Hot Topics in the 6th Edition of FACT-JACIE Standards

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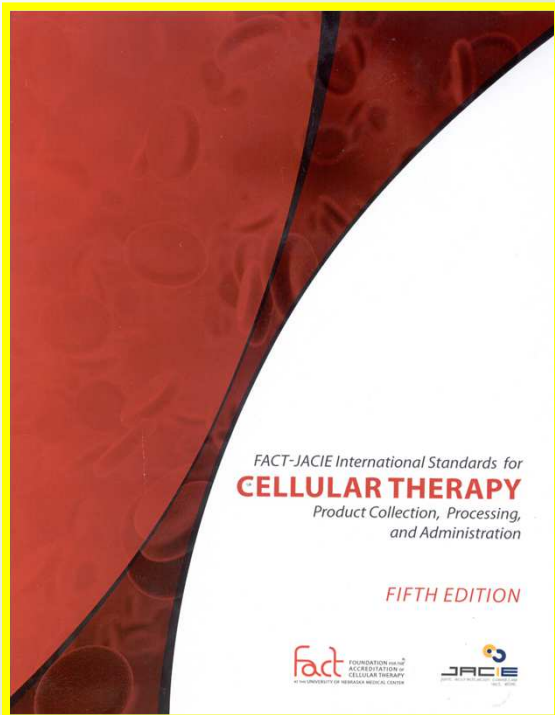
Objectives

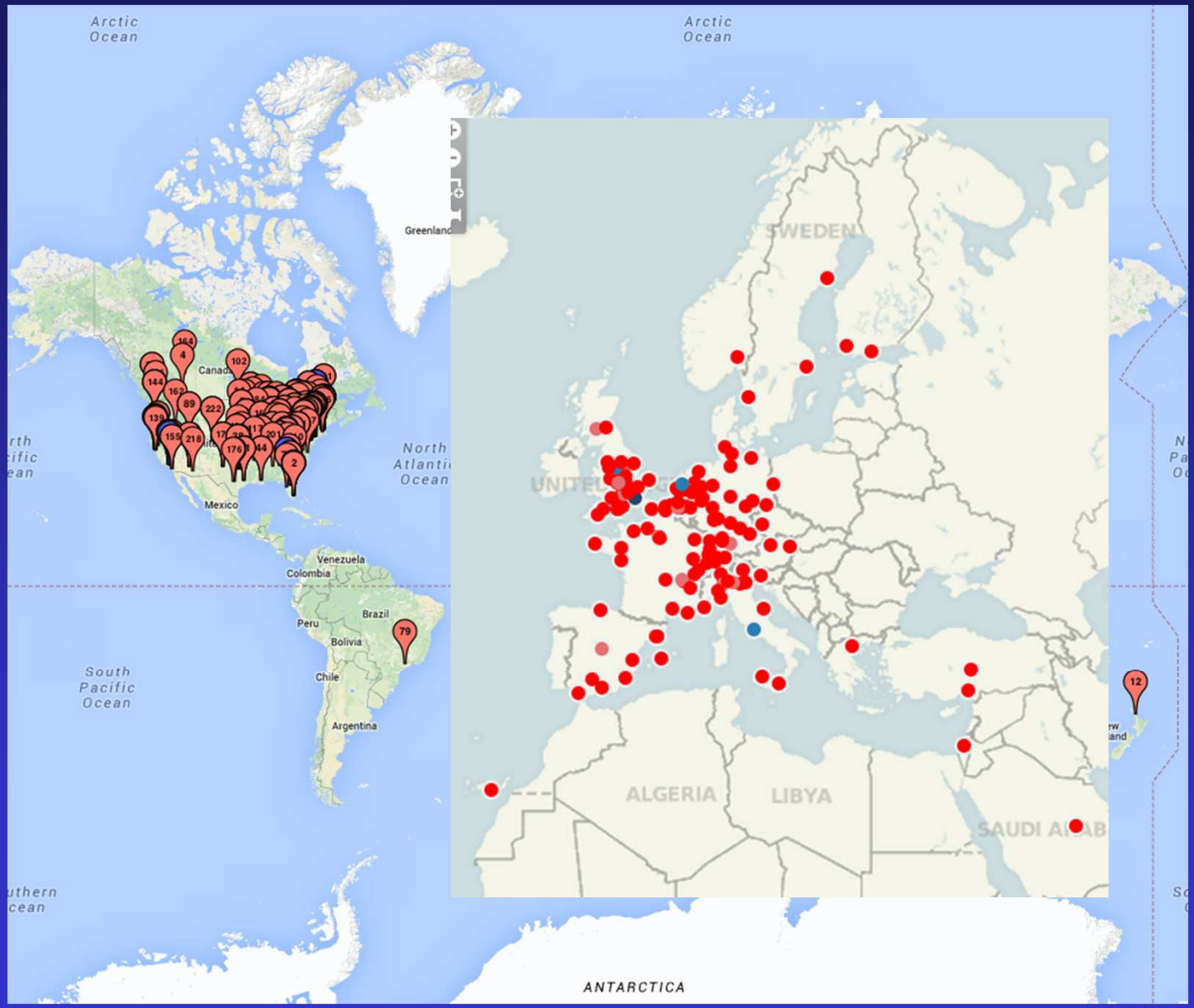
- To review the factors involved in FACT –JACIE Cell Therapy standards' revision
- To review changes in the new 6th edition that affect apheresis facilities participating in cellular therapy product collections

FACT-JACIE International Standards for Hematopoietic Cellular Therapy Product Collection, Processing, and Administration, 6th edition

- Publication: March 1, 2015
- Effective: June 1, 2015



FACT & JACIE Cell Therapy Accredited Facilities



Factors in Standards Revision

- New developments
  - Evidence-based
- Feedback from 5th
  - Standards
  - Accreditation e.g. common citations
- Input from related
  - Organizations
  - Individuals

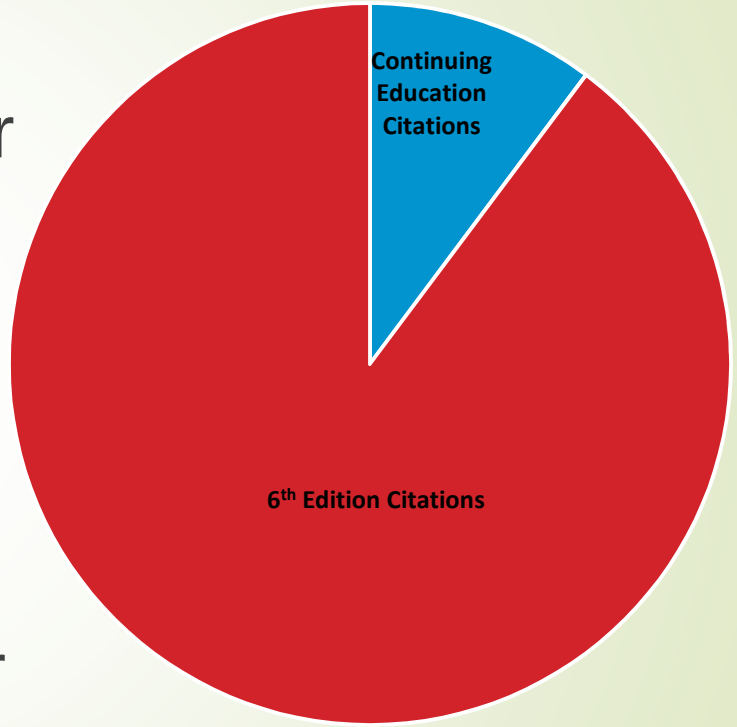
Global Changes in the 6th edition of the Standards that affect Apheresis Collection facilities

Continuing Education (**Global change in all sections:** B3, CM3, **C3,** D3**)**

- 5th edition:
  - "Key Personnel …shall participate regularly in educational activities related to the field of HPC transplantation"
- Applicants and inspectors thought "regular participation" was too vague
- 6th edition:
  - Key personnel must participate in at least 10 hours related to cellular therapy
  - Does not have to be formally recognized (e.g. CME)

6th Ed. Standards: 10 hours of Continuing Education activities

- So far, there have only been 15 inspections (FACT) under the 6th edition Standards
- Of these 15 inspections, 7 programs had citations relating to continuing education
  - So far, 11% of citations for 6th edition Standards relate to continuing education



How to Comply - Continuing Education requirements (all sections)

Does not have to be formally recognized (e.g., CME); Acceptable Continuing Education Examples:

- The annual meeting of several professional societies includes information directly related to the field
- Grand Rounds, if specifically related to cellular therapy or diseases for which transplantation is a therapeutic option
- Presentation of a paper at scientific meeting
- Publication of a manuscript related to cell therapy
- Participation in a webinar or on-line tutorial
- Review of articles in the medical literature related to cellular therapy; including those where the journal offers CME credits
- Local or regional journal club, potentially including the preparation time
- Morbidity and Mortality conferences

Donors: Informed Consent (B6, CM6, C6)

6th edition	5th edition
Informed consent and donor evaluation now must be obtained by a health care professional who is **not** the primary health care professional overseeing care of the recipient	This was only a recommendation
The informed consent process **must** inform the donor of the policy for cellular therapy product discard or disposal	Was not required previously

Donors: Pregnancy Tests

(B6, CM6, C6)

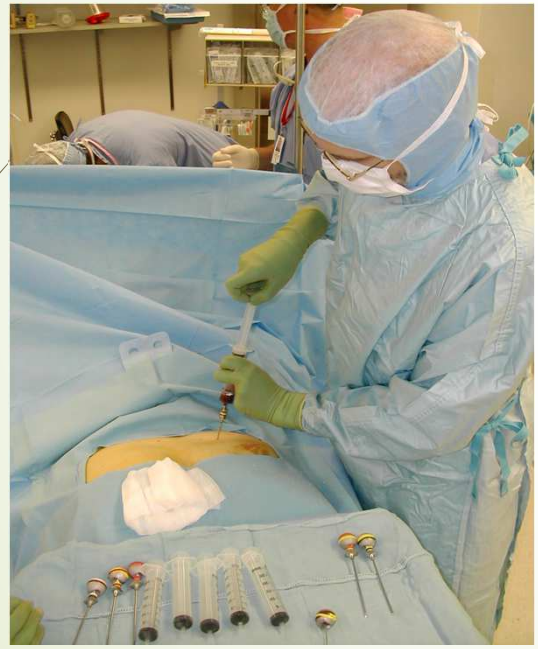
- Previous editions only required a pregnancy assessment for female donors with childbearing potential → was often misinterpreted
- 6th edition : Pregnancy Tests, rather than just assessments, are required
- Must be performed:
  - Within 7 days prior to starting donor mobilization regimen
  - Within 7 days prior to the initiation of the recipient's preparative regimen
- This may require two tests if the recipient is on a long-term preparative regimen

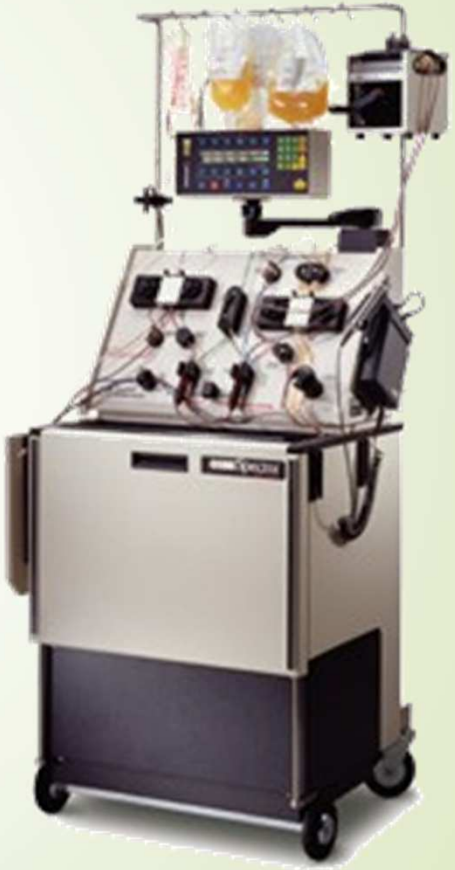
Other Changes to Donor Requirements

(B6, CM6, C6)

- Must have written criteria for selection of allogeneic donors who are elderly
- Must have a policy for anti-HLA antibody testing for mismatched donors and recipients
- Records required for donor eligibility determination must be in English or translated into English when crossing international borders
- Standards throughout the document explicitly reference requirements for incomplete donor eligibility determination in addition to ineligible donors

Changes Specifically to Marrow and Apheresis Standards





Number of Bone Marrow Collections Required (CM1.5)

- 2014 – draft of the 6th edition
- CM1.5 : required minimum average of two BM collections per year (↑ from 1/year)
- Public comments: 46 total!!
- 22/24 agree/disagree; however, those disagreeing strongly dissented
- Back to standards' committee…

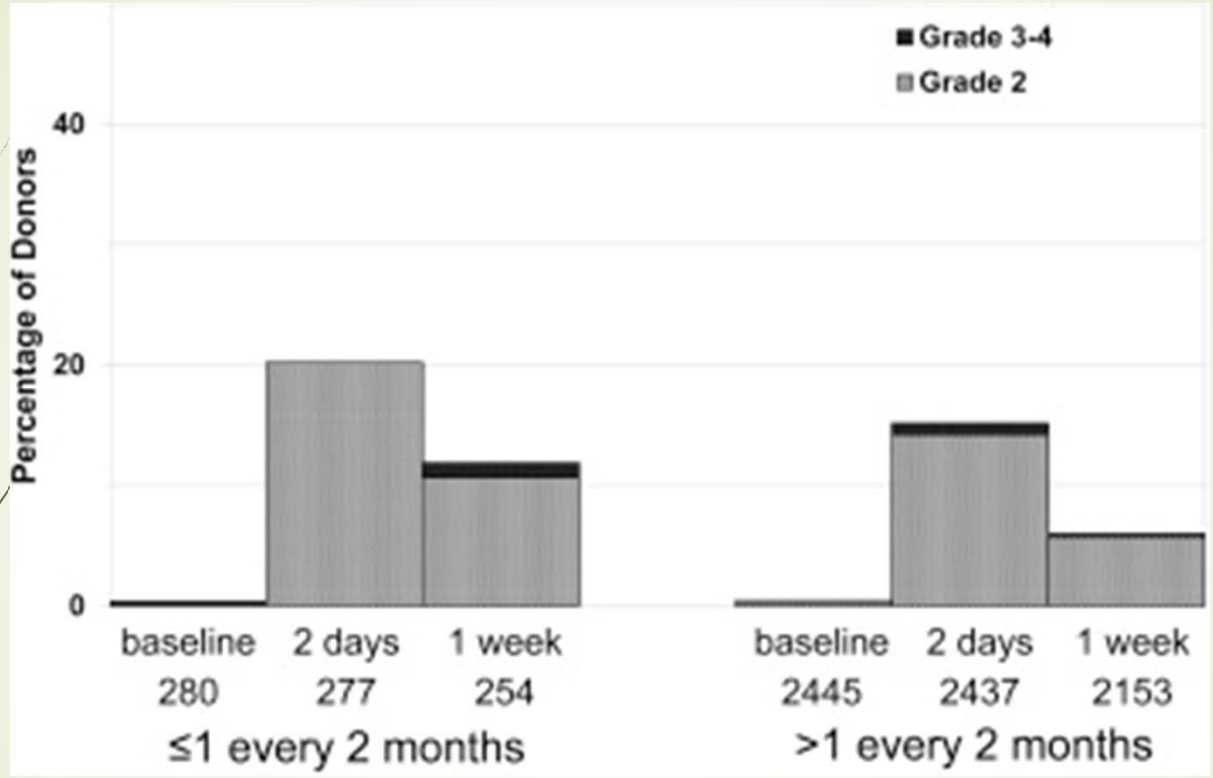
Number of Bone Marrow Collections Required (Cont.)

Concerns	Standards committee thought process
Patients	Access to BM collection could ↓
Donors	Subjected to BM collection to meet numbers
Evidence based	Lack of data: 1. Relationship between no. of collections & competency /outcomes 2. NMDP – no issues with collection centers w/ low numbers
6th edition final Decision	Revert to original requirement - minimum average of 1/BM collection/year

“Just when I discovered the meaning of life, they changed it.”

- George Carlin

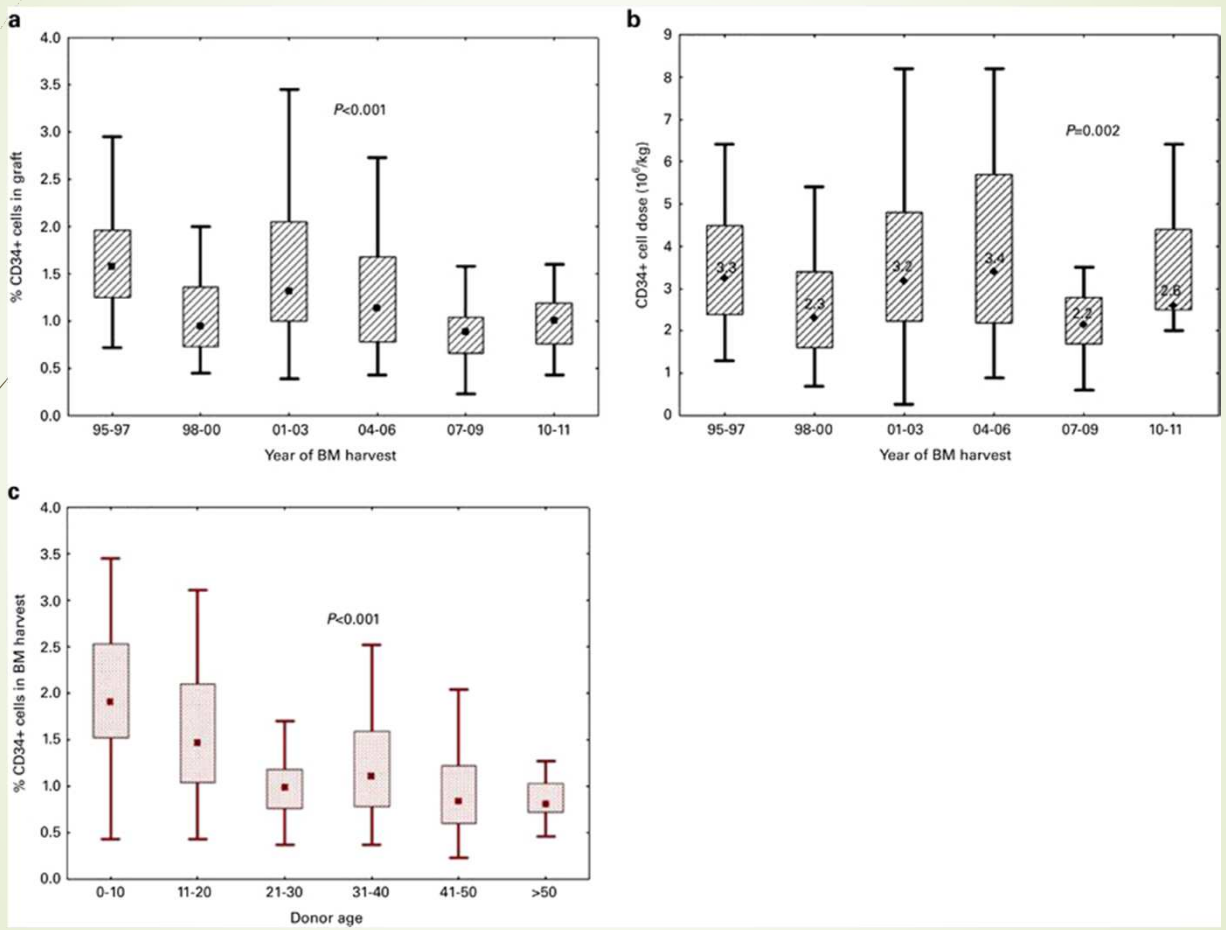
Number of Bone Marrow Collections Required (2015)



Highest toxicity level of key symptoms for BM donors by collection center volume: at baseline, during the pericollection period, and post donation

Bronwen E. Shaw, et al. BBMT, 2015; 21:1830–1838

Number of Bone Marrow Collections Required (2015)



Remberger M, et al. BMT. 2015;50(7):1007-9

Minimum Number of Marrow Collection Procedures – Summary

- For now - remains at a minimum average of one collection per year within the accreditation cycle but stay tuned…
- This minimum number is applied to a single team of collectors and support staff.
  - Different teams at different sites must each meet the minimum

Other Marrow and Apheresis Collection Facility Changes

- Records must identify the person immediately responsible for each significant step (including dates and times) (CM8.15.1, C8.16.1)
- Cellular therapy products must be transported or shipped to the Processing Facility in a validated container (CM10.3, C10.3)
- Marrow Collection Facilities must also control storage areas (CM9.1)
  - Cellular therapy products are always undergoing some process, and temporary holding until they are picked up by another facility is considered storage

Apheresis Equipment (C8.3)

- Inspect for cleanliness prior to each use
- Verify compliance with the maintenance schedule daily prior to use
- Define process for action to take when out of calibration for products collected since the last calibration

Other Apheresis Collection Changes

- When performed in outpatient unit, there must be a designated area with location, space, and design to minimize risk of airborne microbial contamination (C2.1.2)
- Directors and Medical Directors must have performed or supervised a minimum of 5 (initial) or average of 5 (renewal) procedures (C3.1.4, C3.2.4)
- ECP requirements also included in this section based on requests from apheresis professionals (C8.17) and common citations in the clinical part

In the 5th edition: B7- Recipient Care
B7.9: Extracorporeal Photopheresis (ECP)

There shall be a policy addressing safe administration of extracorporeal photopheresis

- Many citations because Clinical Programs did not:
  - Establish SOPs
  - Have a final report of the therapy administered
  - Did not assess response, outcomes, and adverse events
  - ....ECP was in clinical section only. 6th edition- ECP was added to the collection section as well

Extracorporeal Photopheresis (ECP)

- If performed within the Clinical Program or Collection Facility, must be in compliance with the Standards as applicable.
- Additional clinical standards (B7.9 and substandards) apply whether or not ECP is performed within organization.
  - Controlled by Clinical Program: consultation, written order, etc.
  - May need to be in written agreements: final report of ECP, performance in accordance with SOPs, provision of outcome data

Examples of ECP within the Same Institution

Provided by directly affiliated unit

- ECP performed in hospital's infusion center
- Considered an outpatient procedure
- ECP machine can be wheeled to bedside
- SOPs in common apheresis manuals
- Written agreements are not required

Provided by outside vendor

- ECP performed by mobile apheresis service
- Considered a vendor
- Apply written agreements
- Basically applying your own QMP e.g. audits, employees credentials to the vendor and everyone is following your own SOPs.

6th edition: in the apheresis section ECP Requirements Standard C8.17

C8.17	There shall be a policy addressing safe administration of ECP.

C8.17.1	Before ECP is undertaken, there shall be a written therapy plan from a physician specifying the patient's diagnosis and GVHD grade, involved organs, indication, timing of the procedure, proposed regimen, and any other factors that may affect the safe administration of ECP.
C8.17.2	The ECP procedure shall be performed according to written standard operating procedures of the facility performing the procedure appropriate for the clinical condition of the patient.
C8.17.3	A final report of the details of ECP administered shall be documented in the patient's medical record.

Conclusions

- Cellular therapy standards ensure high quality products

  - standardize processes related to collection, processing & administration

- The standards are based on scientific literature, clinical practice, governmental regulations & field input

- It is important to become Familiar with the Standards (especially changes - Use the 5th to 6th edition crosswalk)

Thank you!
GRACIAS!
Todah!
Merci!
Dank Je Wel!
Danke!
THANK YOU!
MERCI!
感謝
謝謝
多謝
どうもありがとう

B/CM/C 6: Donor Section Main Issues

Subgroup	Issue/s	Findings
6.2.1	.Explaination .Donor right .Understanding .Confidentiality	11
6.2.6	.Donor HLA typing information protection .Donor release personal data authorised	8
6.3.1	.Donor suitability evaluation: independent physician. *Related donors*	9
6.3.3	.Recommended risk hemoglobinopathies evaluation	8
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6.3.6	.Donor advocate availability *Minors/menthally incapacitated*	8
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