Accreditation of BMT units & EU Regulations

April 1, 2008

EBMT Annual Meeting
Workshop: EU regulation/standardisation of cellular therapy
Presentation:

- JACIE: aims and current activities
- EU regulation and FACT/JACIE Standards
- Important issues:
  - Import and export;
  - Tissue establishment licensing;
  - The single European Labelling System
- How to go forward
Aims /Role of JACIE

1. Accreditation of Individual Centres
   • Assistance
   • Inspection
   • Certification

2. Information / Education
   • QM courses
   • Training courses
   • Sample documents

3. Regulatory Issues
   • updating standards
   • adjust to regulations
     • International harmonisation
Total applics. 131 (Accredited 53)

BE 6 (1)
NL 16 (9)
AT 2 (1)
FI 3 (2)
CH 10 (7)
ES 5 (1)
D 19 (4)
FR 20 (8)
IT 14 (2)
UK 31 (18)
PL 1
CZ 3
TR 1

ACIE
Regulations and proposals

- EU Directive: procurement and processing of cells
  - 2004/23/EC Quality and safety of tissues and cells.

- Advanced Cell Therapy Regulation 1394/2007
  - Somatic Cell therapy (EUD 2001/83)
  - Gene Therapy (EUD 2001/83)
  - Tissue Engineering
EU Directive 2004/23/EC: Setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells

- This Directive should apply to tissues and cells including hematopoietic peripheral blood, umbilical-cord (blood) and bone marrow stem cells, reproductive cells (eggs, sperm), foetal tissues and cells, and adult and embryonic stem cells.
- This Directive excludes:
  - blood and blood products (2002/98/EC and 2004/33/EC);
  - Tissues and cells used as an autologous graft (tissues removed and transplanted back within the same surgical procedure and without being subjected to any banking);
  - Not applicable for research (animal studies) or for organs, tissues and cells of animal origin;
  - Organs or parts of organs if it is their function to be used for the same purpose as it functions in the human body.

Donor leukocytes?
EUD on T&C and related EUD’s

  - quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells
  - donation, procurement and testing of tissues and cells
  - traceability requirements
  - serious adverse reactions and events
  - coding, processing, preservation, storage and distribution of human tissues and cells
- Implementing Directives in progress
  - Import/export: to be established in 2008-2009
  - A single European coding system: Effective Sept 1, 2008
Accreditation Programme Status:
Total centres registered: 131
Centres in progress: 98
Centres inspected: 93
Facilities accredited: 83*
Reaccredinations in progress: 5
Countries: 13

* Individual facilities e.g. laboratory, apheresis unit, that formed part of a wider application may subsequently be accredited separately for services to other centres

27 March 2008
Due to staff attendance at the 2008 EBMT Congress in Florence, Italy, the JACIE Office will be unattended from the afternoon of Friday 28 March until Wednesday 2 April. We will attend to your emails and messages on our return.

JACIE will be at the EBMT Stand (no. 501), please feel free to meet us there. You should also note the JACIE Session on Monday, 31 March from 12.30-13.30 and the Nurses JACIE Workshop from 13.30-15.00. Check your congress programme for further details.

The 3rd edition of the Accreditation Manual including Guidance is now available for download from the Document Centre on the left-hand side of the screen. The document is listed as 1 Guidance Final Version.Dec.04.07.pdf. This manual is intended to accompany the FACT-JACIE International Standards for Cellular Therapy Product Collection, Processing and Administration. Third Edition. The purpose of the Manual is to provide guidance to applicants for accreditation and to on-site inspectors and to explain the intent and rationale for specific Standards, and to provide explanations, examples and alternative approaches that will be helpful in the accreditation process.

Note: when downloading the files, right-click with your mouse and select the option to save the file to your computer.

26 October 2007: Standards reference numbers: Part D
A minor error was found under Part D of the JACIE release of the Standards. Reference D11.3.3.3 featured as D11.3.2.3. The text is unaffected and the reference appeared correctly in the Inspection Checklist. The corrected version of the 3rd edition of the Standards is now available on the JACIE web site.

In addition, FACT-JACIE has updated the requirements for labelling Cellular Therapy Products. This replaces the information found in the FACT-JACIE International Standards for Cellular Therapy Product Collection, Processing and
<table>
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<tr>
<th>Clinical Programme</th>
<th>Collection (BM / PBPC)</th>
<th>Processing</th>
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<td><strong>Whereas:</strong></td>
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<td>(1) The transplantation of human tissues and cells is a strongly expanding field of medicine offering great opportunities for the treatment of as yet incurable diseases. The quality and safety of these substances should be ensured, particularly in order to prevent the transmission of diseases.</td>
<td>FACT-JACIE sets standards for quality and safety in all aspects of stem cell transplantation.</td>
<td>Consistent</td>
<td>WMDA sets standards for quality and safety as they related to the international exchange of hematopoietic stem cells. The standards include guidelines for health screening of donors to prevent transmission of diseases.</td>
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<td>(2) The availability of human tissues and cells used for therapeutic purposes is dependent on Community citizens who are prepared to donate them. In order to safeguard public health and to prevent the transmission of infectious diseases by these tissues and cells, all safety measures need to be taken during their donation, procurement, testing, processing, preservation, storage, distribution and use.</td>
<td>FACT-JACIE standards cover donation, procurement, testing, processing, preservation, storage, distribution and use.</td>
<td>Consistent</td>
<td>WMDA standards cover health testing of donors, testing for histocompatibility, donation, international transport, and use. They do not cover processing and storage.</td>
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<td>(3) It is necessary to promote information and awareness campaigns at national and European level on the donation of tissues, cells and organs based on the theme 'we are all potential donors'. The aim of these campaigns should be to help European citizens decide to become donors during their lifetime and let their families or legal representatives know their wishes.</td>
<td>FACT-JACIE does not have a role in promoting information and awareness of donation but can assist by assuring of donation.</td>
<td>Consistent</td>
<td>WMDA supports registry activities that provide information and awareness of donation. WMDA standards ensure donor safety.</td>
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Technical requirements of 2004/23/EC: “Crosswalks between JACIE and EU directives”

- Diana Samson performed crosswalks on the 2004/23/EC directive and the 2 technical directives with JACIE standards and WMDA standards (collection).
  - No major differences;
  - JACIE is specifying the issues for cellular therapy products in depth
FACT/JACIE Standards Committee

- JACIE/FACT Subcommittees developing 4th edition of standards and manual
  - Co-Chair & Medical Director: Diana Samson
  - Part B: John Snowden, Jane Apperley, Jacqueline Cornish
  - Part C: Derwood Pamphilon & Cristina Tassi
  - Part D: Ineke Slaper-Cortenbach & Eric Braakman

Available to the membership

Sept 07       Nov 07- Jan 08           Febr 08             March 08 June 08 Oct 08 Nov 08

Crosswalk with cGTP and EU Directive
New edition standards and manual

Consistency, Legal and Board review

Steering Committee Meeting in SD

Membership review

Changes review
Import and export requirements
EUD 2004/23 article 9

For further information, see:
http://europa.eu.int/comm/health/ph_threats/human_substance/tissues
International exchanges in 2006: 38.8%

PERCENTAGE OF STEM CELL DONATIONS PROVIDED FOR NATIONAL AND INTERNATIONAL PATIENTS

UNRELATED STEM CELL DONOR REGISTRIES
Import and export in the EU

ORIGIN OF STEM CELL PRODUCTS
SPECIFIED PER EU COUNTRY

UNRELATED STEM CELL PRODUCTS IN EUROPE
2006/17/EC: technical requirements for donation, procurement and testing of tissues and cells

- Article 2: Requirements for the procurement of human tissues and cells
- Article 3: Selection criteria for donors of tissue and cells
- Article 4: Laboratory tests required for donors
- Article 5: Procurement procedures
- Article 6: requirements for distribution
- Article 7/8: transposition & entry into force

- staff must be properly trained;
- the facilities must be maintained to prevent contamination;
- proper, sterile instruments must be used for procurement;
- SOP’s for
  - the donation and testing process;
  - during transport;
  - at the point of reception in tissue establishments
- selection of tissue and cell donors (live or deceased)
- A unique identifier code for proper identification and traceability.

Article 9: to ensure that imports and exports of tissues and cells ....... meet quality and safety standards equivalent to those laid down in this Directive!
Towards a Global Standard for Donation, Procurement, Testing, and Distribution of HSC and Related Cellular Therapies

Position Paper from the Alliance for Harmonisation of Cellular Therapy Accreditation (AHCTA).

AHCTA represents JACIE, EBMT, WMDA, ISCT-Europe, FACT, FACT-Netcord, ISCT, EFI, ASBMT and the AABB.
Mission statement:

• Harmonisation of respective standards
• Ultimately achieve a single set of quality, safety and professional requirements for cellular therapy including haematopoietic stem cell (HSC) transplantation.
• All aspects of the process from donor recruitment to transplantation and clinical outcome.
• Supported by
  – complementary standards and guidelines,
  – promotion of the concept of a global set of standards
• Inform and support authorities in the area of cellular therapy regulation
Licensing of Tissue Establishments
2006/86/EC: coding, processing, preservation, storage and distribution, procurement and testing

Tissue and cell preparation processes

A. Reception at tissue establishment
B. Processing
C. Storage and release of products
D. Distribution and recall
E. Final labelling for distribution
F. External labelling of the shipping container
Technical requirements in 2006/86/EC: coding, processing, preservation, storage and distribution of tissues and cells

Licensing of Tissues establishments

A. Organisation and management
B. Personnel
C. Equipment and materials
D. Facility and premises
E. Documentation and registry
F. Quality review
Technical requirements: 2006/86/EC: example of a processing requirement

- The *air quality standard*: is a key factor for risk of tissue or cell contamination;

- Unless otherwise specified, where tissues or cells are exposed to the environment during processing, without a subsequent microbial inactivation process, an air quality of **Grade A** as defined in the current European Guide to Good Manufacturing Practice, Annex 1 (Commission Directive 2003/94/EC) is required with a background environment appropriate for the processing of the tissue/cell concerned but at least equivalent to GMP grade D in terms of particles and microbial counts!!
Single European Coding System
EUD 2004/23

For further information see: www.iccbba.org
and: www.cen/isss.org
International Cellular Therapy Coding and Labelling Advisory Group
International Cellular Therapy Coding and Labelling Advisory Group

- Three documents for cellular therapy products:
  - cellular therapy terminology;
  - cellular therapy labelling;
  - implementation plan for cellular therapy products
- Published in Transfusion, BMT and J.Clin. Apher. 2007
- See www.iccbba.org for more information
- Participation with EU in CEN open workshop on the Single European coding system

See www.iccbba.org for more information
Example

- **CLASS**: HPC, APHERESIS
- **MODIFIER**: Cryopreserved

**ATTRIBUTES: Core Conditions**
- Anticoagulant: Citrate
- Collection Volume: NS
- Storage Temperature: $\leq -150^\circ C$

**ATTRIBUTES: Variables**
- Intended Use: For Patient Use
- Manipulation: Plasma reduction
- Cryoprotectant: 10% DMSO
- Additional additives: none
International Cellular Therapy Coding and Labelling Advisory Group
Proposals for Finalising the CWA Report

CEN ISSS Workshop –
Coding & Classification of Human Tissues & Cells

Fourth Plenary Meeting - Brussels, 2008-02-20
Project team: Poniatowski, Reynolds, Trias & Warwick
Product Codes developed by ICCBA with EU support

### EU DG SANCO WG

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<th>Variation 1:</th>
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<th>Variation 3:</th>
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<td>Globally unique donation, product &amp; &quot;key&quot; codes</td>
<td>National, regional, or local donation code + globally unique product &amp; &quot;key&quot; codes</td>
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<th>Country ID + TE</th>
<th>Unique Donation number</th>
<th>Product Code</th>
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Figure 11.2: Proposed EU code structure Variations
Final Consultation - 2008

- Publish for comments < 29th February;
- Close* comments < 13th March;
- Publish for ballot < 20th March;
- Ballot Workshop Members on Final CWA Report < 11th April;
- Publish CWA Report < 30th May 2008?

* No allowance for late comments
How to go forward?

- Translation of EU Directives into national laws in the MS: some are still to be defined;
- Licensing of the tissue establishment by Competent Authorities in MS: co-inspections?
- Crosswalk showing “consistency” between EUD and FACT/JACIE and make an additional list of individual MS laws (ISCT-European LRA Committee)
- Introduction of Cellular Therapy products (MSC, DC etc) in standards: regulation for advanced cell therapies..
More general information:

www.celltherapysociety.org ISCT European LRA committee
www.jacie.org : JACIE standards