EUROPEAN COMMISSION

Health & Consumer Protection
Directorate-General

EU legislation on

Tissues & Cells

The legal basis: Article 152 Public Heath

4 ...Shall contribute to the achievement of the objectives referred to in this Articles through adopting:

(a) Measures setting high standards of quality and safety of organs and substances of human origin, blood and blood derivatives, these measures not prevent any member States from maintaining or introducing more stringent protective measures.

Regulatory framework

Directive 2004/23/EC

of the European Parliament and of the Council setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells

- codecision
- adopted by Parliament and Council on 31 March 2004
- transposed in all Member States by 7 April 2006
- basic principles

Regulatory framework

Commission Directive 2006/17/EC

Implementing Directive 2004/23/EC as regards certain technical requirements for the donation, procurement and testing of human tissues and cells

- comitology
- adopted by the Commission on 8 February 2006
- transposed in all Member States by 1 November 2006
- technical requirements

Regulatory framework

Draft Commission Directive II

Technical requirements 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

- comitology
- to be adopted by mid 2006
- to be in force mid 2007
- technical requirements

Directive 2004/23/EC

GENERAL PROVISIONS

- Objective (Article 1)
  - The Directive doeLay down standards of quality and safety for human tissues and cells intended for human applications, in order to ensure a high level of protection of human health.

Directive 2004/23/EC

GENERAL PROVISIONS

- Scope (Article 2)
  - The Directive applies to Human tissues and cells intended for human applications and of manufactured products derived from human tissues and cells
  - Where manufactured products are covered by other directives, this directive applies only to donation, procurement and testing
  - The Directive does not apply to:
    - tissues and cells used as an autologous graft within the same surgical procedure
    - Research using human tissues and cells when used for purposes other than application to the human body (in vitro research or in animal models)
    - blood and blood components (Directive 2002/98/EC)
    - 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

Directive 2004/23/EC: SCOPE

SOURCE

Donation, Procurement and Testing
Tissues and cells for application in the human body

Tissues and Cells Directive

PROCESSING

Processing, Storage and Distribution

Tissues and cells for application in the human body not covered by other EU Directives

Tissue and Cells Directive

Gene Therapy
Somatic Cell Therapy
Tissue Engineering

Draft Regulation on Advanced Therapies

Directive 2004/23/EC

GENERAL PROVISIONS

- Definitions (Article 3)

- Implementation (Article 4)

  - Designation of Competent Authority(ies) (CA) responsible for implementing the requirements of the Directive

  - Directive shall not prevent MS from maintaining or introducing more stringent protective measures which comply with the provisions of the Treaty

Directive 2004/23/EC

OBLIGATION OF MEMBER STATES AUTHORITIES

- Supervision of human tissues and cells procurement (Article 5)
  - Persons with appropriate training and experience
  - Compliance with requirements on donation, procurement and testing (Directive 2006/17)

Directive 2004/23/EC

Draft Commission Directive II

OBLIGATION OF MEMBER STATES AUTHORITIES

- Accreditation, designation, authorisation, or licensing of tissue establishments (TE) and tissues and cells preparation processes (Article 6
  - Compliance with requirements for processing, preservation, storage and distribution of tissues and cells (Draft Commission Directive II)
  - No substantial change in activities without prior written approval by CA
  - CA may suspend or revoke if inspection or control measures demonstrate tha the TE does not comply with the Directive's requirements
  - Accredited suppliers can distribute specific tissues and cells for immediate transplantation

Draft Commission Directive II to precise the provisions to comply with

Directive 2004/23/EC

OBLIGATION OF MEMBER STATES AUTHORITIES

- Regular inspection and control measures (Article 7)
  - MS shall ensure that the CA organise inspections and appropriate control measures in blood establishments
  - on a regular basis – interval shall not exceed two years
  - by officials representing the CA empowered to inspect TE and facilities of any third parties on its own territory (procedures and documents)
  - as appropriate in the event of any Serious Adverse Event or Reaction or suspicion thereof

Directive 2004/23/EC

Draft Commission Directive II

OBLIGATION OF MEMBER STATES AUTHORITIES

- Traceability (Article 8)
  - MS to ensure that tissues and cells procured, processed, stored or distributed on their territory can be traced from donor to recipient and vice versa (applied also to products and materials into contact with these tissues and cells)
  - Identification and coding procedures (donors and tissues & cells)
  - Record maintenance by TE (Minimum of 30 years after clinical use)

Commission to establish the traceability procedures at community level (Draft Commission Directive II)

Directive 2004/23/EC

OBLIGATION OF MEMBER STATES AUTHORITIES

- Import/export of human tissues and cells (Article 9)
  - Equivalent standards of quality and traceability + accreditation of TE
- Register of Tissue establishment and reporting obligations (Article 10)
  - TEs must keep a record of their activities
  - Annual public reports
  - Public register of accredited TEs
  - European network of TEs registers

Directive 2004/23/EC

Draft Commission Directive II

OBLIGATION OF MEMBER STATES AUTHORITIES

- Notification of Serious adverse events and reactions (Article 11)
  - MS shall ensure that are notified to the CA
    - any Serious Adverse Event or Reaction (SAE/R) related to the procurement, testing, processing, storage and distribution of tissues and cells which may have an influence on their quality and safety
    - as well as any SAE/R observed during or after clinical application which may be attributed to the quality and safety of tissues and cells
  - MS shall ensure that TE have in place a procedure to recall from distribution any product associated with the notification of SAE/R
  - Notification in accordance with procedure and notification format

Draft Commission Directive II to precise the provisions to comply with

Directive 2004/23/EC

DONOR SELECTION AND EVALUATION

- Principles governing tissues and cells donation (Article 12)
  - Voluntary and unpaid donation (Compensation limited to reimbursing the expenses and inconveniences related to the donation)
  - Publicity for donation authorised
  - Member States submit reports to the Commission by April 2006 and every two years thereafter

- Consent (Article 13)

Directive 2004/23/EC

DONOR SELECTION AND EVALUATION

- Data protection and confidentiality (Article 14)
  - MS take measures to ensure that all data, including genetic information, to which third parties have access have been rendered anonymous (donor no longer identifiable)
  - data security measures – safeguards against unauthorised data additions, deletions or modifications
  - procedures to resolve data discrepancies
  - no unauthorised disclosure of information

Whilst guaranteeing the traceability of donations

Directive 2004/23/EC

Directive 2006/17/EC

DONOR SELECTION AND EVALUATION

- Selection, evaluation and procurement (Article 15)
  - Procurement: Article 2 - Directive 2006/17
    - Personnel
    - Facilities
    - Equipment and materials
    - Standard Operating Procedures (Donor identity and consent, Donor selection criteria, laboratory tests)

Directive 2004/23/EC

Directive 2006/17/EC

DONOR SELECTION AND EVALUATION

- Selection, evaluation and procurement (Article 15)
  - Selection Criteria of Donors (Article 3 / Annex I & III – Directive 2006/17)
    - Deceased donors / living donors / donors of reproductive cells
    - Exclusion criteria:
      - malignant/infectious/prions diseases,
      - gaps/unclarities in the medical history,
      - indication that tests on donors will be invalid
      - Transplantation with xenograft
      - …

Directive 2004/23/EC

Directive 2006/17/EC

DONOR SELECTION AND EVALUATION

- Selection, evaluation and procurement (Article 15)
  - Laboratory tests for Donors (Article 4 / Annex II&III Directive 2006/17)
    - HIV 1 and 2 (test Anti-HIV-1, 2)
    - Hepatitis B (test HBsAg, Anti HBc)
    - Hepatitis C (test Anti-HCV-Ab)
    - Syphilis
    - HTLV-I antibody testing 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.
    - In certain circumstances, additional testing 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).

Directive 2004/23/EC

Directive 2006/17/EC

DONOR SELECTION AND EVALUATION

- Selection, evaluation and procurement (Article 15)
  - Selection Criteria and laboratory tests for Donors of Reproductive cells (Annex III Directive 2006/17)
    - Partner donation for Direct use excluded
    - Partner donation (processed and/or stored)
      - HIV 1 and 2 /Hepatitis B/ Hepatitis C
      - Exception for sperm processed for intrauterine insemination and not to be stored, if the risk of cross contamination and staff exposure has been addressed through the use of validated processes.
      - Positive results will not necessarily prevent partner donation in accordance with national rules.

Directive 2004/23/EC

Directive 2006/17/EC

DONOR SELECTION AND EVALUATION

- Selection, evaluation and procurement (Article 15)
  - Selection Criteria and laboratory tests for Donors of Reproductive cells (Annex III Directive 2006/17)
    - Donation other than by partners
      - 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
      - HIV 1 and 2 /Hepatitis B/ Hepatitis C/ Syphilis and Chlamydia
      - In certain circumstances, additional testing may be required depending on the donor's history
      - Genetic screening according with national rules

Directive 2004/23/EC

Draft Commission Directive II

PROVISIONS ON THE QUALITY AND SAFETY OF TISSUES AND CELLS

- Quality management (Article 16)
  - TE must put in place a quality system based on principles of good practices
    - Standard Operating procedures
    - Guidelines
    - Training and reference manuals
    - Reporting forms
    - Donor records
    - Information on the final destination of tissues and cells

Technical requirements to be precised in Draft Commission Directive II

Directive 2004/23/EC

PROVISIONS ON THE QUALITY AND SAFETY OF TISSUES AND CELLS

- Responsible person (Article 17)
  - TE shall designate a responsible person, responsible for:
    - ensuring that human tissues and cells are procured and tested/processed, … in compliance with the Directive and the laws in force in the MS
    - providing info to the CA in the accreditation procedures
    - implementation of requirements on inspections, quality system, record keeping, traceability, selection/evaluation, notification SAR/SAE
  - Minimum conditions of qualification: diploma + 2 year practice
- Personnel (Article 18)
  - Personnel directly involved shall be qualified and be provided with timely, relevant and regularly updated training

Directive 2004/23/EC

Directive 2006/17/EC

PROVISIONS ON THE QUALITY AND SAFETY OF TISSUES AND CELLS

- Reception (Article 19 + Article 5 & Annex IV Directive 2006/17)
  - TE shall verify and record that all donations and the packaging of human tissues and cells comply with the requirements of the Directives
    - Consent and donor identification
    - Donor evaluation.
    - Procurement procedures
    - Donor documentation: Procurement report
    - Packaging and labelling
    - Reception at the tissue establishment

Directive 2004/23/EC

Draft Commission Directive II

PROVISIONS ON THE QUALITY AND SAFETY OF TISSUES AND CELLS

- Processing (Article 20)
  - TE to use processes/equipments/working environment that ensure quality and safety of processed tissues and cells
- Storage conditions (Article 21)
  - Storage processes must adversely affect the functioning and the integrity of the tissues and cells
- Labelling, documentation and distribution (Articles 22 & 23)

Technical requirements to be precised in Draft Commission Directive II

Directive 2004/23/EC

PROVISIONS ON THE QUALITY AND SAFETY OF TISSUES AND CELLS

- Relations with third parties (Article 24)
  - TE to establish written agreements with a third party for any collaboration that influences the quality and safety of tissues and cells processed

Directive 2004/23/EC

Draft Commission Directive II

OTHER PROVISIONS

- Coding system (Article 25)
  - MS to establish a system for the identification of human tissues and cells, to ensure traceability.

  Draft Commission Directive II to precise the provisions + comitology
- Penalties (Article 27)
- Technical requirements and their adaptation to Scientific and technical progress Processing (Article 28)
- Regulatory Committee (Article 29)

Thank you