Practical implications in the sperm bank of the European cell and tissue directives

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I have no commercial relationships or other activities that might be perceived as a potential conflict of interest for this presentation

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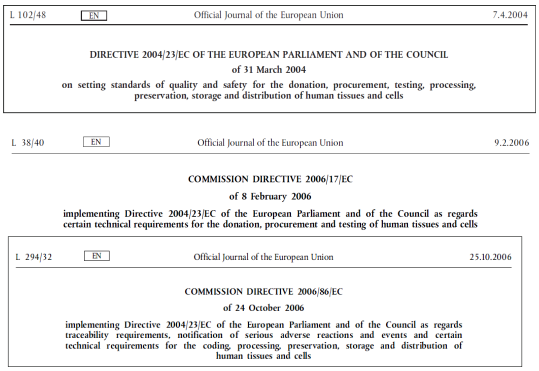
Aims

- An overview of the EU directives on Cells and Tissues …
- Consequences for processing of semen samples:
  - Air quality
  - Quarantine
  - Cryo preservation
  - Transportation
  - Documentation - Traceability
- A future with increased availability of cells and tissues within Europe?

Background to the EU Directives

- Contamination of blood products (HIV, Hep C, Hep B)
  - Lack of control systems to protect recipients
  - Lack of documentation to allow traceability
- Shortage of cells and tissues to use in humans
- Quality Management
  - Protection for Donor and Recipient
  - Increased availability of cells and tissues

The EU Directives



L 102/48 EN Official Journal of the European Union 7.4.2004

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

L 38/40 EN Official Journal of the European Union 9.2.2006

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

L 294/32 EN Official Journal of the European Union 25.10.2006

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

Directive 2004:23 – Parliament and Council

- **Quality** and **Safety** – *prevent transmission of disease*
- Increase **availability**
  - **Unified standards** – same level of security
- **Promote** unified standards, quality and safety worldwide
- **Reproductive cells** (eggs, sperm) included

Directive 2004:23 – Parliament and Council

- Tissues and cells intended for **human applications**
- **Not** research using human tissues and cells, e.g. *in vitro research* or in animal models

Directive 2004:23 – Parliament and Council

- **MEMBER STATES' AUTHORITIES**
  - Supervision, inspections, control measures
  - Accreditation of Tissue Establishments
  - Import and Export of Cells and Tissues
  - Reporting

Directive 2004:23 – Parliament and Council

- **DONOR SELECTION and EVALUATION; PROCUREMENT**
  - Voluntary and unpaid donations of tissues and cell
  - Informed Consent, data protection, confidentiality
    - Some countries (incl Sweden)
      - laws enabling child to obtain information of the genetic origin – data to be saved 70 years
  - Procurement of cells and tissues

Directive 2004:23 – Parliament and Council

- **TISSUE ESTABLISHMENT**
  - Organization, competencies, Quality Management
  - Practical handling of cells and tissues
    - Procurement / Reception
    - Processing
    - Testing
    - Storage
    - Labelling (coding)
    - Distribution

COMMISSION DIRECTIVE 2006/17/EC

- **Technical requirements for the donation, procurement and testing of human tissues and cells**
- Reproductive cells have, due to the specific nature of their application, specific quality and safety characteristics that are taken into account in this Directive

COMMISSION DIRECTIVE 2006/17/EC

- "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**."

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- **Non partner donors** of reproductive cells:
  - Age, health and medical history
  - Identifying risks for donor or recipient
  - Biological tests:
    - HIV 1 and 2
    - Hepatitis B
    - Hepatitis C
    - Syphilis
    - Chlamydia in urine (NAT) for **sperm donors**
    - Other diseases depending on prevalence
    - Genetic screening

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- **Non partner donors** of *sperm*:
  - Sperm quarantined for a minimum of 180 days
    - ***repeated*** tests of donor:
      - HIV 1
      - Hepatitis B
      - Hepatitis C
    - ***Unless NAT (PCR) test is used***

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- **Partner donation (not direct use)**:
  - Justification for the donation and its safety for the recipient and any child(ren) that might result
  - Biological tests*:
    - HIV 1 and 2
    - Hepatitis B
    - Hepatitis C
    - Other depending on prevalence

*) "In order to minimize the risk of cross-contamination, biological testing of the donor will be necessary **only when the donated cells will be processed, cultured or stored**."

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- **Traceability**
  - "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"

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- **Packaging**
  - minimise the *risk of contamination* and
  - stored at temperatures that *preserve the required characteristics and biological function* of the cells/tissues.
  - prevent *contamination of those responsible* for packaging and transportation

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- **traceability** requirements, notification of se**rious adverse reactions** and **events**
- technical requirements for the **coding**, **processing**, **preservation**, **storage** and **distribution** of human tissues and cells

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- The air quality standard during the processing of tissues and cells
  - **in certain situations**, an air quality with particle counts and microbial colony counts equivalent to those of Grade A standard is not indicated.
  - it should be **demonstrated and documented** that the **chosen environment achieves the quality and safety required** for the type of tissue and cells, process and human application concerned.

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- Reports on suspected and serious adverse events and reactions reactions
- Annual reports (numbers of cells/tissues)
- Implentation of IT-solution to reduce costs
- A single European Code system (?)

Aims

- An overview of the EU directives on Cells and Tissues …
- **Consequences for processing of semen samples:**
  - **Air quality**
  - **Quarantine**
  - **Cryo preservation**
  - **Transportation**
  - **Documentation - Traceability**
- Aspects of increased availability of cells and tissues within Europe

Air Quality

- Protection of the recipient
- Contamination from staff or other cells/tissues
- Basic requirement is Air Quality Grade A
- Four possible exceptions – standpoint by ESHRE/EACC and Swedish Gamete Expert Group
  a) Microbial inactivation or terminal sterilisation
     - Not applicable

Air Quality

- Four possible exceptions (cont'd):
  b) Grade A environment has a detrimental effect
    - Rapid temperature fall (disturbed cell cleavage)
    - Decreased pH (loss of CO_2)
    - Vibrations jeopardizing microinjection
    - Turbulent air flow if a microscope is put into a Laminar Air Flow hood increases risk for contamination

Air Quality

- Four possible exceptions (cont'd):
  c) Lower risk of transmitting infections than with cell and tissue transplantation
    - The risk for a serious infection after embryo transfer or IUI is much lower compared to other cell and tissue transplantation.
    - With ART, embryos or sperm processed under controlled environment are transferred to the physiological recipient (the uterus) without the need for immunosuppression.

Air Quality

- Four possible exceptions (cont'd):
  d) Not technically possible in a Grade A environment
    - ICSI – requires a non vibrating microscope
    - Turbulent air flow caused by inverted microscope in LAF hood increases the risk for contamination

Quarantine of semen samples

- The issue is to keep different samples apart – to avoid cross contamination
  - Efficiently sealed sample containers
  - Disinfection of the exterior surfaces of the containers before and after storage

Cryopreservation

- The issue is the safe storage without cross contamination
  - Sealed containers with disinfected exterior surfaces
  - Safe temperatures?
    - Dry ice (-79°C)?
    - < -100°C?
    - < -130°C – vitrification = cessation of crystallization

Transportation

- Prevent any loss of sample identity or occurrance of other causes for errors or damage to the cells
  - Standardized codes for identification and “product” characteristics
  - Correct documentation provided for receiving part
  - Correct conditions (temperature) during transport

Documentation - Traceability

- Source: donor, as required in each country
  - Donor record; sometimes specifics about donor
  - Results of testing for contagious diseases
- Process
  - Media (lot), consumables (lot) in direct contact, etc
  - Staff performing different steps
  - Decisions: accepted for use (who, when)
- Distribution
  - Feed back of use

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  - Documentation - Traceability
- **A future with increased availability of gametes within Europe**

A future with increased availability of donor gametes?

- Tissue Establishments can exchange donor gametes
  - Ethnic groups – comparison with social parent
  - Decreased risk for siblings to meet and procreate
  - Still differencies between countries
    - Sweden:
      - Child has right to get information about the donor (when adult)
      - Documentation must be saved by the clinic for 70 years

Thanks for your attention

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References

– EU Directives 2004:23, 2006/17, 2006/86: (select language!)
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http://www.eshre.eu/ESHRE/English/Specialty-Groups/Data-collection-Consortia/European-Assisted-Conception-Consortium/page.aspx/283