<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
<th>Speaker/Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>09.00 – 09.15</td>
<td>Welcome and goals of the day <em>Osman İlhan</em></td>
<td></td>
</tr>
<tr>
<td>09.15 – 09.45</td>
<td>Current Status of Accreditation in Europe <em>Eoin McGrath</em></td>
<td></td>
</tr>
<tr>
<td>09.45 – 10.15</td>
<td>Current and future regulatory environment for transplant teams <em>Evren Özdemir</em></td>
<td></td>
</tr>
<tr>
<td>10.15 – 10.30</td>
<td><strong>Break</strong></td>
<td></td>
</tr>
<tr>
<td>10.30 – 11.00</td>
<td>Resources available to assist centres in preparation <em>Eoin McGrath</em></td>
<td></td>
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<tr>
<td>11.00 – 12.30</td>
<td>Working Groups – Topic: What are the main challenges to establishing a Quality Management System in our units?</td>
<td></td>
</tr>
<tr>
<td>12.30 – 14.00</td>
<td><strong>Lunch</strong></td>
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<tr>
<td>14.00 – 14.45</td>
<td>Common deficiencies found in JACIE inspections.</td>
<td></td>
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<tr>
<td>14.45 – 15.45</td>
<td>Experience of an accredited centre <em>Nina Som, Bristol, UK</em></td>
<td></td>
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<tr>
<td>15.45 – 16.00</td>
<td><strong>Break</strong></td>
<td></td>
</tr>
<tr>
<td>16.00 – 16.30</td>
<td>Presentations by working groups + discussion</td>
<td></td>
</tr>
<tr>
<td>16.15 – 16.30</td>
<td><strong>Summary</strong></td>
<td></td>
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</table>
Current status of accreditation in EU

Eoin McGrath
JACIE Office, Barcelona
Inspections since 2003

- Centres registered: 126
- Centres in progress: 48
- Centres inspected: 78
  - Facilities accredited: 39
  - Post-inspection, not accredited: 37
  - Accreditation expired: 2 (Spanish pilot programme)
- Countries: 13

- 9 audits scheduled up to end 2007.
Applications

Total apps. 126 (Accredited 39)

- FI 3 (2)
- PL 1
- CZ 3
- AT 2 (2)
- D 28
- NL 13 (7)
- BE 5
- UK 27 (12)
- FR 18 (6)
- ES 6
- CH 10 (9)
- IT 9 (1)
- TR 1

BE 5
FR 18 (6)
ES 6
CH 10 (9)
IT 9 (1)
TR 1

UK 27 (12)
FR 18 (6)
ES 6

Total apps. 126 (Accredited 39)
**JACIE Board**

**EBMT - ISCT**

**Structure**

**21 Countries:** Austria; Belgium; Czech Republic; Denmark; Estonia; Finland; France; Germany; Greece; Hungary; Italy; The Netherlands; Norway; Poland; Switzerland; Slovakia; Slovenia; Spain; Sweden; Turkey; United Kingdom; Sectoral representatives for Cord Blood, Nursing & Paediatrics

President: Ineke Slaper-Cortenbach (ISCT)
Vice-President: Jane Apperley (EBMT)
Medical Director: Diana Samson, Accreditation chair: Derwood Pamphilon

**JACIE Office**

**Accreditation Committee**

Eoin James MacHale
International status
Contacts

- Contacts with
  - EU
  - WHO
  - EUSTITE project
  - Council of Europe
  - National health authorities
  - Other accrediting bodies
Regulatory context -EU

  - quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells
  - donation, procurement and testing of human tissues and cells
  - traceability requirements
  - serious adverse reactions and events
  - coding, processing, preservation, storage and distribution of human tissues and cells
- Directives in progress
  - Import/export
  - Coding Effective Sept 2008
International status

Spain
The Spanish National Transplant Organisation (ONT) is the Competent Authority.

Agreement signed 30 Oct 2006 between ONT, Spanish scientific societies and JACIE officially supporting voluntary accreditation for HSC centres
International status

The Netherlands
Dutch Health Care Inspectorate (IGZ) underlines the importance of JACIE accreditation as a tool to show compliance with the EU directive for tissue banks.

Agreement with CCKL (national lab accreditation body) to manage JACIE inspections.

- Includes condition that centers must have JACIE accreditation within 2 years from now.
International status

Italy

The Centro Nazionale Trapianti (CNT) considering assigning JACIE inspectors, via Italian Bone Marrow Transplant Group (GITMO), to perform inspections of HSC transplant programs and investigate that any additional EU directive requirements are checked during the inspections.
International status

**France**
The French Health Authority (HAS) recognises JACIE as an exemplary and innovative process.

HAS policy is to recognise different evaluation systems in order to benefit from complementary aspects and avoid duplication and includes JACIE within this policy.  
[ANAES Accreditation Manual For Healthcare Organisations](#), Sept 2004
International status

United Kingdom
Human Tissue Authority (HTA) propose to use JACIE inspectors as advisors when visiting SCT facilities and two have now been trained as HTA Specialist Assessors.

JACIE accredited centres have been classified as low-risk by HTA.

NHS service commissioners are considering JACIE accreditation as a quality standard for provision of HSCT services to the NHS.
International status

Austria
The Austrian Health Institute (ÖBIG) provided financial support to centres preparing for JACIE accreditation

Belgium
Health authorities have asked that JACIE inspectors act as advisors on implementation of Directive and Belgian regulations will take JACIE Standards as a base

Poland
Ministry of Health plans to support accreditation expenses within the scope of the POLGRAFT program
JACIE developments
Standards

- Designed to cover all phases/tasks in transplantation from donor to infusion
- **Interaction** between clinical unit, cell collection facility and laboratory fundamental
CLINICAL UNIT

OTHER HOSPITAL

PROGRAMME MUST DEMONSTRATE ALL INTERACTIONS

PROCESSING LABORATORY

APHERESIS UNIT

BONE MARROW COLLECTION

19
Standards: 3rd edition

- In effect since 19th August
- First inspection using 3rd edition took place in UK, September
- Manual:
  - FACT Office coordinating drafting and release
  - JACIE contribution
  - Provisional date November 9 for release
Major changes

1. Restructure of Document
   Three sections compared and aligned to be parallel and consistent throughout.

2. International Language and Content
   “FACT-JACIE International Standards…”

3. Regulatory requirements (FDA and EU Directive) included
   Includes labeling requirements – 2 tables as appendices

4. Redefined numbers requirements
   B1.5 for clinical programs
   C1.3, C1.4, C1.5 for collection facilities (12 months, 30 aphereses/3 years; 3 marrows/3 years)
   D1.3 for Processing facilities (12 months)

5. Expanded Quality Management section (B4; C4; D4)

6. Collection:
   Added Pediatric competencies
   Duplicated Donor Selection, Evaluation and Management

7. Processing Facility
   GTP issues, primarily of donor eligibility, documentation, and labeling
Inspectors

- 141 certified inspectors in total
- 18 countries
- All inspectors required to have attended training course and submitted CV, qualifications, exam and registration
- Half-day refresher course planned for Florence EBMT meeting
The Alliance for Harmonisation of Cellular Therapy Accreditation (AHCTA) is formed by representatives of the following organisations:

- American Association of Blood Banks (AABB)
- American Society for Blood & Marrow Transplantation (ASBMT)
- European Group for Blood & Marrow Transplantation (EBMT)
- Foundation for the Accreditation of Cellular Therapy (FACT)
- International NETCORD Foundation
- International Society for Cellular Therapy (Europe) (ISCT)
- Joint Accreditation Committee ISCT-EBMT (JACIE)
- World Marrow Donor Association (WMDA)
Mission statement

- harmonisation of respective standards
- 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
- Import/export discussion document
  - Min guidelines to support TC Directive
  - Input on cord blood from NetCord
- Crosswalk of respective standards to highlight areas of discrepancy
• Any questions?
Resources Available to Assist Centers in Preparation
Tools & assistance

- Standards
- Manual
- Inspection Guide
- JACIE Office
- JACIE Online
- Medical Director
- Other inspectors
- Online documentation
Documents on web site

- Inspection Checklist
- 3rd ed FACT-JACIE Standards
- Significant Changes
- Online Guide
- Accreditation deficiencies v2.0
- Accreditation process
- Pre-inspection Document Checklist
- Inspection guide 2.5
- JACIE CV template
- Potential Inspection Outcomes July 2006
- JACIE information leaflet
International Cellular Therapy Coding and Labelling Advisory Group

- Review existing regulation regarding labeling
- Design product label templates that satisfy regulatory requirements;
- Provide a focus for the standardization of terminology and product naming;
- Promote the adoption of the ISBT 128 standard in cellular therapy facilities around the world;
- Provide advice and support to facilities introducing the standard;
- Advise on the ongoing development of the ISBT 128 standard to support new developments in cellular therapy.
International Cellular Therapy Coding and Labelling Advisory Group

- Final release of terminology and label design at ISCT meeting, June 2007
- [http://iccbba.org/cellulartherapy_educational_material.html](http://iccbba.org/cellulartherapy_educational_material.html)
- Contribute to the work of the CEN (European Committee for Standardization): CEN/ISSS Workshop on Coding of Information and Traceability of human Tissues and Cells (WS/Tissues & Cells)
CEN/ISSS Workshop on Coding of Information and Traceability of human Tissues and Cells (WS/Tissues & Cells)

● “…..propose guidelines and recommendations to permit the implementation of the European Coding System respecting the Tissue and Cells Directive’s requirements.”

CEN/ISSS Workshop on Coding of Information and Traceability of human Tissues and Cells (WS/Tissues & Cells)

- 11 months duration
- Expect to complete work in mid-March 2008
- Recommendation to the EU Commission
  - Commission decides on adoption
  - In place by September 2008
Quality Management Guide

● ‘Practical reference guide to implementing quality management in a stem cell transplantation (SCT) programme in accordance with JACIE Standards’

● **Phase 1:** To write and publish a guide to implementing quality systems in stem cell transplant programmes in line with the JACIE Standards on quality management

● **Phase 2:** To update the guide on a regular basis based on continued accrual of experience and best practice

● The project to be fully funded by an unrestricted educational grant from Chugai Sanofi Aventis.
Quality Management Guide

- To help applicants move from the ‘blank page’ when they start preparing
- To distribute experience and best practice
- To train inspectors
- Release early 2008
- Copies sent to EBMT member centres and ISCT Europe members
Deficiencies data
Deficiencies library

- Currently 570 items from 35 reports
- Very useful for applicant centres, inspectors
- Helps JACIE maintain consistency in recommendations
- Public anonymous version will be on website.
<table>
<thead>
<tr>
<th>ManSection</th>
<th>Edition</th>
<th>Markers D / F / S</th>
<th>Inspector's Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>B03000</td>
<td>3421</td>
<td>Red</td>
<td>The Programme has used CPD and programme participation as evidence of competency for attending physicians. There is no clear indication of how competency is judged. A number of the activities listed in this standard are generic to haematology but others are more specific to allogeneic BMT. A checklist for attending haematologists was not available. Dr McEugy indicated he was not competent in all areas but this may be clinically appropriate as he only attends SCT patients on an on call basis. Assessment of competencies for trainees is ongoing during their training period. We did not see detailed records of participation in educational activities related to the field of haematopoietic stem cell transplantation.</td>
</tr>
<tr>
<td>B03000</td>
<td>3422</td>
<td>Red</td>
<td>All physicians in the program have clinical training and competency regarding items of paragraph B 3.4.2, but some of them reveal a lack of education to improve their competency in some fields (e.g. management of ABO incompatible haematopoietic progenitor cell components, methodology of HLA typing, identification and selection of haematopoietic progenitor cell source.)</td>
</tr>
<tr>
<td>B03000</td>
<td>3432</td>
<td>Yellow</td>
<td>The answer given by the team is NO. Bone marrow harvest is becoming increasingly less frequent and is replaced by peripheral blood progenitor cells harvest. Nonetheless, the auditors found that the team has enough trained physicians to perform bone marrow harvest when requested. Transplant physicians in the clinical program are proficient in HPC infusions.</td>
</tr>
<tr>
<td>B03000</td>
<td>3600</td>
<td>Red</td>
<td>Not all physicians provided evidence of certification and subspecialty training. Documentation of higher specialist accreditation and certification was not always available. Documentation should be provided on CoC-years of GMC centres entering will suffice.</td>
</tr>
<tr>
<td>B03000</td>
<td>3600</td>
<td>Red</td>
<td>No access to clinical psychology. There should be access to clinical psychology. Presumably this can be accessed through psychiatric referral. The applicant should clarify this.</td>
</tr>
<tr>
<td>B03000</td>
<td>3610</td>
<td>Red</td>
<td>Based on the PDF file received via JACIE website, the liaison consultant for Infectious Disease and Psychiatry were not in the specialist register. It is unclear who produced this PDF file – I suspect this may be an administrative error; the Consultant staff at the Hammersmith have a high academic reputation. The Inspector noted that the consultant’s junior physicians for Infectious disease and psychiatry were not found in the specialist register. Evidence of their correct registration as consultants should be submitted for review.</td>
</tr>
<tr>
<td>B03000</td>
<td>3710</td>
<td>Red</td>
<td>Nurse and nurse practitioners in the program have been trained and provide the management of...</td>
</tr>
</tbody>
</table>

Training

Stafing
● Experience generally same as FACT in US

● Listing of deficiencies
  ● On web site shortly
EBMT Annual Meeting, 2008

Florence • Italy • March 30 – April 2, 2008

1. JACIE Session: Monday 12.30-13.30 (to be confirmed)

2. JACIE & Nursing: time and day to be advised

3. Quality management workshop : Monday (to be confirmed)
Work groups
WORKING GROUPS

- Processing
- Clinical + Collection (incl. Nurses)
- Quality Manager + Data Manager

“Challenges in establishing a quality system in my facility”
Discuss in groups

“Challenges in establishing a quality system in my facility”

- What is objective?
- Who should be involved?
- What resources and support do we need?
- What methodology will we use?
- What/who are potential threats to success?
Rogers achieved academic fame for his Diffusion of innovations theory. He proposed that adopters of any new innovation or idea could be categorized as innovators, early adopters, early majority, late majority and laggards.
Rogers Adoption / Innovation Curve

Innovators: 2.5%
Early Adopters: 13.5%
Early Majority: 34%
Late Majority: 34%
Laggards: 16%
Common deficiencies found in JACIE inspections
Breakdown of deficiencies by section

- Clinical, 24%
- Collection BM, 9%
- Collection PB, 26%
- Processing, 42%
% of deficiencies per section of standards
Categories of deficiencies as % of total deficiencies across all parts of standards
**Minor vs Significant Deficiencies**

- Difference between a minor deficiency and a significant deficiency is a matter of judgement

- **Minor deficiencies**
  - generally involve correction to existing SOPs or other documentation

- **Significant deficiencies - examples**
  - Inpatient isolation facilities inadequate
  - No continuous temperature monitoring of freezers
  - Inadequate quality management programme
Clinical Programme

- Single Clinical Programmes
- Consultants/Attending Physicians
- Adverse Event Reporting
- Audits & Outcome Reviews
- Donor Evaluation, Selection and Care
- Therapy Administration
Single Clinical Programmes

B1 “
...integrated medical team...
single PD..common staff training programmes, protocols & QMS”

• Lack of integration
• Poor interaction between staff in the 2 units
• Little sharing of expertise
• QMP’s essentially separate
• Who is the designated person for QM?
Senior Clinical Staff

- B3.1..”dedicated BMT team including PD + 1 physician trained or experienced in HPC therapy for 1 year”
- Also adult and paeds expertise as appropriate
- BMH proficiency

- Not all 1 year experience
- Not correct speciality
- CV’s - documentation of appropriate training
- Are they competent?
- Not proficient in BMH
QM: Adverse Event Reporting

- B4.10 “must have a system, document corrective actions & review, evaluate promptly
- Report to regulatory agency”

- Uses hospital based system: under-reporting
- No SOP: PD/patients physician
- No evidence of AE evaluation
- Must include in quality review
Audit and Outcome Review

B4.8 “collect, analyse & audit performance data”

• Should include TRM, engraftment, line infections

• No plan for review

• Range of acceptability?

• Deviation - ? what action

• No SOP for audits - communicate results
B6 Donor evaluation testing & consent

- Patient / Donor issues -1
  - no record of verification of patients diagnosis
  - no formally documented criteria for defining suitable donor
  - no explicit documentation of suitability of donors
  - not clear how the decision is made to use a donor not meeting the programme’s selection criteria
  - donor’s medical record does not record where applicable that the donor was informed of any abnormalities and of recommended follow-up
  - policy for disposal not mentioned in donor consent forms
Donor Evaluation, Selection & Management

B6 Donor evaluation testing & consent

- Patient / Donor issues 2
  - pregnancy assessment not routinely performed
  - donor medical history does not include a travel history
  - donor medical history does not include questions to identify persons at high risk of significant transmissible infections.
  - HLTV I and 2 serology not performed
  - no SOP or controlled document for transmitting the results of donor evaluation from the clinical team to the collection facility
Therapy Administration

B7 Written policies for HD therapy and HPC products

- No SOP’s for all regimes
- Dose of drugs not checked by 2 people
- Instructions for infusion not clear
- No documentation in notes of unit identifiers for all products
Stem Cell Collection

Bone Marrow

- Personnel
- Protocols and procedures
- Cell collection

Peripheral Blood

- Personnel
- Labels
- Collection facilities
Bone Marrow Collection

C3 Personnel

- BMH - documented training & proficiency
- MD responsible for donor evaluation & safety
- How many procedures are done
Bone Marrow Collection
Policies and Procedures

C5

BM Collection Procedures

- no SOP for BM collection
- SOP present but inadequate e.g. no acceptable results and tolerance limits / no instruction for action if these are not met
- no procedure for recording deviation from the SOPs relating to marrow collection, or whether and how such deviations are approved
- expiration dates and lot numbers of the reagents/equipment used for BM harvest not recorded
- records of collection not regularly reviewed by CF Director
- no systematic outcome review / audit
Bone Marrow Collection: cells and labels

C7 & C8

- No written orders
- SOP must cover transportation
- Labels must be alphanumeric
- Must give proper name
- CF and PL need to agree HPC identifiers
PBSC Collection

- No formal policy/SOP for assessment of venous line placement
- Assessment of venous line placement not documented in patient record
- Range of expected results not defined in SOP for stem cell collection
- Tolerance limits and corrective actions for collection not defined
- No SOP covering transportation from the apheresis unit to the processing facility
- No procedure/documentation relating to validation of equipment/procedures
- Records of collection not regularly reviewed by CF Director
- No systematic outcome review/audit
PBSC Collection:

- Inadequate documentation of training
- MD does not have appropriate contract with facility
- QMP should cover H&S
- TTI testing by clinical programme - communication
- Reporting AE’s to clinical unit - SOP

- Communication from clinical to collection team
- Suitable space for donor examination
- Proper disposal of apheresis kits
PBSC Collection: Labels

C7 Operations, product identification and label content

- Examples appended to SOP
- Unique alphanumeric identifier
- SOP to include Biohazard label
- Pre- or demand-printed labels
  ‘Human HPC-A
- Name + volume of AC/additives
Cell Processing Laboratory

- Quality Management
- Labels
- Storage Conditions
Quality Management

- Processing Facility
  - no written request for processing
  - methods used for processing not validated
  - no SOP for handling ABO incompatible graft
  - alarm system not adequate
  - temperature not monitored during transport
  - engraftment data not regularly monitored
  - no formal criteria for acceptable engraftment
LABELS

Labelling

- components labelled only with the donor name. (A unique alphanumeric code must be used)
- proper component name not used (Haematopoietic Progenitor Cells, Marrow / Apheresis - HPC-M / HPC-A)
- Biohazard label not used as specified
- missing information
  - date / time / volume of collection
  - name and volume of anticoagulant / other additives
  - donor ABO and Rh group
  - instruction ‘Do not irradiate’
  - instruction ‘for autologous use only’
  - time of expiry
Conditions for Storage

D9 Cryopreservation samples, procedures and cooling rate

- Continuous monitoring required
- Procedure for notifying personnel
- Room must be secure
- ‘No provision for back up storage’
- ‘No storage temp records’
Typical Deficiencies - General

- Interactions must be documented
  - written request for collection
    - From clinical programme to collection facility
  - written request for processing
    - From clinical programme to processing facility
  - results of infections disease marker testing
    - must be available to both collection and processing facilities
  - engraftment data
    - must be available to both collection and processing facilities
  - report of adverse events
    - Must be available to all relevant facilities
  - transport log form
    - For handover between collection/processing and processing /clinical facilities
Don’t forget….

- Listing of deficiencies
  - On web site
THE END
Teşekkür ederim
Thank you for listening