The new EU directives
What do they mean for us dealing with treating male infertility?

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ESHRE CampusPrague, April 2007

Outline lecture

- EU Directives: political background
- EU Directives: definitions
- Comply with TD1: Screening
- Comply with TD2: Processing and preservation
- European Assisted Conception Consortium

2

European Union

- The European Union was founded in 1957
- Political treaties between the member states define strategy
- European directives are made to implement these treaties
- Directives are made and decided upon by European Institutions

3

European Treaties

- Treaty of Rome (1957) (EEC)
  - → economic cooperation
  - → no formal basis for measures in field of public health
- Treaty of Maastricht (1992) (EU)
  - → European citizenship
  - → + defense, justice, public health

    Article 129: information, education, surveillance

4

European Treaties

- Treaty of Amsterdam (1999)
  - → + public health protection
  - → Article 152 (former article 129) provides legal tools to ensure a high level of human health protection
- EU Directive 2004/23/EC on tissues and cells is part of the EU Public Health Programme

5

Directive 2004 / 23 / EC

- A legal document on setting standards of quality and safety for the donation, procurement, testing, coding, processing, preservation, storage and distribution of human tissues and cells intended for application to the human body
- Including ... reproductive cells (eggs, sperm), foetal tissues and cells and adult and embryonic stem cells
- In order to prevent prevention of transmission of infectious disease and prevention of gamete/embryo exchange (mix-up).

6

Mother and daughter Directives

2004/23/EC Mother Directive
Into force in EU on 7 April 2006

2006/17/EC Technical directive 1 (TD1)
Mainly donor screening criteria
Into force in EU on 1 November 2006

2007/86 / EC Technical directive 2 (TD2)
Mainly conditions under which cells and tissues need to be processed and preserved
Into force in EU on 1 September 2007

7

Requirements on fertility units and member states

- Fertility units will be regarded as tissue establishments and will have to fullfil requirements of TD 1 and TD2
- EU member states
  - → Have to implement EU directive into national law
  - → Have to design national competent authorities to
    - Set up licensing system for tissue establishments
    - Organize inspections
    - Report back to the EC

8

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9

Tissue directives: definitions

- “Donor” means every human source, whether living or deceased, of human cells and tissues.
- Partner donation means the donation of reproductive cells between a man and a woman who declare to have an intimate physical relationship. In a couple, man and woman are considered donors to each other.
- Classical donation is called non-partner donation under the Directive.

10

Tissue directives: definitions

- The directive applies to fresh and cryopreserved reproductive tissues and cells for application to the human body. This covers gametes, pronuclear stages, embryos and ovarian and testicular tissues.
- The directive applies to all procedures where reproductive cells and tissues are being processed, cultured, banked or stored. This means that intra-uterine insemination falls under the directive.

11

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12

TD1: donation

- Voluntary
- unpaid
- informed consent
- unique donor identification
- data to be kept for minimum 30 years

13

TD1: Laboratory testing

- Partner donation, direct use
  - → No testing necessary
  - → Not applicable in IUI/IVF/ICSI
- Partner donation (not direct use)
  - → Anti - HIV 1,2
  - → Hepatitis B
    - HBsAg, Anti-HBc
  - → Hepatitis C
    - Anti - HCV
- Positivity does not exclude patients from treatment

14

TD1: Laboratory testing

- Donation other than by partners (sperm donors)
  - → Serological screening for HIV, HBV, HCV must be negative
  - → + Syphilis negative
  - → + Chlamydia negative
  - → Quarantine 180 days
  - → genetic screening for autosomal recessive genes prevalent in the donor's ethnic background

15

TD1: Laboratory testing

- Separate storage obliged
  - → when positive tests
  - → when results unknown at moment of storage
- Systems for separate storage
  - → High security straws
  - → Separate storage tanks for each distinct separate serological profile

16

TD1: Laboratory testing

- Unresolved question so far: frequency of screening
- TD1 says “at the time of donation”
- But ART is repetitive treatment
- Largely among partners
- This makes it distinct from non-reproductive cells
- It is as yet not specified if it is required to re-test the patient prior to each treatment or whether a specified interval will be acceptable

17

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18

TD 2: requirements

- Quality Management System
- Air quality conditions
- Traceability
- Coding
- Notification of adverse reactions and events

19

QMS

- Quality Management System
  - → organization,
  - → personnel,
  - → facilities,
    - Air quality
  - → equipment
  - → documentation and records
- Examples ISO 9001, ISO 15189
- EUTD > QMS

20

Air quality requirements

- a GMP defined Grade A on a background air quality of Grade D is required
- A less stringent environment can be allowed in case of:
  - → final process of product sterilisation
  - → air quality requirements with detrimental effect on tissues or cells
  - → low additional risk of transmitting infection upon application to the human body
  - → technical incompatibility
  - → The air quality still needs to be documented

21

Traceability

- Keep record of all data on donor, donation, and critical materials and reagents used that can influence safety and quality of tissues and cells
  - → media lot and batch numbers
  - → disposables
- storage for 30 years

22

Coding

- → unique internal code always needed
- → unique European coding system
  - only needed for non-partner donation
  - Unique European coding system is now being worked on by EC in collaboration with CEN (European Committee for Standardization)

23

Notification of adverse reactions - events

- Reporting of adverse reactions - adverse events to the national competent authorities
  - → relating to risk of transmission of infectious disease
  - → relating to risk of gamete mix up

24

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25

EACC: an ESHRE offer you can't refuse

- European Assisted Conception Consortium
- Joint venture between ESHRE and HFEA
  - → ESHRE = European Society for Human Reproduction and Embryology
  - → HFEA = Human Fertilisation and Embryology Authority (UK)
- Member state organisation
- Not - for - profit initiative
- Established at ESHRE 2005 Copenhagen

26

EACC Objectives

- Bring together IVF professionals and national authorities from European member states
  - To share learning and best practice
  - Provide advice to member states
- Communication to European Commission
  - → present joint position of regulators and practitioners
  - → give expert advice to EC

27

EACC Members

Per member state / three members

→ Two practitioners

- one clinician
- one embryologist

→ One regulator

Please check ESHRE Website – link to EACC - membership:
check for members of your country; they are
your representatives

28

EACC Format: Executive Committee

→ Five practitioners

→Anna Veiga (Spain)
→Ioannis Messinis (Greece)
→Josiane Van der Elst (Belgium)
→Cristina Magli (Italy)
→Arne Sunde (Norway)

→ Three regulators

→Angela McNAb (chair) (UK)
→Bernard Loty (Fr)
→Basil Tarlatzis (Greece)


Josiane Van der Elst


Anna Veiga


Cristina Magli


Ioannis Messinis


Arne Sunde


Basil Tarlatzis


Angela McNab


Bernard Loty

29

EACC activities

- Full Consortium meetings for members
- Meetings of Executive Board
- Meetings of Executive Board with European Commission
- EACC Newsletter

30

ESHRE / EACC links

- Members' Information Session at ESHRE meetings
- EACC direct link on ESHRE website
- Focus on Reproduction
- ESHRE position paper on Directive coming out soon in next FoR

31