

Draft

COMMISSION DIRECTIVE ../.../EC

of

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

(Text with EEA relevance)

THE COMMISSION OF THE EUROPEAN COMMUNITIES,

Having regard to the Treaty establishing the European Community, and in particular Article 152(4)(a) thereof,

Having regard to 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 cells¹, and in particular points (b), (d), (e), (f), and (i) of Article 28 thereof,

Whereas:

- (1) Directive 2004/23/EC lays down standards of quality and safety for the donation, procurement and testing of all human tissues and cells intended for human applications, and of manufactured products derived from human tissues and cells intended for human applications, so as to ensure a high level of human health protection.
- (2) In order to prevent the transmission of diseases by human tissues and cells for human applications and to ensure an equivalent level of quality and safety, Directive 2004/23/EC calls for the establishment of specific technical requirements for each one of the steps in the human tissue and cell application process.
- (3) The use of tissues and cells for application in the human body carries a risk of disease transmission and other potential adverse effects in recipients. That risk can be reduced by careful donor selection, testing of each donation and the application of procedures to procure tissues and cells in accordance with rules and processes established and updated according to the best available scientific advice. Therefore, all tissues and cells, including those used as starting material for the manufacture of medicinal products, to be used in the Community should meet the quality and safety requirements laid down in this Directive.

¹ OJ L 102, 7.4.2004, p. 48.

- (4) Reproductive cells have, due to the specific nature of their application, specific quality and safety characteristics that are taken into account in this Directive.
- (5) For the donation of reproductive cells between partners that have an intimate physical relationship, it is justified to require less stringent biological testing, given that in this case the risk for the recipient is considered less than for donation from third parties. In order to minimise the risk of cross-contamination, biological testing of the donor will be necessary only when the donated cells will be processed, cultured or stored.
- (6) This Directive is based on international experience drawn upon through an extensive consultation, the Council of Europe's Guide to safety and quality assurance for organs, tissues and cells, the European Convention on Human Rights, the Council of Europe's Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine (Oviedo, 4.IV.1997), with its additional protocols, and recommendations from the World Health Organisation. In particular, with regard to further additional biological testing for donors originating from high-incidence areas of specific diseases or whose sexual partners or parents originate from high-incidence areas, Member States will refer to existing international scientific evidence. The Directive is consistent with the fundamental principles set out in the European Charter of Fundamental Rights.
- (7) The measures provided for in this Directive are in accordance with the opinion of the Committee set up by Directive 2004/23/EC,

HAS ADOPTED THIS DIRECTIVE:

Article 1

Definitions

For the purposes of this Directive, the following definitions apply:

- (a) '*reproductive cells*' means all tissues and cells intended to be used for the purpose of assisted reproduction;
- (b) '*partner donation*' means the donation of reproductive cells between a man and a woman who declare that they have an intimate physical relationship;
- (c) '*direct use*' means any procedure where cells are donated and used without any banking;
- (d) '*quality system*' means the organisational structure, defined responsibilities, procedures, processes, and resources for implementing quality management and includes all activities which contribute to quality, directly or indirectly;
- (e) '*Standard Operating Procedures*' (*SOPs*) means written instructions describing the steps in a specific process, including the materials and methods to be used and the expected end product;

- (f) *'validation'* (or *'qualification'* in the case of equipment or environments) means establishing documented evidence that provides a high degree of assurance that a specific process, SOPs, piece of equipment or environment will consistently produce a product meeting its predetermined specifications and quality attributes; a process is validated to evaluate the performance of a system with regard to its effectiveness based on intended use;
- (g) *'traceability'* means the ability to locate and identify the tissue/cell 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 the manufacturing facility receiving, processing or storing the tissue/cells, and the ability to identify the recipient(s) at the medical facility/facilities applying the tissue/cells to the recipient(s); traceability also covers the ability to locate and identify all relevant data relating to products and materials coming into contact with those tissues/cells;
- (h) *'procurement organisation'* means a health care establishment or a unit of a hospital or another body that undertakes the procurement of human tissues and cells and that may not be accredited, designated, authorised or licensed as a tissue establishment.

Article 2

Requirements for the procurement of human tissues and cells

1. With the exception of partner donation of reproductive cells for direct use, Member States shall ensure that the procurement of human tissues and cells is accredited, designated, authorised or licensed only when the requirements in paragraphs 2 to 12 are met.
2. Procurement of human tissues and cells shall be carried out by persons who have successfully completed a training programme specified by a clinical team specialising in the tissues and cells to be procured or a tissue establishment authorised for procurement.
3. The tissue establishment or procurement organisation shall have written agreements with the staff or clinical teams responsible for donor selection, unless they are employed by the same organisation or establishment, specifying the procedures to be followed to assure compliance with the selection criteria for donors set out in Annex I.
4. The tissue establishment or procurement organisation shall have written agreements with the staff or clinical teams responsible for tissue/cell procurement, unless they are employed by the same establishment or organisation, specifying the type(s) of tissues and/or cells and/or test samples to be procured and the protocols to be followed.
5. There shall be Standard Operating Procedures (SOPs) for the verification of:
 - (a) donor identity;

- (b) the details of donor or donor family consent or authorisation;
- (c) the assessment of the selection criteria for donors as detailed in Article 3;
- (d) the assessment of the laboratory tests required for donors as detailed in Article 4.

There shall also be SOPs describing the procedures for procurement, packaging, labelling and transportation of the tissues and cells to the point of arrival at the tissue establishment or, in the case of direct distribution of tissues and cells, to the clinical team responsible for their application or, in the case of tissue/cell samples, to the laboratory for testing, in accordance with Article 5 of this Directive.

- 6. Procurement shall take place in appropriate facilities, following procedures that minimise bacterial or other contamination of procured tissues and cells, in accordance with Article 5.
- 7. Procurement materials and equipment shall be managed in accordance with the standards and specifications laid down in Annex IV, section 1.3, and with due regard to relevant national and international regulation, standards and guidelines covering the sterilisation of medicines and medical devices. Qualified, sterile instruments and procurement devices shall be used for tissue and cell procurement.
- 8. Procurement of tissues and cells from living donors shall take place in an environment that ensures their health, safety and privacy.
- 9. Where appropriate, the staff and equipment necessary for body reconstruction of deceased donors shall be provided. Such reconstruction shall be completed effectively.
- 10. The procedures for the procurement of tissues and cells shall be carried out in accordance with the requirements specified in Article 5.
- 11. A unique identifying code shall be allocated to the donor and the donated tissues and cells, during procurement or at the tissue establishment, to ensure proper identification of the donor and the traceability of all donated material. The coded data shall be entered in a register maintained for the purpose.
- 12. Donor documentation shall be maintained in accordance with point 1.4 of Annex IV.

Article 3

Selection criteria for donors of tissues and cells

The competent authority or authorities shall ensure that donors comply with the selection criteria set out in:

- (a) Annex I for donors of tissues and cells, except donors of reproductive cells;
- (b) Annex III for donors of reproductive cells.

Article 4

Laboratory tests required for donors

1. The competent authority or authorities shall ensure that:
 - (a) donors of tissues and cells, except donors of reproductive cells, undergo the biological tests set out in point 1 of Annex II;
 - (b) the tests referred to in point (a) are carried out in compliance with the general requirements set out in point 2 of Annex II.
2. The competent authority or authorities shall ensure that:
 - (a) donors of reproductive cells undergo the biological tests set out in points 1, 2 and 3 of Annex III;
 - (b) the tests referred to in point (a) above are carried out in compliance with the general requirements set out in point 4 of Annex III.

Article 5

Tissue and/or cell donation and procurement procedures and reception at the tissue establishment

The competent authority or authorities shall ensure that the tissue and/or cell donation and procurement procedures and the reception of tissues and/or cells at the tissue establishment comply with the requirements set out in Annex IV.

Article 6

Requirements for direct distribution to the recipient of specific tissues and cells

The competent authority or authorities may authorise the direct distribution of specific tissues and cells from where the procurement is carried out to a health care establishment for immediate transplantation .

Article 7

Transposition

1. Member States shall bring into force the laws, regulations and administrative provisions necessary to comply with this Directive by 1 November 2006, at the latest. They shall forthwith communicate to the Commission the text of those provisions and a correlation table between those provisions and this Directive.

When Member States adopt those provisions, they shall contain a reference to this Directive or be accompanied by such a reference on the occasion of their official publication. Member States shall determine how such reference is to be made.

2. Member States shall communicate to the Commission the text of the main provisions of national law which they adopt in the field covered by this Directive.

Article 8

Entry into force

This Directive shall enter into force on the twentieth day following that of its publication in the *Official Journal of the European Union*.

Article 9

Addressees

This Directive is addressed to the Member States.

Done at Brussels,

For the Commission

Member of the Commission

ANNEX I

Selection criteria for donors of tissues and/or cells (except donors of reproductive cells) as referred to in Article 3(a)

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 person as defined in Article 17 of Directive 2004/23/EC, donors must be excluded from donation if any of the following criteria applies:

1. Deceased Donors

1.1. General criteria for exclusion

- 1.1.1. 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.
- 1.1.2. History of a disease of unknown aetiology.
- 1.1.3. Presence, or previous history, of malignant disease, except for primary basal cell carcinoma, carcinoma *in situ* of the uterine cervix, and 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.
- 1.1.4. Risk of transmission of diseases caused by prions. This risk applies, for example, to:
 - (a) people diagnosed with Creutzfeldt–Jakob Disease, or variant Creutzfeldt-Jacob Disease, or having a family history of non-iatrogenic Creutzfeldt-Jacob Disease;
 - (b) people with a history of rapid progressive dementia or degenerative neurological disease, including those of unknown origin;
 - (c) recipients of hormones derived from the human pituitary gland (such as growth hormones) and recipients of grafts of cornea, sclera and dura mater, and persons that have undergone undocumented neurosurgery (where dura mater may have been used);

For variant Creutzfeldt-Jacob Disease, further precautionary measures may be recommended.

- 1.1.5. Systemic infection which is not controlled at the time of donation, including bacterial diseases, systemic viral, fungal or parasitic infections, or significant local infection 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.

- 1.1.6. 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.
- 1.1.7. History of chronic, systemic autoimmune disease that could have a detrimental affect on the quality of the tissue to be retrieved.
- 1.1.8. Indications that test results of donor blood samples will be invalid due to:
 - (a) the occurrence of haemodilution, according to the specifications in Annex II, section 2, where a pre-transfusion sample is not available; or
 - (b) treatment with immunosuppressive agents.
- 1.1.9. Evidence of any other risk factors for transmissible diseases on the basis of a risk assessment, taking into consideration donor travel and exposure history and local infectious disease prevalence.
- 1.1.10. Presence on the donor's body of physical signs implying a risk of transmissible disease(s) as described in Annex IV, point 1.2.3.
- 1.1.11. Ingestion of, or exposure to, a substance (such as cyanide, lead, mercury, gold) that may be transmitted to recipients in a dose that could endanger their health.
- 1.1.12. Recent history of vaccination with a live attenuated virus where a risk of transmission is considered to exist.
- 1.1.13. Transplantation with xenografts.

1.2. Additional exclusion criteria for deceased child donors.

1.2.1. Any children born from mothers with HIV infection or that meet any of the exclusion criteria described in section 1.1 must be excluded as donors until the risk of transmission of infection can be definitely ruled out.

- (a) 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;
- (b) 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.

2. Living Donors

2.1. Autologous Living Donor

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

2.2. Allogeneic Living Donor

- 2.2.1. Allogeneic living donors must be selected on the basis of their health and medical history, provided on a questionnaire and through an interview performed by a qualified and trained healthcare professional with the donor, in compliance with point 2.2.2. This assessment must include relevant factors that may assist in identifying and screening out persons whose donation could present a health risk to others, such as 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.
- 2.2.2. 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 donor's physical status and medical and behavioural history and the results of clinical investigations and laboratory tests establishing the donor's state of health.
- 2.2.3. The same exclusion criteria must be applied as for deceased donors with the exception of point 1.1.1. Depending on the tissue or cell to be donated, other specific exclusion criteria may need to be added, such as:
- (a) pregnancy (except for donors of umbilical cord blood cells and amniotic membrane and sibling donors of haematopoietic progenitors);
 - (b) breast feeding;
 - (c) in the case of haematopoietic progenitor cells, the potential for transmission of inherited conditions.

ANNEX II

Laboratory tests required for donors (except donors of reproductive cells) as referred to in Article 4(1)

1. Biological tests required for donors

- 1.1. The following biological tests must be performed for all donors as a minimum requirement:

HIV 1 and 2	Anti-HIV-1,2
Hepatitis B	HBsAg Anti HBc
Hepatitis C	Anti-HCV-Ab
Syphilis	See 1.4 (below)

- 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 the donor's parents originate from those areas.
- 1.3. When 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. When 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 donor's history and the characteristics of the tissue or cells donated (e.g. RhD, HLA, malaria, CMV, toxoplasma, EBV, *Trypanosoma cruzi*).
- 1.6. For autologous donors, Annex I, point 2.1.1, applies.

2. General requirements to be met for determining biological markers

- 2.1. The tests must be carried out by a qualified laboratory, authorised as a testing centre by the competent authority in the Member State, using CE-marked testing kits where appropriate. The type of test used must be validated for the purpose in accordance with current scientific knowledge..
- 2.2. The biological tests will be carried out on the donor's serum or plasma; they must not be performed on other fluids or secretions such as the aqueous or vitreous humour unless specifically justified clinically using a validated test for such a fluid.

2.3. When 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:

- (a) **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;
- (b) **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.

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.

2.4. 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.

2.5. a) In the case of living donors (except allogeneic bone marrow stem-cell and peripheral blood stem-cell donors, for practical reasons), blood samples must be obtained at the time of donation or if not possible, within 7 days post donation (this is the 'donation sample').

b) Where 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 7 days post donation.

c) Where tissues and cells of allogeneic living donors cannot be stored for long periods and repeat sampling is therefore not possible, paragraph 2(5)(a) above applies.

2.6. If in a living donor (except bone marrow stem-cell and peripheral blood stem-cell donors) the 'donation sample', as defined in paragraph 2.(5).(a) above, 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 the viruses concerned.

2.7. 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.

2.8. In the case of neonatal donors, the biological tests may be carried out on the donor's mother to avoid medically unnecessary procedures upon the infant.

ANNEX III

Selection criteria and laboratory tests required for donors of reproductive cells as referred to in Article 3(b) and Article 4(2)

1. Partner donation for direct use

Donor selection criteria and laboratory testing do not need to be applied in the case of partner donation of reproductive cells for direct use.

2. Partner donation (not direct use)

Reproductive cells that are processed and/or stored and reproductive cells that will result in the cryopreservation of embryos must meet the following criteria:

- 2.1. The clinician responsible for the donor must determine and document, based on the patient's medical history and therapeutic indications, the justification for the donation and its safety for the recipient and any child(ren) that might result.
- 2.2. The following biological tests must be carried out to assess the risk of cross-contamination:

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

In case of sperm processed for intrauterine insemination, not to be stored and if the Tissue establishment can demonstrate that the risk of cross contamination and staff exposure has been addressed through the use of validated standard operation procedures, the biological testing may not be required.

- 2.3. Where HIV 1 and 2, hepatitis B or hepatitis C test results are positive or unavailable, or where 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 donor's parents originate from those areas.
- 2.5. In certain circumstances, additional testing may be required depending on the donor's travel and exposure history and the characteristics of the tissue or cells donated (e.g. Rh D, malaria, CMV, T. cruzi).
- 2.6. Positive results will not necessarily prevent partner donation in accordance with national rules.

3. Donations other than by partners

The use of reproductive cells other than for partner donation must meet the following criteria:

- 3.1. Donors must be selected on the basis of their age, health and medical history, provided on a questionnaire and through a personal interview performed by a qualified and trained healthcare professional. This assessment must include relevant factors that may assist in identifying and screening out persons whose donation could present a health risk to others, such as the possibility of transmitting diseases (such as sexually transmitted infections), or health risks to themselves (e.g.; superovulation, sedation or the risks associated with the egg collection procedure or the psychological consequences of being a donor).
- 3.2. The donors must be negative for HIV 1 and 2, HCV, HBV and syphilis on a serum or plasma sample, tested in accordance with Annex II, point 1.1, and sperm donors must additionally be negative for chlamydia on a urine sample tested by the nucleic acid amplification technique (NAT).
- 3.3. 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 donor's parents originate from those areas.
- 3.4. In certain circumstances, additional testing may be required depending on the donor's history and the characteristics of the tissue or cells donated (e.g. RhD, malaria, CMV, T. cruzi).
- 3.5. For autologous donors, Annex I, point 2.1.1, applies.
- 3.6. Genetic screening for autosomal recessive genes known to be prevalent, according to international scientific evidence, in the donor's ethnic background 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 must be provided, in accordance with the requirements in force in Member States. 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 met for determining biological markers

- 4.1 The tests must be carried out in accordance with Annex II, points 2.1 and 2.2.
- 4.2 Blood samples must be obtained at the time of donation.
- 4.3 Sperm donations will 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 an inactivation step that has been validated for the viruses concerned.

ANNEX IV

Cell and/or tissue donation and procurement procedures and receipt at the tissue establishment as referred to in Article 5

1. Donation and procurement procedures

1.1. Consent and donor identification

1.1.1. Before the procurement of tissues and cells proceeds, an authorised person must confirm and record:

- (a) that consent for the procurement has been obtained in accordance with Article 13 of Directive 2004/23/EC; and
- (b) how and by whom the donor has been reliably identified.

1.1.2. In the case of living donors, the health professional responsible for obtaining the health history must ensure that the donor has:

- (a) understood the information provided,
- (b) had an opportunity to ask questions and been provided with satisfactory responses;
- (c) confirmed that all the information provided is true to the best of his/her knowledge.

1.2. Donor evaluation (this section does not apply to partner donation of reproductive cells or to autologous donors)

1.2.1. An authorised person must collect and record the donor's relevant medical and behavioural information according to the requirements described in section 1.4.

1.2.2. In order to acquire the appropriate information, different relevant sources must be used, including at least an interview with the donor, for living donors, and the following when appropriate:

- (a) the medical records of the donor;
- (b) an interview with a person who knew the donor well, for deceased donors;
- (c) an interview with the treating physician,
- (d) an interview with the general practitioner;
- (e) the autopsy report.

1.2.3. In addition, in the case of a deceased donor, and in the case of a living donor when justified, a physical examination of the body must be performed to detect any signs that may be sufficient in themselves to exclude the donor or which must be assessed in the light of the donor's medical and personal history.

- 1.2.4. The complete donor records must be reviewed and assessed for suitability and signed by a qualified health professional.

1.3. Procurement procedures for tissues and cells

- 1.3.1. The procurement procedures must be appropriate for the type of donor and the type of tissue/cells donated. There must be procedures in place to protect the safety of the living donor.
- 1.3.2. The procurement procedures must protect those properties of the tissue/cells that are required for their ultimate clinical use, and at the same time minimise the risk of microbiological contamination during the process, particularly when tissues and cells cannot subsequently be sterilised.
- 1.3.3. For deceased donation, the area of access must be restricted. A local sterile field using sterile drapes must be used. Staff conducting procurement must be clothed appropriately for the type of procurement. Usually, this will extend to being scrubbed, gowned in sterile clothing and wearing sterile gloves, face shields and protective masks.
- 1.3.4. In the case of a deceased donor, the place of procurement must be recorded and the time interval from death to procurement must be specified so as to ensure that the required biological and/or physical properties of the tissues/cells are retained.
- 1.3.5. 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.
- 1.3.6. Any adverse event occurring during procurement that has or may have resulted in harm to a living donor and the outcome of any investigation to determine the cause must be recorded and reviewed.
- 1.3.7. Policies and procedures must be in place to minimise the risk of tissue or cell contamination by staff who might be infected with transmissible diseases.
- 1.3.8. Sterile instruments and devices must be used for tissue and cell procurement. Instruments or devices must be of good quality, validated or specifically certified and regularly maintained for the procurement of tissues and cells.
- 1.3.9. When reusable instruments must be used, a validated cleaning and sterilisation procedure for removal of infectious agents has to be in place.
- 1.3.10. Wherever possible, only CE marked medical devices must be used and all concerned staff must have received appropriate training on the use of such devices.

1.4. Donor documentation

- 1.4.1. For each donor, there must be a record containing:
 - (a) the donor identification (first name, family name and date of birth — if a mother and child are involved in the donation, both the name and date of birth of the mother and the name, if known, and date of birth of the child);

- (b) age, sex, medical and behavioural history (the information collected must be sufficient to allow application of the exclusion criteria, where required);
- (c) outcome of body examination, where applicable,
- (d) haemodilution formula, where applicable;
- (e) the consent/authorisation form, where applicable;
- (f) clinical data, laboratory test results, and the results of other tests carried out;
- (g) if an autopsy was performed, the results must be included in the record (for tissues and cells that cannot be stored for extended periods, a preliminary verbal report of the autopsy must be recorded);
- (h) for haematopoietic progenitor cell donors, the donor's suitability for the chosen recipient must be documented. For unrelated donations, when the organisation responsible for procurement has limited access to recipient data, the transplanting organisation must be provided with donor data relevant for confirming suitability.

1.4.2. The organisation performing the procurement must produce a procurement report, which is passed on to the tissue establishment. This report must contain at least:

- (a) the identification, name and address of the tissue establishment to receive the cells/tissues;
- (b) donor identification data (including how and by whom the donor was identified);
- (c) description and identification of procured tissues and cells (including samples for testing);
- (d) identification of the person who is responsible for the procurement session, including signing;
- (e) date, time (where relevant, start and end) and location of procurement and procedure (SOP) used, including any incidents that occurred; where relevant, environmental conditions at the procurement facility (description of the physical area where procurement took place);
- (f) for deceased donors, conditions under which the cadaver is kept: refrigerated (or not), time of start and end of refrigeration;
- (g) ID/batch numbers of reagents and transport solutions used.

The report must also contain the date and time of death where possible.

Where sperm is procured at home, the procurement report must state this and must contain only:

- (a) the name and address of the tissue establishment to receive the cells/tissues;
- (b) the donor identification.

The date and time of procurement may be included, where possible.

- 1.4.3. All the records must be clear and readable, protected from unauthorised amendment and retained and readily retrieved in this condition throughout their specified retention period in compliance with data protection legislation.
- 1.4.4. Donor records required for full traceability must be kept for a minimum of 30 years after clinical use, or the expiry date, in an appropriate archive acceptable to the competent authority.

1.5. Packaging

- 1.5.1. Following procurement, all recovered tissues and cells must be packaged in a manner which minimises the risk of contamination and must be stored at temperatures that preserve the required characteristics and biological function of the cells/tissues. The packaging must also prevent contamination of those responsible for packaging and transportation of the tissues and cells.
- 1.5.2. The packaged cells/tissues must be shipped in a container which is suitable for the transport of biological materials and which maintains the safety and quality of the contained tissue or cells.
- 1.5.3. Any accompanying tissue or blood samples for testing must be accurately labelled to ensure identification with the donor, and must include a record of the time and place the specimen was taken.

1.6. Labelling of the procured tissues/cells

At the time of procurement, every package containing tissues and cells must be labelled. The primary tissue/cell container must indicate the donation identification or code and the type of tissues and cells. Where the size of the package permits, the following information must also be provided:

- (a) date (and time where possible) of donation;
- (b) hazard warnings;
- (c) nature of any additives (if used);
- (d) in the case of autologous donations, the label must state 'for autologous use only';
- (e) in case of directed donations, the label must identify the intended recipient.

If any of the information under points (a) to (e) above cannot be included on the primary package label, it must be provided on a separate sheet accompanying the primary package.

1.7. Labelling of the shipping container

When tissues/cells are shipped by an intermediary, every shipping container must be labelled at least with:

- (a) TISSUES AND CELLS and HANDLE WITH CARE;

- (b) the identification of the establishment from which the package is being transported (address and phone number) and a contact person in the event of problems;
- (c) the identification of the tissue establishment of destination (address and phone number) and the person to be contacted to take delivery of the container;
- (d) the date and time of the start of transportation;
- (e) specifications concerning conditions of transport relevant to the quality and safety of the tissues and cells;
- (f) in the case of all cellular products, the following indication: DO NOT IRRADIATE;
- (g) when a product is known to be positive for a relevant infectious disease marker, the following indication: BIOLOGICAL HAZARD;
- (h) in the case of autologous donors, the following indication: 'FOR AUTOLOGOUS USE ONLY';
- (i) specifications concerning storage conditions (such as DO NOT FREEZE)

2. Receipt of the tissue/cells at the tissue establishment

- 2.1. When the retrieved tissues/cells arrive at the tissue establishment, there must be documented verification that the consignment, including the transport conditions, packaging, labelling and associated documentation and samples, meet the requirements of this Annex and the specifications of the receiving establishment.
- 2.2. Each establishment must ensure that the tissue and cells received are quarantined until they, along with the associated documentation, have been inspected or otherwise verified as conforming to requirements. The review of relevant donor/procurement information and thus acceptance of the donation needs to be carried out by specified/authorised persons.
- 2.3. Each tissue establishment must have a documented policy and specifications against which each consignment of tissues and cells, including samples, are verified. These must include the technical requirements and other criteria considered by the tissue establishment to be essential for the maintenance of acceptable quality. The tissue establishment must have documented procedures for the management and segregation of non-conforming consignments, or those with incomplete test results, to ensure that there is no risk of the contamination of other tissues and cells being processed, preserved or stored.
- 2.4. The data that must be registered at the tissue establishment (except for donors of reproductive cells intended for partner donation) include:
 - (a) consent/authorisation; including the purpose(s) for which the tissues and cells may be used (i.e. therapeutic or research, or both therapeutic use and research) and any specific instructions for disposal if the tissue or cells are not used for the purpose for which consent was obtained;

- (b) all required records relating to the procurement and the taking of the donor history, as described in the donor documentation section;
- (c) results of physical examination, of laboratory tests and of other tests (such as the autopsy report, if used in accordance with section 1.2.2.);
- (d) for allogeneic donors, a properly documented review of the complete donor evaluation against the selection criteria by an authorised and trained person;
- (e) in the case of cell cultures intended for autologous use, documentation of the possibility of medicinal allergies (such as to antibiotics) of the recipient.

2.5. In the case of reproductive cells intended for partner donation, the data to be registered at the tissue establishment include:

- (a) consent; including the purpose(s) for which the tissues and cells may be used (such as reproductive only and/or for research) and any specific instructions for disposal if the tissue or cells are not used for the purpose for which consent was obtained;
- (b) donor identification and characteristics: type of donor, age, sex, presence of risk factors and, in the case of a deceased donor, the cause of death;
- (c) partner identification;
- (d) place of procurement;
- (e) tissues and cells obtained and relevant characteristics.