristics.

**3.7. Traceability Requirements for the Tissues and Cells**

79. Tissue establishments and tissue application organisations shall ensure traceability of the tissues and cells in accordance with the requirements of this Regulation through documentation and the use of the Single European Code from procurement to human application or disposal and vice versa.

[*14 March 2017*]

79.1 The tissues and cells used for the manufacture of advanced therapy medicinal products shall be traceable in accordance with this Regulation until the transfer thereof to the manufacturer of advanced therapy medicinal products.

[*14 March 2017*]

79.2 If the personnel involved in retrieval of the tissues and cells from a deceased donor is employed by two or more tissue establishments, the medical treatment institution shall ensure a traceability system corresponding to this Regulation and covering the procurement of the tissues and cells at various tissue establishments.

[*14 March 2017*]

80. All tissues and cells procured, processed, stored, and distributed in the tissue establishment and the tissue application organisation shall be traceable from donor to recipient and from recipient to donor, regardless of the intended purpose of use of the tissues and cells and the medical treatment institution to which the tissues and cells are delivered. This traceability shall also apply to all data relating to articles and materials that have come into contact with the tissues and cells.

81. In order to ensure donor identification and traceability, each tissue and cell sample obtained and the graft prepared therefrom shall be allocated an identification code in accordance with Paragraph 58 of this Regulation.

82. The tissue establishment shall include at least the following information in the traceability system:

82.1. donor identification;

82.2. donation identification that shall include at least the following information:

82.2.1. identification of the tissue establishment or procurement organisation (including contact details);

82.2.2. unique donation number;

82.2.3. the date of procurement of the tissues and cells;

82.2.4. the place of procurement of the tissues and cells;

82.2.5. the type of donation (for example, single or multi-tissue, autologous, a living or deceased donor);

82.3. product identification that shall include at least the following information:

82.3.1. identification of the tissue establishment;

82.3.2. the type of the tissues and cells (product) (basic nomenclature);

82.3.3. pool number (in case of pooling);

82.3.4. split number (if applicable);

82.3.5. expiry date (if applicable);

82.3.6. tissue or cell status (for example, quarantined, suitable for use);

82.3.7. description and origin of the product, processing steps applied, materials and additives coming into contact with the tissues and cells and having an effect on their quality and safety;

82.3.8. institution (unit) issuing the final label;

82.4. Single European Code (if applicable);

82.5. identification of the tissues and cells intended for human application:

82.5.1. the date of distribution (disposal);

82.5.2. identification of the medical practitioner or end-user (institution (unit)).

[*14 March 2017*]

83. The tissue application establishment shall include at least the following information in the traceability system:

83.1. identification of the supplier tissue establishment;

83.2. identification of the medical practitioner or end-user (institution (unit));

83.3. the type of the tissues and cells;

83.4. product identification;

83.5. identification of the recipient of tissues or cells;

83.6. the date of application of tissues or cells;

83.7. Single European Code (if applicable).

[*14 March 2017*]

84. The tissue establishment shall enter into a written agreement with the third parties in all cases where there is an external activity that affects the quality and safety of the tissues and cells processed in cooperation with the third party, and also in the following cases:

84.1. the tissue establishment entrusts the third party with one of the steps in the processing of tissues or cells;

84.2. the third party supplies goods and services affecting the quality and safety of the tissues or cells, including their distribution;

84.3. the tissue establishment provides services to an unauthorised tissue establishment;

84.4. the tissue establishment distributes tissues or cells processed by the third party.

85. Tissue establishments shall evaluate and enter into contracts with the third parties according to their capacity to comply with the requirements laid down in this Regulation.

86. The tissue establishment may enter into contracts for the transportation of the tissues and cells and the provision of other processes not related to the procurement and application of the tissues and cells with the third parties that may be other than a medical treatment institution.

87. Contracts entered into between the tissue establishments and the third parties shall specify the obligations and responsibilities of the parties and the detailed arrangements for cooperation. Tissue establishments shall maintain a complete database of the abovementioned contracts.

88. The tissue establishment, the procurement organisation, and the tissue application organisation shall ensure the anonymity of the tissue and cell donor, the protection and confidentiality of personal data, and also genetic data.

89. In order to ensure compliance with the requirements specified in Paragraph 82 of this Regulation, including the circulation of information, the organisations referred to in Paragraph 88 of this Regulation shall:

89.1. organise security measures to prevent unauthorised addition, deletion, or modification of data in the donor records or in the register of rejected grafts and to ensure secure transmission of information;

89.2. take appropriate action in the event of a data discrepancy;

89.3. ensure non-disclosure of personal data, and also the functioning of the traceability system.

90. The tissue establishment and the tissue application organisation shall ensure that information on the personal data of the donor is not disclosed to the recipient and his or her relatives and information on the personal data of the recipient is not disclosed to the donor and his or her relatives, in particular with regard to the donation of gametes.

91. The donor records referred to in Paragraph 56 and the data referred to in Paragraphs 82 and 83 of this Regulation shall be kept for at least 30 years after the clinical use of tissues or cells in accordance with the requirements of the laws and regulations governing the management of documents and archives.

**3.7.1 European Coding System**

[*14 March 2017*]

91.1 The Single European Code shall be allocated to all tissues and cells (except for the cases referred to in Paragraph 91.2 of this Regulation) distributed for human application. In other cases, where the tissues and cells are released for circulation, the donation identification sequence shall be applied (at least in the accompanying documentation).

[*14 March 2017*]

91.2 The Single European Code shall not be allocated to:

91.21. reproductive cells donated by the partner;

91.22. tissues and cells other than reproductive cells donated by the partner if the tissues and cells remain within the same medical treatment institution;

91.23. tissues and cells distributed directly for immediate transplantation to the recipient in accordance with Sub-paragraph 27.1 of this Regulation;

91.24. tissues and cells imported to a European Union Member State or a country of the European Economic Area in case of emergency expressly authorised by the Agency;

91.25. tissues and cells imported into a European Union Member State or a country of the European Economic Area if the relevant tissues and cells remain in the same medical treatment institution from import to application, provided that there is a tissue establishment located in the relevant medical treatment institution which has obtained the authorisation to carry out import activities.

[*14 March 2017*]

91.3 The Single European Code shall comply with the requirements laid down in Annex 10 to this Regulation, and also:

91.31. has been drawn up in easily legible format. The Code shall be preceded by the acronym SEC. The parallel use of other labelling and traceability systems is possible;

91.32. when drawing up the Single European Code, the donation identification sequence and the product identification sequence shall be separated by a single space or printed as two successive lines.

[*14 March 2017*]

91.4 The tissue establishment shall comply with the following minimum requirements in the application of the Single European Code:

91.41. allocate a Single European Code to all tissues and cells requiring application of this code at the latest before their distribution for human application;

91.42. allocate a donation identification sequence after procuring the tissues and cells or after receipt thereof from a procurement organisation or a third country supplier. The tissue establishment where the tissues and cells are pooled shall ensure the traceability of each individual donation by allocating a new donation identification number to the end product;

91.43. not alter the donation identification sequence once it is allocated to the tissues and cells released for circulation unless it is necessary to correct an encoding error. Any correction requires proper documentation;

91.44. use the EUTC, ISBT128 or Eurocode coding system and the relevant tissue and cell product numbers included in the European Union Tissue and Cell Product Compendium before their distribution for human application;

91.45. use an appropriate split number and expiry date. For the tissues and cells for which no expiry date is defined, the expiry date shall be 00000000 before their distribution for human application;

91.46. apply the Single European Code on the label of the relevant product and accompanying documentation before its distribution for human application. The indication shall be indelible and permanent. If the label size precludes the application of the Single European Code on the label, the code shall be unambiguously linked to the tissues and cells packaged with such a label through the accompanying documentation. The tissue establishment may entrust indication of the Single European Code to a third party, provided that the tissue establishment ensures compliance with the requirements laid down in this Regulation, in particular in terms of uniqueness of the code;

91.47. notify the Agency of the following:

91.47.1. the information contained in the European Union Tissue Establishment Compendium requires an update or correction;

91.47.2. the European Union Tissue and Cell Product Compendium requires an update;

91.47.3. the tissue establishment observes a situation of significant non-compliance with the requirements relating to the Single European Code concerning the tissues and cells received from other European Union tissue establishments;

91.48. take the necessary measures in case of incorrect application of the Single European Code on the label.

[*14 March 2017*]

91.5 The Agency shall:

91.51. enter tissue establishment data into the database in order to ensure the allocation of a unique tissue establishment number to all tissue establishments which have obtained the authorisation:

91.51.1. if a tissue establishment has different physical locations, but has one system for allocating unique donation numbers, it may be deemed to be one and the same tissue establishment;

91.51.2. if a tissue establishment uses two or more systems to allocate unique donation numbers, such unit of the tissue establishment or location shall be allocated separate tissue establishment numbers corresponding to the number of allocation systems used;

91.52. monitor and enforce the full implementation of the Single European Code by the tissue establishment;

91.53. ensure the validation of the data on the tissue establishments contained in the European Union Tissue Establishment Compendium and, within 10 working days after any change significantly affecting the activities specified in the authorisation of the relevant tissue establishment, update the Compendium in particular in the following situations:

91.53.1. a new tissue establishment obtains the authorisation;

91.53.2. the information of the tissue establishment changes or is not correctly registered in the European Union Tissue Establishment Compendium;

91.53.3. in the case of change of detailed information of the tissue establishment specified in Paragraph 24.1 of this Regulation related to the authorisation, including:

91.53.3.1. issuance of the authorisation in relation to a new tissue or cell type;

91.53.3.2. issuance of the authorisation in relation to a new prescribed activity for the use of tissues and cells;

91.53.3.3. detailed information on any conditions or exceptions which supplement the conditions for the activity of the tissue establishment;

91.53.3.4. complete or partial suspension of a specific authorisation for a particular activity or tissue or cell type;

91.53.3.5. complete or partial cancellation of the authorisation of a tissue establishment;

91.53.3.6. situations where a tissue establishment voluntarily ceases the activity for which it has obtained the authorisation;

91.54. alert the competent authorities of another Member State when they observe incorrect information in the European Union Tissue Establishment Compendium relating to the other Member State or when they observe a situation of significant non-compliance with the provisions relating to the Single European Code relating to the other Member State;

91.55. alert the Commission and other competent authorities when in their assessment the European Union Tissue and Cell Product Compendium requires an update.

[*14 March 2017*]

91.6 The tissue establishment shall use one of the following systems to allocate a unique donation number:

91.61. a system of the tissue establishment;

91.6 2. an international system for allocating a unique donation number compatible with the Single European Code.

[*14 March 2017*]

**3.8. Import and Export of the Tissues and Cells**

92. The import and export of the tissues and cells from and to third countries shall be carried out by a tissue establishment which has obtained the authorisation from the Agency for carrying out such activities. The customs authorities shall verify that the tissue establishment is entitled to import or export the relevant tissues and cells.

[*14 March 2017*]

93. If the importing tissue establishment carries out activities (for example, donation, procurement, testing, processing, preservation, storage, or export) with the tissues and cells intended for import into a European Union Member State or a country of the European Economic Area outside the European Union or the European Economic Area, it shall enter into a contract with third country suppliers.

[*14 March 2017*]

94. The contract between the importing tissue establishment and the third country supplier shall specify the quality and safety requirements to ensure that the quality and safety standards of the tissues and cells to be imported are equivalent to those laid down in this Regulation, and also shall include at least the following information:

94.1. detailed information on the specifications of the importing tissue establishment aimed at ensuring compliance with the quality and safety standards laid down in this Regulation and the obligations of both parties to ensure the compliance of the imported tissues and cells with equivalent quality and safety standards;

94.2. the condition that the third country supplier provides to the importing tissue establishment the information specified in Sub-paragraph 8.52 of this Regulation;

94.3. the condition that the third country supplier informs the importing tissue establishment of any suspected or actual serious adverse events or reactions which may affect the quality and safety of the tissues and cells imported or intended to be imported by the importing tissue establishment;

94.4. the condition that the third country supplier informs the importing tissue establishment of any significant changes in its activity, including complete or partial cancellation or suspension of the authorisation to export tissues and cells or other such decisions by the competent authority or authorities of the third country relating to non-compliance which may affect the quality and safety of tissues and cells imported or intended to be imported by the importing tissue establishment;

94.5. the requirement to guarantee the right of the competent authority or authorities to inspect the activities of third country suppliers, including, where appropriate, to carry out inspection of the relevant establishment as part of the inspection of the importing tissue establishment. This requirement shall guarantee the right of the importing tissue establishment to regularly audit the third country supplier;

94.6. the agreed conditions to be complied with during the transportation of the tissues and cells between the third country supplier and the importing tissue establishment;

94.7. the requirement for the third country supplier or its sub-contractor to keep donor data relating to the imported tissues and cells for 30 years after their procurement in accordance with the laws and regulations regarding data protection and to ensure that arrangements are made for the storage of such data in the event that the third country supplier ceases its activity;

94.8. the arrangements for regular review and, where necessary, revision of the contract, including to reflect any changes in the quality and safety standards laid down in this Regulation;

94.9. a list of all standard operating procedures of the third country supplier relating to the quality and safety of the imported tissues and cells, and also the commitment to submit the list upon request.

[*14 March 2017*]

94.1 The contract entered into between the importing tissue establishment and the third country supplier shall establish the right of the Agency to inspect the activities, including the facilities, of any third country supplier during the duration of the contract and for a period of two years following its termination.

[*14 March 2017*]

94.2 The requirements referred to in Paragraph 94 of this Regulation shall not apply in the case of one-off import, provided that the importing tissue establishment takes the necessary measures to ensure that the import of tissues and cells complies with the quality and safety standards and requirements laid down in this Regulation and that the imported tissues and cells can be traced from donor to recipient and vice versa and are used only for the intended recipients.

[*14 March 2017*]

94.3 The importing tissue establishment shall keep a record of its activities, indicating the type and quantity of the tissues and cells imported, including one-off import, and also their origin and destination. The annual report referred to in Paragraph 142 of this Regulation shall include information on the activities carried out and written confirmation that the imported tissues and cells were used for the intended recipient.

[*14 March 2017*]

94.4 The authorised persons of the Agency shall regularly, but not less than once every two years, carry out inspections of importing tissue establishments and, where appropriate, third country suppliers and shall verify that the importing tissue establishments are taking the necessary measures to ensure quality standards for the imported tissues and cells equivalent to those laid down in this Regulation. The following shall be ensured during the inspection:

94.41. the procedures and activities carried out in the facilities of the importing tissue establishment and the third country supplier which are essential to ensure that the quality and safety standards of the imported tissues and cells are equivalent to the standards laid down in this Regulation are evaluated and verified;

94.42. all documents (including records) relating to the fulfilment of the requirements referred to in Chapters 3 and 4 of this Regulation (which are relevant to the evaluation and inspection) are examined.

[*14 March 2017*]

94.5 The Agency may carry out an inspection or other control measures of an importing tissue establishment or third country supplier on the basis of a justified request from the competent authority of the European Union Member State or a country of the European Economic Area where the imported tissues were distributed. The Agency shall decide on the necessary measures after consulting the competent authority which submitted the request.

[*14 March 2017*]

94.6 Where an on-site inspection takes place following such a request, the Agency shall reach agreement with the competent authority of the relevant European Union Member State or country of the European Economic Area which made such a request on whether the competent authority of the relevant country participates in the inspection. The final decision on any such participation shall be taken by the Agency. If participation is refused, the Agency shall provide the reasons for such refusal to the competent authority of the relevant European Union Member State or country of the European Economic Area which made such a request.

[*14 March 2017*]

94.7 The costs related to the inspection or control measures of the importing tissue establishment or third country supplier shall be borne by the importing tissue establishment or third country supplier according to the price list of paid services of the State Agency of Medicines.

[*14 March 2017*]

94.8 The Agency shall provide information on the inspections and other control measures of the importing tissue establishment and the third country supplier and the results thereof on the basis of a justified request from another European Union Member State or country of the European Economic Area, or the European Commission.

[*14 March 2017*]

**3.9. Notification of Serious Adverse Reactions and Serious Adverse Events**

95. The procurement organisation shall have standard operating procedures in place to retain the records of the tissues and cells procured and to notify tissue establishments without delay of any serious adverse reactions in the living donor which may affect the quality and safety of the tissues and cells.

96. The procurement organisation and the tissue establishment shall have standard operating procedures in place to retain the records and to notify tissue establishments without delay of any serious adverse events during procurement which may affect the quality and safety of human tissues and cells.

97. The application organisation shall have standard operating procedures in place to retain the records of the tissues and cells used and to notify the tissue establishment without delay of any serious adverse reactions and serious adverse events observed during or after clinical use of the tissues or cells which may be related to the quality and safety of the tissues and cells.

98. The tissue establishment shall provide information to the tissue application organisation on the notification of serious adverse reactions and serious adverse events which may affect the quality and safety of the tissues and cells.

99. The tissue establishment shall develop the procedures for informing the Agency of suspected serious adverse reactions and suspected serious adverse events, and also shall inform without delay of the findings of the investigation to analyse the causes and consequences of serious adverse reactions and events.

99.1 The importing tissue establishment shall, in accordance with Annexes 5 and 6 to this Regulation, immediately inform the Agency of any suspected or actual serious adverse events or reactions notified to it by third country suppliers which may affect the quality and safety of the tissues and cells they import.

[*14 March 2017*]

100. The responsible person shall ensure that the Agency is notified of serious adverse reactions as soon as they become known, but not later within 48 hours, by sending a notification in accordance with Part A of Annex 5 to this Regulation and of serious adverse events by sending a notification in accordance with Part A of Annex 6 to this Regulation. Within five days after completion of the investigation, tissue establishments shall submit to the Agency an investigation report on serious adverse reactions by sending a notification in accordance with Part B of Annex 5 to this Regulation and on serious adverse events by sending a notification in accordance with Part B of Annex 6 to this Regulation.

101. The tissue establishment shall notify the Agency of the actions taken in relation to other tissues and cells that have been distributed for human applications.

102. The tissue establishment shall evaluate serious adverse events and their causes in order to prevent them in a timely manner during the procurement, testing, processing, storage, and distribution of the tissues and cells.

103. In the case of medical assisted insemination, any type of gamete or embryo misidentification or mix-up shall be considered to be a serious adverse event. The procurement organisation or tissue application organisation that has carried out the medical assisted insemination shall report such events to the supplying tissue establishment for investigation and notification to the Agency.

**4. Quality and Safety Standards for the Use of the Tissues and Cells of a Living Donor and a Deceased Human Being at the Tissue Establishment**

104. In determining the procedures for work organisation and management, the tissue establishment shall ensure the following:

104.1. the qualification of the responsible person complies with the requirements referred to in Sub-chapter 3.1 of this Regulation;

104.2. the tissue establishment must have a specific and clearly defined structure and operating procedures, including a clearly defined hierarchy of accountability and reporting;

104.3. the tissue establishment must have a medical practitioner to advise on and oversee the medical activities of the tissue establishment (donor selection, review of clinical outcomes of applied tissues and cells) or interaction with the patients of the tissue establishment;

104.4. the tissue establishment must develop a quality certification system in accordance with this Regulation;

104.5. the risks inherent in the use and handling of biological material are identified and minimised, and the activities to be carried out comply with the specified quality and safety requirements. It is important to carry out a risk analysis relating to standard operating procedures, the environment, the health status of personnel;

104.6. the contract between the tissue establishment and the third parties on any of the stages in the processing of tissues or cells shall specify the obligations and responsibilities of the third parties, and also the procedures to be complied with in order to comply with the required performance specification;

104.7. there must be a documented system in place, supervised by the responsible person, for ratifying that the tissues and cells comply with the quality and safety standards defined for their release and distribution;

104.8. in the event of termination of activities of the tissue establishment, the contracts and standard operating procedures must include traceability data and materials concerning the quality and safety of the cells and tissues;

104.9. there must be procedures to ensure the identification of every unit of tissues or cells at all stages of the activities.

105. There must be a sufficient number of qualified personnel at the tissue establishment.

106. The competency of the personnel must be evaluated at regular intervals in accordance with the requirements specified in the quality system. For that purpose:

106.1. personnel job descriptions must be drawn up, defining the scope of the responsibility and obligations;

106.2. initial training of personnel is provided and, in the event of changes in standard operating procedures or scientific knowledge, advanced training and adequate opportunities for professional development must be ensured;

106.3. the personnel is informed of the broader ethical, legal and regulatory context of their work. The training programme ensures and documents that each person:

106.3.1. has demonstrated competence in the performance of their designated tasks;

106.3.2. has an adequate knowledge and understanding of the scientific (technical) processes and principles relevant to their designated tasks;

106.3.3. understands the organisational structure, quality system, and safety rules of the tissue establishment.

107. In determining the necessary equipment and materials, the tissue establishment shall ensure the following:

107.1. equipment and materials must be designed and maintained in a way to comply with their intended purpose, minimising any hazard to the recipient and personnel;

107.2. all critical equipment and technical devices must be identified, validated, and regularly inspected, and also preventively maintained in accordance with the instructions of the manufacturer. If equipment or materials affect critical processing or storage parameters (for example, temperature, pressure, particle counts, microbial contamination levels), they must be identified and must be the subject of appropriate monitoring, alerts, alarms and corrective action, as required, to detect malfunctions and defects and to ensure that the critical parameters are maintained within acceptable limits at all times. All equipment with a critical measuring function must be calibrated against a traceable standard, if available;

107.3. new or repaired equipment must be tested when installed and must be validated before use and test results must be documented;

107.4. disinfection, cleaning, and maintenance of all critical equipment must be performed regularly and actions related thereto must be documented;

107.5. standard procedures for the operation of each piece of critical equipment, detailing the action to be taken in the event of malfunctions or failure, must be available;

107.6. standard procedures must be developed for the validated cleaning and sterilisation of reusable equipment (instruments) to remove infectious agents;

107.7. standard procedures for materials and equipment must be in place for all critical materials and reagents. In particular, specifications for additives (for example, solutions) and packaging materials must be defined. Critical reagents and materials must comply with documented requirements and specifications and, where applicable, with the laws and regulations governing the procedures for the registration, conformity assessment, distribution, operation, and technical supervision of medical devices.

108. The tissue establishment must have suitable facilities to carry out the special activities with the tissues and cells included in the authorisation.

109. The tissue establishment shall ensure compliance with the following requirements:

109.1. activities which include processing of the tissues and cells must take place in an environment with specified air quality and cleanliness in order to minimise the risk of contamination, including cross-contamination between donations. The effectiveness of these measures must be validated and monitored;

109.2. in facilities and work environment where the donor tissues and cells are in direct contact with the external environment, where it is not possible to ensure a microbiological inactivation process (sterilisation), the air quality with particle counts and microbial colony counts must comply with the requirements for Grade A specified in Annex 7 to this Regulation, whereas for the work environment in the surrounding facilities it must be suitable for the handling of the relevant tissues or cells and not below the requirements for Grade D;

109.3. justifying and documenting that the necessary quality and safety requirements are achieved, at least by assessing the purpose and type of use of the donor tissues and cells and the immunological status of the recipient, air quality requirements lower than those laid down in Sub-paragraph 109.2 of this Regulation may be applied in the following cases:

109.3.1. a validated microbial inactivation or validated terminal sterilisation process is ensured for the tissues and cells;

109.3.2. if there is proof that the application of requirements has a negative impact on clinically relevant tissue and cell properties;

109.3.3. the use of donor tissues and cells implies a significantly lower risk of transmitting bacterial or fungal infection to the recipient than with cell and tissue transplantation;

109.3.4. if it is not technically possible to carry out the required process of tissue and cell processing in a Grade A environment, for example, due to requirements for specific equipment in the processing area that is not fully compatible with Grade A;

109.4. the storage of the tissues and cells shall be included in the activities for which authorisation is required, determining the storage conditions necessary to maintain the required properties of the tissues and cells, including appropriate parameters such as temperature, humidity and air quality, which shall be controlled (monitored) and documented;

109.5. ensure that donor tissues and cells are stored separately from other donor tissues and cells that have already been separated for future use, in order to prevent the risk of contamination. Quarantined tissues and cells shall be stored separately from other tissues and cells intended for further use. Unused or damaged tissues and cells shall be disposed of in accordance with the laws and regulations governing the management of waste generated in a medical treatment institution;

109.6. the personnel shall be provided with appropriate clothing and equipment, and also written instructions setting out hygiene and clothing requirements for personnel must be developed.

[*14 March 2017*]

110. The tissue establishment shall ensure that the bacteriological examination parameters of the environment in facilities correspond to the parameters laid down in Annex 7 to this Regulation.

[*14 March 2017*]

111. The tissue establishment shall develop a system that clearly defines how documentation, including electronic documents, records, and registers, is created and maintained and standard operating procedures for activities requiring authorisation are approved:

111.1. the documents shall be regularly reviewed to ensure that they correspond to the requirements laid down in this Regulation. The system shall ensure that the work performed is standardised and that all stages, i.e. coding, donor eligibility assessment, procurement, processing, preservation, storage, transportation, distribution or disposal, are transparent, including aspects related to quality control and quality assurance;

111.2. for all critical activities, the materials, equipment, and personnel involved shall be identified and documented;

111.3. the responsible person of the tissue establishment shall review, record, approve, document, and accurately implement all changes to records, including electronic records;

111.4. the tissue establishment shall establish standard document management procedures in order to ensure the history of document reviews and changes, and also to ensure that only current versions of documents, including electronic documents, are in use;

111.5. records must be shown to be reliable and a true representation of the results;

111.6. records must be legible and indelible and may be handwritten or transferred to another validated system, for example, a computer;

111.7. records (except data needed for full traceability), including data initially generated which are critical to the safety and quality of the tissues and cells shall be kept for at least 10 years after expiry date;

111.8. records must meet the data protection requirements for natural persons and the requirements laid down in Sub-chapter 3.3 of this Regulation. Access to registers and data must be restricted to persons authorised by the responsible person, and also to the Agency for the purpose of inspection and control measures.

112. In order to ensure the fulfilment of the requirements laid down in this Regulation, control and quality testing shall be carried out at the tissue establishment:

112.1. an audit system shall be established for activities requiring authorisation. Audit shall be carried out by independent trained and competent persons at least every two years in order to verify compliance with the approved procedures and the requirements of this Regulation. The results and corrective actions shall be documented;

112.2. where there are deviations from the established quality and safety standards, documented actions (procedures) shall be carried out, including a decision on possible corrective and preventive actions. The fate of non-conforming tissues and cells must be decided in accordance with written standard operating procedures supervised by the responsible person and these non-conformities shall be recorded. All affected tissues and cells must be identified and notified to the Agency;

112.3. corrective actions shall be documented, initiated, and completed in a timely manner. The effectiveness of preventive and corrective actions shall be evaluated after the implementation thereof;

112.4. the tissue establishment shall have processes in place to review the performance of the quality system in order to ensure continuous and systematic improvement thereof.

**5. Procedures for the Issuance of the Authorisation, Duplicate Thereof to the Higher Education Institution, for the Cancellation of the Authorisation, Suspension and Renewal of the Validity Thereof**

113. The higher education institution seeking the authorisation shall:

113.1. submit an application to the Agency. The following information shall be indicated in the application:

113.1.1. the name, registration number, legal address, and actual address of the higher education institution;

113.1.2. the given name surname, position, and contact details (telephone number, electronic mail address) of the person responsible for cooperation with the Agency;

113.2. append the descriptions of standard operating procedures for the activity of the use of the tissues and cells related to the implementation of medical study programmes to the application referred to in Sub-paragraph 113.1 of this Regulation.

114. The Agency shall assess the application and descriptions of standard operating procedures for the activity of the use of the tissues and cells related to the implementation of medical study programmes referred to in Paragraph 113 of this Regulation, evaluate compliance of the higher education institution with the requirements laid down in Chapter 6 of this Regulation in relation to the use of the tissues and cells, and, within one month after receipt of the application, take the decision (Annex 8) on issuance of the authorisation or refusal to issue the authorisation. The Agency shall notify the applicant of the decision on issuance of the authorisation or refusal to issue the authorisation in accordance with the procedures laid down in the Law on Notification.

115. If, during examination of the application referred to in Paragraph 113 of this Regulation and the descriptions of standard operating procedures for the use of the tissues and cells for activities related to the implementation of medical study programmes, the Agency establishes that they are incomplete or do not meet the requirements referred to in Chapter 6 of this Regulation, it shall, within five working days after receipt of the application referred to in Paragraph 113 of this Regulation, request the higher education institution in writing to clarify the information.

116. The higher education institution shall, within 10 working days after receipt of the request referred to in Paragraph 115 of this Regulation, submit to the Agency documents certifying the elimination of the deficiencies.

117. The Agency shall assess the submitted documents referred to in Paragraph 116 of this Regulation, evaluate the compliance of the higher education institution with the requirements referred to in Chapter 6 of this Regulation in relation to the use of the tissues and cells and, within one month after receipt of the application referred to in Sub-paragraph 113.1 of this Regulation, take the decision on issuance of the authorisation or refusal to issue the authorisation. The Agency shall notify the applicant of the decision on issuance of the authorisation or refusal to issue the authorisation in accordance with the procedures laid down in the Law on Notification.

118. For the purposes of taking the decision referred to in Paragraphs 114, 117, and 123 of this Regulation, an official of the Agency has the right to visit the higher education institution and the higher education institution has the obligation to ensure access for the official of the Agency to the documents, facilities, and equipment necessary for taking the decision, and also the presence of the responsible person of the higher education institution during the visit.

119. The Agency shall take the decision on refusal to issue the authorisation if at least one of the following conditions have set in:

119.1. the documents submitted by the higher education institution contain false information;

119.2. the higher education institution does not comply with the requirements referred to in Chapter 6 of this Regulation and is unable to ensure compliance with the conditions for the use of the tissues and cells;

119.3. the higher education institution has not submitted all the information referred to in Paragraph 113 of this Regulation within the time limit referred to in Paragraph 116 of this Regulation.

120. If the authorisation is damaged, destroyed, lost, or stolen, the higher education institution shall inform the Agency in writing thereof within three working days and apply for a duplicate of the authorisation. The Agency shall, within three working days after receipt of the application, take the decision on issuance of a duplicate of the authorisation and issue a duplicate thereof. The Agency shall notify the applicant of the decision to issue a duplicate of the authorisation in accordance with the procedures laid down in the Law on Notification.

121. If the Agency establishes that the higher education institution does not ensure compliance with the requirements referred to in Chapter 6 of this Regulation, it shall suspend the validity of the authorisation and determine a time period for the elimination of the deficiencies.

122. In order to renew the validity of the authorisation, the higher education institution shall submit to the Agency an application for the renewal of the validity of the authorisation and documents certifying the elimination of the deficiencies due to which the validity of the authorisation has been suspended.

123. The Agency shall assess the application referred to in Paragraph 122 of this Regulation and the documents attached thereto, evaluate the compliance of the higher education institution with the requirements referred to in Chapter 6 of this Regulation in relation to the use of the tissues and cells and shall, within one month after receipt of the application, take the decision on renewal of the validity of the authorisation if the deficiencies due to which the validity of the authorisation has been suspended have been eliminated or on cancellation of the authorisation if the deficiencies due to which the validity of the authorisation has been suspended have not been eliminated. The Agency shall notify the applicant of the decision in accordance with the procedures laid down in the Law on Notification.

124. The Agency shall cancel the authorisation due to at least one of the following reasons:

124.1. the higher education institution has requested to cancel the authorisation issued to it;

124.2. the higher education institution does not comply with the conditions for activities specified in the authorisation;

124.3. the higher education institution has not eliminated the deficiencies within the time period referred to in Paragraph 121 of this Regulation due to which the validity of the authorisation has been suspended;

124.4. the higher education institution has provided false information.

125. The Agency shall notify the decision on cancellation of the authorisation to the higher education institution in accordance with the procedures laid down in the Law on Notification.

126. The decisions taken by the Agency on issuance of the authorisation or refusal to issue the authorisation, and also on suspension of the validity of the authorisation or cancellation thereof may be contested by the higher education institution in the Ministry of Health in accordance with the procedures laid down in the Administrative Procedure Law.

127. The decision of the Ministry of Health may be appealed to a court in accordance with the procedures laid down in the Administrative Procedure Law.

128. The Agency shall post the information on the issued authorisations (name of the higher education institution, telephone number, actual address of the use of the tissues and cells, number and date of the authorisation), on the suspension of the validity of the issued authorisations or the cancellation thereof within three working days after taking the relevant decision on the website of the Agency.

**6. Requirements for the Receipt of the Authorisation by the Higher Education Institution, Conditions for the Use of the Tissues and Cells at the Higher Education Institution, and Procedures for the Use of Living Donor Tissues and Cells for Medical Studies**

129. The tissues and cells shall be used in accordance with study programmes.

130. In the implementation of medical study programmes at the higher education institution, the use of the tissues and cells shall be carried out in accordance with the established standard operating procedures.

131. The requirements for the use of hygiene and personal protective equipment for personnel and students shall be laid down in writing at the higher education institution.

132. The tissues and cells shall be stored by the higher education institution under specific laboratory conditions in accordance with the standard operating procedures.

**7. Procedures for the Supervision and Control of the Evaluation of the Use of the Tissues and Cells, and also Procedures for Reporting to the European Commission on Serious Adverse Reactions and Serious Adverse Events**

133. The Agency shall take all measures to ensure the procurement and receipt of the tissues and cells in accordance with the requirements referred to in Sub-chapters 3.4 and 3.6 of this Regulation.

134. The authorised persons of the Agency shall regularly, but not less than once every two years, carry out supervision of the activities of the tissue establishment. The following shall be carried out during the supervision:

134.1. inspection of the equipment used by the tissue establishment and the third parties, taking into account the contracts referred to in Paragraphs 84, 85, and 86 of this Regulation;

134.2. assessment and verification of the standard operating procedures and activities carried out by tissue establishments and third party equipment which is subject to the requirements referred to in Chapters 3 and 4 of this Regulation;

134.3. examination of all documents (records) related to the fulfilment of the requirements referred to in Chapters 3 and 4 of this Regulation;

134.4. examination of the contracts entered into between the tissue establishment and the third parties and assessment of their compliance with the requirements referred to in Paragraph 87 of this Regulation.

135. During the inspections carried out by the Agency, the tissue establishment shall ensure the availability of the documents referred to in Sub-paragraph 8.2 of this Regulation, and also other information.

136. In order to ensure the compliance with the requirements referred to in this Regulation, the authorised persons of the Agency shall regularly, but not less than once every three years, carry out the supervision of the higher education institution. The following shall be carried out during the supervision:

136.1. assessment of the facilities and equipment of the higher education institution where activities related to the use of the tissues and cells take place;

136.2. assessment of all records, standard operating procedures of the activity, and activities related to the fulfilment of the requirements referred to in this Regulation.

137. The higher education institution shall ensure the availability of the description of the standard operating procedures referred to in Sub-paragraph 113.2 of this Regulation for the use of the tissues and cells for activities related to the implementation of medical study programmes, and also other information during the inspections carried out by the Agency.

138. The Agency shall organise and carry out the supervision referred to in Paragraph 134 of this Regulation in the tissue establishment (including extraordinary) in the event of the detection or suspicion of serious adverse reactions or serious adverse events, and also in the event of a justified request from the competent authority of another European Union Member State.

139. The Agency shall, every three years, prepare and submit to the European Commission a report on the activities related to the procurement, testing, processing, preservation, storage, and use of the tissues and cells carried out in tissue establishments, and also on the inspections carried out in tissue establishments.

140. The Agency shall, each year by 30 June, submit to the European Commission an annual notification of reports received on serious adverse reactions and serious adverse events (Annex 9).

141. The Agency shall provide other Member States and the European Commission with information on serious adverse reactions and serious adverse events, and also, upon request of another Member State or the European Commission, provide information on the results of inspections and control measures carried out in relation to compliance with the quality and safety standards in the field of donation, procurement, testing, processing, preservation, storage, and distribution of human tissues and cells.

142. The tissue establishment shall prepare an annual report on its activities for the previous year and submit it to the Agency by 15 February of the current year. The annual report shall keep an account of the activities of the tissue establishment, including the type and quantity of the tissues or cells obtained, tested, preserved, processed, stored, and distributed or otherwise used, and also the origin and destination of the tissues and cells intended for human application.

143. The Agency shall publish the annual report referred to in Paragraph 142 of this Regulation on its website, and also shall make available summaries of reports submitted by other Member States to the European Commission. The Agency shall keep the acquired information in accordance with the requirements of the laws and regulations in the field of personal data protection.

**8. Closing Provisions**

[*14 March 2017*]

144. The tissues and cells that were in storage until 29 October 2016 may be exempted from the assignment of the Single European Code provided that the relevant tissues and cells are placed in circulation in European Union Member States or countries of the European Economic Area within five years after the abovementioned date and that complete traceability thereof is ensured.

[*14 March 2017*]

145. For the tissues and cells which remain in storage and which are only released for circulation after expiry of the five-year period referred to in Paragraph 144 of this Regulation and for which the application of the Single European Code is not possible, in particular because the tissues and cells are stored under deep-freeze conditions, the tissue establishments shall use the procedures applicable to products with small labels in accordance with Sub-paragraph 91.46 of this Regulation.

[*14 March 2017*]

**Informative Reference to European Union Directives**

[*26 May 2014; 14 March 2017*]

The Regulation contains legal norms arising from:

1) Directive 2004/23/EC of the European Parliament and of the Council of 31 March 2004 on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells;

2) Commission Directive 2006/17/EC of 8 February 2006 implementing Directive 2004/23/EC of the European Parliament and of the Council as regards certain technical requirements for the donation, procurement and testing of human tissues and cells;

3) Commission Directive 2006/86/EC of 24 October 2006 implementing Directive 2004/23/EC of the European Parliament and of the Council as regards traceability requirements, notification of serious adverse reactions and events and certain technical requirements for the coding, processing, preservation, storage and distribution of human tissues and cells;

4) Commission Directive 2012/39/EU of 26 November 2012 amending Directive 2006/17/EC as regards certain technical requirements for the testing of human tissues and cells;

5) Commission Directive (EU) 2015/565 of 8 April 2015 amending Directive 2006/86/EC as regards certain technical requirements for the coding of human tissues and cells;

6) Commission Directive (EU) 2015/566 of 8 April 2015 implementing Directive 2004/23/EC as regards the procedures for verifying the equivalent standards of quality and safety of imported tissues and cells.

Prime Minister Valdis Dombrovskis

Minister for Health Ingrīda Circene

**Annex 1**

Cabinet Regulation No. 1176

22 October 2013

[*14 March 2017*]

**AUTHORISATION TO USE TISSUES AND CELLS No. \_\_\_\_\_\_\_\_\_\_**

Rīga

**State Agency of Medicines**

|  |  |  |
| --- | --- | --- |
|  |  |  |
|  | (address, telephone, registration No.) |  |

**certifies that**

|  |  |
| --- | --- |
| 1. |  |
| (name of the medical treatment institution (unit)) | |

|  |  |  |
| --- | --- | --- |
| 2. | Registered in the register of medical treatment institutions under No. |  |

|  |  |
| --- | --- |
| 3. |  |
| (legal address and actual address, telephone, e-mail address of the medical treatment institution) | |

|  |  |
| --- | --- |
| 4. | Responsible person of the institution (unit) |
|  | |
| (given name, surname, telephone, e-mail address) | |
|  | |

**has been assessed and complies with the requirements laid down in Cabinet Regulation No. 1176 of 22 October 2013, Procedures for the Use of Human Tissues and Cells, and is entitled to carry out the following activities of the use of tissues and cells:**

|  |
| --- |
|  |
| (indicate the necessary type(-s) of use of tissues and (or) cells) |

5. Date \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

|  |  |  |
| --- | --- | --- |
| 6. | Director of the State Agency of Medicines |  |
|  |  | (given name, surname, signature) |

Place for a seal

|  |  |  |
| --- | --- | --- |
| 7. | Annexes to the authorisation and the number of pages of annexes |  |

Note. The details of the document “signature” and “place for a seal” shall not be completed if the electronic document has been prepared in accordance with the laws and regulations regarding drawing up of electronic documents.

Annex 1

Authorisation for the Use of Tissues and Cells

No. \_\_\_\_\_\_\_\_

**Conditions for special activity**

(*mark as appropriate*)

|  |  |  |
| --- | --- | --- |
| **Tissue or cell type** | **Field of activity** | **Processing method** |
| Bones |  |  |
| Skin |  |  |
| Blood vessels |  |  |
| Ocular tissues |  |  |
| Amniotic membrane |  |  |
| Ovarian tissues |  |  |
| Testicular tissues |  |  |
| Other tissues (please, specify) |  |  |
| Bone marrow |  |  |
| Peripheral blood stem cells |  |  |
| Cord blood |  |  |
| Oocytes |  |  |
| Spermatozoa |  |  |
| Other cells (please, specify) |  |  |
| Embryos |  |  |
| Zygotes |  |  |
| Other (please, specify) |  |  |

|  |  |
| --- | --- |
| Director of the State Agency of Medicines |  |
|  | (given name, surname, signature) |

Note. The detail of the document “signature” shall not be completed if the electronic document has been prepared in accordance with the laws and regulations regarding drawing up of electronic documents.

Annex 2

Authorisation for the Use of Tissues and Cells

No. \_\_\_\_\_\_\_\_

**Information on Procurement Organisations and Third Parties which Carry out Activities in Accordance with the Contracts Entered Into**

|  |  |
| --- | --- |
| 1. Name of the institution |  |

|  |  |
| --- | --- |
| 2. Address, telephone of the institution |  |

|  |  |
| --- | --- |
| 3. Given name, surname of the responsible person |  |

|  |  |
| --- | --- |
| 4. Scope of activity of the contract |  |

|  |  |
| --- | --- |
| Director of the State Agency of Medicines |  |
|  | (given name, surname, signature) |

Note. The detail of the document “signature” shall not be completed if the electronic document has been prepared in accordance with the laws and regulations regarding drawing up of electronic documents.

Annex 3

Authorisation for the Use of Tissues and Cells

No. \_\_\_\_\_\_\_\_

**Information on the Laboratory(-ies) Carrying out Laboratory Testing of Donor Blood or Donation Samples on a Contractual Basis and Comply with the Mandatory Requirements Laid Down in Laws and Regulations for Medical Laboratories**

|  |  |
| --- | --- |
| 1. Name of the laboratory |  |

|  |  |
| --- | --- |
| 2. Address, telephone of the laboratory |  |

|  |  |
| --- | --- |
| 3. Given name, surname of the responsible person |  |

|  |  |
| --- | --- |
| 4. Scope of activity of the contract |  |

|  |  |
| --- | --- |
| Director of the State Agency of Medicines |  |
|  | (given name, surname, signature) |

Note. The detail of the document “signature” shall not be completed if the electronic document has been prepared in accordance with the laws and regulations regarding drawing up of electronic documents.

Annex 4

Authorisation for the Use of Tissues and Cells

No. \_\_\_\_\_\_\_\_

**Authorisation to the Tissue Establishment for the Import of Tissues and Cells**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| 1. Information on the importing tissue establishment (ITE) | | | | | | | | | | |
| 1.1. Name of the importing tissue establishment | | | | |  | | | | | |
| 1.2. Code in the EU Tissue Establishment Compendium | | | | |  | | | | | |
| 1.3. Address of the importing tissue establishment and legal address (if different) | | | | |  | | | | | |
| 1.4. Site of reception of import (if different from the previously specified address) | | | | |  | | | | | |
| 1.5. Name of the holder of the authorisation | | | | |  | | | | | |
| 1.6. Address of the holder of the authorisation | | | | |  | | | | | |
| 1.7. Telephone number of the holder of the authorisation (if available) | | | | |  | | | | | |
| 1.8. E-mail address of the holder of the authorisation (if available) | | | | |  | | | | | |
| 1.9. Website of the importing tissue establishment | | | | |  | | | | | |
| 2. Field of activity | | | | | | | | | | |
| 2.1. Tissue and cell type (listed using the tissue and cell categories specified in the EU Tissue Establishment Compendium and adding rows as required) | Activities in third countries | | | | | | | | | Status of the import authorisation |
| donation | procurement | testing | | | preservation | processing | storage | |
|  |  |  |  | | |  |  |  | |  |
|  | 3CS – third country supplier  SC – sub-contractor of the third country supplier | | | | | | | | | G – granted  S – suspended  R – revoked  C – ceased |
| 2.2. One-off import | | | | | | | | | | |
| 2.3. Name(-s) of the imported tissue and cell product | | | |  | | | | | | |
| 2.4. Import conditions or further notations | | | |  | | | | | | |
| 2.5. Third country or countries where the tissue or cells were procured (for each type of imported tissues and cells) | | | |  | | | | | | |
| 2.6. Third country or countries where other activities are carried out (if different) | | | |  | | | | | | |
| 2.7. Name and country of the third country supplier(-s) (for each type of imported tissues and cells) | | | |  | | | | | | |
| 2.8. EU Member States where the imported tissues and cells will be distributed (if known) | | | |  | | | | | | |
| 3. Competent authority that issued the authorisation | | | | | | | | | | |
| 3.1 National authorisation number | | | |  | | | | | | |
| 3.2. Legal basis of the authorisation | | | |  | | | | | | |
| 3.3. Duration of the authorisation (if any) | | | |  | | | | | | |
| 3.4. First-time authorisation or renewal of the importing tissue establishment | | | | first-time | | | | | renewal | |
| 3.5. Additional information | | | |  | | | | | | |
| 3.6. State Agency of Medicines | | | |  | | | | | | |
| 3.7. Name of the Director of the State Agency of Medicines | | | |  | | | | | | |
| 3.8. Signature (electronic or other) of the Director of the State Agency of Medicines | | | |  | | | | | | |
| 3.9. Date of issuing the authorisation | | | |  | | | | | | |
| 3.10. Seal of the State Agency of Medicines | | | |  | | | | | | |

Minister for Health Ingrīda Circene

**Annex 2**

Cabinet Regulation No. 1176

22 October 2013

**Selection Criteria for Tissue or Cell Donors (Except for Gamete Donors)**

[*14 March 2017*]

Selection criteria for donors are based on an analysis of the risks related to the application of the specific cells/tissues. Indicators of these risks must be identified by physical examination, review of the medical and behavioural history, biological testing, post-mortem examination (for deceased donors), and any other appropriate investigation. Unless justified on the basis of a documented risk assessment approved by the responsible persons, donors must be excluded from donation if any of the following criteria applies:

1. General criteria for exclusion of a deceased donor:

1.1. cause of death unknown, unless autopsy provides information on the cause of death after procurement and none of the general criteria for exclusion set out in the present section applies;

1.2. history of a disease of unknown aetiology;

1.3. presence, or previous history, of malignant disease, except for primary basal cell carcinoma, carcinoma *in situ* of the uterine cervix, and also some primary tumours of the central nervous system that have to be evaluated according to scientific evidence. Donors with malignant diseases can be evaluated and considered for cornea donation (except for those with retinoblastoma, haematological neoplasm, and malignant tumours of the anterior segment of the eye);

1.4. risk of transmission of diseases caused by prions which applies to:

1.4.1. people diagnosed with Creutzfeldt–Jakob disease, or variant Creutzfeldt–Jacob disease, or having a family history of non-iatrogenic Creutzfeldt–Jakob disease. Further precautions may be recommended for the variant Creutzfeldt–Jakob disease;

1.4.2. people with a history of rapid progressive dementia or degenerative neurological disease, including those of unknown origin;

1.4.3. recipients of hormones derived from the human pituitary gland (for example, growth hormones) and recipients of grafts of cornea, sclera and dura mater, and also persons that have undergone undocumented neurosurgery (where dura mater may have been used);

1.5. systemic infections which are not controlled at the time of donation, including bacterial diseases, systemic viral, fungal or parasitic infections, or significant local infections in the tissues and cells to be donated. Donors with bacterial septicaemia may be evaluated and considered for eye donation but only where the corneas are to be stored by organ culture to allow detection of any bacterial contamination of the tissue;

1.6. history, clinical evidence, or laboratory evidence of HIV, acute or chronic hepatitis B (except in the case of persons with a proven immune status), hepatitis C and HTLV I/II, transmission risk or evidence of risk factors for these infections;

1.7. history of chronic, systemic autoimmune diseases that could have a detrimental effect on the quality of the tissues to be retrieved;

1.8. indications that test results of donor blood samples will be invalid due to the occurrence of haemodilution or treatment with immunosuppressive agents;

1.9. evidence of any other risk factors for transmissible diseases on the basis of a risk assessment, and also local infectious disease prevalence, and also taking into consideration medical history of the donor;

1.10. presence on the donor’s body of physical signs implying a risk of transmissible diseases;

1.11. information on the ingestion of, or exposure to, a substance (for example, cyanide, lead, mercury, gold) that may be transmitted to recipients in a dose that could endanger their health;

1.12. recent history of vaccination with a live attenuated virus (where a risk of transmission is considered to exist);

1.13. transplantation with xenografts;

1.14. a stay in a prison or remand prison before death (more than 72 hours in the last six months).

2. Deceased child donors. Any children born from mothers with HIV infection or that meet any of the exclusion criteria referred to in Paragraph 1 of this Annex must be excluded as donors until the risk of transmission of infection can be definitely ruled out:

2.1. children aged less than 18 months born from mothers with HIV, hepatitis B, hepatitis C, or HTLV infection, or at risk of such infection, and who have been breastfed by their mothers during the previous 12 months, cannot be considered as donors regardless of the results of the analytical tests (in addition to the exclusion criteria referred to in Paragraph 1 of this Annex);

2.2. children of mothers with HIV, hepatitis B, hepatitis C, or HTLV infection, or at risk of such infection, and who have not been breastfed by their mothers during the previous 12 months and for whom analytical tests, physical examinations, and reviews of medical records do not provide evidence of HIV, hepatitis B, hepatitis C, or HTLV infection, can be accepted as donors.

3. Selection criteria for an autologous living donor:

3.1. if the removed tissues and cells are to be stored or cultured, the same minimum set of biological testing requirements must apply as for an allogeneic living donor;

3.2. positive test results will not necessarily prevent the tissues or cells or any product derived from them being stored, processed, or reimplanted, if appropriate isolated storage facilities are available to ensure no risk of cross-contamination with other grafts or no risk of contamination with adventitious agents and mix-ups.

4. Selection criteria for an allogeneic living donor:

4.1. allogeneic living donors must be selected on the basis of their health and medical history, provided on a questionnaire, and also through an interview. This assessment must include relevant factors that may assist in identifying and screening out persons whose donation could present a health risk to others, the possibility of transmitting diseases or health risks to themselves. For any donation, the collection process must not interfere with or compromise the health or care of the donor. In the case of cord blood or amniotic membrane donation, this applies to both mother and baby;

4.2. selection criteria for allogeneic living donors must be established and documented by the tissue establishment (and the transplanting clinician in the case of direct distribution to the recipient), based on the specific tissue or cells to be donated, together with the physical status and medical and behavioural history of the donor and the results of clinical investigations and laboratory tests establishing the state of health of the donor;

4.3. the same exclusion criteria must be applied as for deceased donors, except for Sub-paragraph 1.1 of this Annex. Depending on the tissue or cell to be donated, other specific exclusion criteria shall be applied:

4.3.1. pregnancy (except for donors of umbilical cord blood cells and amniotic membrane and sibling donors of haematopoietic progenitors);

4.3.2. breastfeeding;

4.3.3. in the case of haematopoietic progenitor cells, the potential for transmission of inherited conditions.

Minister for Health Ingrīda Circene

**Annex 3**

Cabinet Regulation No. 1176

22 October 2013

**Laboratory Testing of Tissue and Cell Donors (Except for Gamete Donors)**

[*26 May 2014*]

1. Screening of donors for infection markers:

1.1. all donors shall be subject to at least the following laboratory tests:

|  |  |
| --- | --- |
| HIV 1 and 2 | Anti HIV-1,2 |
| Hepatitis B | HBsAg  Anti HBc |
| Hepatitis C | Anti-HCV-Ab |
| Syphilis | see Sub-paragraph 1.4 |

1.2. HTLV-I antibody testing must be performed for donors living in, or originating from, high-incidence areas or with sexual partners originating from those areas or where parents of the donor originate from those areas;

1.3. if anti-HBc is positive and HBsAg is negative, further investigations are necessary with a risk assessment to determine eligibility for clinical use;

1.4. a validated testing algorithm must be applied to exclude the presence of active infection with *Treponema pallidum*. A non-reactive test, specific or non-specific, can allow tissues and cells to be released. If a non-specific test is performed, a reactive result will not prevent procurement or release if a specific *Treponema* confirmatory test is non-reactive. A donor whose specimen tests reactive on a *Treponema*-specific test will require a thorough risk assessment to determine eligibility for clinical use;

1.5. in certain circumstances, additional testing may be required depending on the health history of the donor and the characteristics of the tissue or cells donated (for example, RhD, HLA, malaria, CMV, toxoplasma, EBV, *Trypanosoma cruzi*);

1.6. Paragraph 3 of Annex 2 to this Regulation shall apply to autologous donors.

2. General requirements to be complied with for determining biological markers:

2.1. screening for infection markers must be carried out by a qualified laboratory, authorised by the Agency as a testing centre, using EC-marked testing kits where appropriate. The type of screening test for infection markers used must be validated for the purpose in accordance with scientific knowledge;

2.2. screening for markers of infection must be carried out on the serum or plasma of the donor. It must not be performed on other fluids or secretions, for example, the aqueous or vitreous humour unless specifically justified clinically using a validated test for such a fluid;

2.3. if potential donors have lost blood and have recently received donated blood, blood components, colloids or crystalloids, blood testing may not be valid due to haemodilution of the sample. An algorithm must be applied to assess the degree of haemodilution in the following circumstances:

2.3.1. ante-mortem blood sampling: if blood, blood components and (or) colloids were infused in the 48 hours preceding blood sampling or if crystalloids were infused in the hour preceding blood sampling;

2.3.2. post-mortem blood sampling: if blood, blood components and (or) colloids were infused in the 48 hours preceding death or if crystalloids were infused in the hour preceding death;

2.4. tissue establishments may accept tissues and cells from donors with plasma dilution of more than 50 % only if the testing procedures used are validated for such plasma or if a pre-transfusion sample is available;

2.5. in the case of a deceased donor, blood samples must have been obtained just prior to death or, if not possible, the time of sampling must be as soon as possible after death and in any case within 24 hours after death;

2.6. in the case of a living donor (except allogeneic bone marrow stem-cell and peripheral blood stem-cell donors):

2.6.1. blood samples must be obtained at the time of donation or, if not possible, within seven days post donation (this is the “donation sample”);

2.6.2. if tissues and cells of allogeneic living donors can be stored for long periods, repeat sampling and testing is required after an interval of 180 days. In these circumstances of repeat testing, the donation sample can be taken up to 30 days prior to and seven days post donation;

2.6.3. if tissues and cells of allogeneic living donors cannot be stored for long periods and repeat sampling is therefore not possible, Sub-paragraph 2.6.1 of this Annex shall be applied;

2.7. if in a living donor (except for bone marrow stem-cell and peripheral blood stem-cell donors) the “donation sample”, as defined in Sub-paragraph 2.6.1 of this Annex, is additionally tested by the nucleic acid amplification technique (NAT) for HIV, HBV, and HCV, testing of a repeat blood sample is not required. Retesting is also not required if the processing includes an inactivation step that has been validated for specific viruses;

2.8. in the case of bone marrow and peripheral blood stem-cell collection, blood samples must be taken for testing within 30 days prior to donation;

2.9. in the case of neonatal donors, the biological tests may be carried out on the mother of the donor to avoid medically unnecessary procedures upon the infant.

**Annex 4**

Cabinet Regulation No. 1176

22 October 2013

**Selection Criteria and Laboratory Tests Required for Gamete Donors**

[*26 May 2014; 14 March 2017*]

1. Donor selection criteria and laboratory testing need not be applied in the case of gametes donated by partners for direct use.

2. Requirements for working with processed and stored gametes (partner donation not intended for direct use), and also gametes intended for the cryopreservation of embryos:

2.1. the physician responsible for the selection of donors must determine and document, based on the medical history and therapeutic indications of patients, the justification for the donation and its safety for the recipient and any child that might be born as a result of donation;

2.2. the following biological tests must be carried out to prevent the risk of cross-contamination:

|  |  |
| --- | --- |
| HIV 1 and 2 | Anti-HIV 1 and 2 |
| Hepatitis B | HBsAg, anti-HBc |
| Hepatitis C | Anti-HCV-Ab |

In case of sperm procured (intended) for intrauterine insemination and not to be stored, laboratory investigations are not mandatory provided that the tissue establishment, through the use of validated processes, can demonstrate that the risks of infection have been prevented;

2.3. if HIV 1 and 2, hepatitis B or hepatitis C test results are positive or unavailable, or if the donor is known to be a source of infection risk, a system of separate storage must be devised;

2.4. HTLV-I antibody testing must be performed for donors living in or originating from high-incidence areas or with sexual partners originating from those areas or where the parents of the donor originate from those areas;

2.5. in certain circumstances, additional testing may be required depending on the travel and exposure history of the donor and the characteristics of the tissue or cells donated (for example, RhD, malaria, CMV, *T. cruzi*);

2.6. positive results do not necessarily prevent partner donation.

3. The following conditions must be complied with in order to use gametes other than a partner donation:

3.1. donors must be selected on the basis of their age, medical examination, anamnesis data provided on a questionnaire, and also through a personal interview performed by a qualified and trained healthcare personnel. This assessment must include relevant factors that may assist in identifying and screening out persons whose donation could present a health risk to others, for example, the possibility of transmitting diseases (for example, sexually transmitted infections (gonorrhea, trichomoniasis, chlamydiosis), severe and inherited extragenital diseases), or health risks to themselves (for example, superovulation, sedation or the risks associated with the egg collection procedure or the psychological consequences of being a donor). Donors shall submit the conclusion of a narcologist and a psychiatrist;

3.2. the donors must be negative for HIV 1 and 2, HBV, HCV, syphilis tested in accordance with Sub-paragraph 1.1 of Annex 3 to this Regulation, and sperm donors must be negative for chlamydia on a urine sample tested by the nucleic acid amplification technique (NAT), and also a spermogram must be carried out for sperm donors;

3.3. HTLV-1 antibody testing must be performed for donors living in or originating from high-incidence areas or with sexual partners originating from those areas or where the parents of the donor originate from those areas;

3.4. in certain circumstances, additional testing may be required depending on the health history of the donor and the characteristics of the tissue or cells donated (for example, RhD, malaria, CMV, *T. cruzi*);

3.5. Paragraph 3 of Annex 2 to this Regulation shall apply to autologous donors;

3.6. genetic screening for autosomal recessive genes known to be prevalent, according to international scientific evidence, in the ethnic background of the donor and an assessment of the risk of transmission of inherited conditions known to be present in the family must be carried out, after consent is obtained. Complete information on the associated risk and on the measures undertaken for its mitigation must be communicated and clearly explained to the recipient.

4. General requirements to be complied with for determining screening for infection (biological) markers:

4.1. the tests must be carried out in accordance with Sub-paragraphs 2.1 and 2.2 of Annex 3 to this Regulation;

4.2. for donations from other persons (other than partners), blood samples shall be taken at the time of each donation. For a donation from a partner (other than for direct use), blood samples shall be taken within three months prior to the first donation. For subsequent donations from the same donor, blood samples shall be taken no later than 24 months after the last sample was taken;

4.3. sperm donations of other persons (other than partners) shall be quarantined for a minimum of 180 days, after which repeat testing is required. If the blood donation sample is additionally tested by the nucleic acid amplification technique (NAT) for HIV, HBV, and HCV, testing of a repeat blood sample is not required. Retesting is also not required if the processing includes inactivation that has been validated for specific viruses.

**Annex 5**

Cabinet Regulation No. 1176

22 October 2013

[*14 March 2017*]

**Notification of Serious Adverse Reactions**

**Part A**

**Rapid Notification for Suspected Serious Adverse Reactions**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| 1. Name of the tissue establishment | |  | | | |
| 2. EU tissue establishment code (if applicable) | |  | | | |
| 3. Report identification | |  | | | |
| 4. Reporting date (yyyy.mm.dd.) | | | . . . | | |
| 5. Individual affected (mark as appropriate): | | | | | |
| 5.1. recipient |  | | | | |
| 5.2. donor |  | | | | |
| 6. Date and place of procurement or human application (yyyy.mm.dd.) | | | . . . | |  |
| 7. Unique donation identification number | | | |  | |

|  |  |
| --- | --- |
| 8. Date of suspected serious adverse reaction  (yyyy.mm.dd.) | . . . |

9. Type of tissues and cells involved in the suspected serious adverse reaction (please, specify)

|  |
| --- |
|  |

10. Single European Code of tissues or cells involved in the suspected serious adverse reaction (if applicable)

|  |
| --- |
|  |

11. Type of suspected serious adverse reaction(-s) (please, specify)

|  |
| --- |
|  |

**Part B**

**Conclusions of Serious Adverse Reactions Investigation**

|  |  |  |
| --- | --- | --- |
| 12. Name of the tissue establishment |  | |
| 13. EU tissue establishment code (if applicable) |  | |
| 14. Report identification |  | |
| 15. Confirmation date (yyyy.mm.dd.) | | . . . |

16. Date of serious adverse reaction (yyyy.mm.dd.) . . .

|  |  |
| --- | --- |
| 17. Unique donation identification number |  |

18. Confirmation of serious adverse reaction (mark as appropriate):

|  |  |
| --- | --- |
| 18.1. yes |  |
| 18.2. no |  |

19. Single European Code of the tissues and cells involved in the confirmed serious adverse reaction (if applicable)

|  |
| --- |
|  |

20. Change of type of serious adverse reaction (mark as appropriate):

|  |  |
| --- | --- |
| 20.1. yes |  |
| 20.2. no |  |

21. Please, specify if the answer to Paragraph 20 of this Annex is affirmative

|  |
| --- |
|  |

22. Clinical outcome (if known) (mark as appropriate):

|  |  |
| --- | --- |
| 22.1. complete recovery |  |
| 22.2. minor sequelae |  |
| 22.3. serious sequelae |  |
| 22.4. death |  |

23. Outcome of the investigation and final conclusions

|  |
| --- |
|  |

24. Recommendations for preventive and corrective actions

|  |
| --- |
|  |

**Annex 6**

Cabinet Regulation No. 1176

22 October 2013

[*14 March 2017*]

**Notification of Serious Adverse Events**

**Part A**

**Rapid Notification for Suspected Serious Adverse Events**

|  |  |  |
| --- | --- | --- |
| 1. Name of the tissue establishment |  | |
| 2. EU tissue establishment code (if applicable) |  | |
| 3. Report identification |  | |
| 4. Reporting date (yyyy.mm.dd.) | | . . . |

5. Date of serious adverse event (yyyy.mm.dd.) . . .

6. Information on serious adverse event

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Serious adverse event which may affect quality and safety of tissues and cells due to a deviation in the following stages | Specification | | | |
| tissue and cell defect | equipment failure | human error | other (please, specify) |
| Procurement |  |  |  |  |
| Testing |  |  |  |  |
| Transportation |  |  |  |  |
| Processing |  |  |  |  |
| Storage |  |  |  |  |
| Distribution |  |  |  |  |
| Materials |  |  |  |  |
| Other (please, specify) |  |  |  |  |

**Part B**

**Conclusions of Serious Adverse Events Investigation**

|  |  |  |
| --- | --- | --- |
| 7. Name of the tissue establishment |  | |
| 8. EU tissue establishment code (if applicable) |  | |
| 9. Report identification |  | |
| 10. Confirmation date (yyyy.mm.dd.) | | . . . |

11. Date of serious adverse event (yyyy.mm.dd.) . . .

12. Root cause analysis (details)

|  |
| --- |
|  |

13. Corrective measures taken (detailed information)

|  |
| --- |
|  |

**Annex 7**

Cabinet Regulation No. 1176

22 October 2013

**Particle Level Parameters of the Environment in Facilities of a Tissue Establishment**

[*14 March 2017*]

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Grade | Maximum permissible level of particles per one cubic metre which are equal to or above the level specified in the table | | | |
| at-rest\* | | in operation\*\* | |
| 0.5 μm | 5.0 μm | 0.5 μm | 5.0 μm |
| A | 3520 | 20 | 3520 | 20 |
| B | 3520 | 29 | 352 000 | 2900 |
| C | 352 000 | 2900 | 3 520 000 | 29 000 |
| D | 3 520 000 | 29 000 | Not regulated | Not regulated |

Notes.

1. \* At-rest is a condition in which the equipment and all necessary machines are installed and operating, but with no personnel present in the facilities.

2. \*\* Operational is a condition where the equipment and machines are installed and operating in the specified manner for the process and the specified personnel required to carry out the process is present in the facilities.

Each processing operation in which tissues or cells come into direct contact with the environment must ensure an appropriate level of cleanliness of the environment to minimise the risk of particulate or microbiological contamination of the products or materials being processed.

In order to meet the conditions necessary for the “in operation”, these areas must be designed to achieve a specified degree of air purity in “at-rest”. “At-rest” is a condition with the equipment installed and operating, all production accessories present, but with no personnel present. “In operation” is a condition where the equipment is operating in the specified manner and with the specified number of personnel present. The “in operation” and “at-rest” states are to be defined for each clean room or group of clean rooms.

Within the meaning of this Regulation, there are four grades of rooms.

Grade A – a local zone where high-risk activities, for example, the aseptic processing of tissues or cells when they come into contact with the environment, take place. These conditions are usually provided in a laminar flow cabinet. Laminar flow systems operating in open clean rooms should provide a homogeneous air flow with a velocity range from 0.36 to 0.54 m/s (guidance value). The maintenance of laminar flow shall be demonstrated and validated. In insulated cabinets and gloved cabinets, a unidirectional air flow at a lower velocity may be used.

Grade B – in aseptic processing, this is the background environment of a Grade A area.

Grades C and D – clean areas for less significant processing stages.

**Bacteriological Examination (Monitoring in Action) Parameters of the Environment in Facilities of a Tissue Establishment \***

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Grade | Air sample (CFU\*\*/m 3) | Plate diameter size 90 mm (CFU/4h)\*\*\* | Contact plate diameter size 55 mm  (CFU/plate)\*\*\*\* | Glove print – five fingers  (CFU/glove)\*\*\*\*\* |
| A | <1 | <1 | <1 | <1 |
| B | 10 | 5 | 5 | 5 |
| C | 100 | 50 | 25 | – |
| D | 200 | 100 | 50 | – |

Notes.

1. \* Average values.

2. \*\* Colony-forming units.

3. \*\*\* Individual sedimentation plates may be exposed for less than four hours, the result being recalculated accordingly to a four-hour period.

4. \*\*\*\* Contact plates of the same size as the specified contact plate diameter can be used. Contact with the surface during sampling should be at least 10 seconds.

5. \*\*\*\*\* Gloves must not be disinfected before taking impressions. The sample must be taken at the end of the working session, contact time with the plate 5–10 seconds.

**Annex 8**

Cabinet Regulation No. 1176

22 October 2013

**AUTHORISATION TO USE TISSUES AND CELLS No. \_\_\_\_\_\_\_\_\_\_**

Rīga

**State Agency of Medicines**

|  |  |  |
| --- | --- | --- |
|  |  |  |
|  | (address, telephone, registration No.) |  |

**certifies that**

|  |  |
| --- | --- |
| 1. |  |
|  | (name of the higher education institution) |

|  |  |  |
| --- | --- | --- |
| 2. | Registered in the register of educational institutions under No. |  |

|  |  |
| --- | --- |
| 3. |  |
|  | (legal address and actual address, telephone, e-mail address of the higher educational institution) |

|  |  |  |
| --- | --- | --- |
| 4. | Responsible person of the institution |  |
|  |  | (given name, surname, telephone, e-mail address) |

**has been assessed and complies with the requirements laid down in Cabinet Regulation No. 1176 of 22 October 2013, Procedures for the Use of Human Tissues and Cells, and is entitled to use tissues and cells for the implementation of a medical study programme(-s).**

5. Date \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

|  |  |
| --- | --- |
| 6. Director of the State Agency of Medicines |  |
|  | (given name, surname, signature) |

Place for a seal

Note. The details of the document “signature” and “place for seal” shall not be completed if the electronic document has been prepared in accordance with the laws and regulations regarding drawing up of electronic documents.

Minister for Health Ingrīda Circene

**Annex 9**

Cabinet Regulation No. 1176

22 October 2013

[*14 March 2017*]

**ANNUAL NOTIFICATION SAMPLE FORM**

PART A

**Annual Notification of Serious Adverse Reactions**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Reporting country | |  | | |
| Reporting date | |  | | |
| Number of serious adverse reaction(-s) per tissue and cell type (or the product coming into contact with cells and tissues) | | | | |
| No. | Tissue/cell type (or the product coming into contact with tissues and cells) | | Number of serious adverse reaction(-s) | Total number of tissues/cells of the relevant type (if available) |
| 1. |  | |  |  |
| 2. |  | |  |  |
| 3. |  | |  |  |
| 4. |  | |  |  |
| … |  | |  |  |
| Total | | |  |  |
| Total number of tissues and cells distributed (including types of tissues and cells for which no serious adverse reactions were reported) | | | | |
| Number of recipients affected (total number of recipients) | | | | |
| Type of reported serious adverse reactions | | | Total number of serious adverse reaction(-s) | |
| Transmitted bacterial infection | | |  | |
|  | | HBV |  | |
| HCV |  | |
| HIV-1/2 |  | |
| Other (please, specify) |  | |
| Transmitted parasite infection | | Malaria |  | |
| Other (please, specify) |  | |
| Transmitted malignant diseases | | |  | |
| Other cases of spread of disease | | |  | |
| Other serious adverse reactions (please, specify) | | |  | |

PART B

**Annual Notification of Serious Adverse Events**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Reporting country |  | | | |
| Reporting date |  | | | |
| Total number of tissues and cells processed | | | | |
| Total number of adverse events which has affected quality and safety of tissues and cells due to a deviation in the following stages | Specification | | | |
| specific tissues and cells (please, specify) | equipment failure (please, specify) | human error (please, specify) | other (please, specify) |
| Procurement |  |  |  |  |
| Testing |  |  |  |  |
| Transportation |  |  |  |  |
| Processing |  |  |  |  |
| Storage |  |  |  |  |
| Distribution |  |  |  |  |
| Materials |  |  |  |  |
| Other (please, specify) |  |  |  |  |

Minister for Health Ingrīda Circene

**Annex 10**

Cabinet Regulation No. 1176

22 October 2013

**Structure of the Single European Code (SEC)**

[*14 March 2017*]

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Donation identification sequence | | | Product identification sequence | | | |
| EU tissue establishment code | | unique donation number | product code | | split number | expiry date  (yyyy.mm.dd.) |
| ISO country code | tissue establishment number | product coding system identifier | product number |
| two alphabetic characters | six alpha-numeric characters | 13 alpha-numeric characters | one alphabetic character | seven alpha-numeric characters | three alpha-numeric characters | eight numeric characters |