Foundation for the Accreditation of Cellular Therapy

FACT

Phyllis I Warkentin, MD

September 13, 2013

Update FACT Presentation

- History of FACT
- Standards / Accreditation
  - Accomplishments and recent changes – Fifth Editions
  - HRSA-designated Accrediting Body / criteria
- What's new:
  - FACTWeb
  - New Accreditation Goals
  - International expansion
  - Core Standards / Regen Med
- Inter-organizational Cord Blood Survey
  - Characterization; Identity confirmation; Processing

FACT History

- An organization of practicing professionals, encompassing all aspects of cellular therapy; co-founded in 1996 by:
  - American Society for Blood and Marrow Transplant
  - International Society For Cellular Therapy
- Mission:
  - *Promote quality medical and laboratory practice of cellular therapy through its peer-developed standards and voluntary inspection and accreditation program.*
- Goals:
  - Promote quality patient care and quality laboratory performance

    a valid accreditation process for HPC transplant must include assessment of clinical practice, cell collection, and laboratory services
  - Improve treatment outcomes
  - Foster research and continued development of cellular therapies

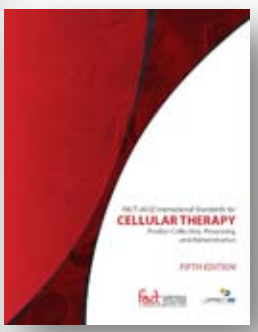
ASBMT™ American Society for Blood and Marrow Transplantation

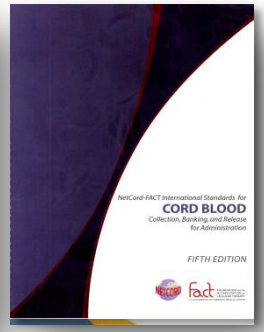
International Society for Cellular Therapy ISCT

The Goals of the FACT Community Today

- Promote quality patient care and laboratory practice
- Improve treatment outcomes
- Foster continued development of cellular therapies

Pursued through three core services:





Standards

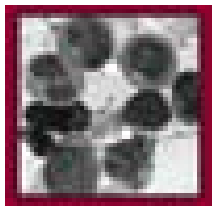
Accreditation

Education

Partners

FACT
FOUNDATION FOR THE ACCREDITATION OF CELLULAR THERAPY
AT THE UNIVERSITY OF NEBRASKA MEDICAL CENTER

JACIE
joint accreditation committee
isct ebmt


ASBMT
American Society for Blood and Marrow Transplantation

unique source
NETCORD
for stem cells

International Society for Cellular Therapy
ISCT


CELLULAR THERAPY
FIFTH EDITION
NetCord-FACT International Standards for
CORD BLOOD
Collection, Banking, and Release
for Administration
FIFTH EDITION
NETCORD
Fact

STANDARDS

Standards Development

- FACT Standards are minimal requirements for quality practice; not intended to establish best practices.
- All FACT Standards are developed by experts in the field, functioning in variety of roles: clinicians, scientists, technologists, nurses, pharmacists, quality experts, others.
- Standards are evidence-based.
  - Based on published medical literature wherever available
  - Developed by consensus of experts
  - Legal review; regulatory review; public comment period. Each comment reviewed, incorporated as appropriate.
- Board approval; publication

Interim Standards

- Proposed by Standards Committee, Board member or any participant
- Indicated to address urgent situations
  - Newly emergent diseases
  - New process developments
  - Correction or regulatory change
- Standards Committee review
- Approval and adoption:
    - FACT Board of Directors
    - NetCord or JACIE Board of Directors
- Publish and distribute for immediate implementation

Cellular Therapy Standards

- First edition published 1996
  - Clinical Guidelines of ASBMT
  - Laboratory Standards of ISCT
- Cover all phases of collection, processing, and administration of hematopoietic progenitor or therapeutic cells
- Clinical Program must utilize a collection service and a cell processing laboratory that meet FACT Standards:
  - FACT - accredited or successfully inspected
- No specific program structure is required
- Functional coordination and cooperation required
- Maintain comprehensive Quality Management Program
- Follow and analyze patient outcomes

Collaboration with JACIE

Joint Accreditation Committee – ISCT & EBMT

Established in 1998 to assess and accredit programs in hematopoietic cellular therapy – adopted FACT Standards

- Joint review of 2nd edition Standards – 2002
- International Standards for subsequent editions
  - Overall FACT Standards Chairperson
  - Joint FACT / JACIE leadership and membership for each Subcommittee for development

Current: Fifth edition; March 2012.

- Inclusive internationally applicable language
- Expanded guidance; regulatory considerations

FACT-JACIE Cellular Therapy Standards Key Changes - Fifth edition

- Clarify scope: cover all phases of collection, transportation, processing, storage, and clinical administration of cellular therapy products (hematopoietic progenitor cells; therapeutic cells) derived from marrow or peripheral blood
  - Include clinical administration of cord blood cells, not collection or banking
- Separate section for bone marrow collection services
- Extracorporeal photopheresis explicitly included
- Donors: advocate available, independent clinician to evaluate suitability, IDMs not required in autologous donors
- Implementation plan required for ISBT 128

FACT-JACIE Cellular Therapy Standards Key Changes - Fifth edition

- Cord blood administration
  - Clinical service must communicate with Processing Facility prior to requesting a CBU
  - Policies for determining appropriate volume of RBCs, cryoprotectant, and other additives required
  - Processing Facility: ensure adequate storage capability
  - If inexperienced with type of unit, obtain a practice unit
  - RED-cell replete unit: must be diluted and/or washed
  - Red-cell depleted: should be diluted and/or washed
  - Double cord blood units: ensure first has been administered safely prior to administration of the second.

Cord Blood Banking Standards

- FACT Standards (1st edition) included a few CBB Standards
- Complexity of cord blood banking required separate Standards
- Collaboration with NetCord brought together the expertise of NetCord with the proven accreditation process of FACT
- **The International NetCord Foundation**

  A network of Cord Blood Banks / CBB experts
  - Promote the highest quality in cord blood products
  - Balance global supply and demand for cord blood
  - Encourage and facilitate the use of cord blood transplants by promoting laboratory and clinical research and providing professional and public education

NetCord-FACT International Standards for Cord Blood Collection, Processing, and Release for Administration Fifth Edition, 2013

- Established by consensus by experts in CB Banking under the direction of the FACT Standards Committee Chair
- Guidelines of International NetCord Foundation used as start
- Standards based on published literature whenever available
- **SCOPE:**
  - All aspects of CB banking – donor recruitment, screening, testing, consents, collection, transport, processing, storage, search and matching, and clinical outcome.
  - Do not cover clinical uses of CB or transplantation
  - Inclusive of unrelated donor units and directed or family units
- Bank is responsible to follow clinical outcomes in sufficient detail to assess quality of product.

ACCREDITATION

FACT Inspection /Accreditation

- Voluntary accreditation
  - Educational, collegial, helpful inspections
  - Accredited programs published – newsletters, website
- Basis for accreditation: NetCord-FACT Standards
  - Written application and on-site inspection
  - Central office preview and review
- Volunteer inspectors, experts in the field; peers
- Accreditation Committee reviews each report; determines next steps and accreditation status;
- Results & appeals to Boards of Directors
- Inspections periodically audited

FACT Accreditation

- Accreditation based on documented compliance with all Standards
  - Written documents
  - On-site inspection
  - Expert volunteer inspectors, trained, active in the field
  - Educational; collegial rather than punitive
  - Three years duration
- FACT and JACIE Accreditation Programs:
  - Similar but separate
- FACT Cell Therapy Accreditation:
  - U.S., Canada, Australia, New Zealand, Brazil, Singapore
- FACT-NetCord CBB Accreditation:
  - Cord Blood Banks world-wide (19 countries)

FACT Accreditation Eligibility

Hematopoietic Progenitor Cell Facility

- Clinical Transplantation Program
  - Allogeneic HPC Transplantation (all graft sources)
    Minimum volume 10 new recipients per year
  - Autologous HPC Transplantation
- Hematopoietic Cell Collection Facility
  - Bone Marrow Collection
  - Peripheral Blood Progenitor Cells, Apheresis
- HPC Processing Facility

Cord Blood Bank (URD and/or Related)

Minimum 500 units; actively banking

Accreditation Process

- Applicant submits application to confirm eligibility
- Applicant submits document checklist and inspection checklist via FACTWeb; Checklist documentation
- Applicant and inspectors plan on-site inspection
  - FACT Coordinators assist banks; inspectors
- Inspectors conduct on-site inspection and submit report
- Accreditation Committee determines outcome
  - Separate Committees for Cell Therapy and Cord Blood Banks
- Applicant submits responses; documents all standards have been met
  - Focused reinspection may be required
- Accreditation is awarded

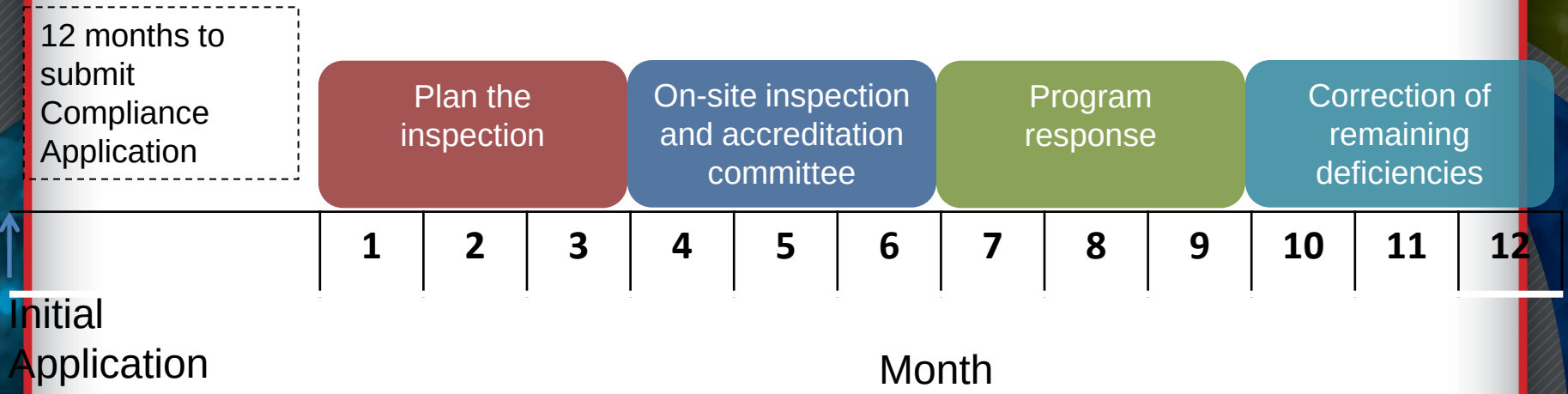
On-site Inspections: Fixed Collection Sites

- See at least one example of each variable:
  - Individual Facility Medical Director other than CBB MD
  - Type of unit – related donor, unrelated, both
  - Method of Collection – in utero, ex utero
  - Collection personnel: bank staff, hospital staff, physician / midwife
  - Transport to bank:
    - By hand, bank personnel, courier service,
    - Ship (unaccompanied): plane, train, cab, other
    - Interim stop (temporary storage)
  - Distance from bank
  - Number of units collected on average per week

CBB Collection Site Algorithm

Collection sites (Fixed)	Number inspected
1	1
2 - 5	2
6 - 10	3
11 - 20	4
21 - 50	5
51 – 100	7
101 - 150	9

Accreditation Timeline



- Accreditation cycle is three years
  - Reduces burden on organizations
  - Ensures continuous improvement and adaptation to the evolving field

FACT-NetCord Inspections
Potential Outcomes


Foundation for the Accreditation of Cellular Therapy

Certifies That

MD Anderson Cord Blood Bank

Houston, Texas

Having Met the Requirements of FACT and NetCord
is Granted Accreditation for

Cord Blood Collection, Processing, Testing, Banking,
Selection and Release of Unrelated Allogeneic and Directed Allogeneic Donations

From: March 31, 2006 To: March 31, 2009

Accreditation does not automatically survive a change in director, ownership,
or location and assumes that all interim requirements are met.

C. Fred LeMaistre, MD
FACT President

Phyllis I. Warkentin, MD
Chairman, Accreditation Committee

Joan Garcia, MD
NetCord President

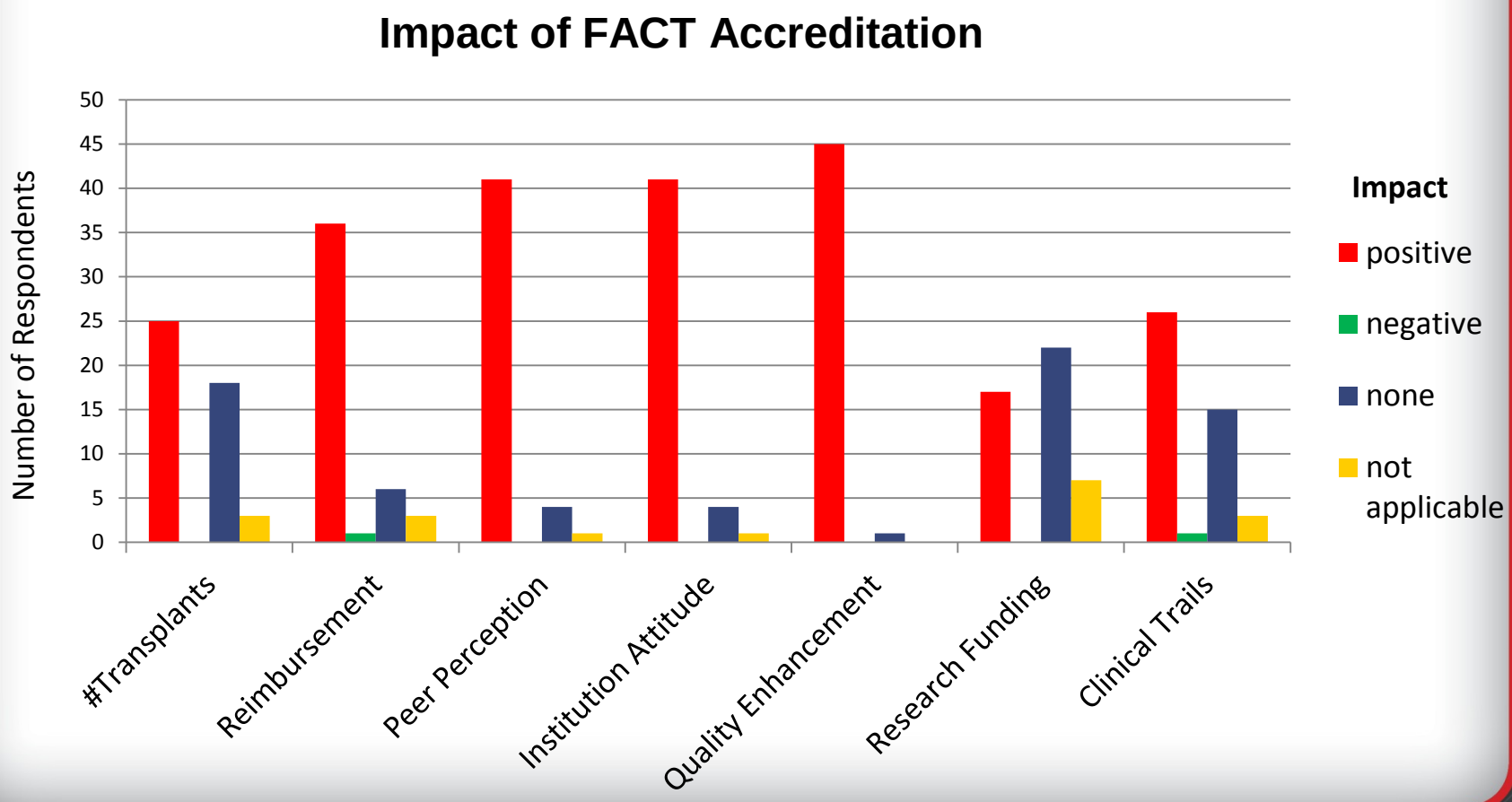
- No deficiencies
  - Full accreditation - 3 years
- Few and scattered deficiencies
  - Written response
  - Chairman and staff evaluate responses
    ± review by CBB Accreditation Committee
  - Accreditation
- Major and Systemic deficiencies
  - Written response
  - Focused reinspection of specific areas
    OR reinspection of entire program
  - Accreditation Committee review
- Non-accreditation
  - Reapplication

FACT Accreditation – Sept. 2013

Hematopoietic Cellular Therapy Programs						
US	Canada	Australia	New Zealand	Brazil	Singapore	**TOTAL**
177	15	4	1	1	1	**199**

CORD BLOOD BANKS 44					
	URD Units	**Related / Family**	**Both**	**TOTAL**	**HRSA CBB**
US	5	0	4	**9**	**8**
Non-US	8	6	21	**35**	**0**
TOTAL	**13**	**6**	**25**	**44**	**8**

Survey of HPC Programs with 10 Years Continuous Accreditation



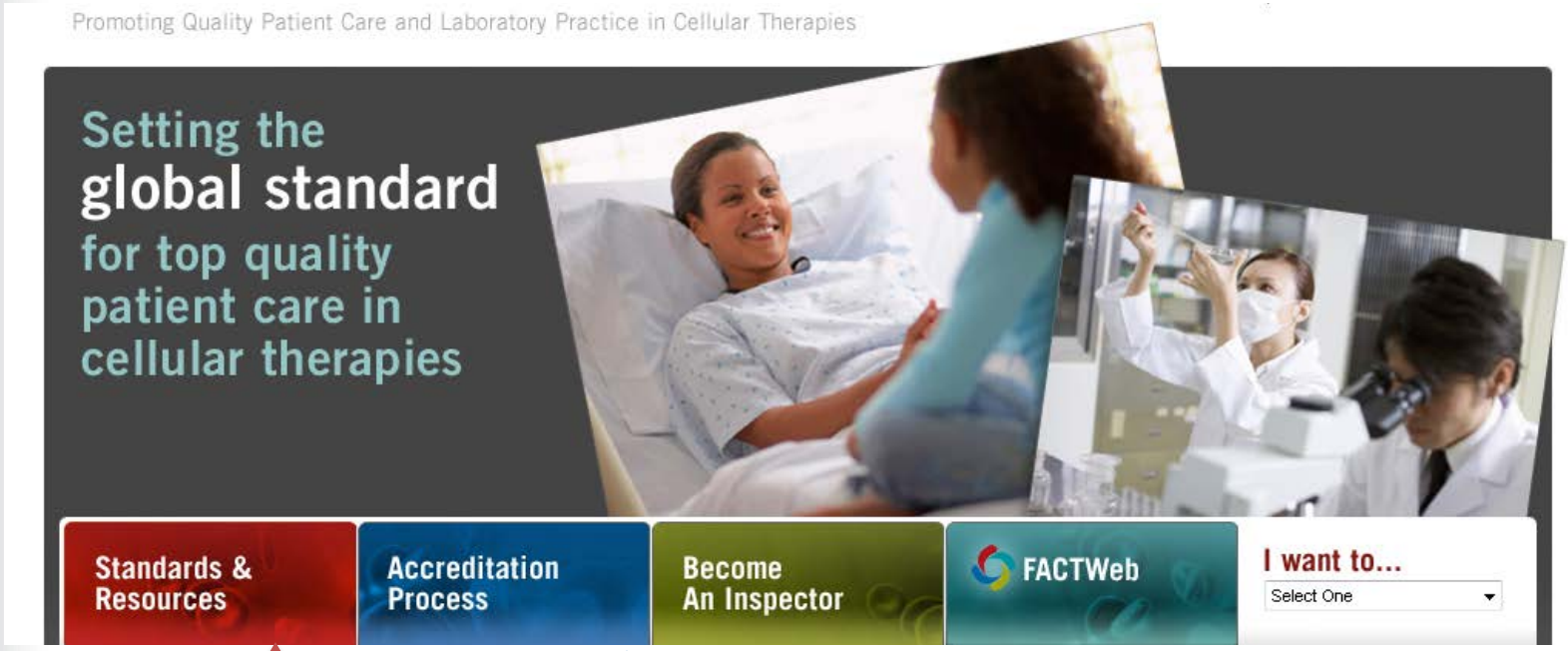
Interim Reports

- All accredited facilities submit annual report:
  - Significant personnel changes
  - Identify new fixed collection sites; other facility changes / moves
  - Significant process changes
  - Inventory
- Individualized submissions include specific follow up reports related to prior deficiencies, FDA citations, other issues
- Additionally, if not inspected under current edition of Standards, may be asked for documentation of compliance with significant new standard: eg, cord blood processing standards

FACT: New Initiatives

- FACTWeb
- International Accreditation
- New Accreditation Goals
  - Collection Centers – licensed or IND products
  - Processing more than minimal manipulation
- Core Standards:
  - Regenerative Medicine
  - Outreach to other disciplines

The FACT Website



provides details regarding the scope of the Standards and links to regulatory and industry resources.

includes general information pertinent to obtaining initial or renewal accreditation, including accreditation timelines, process overview, and fees.

lists the benefits and expectations of inspectors and provides directions on how to apply to become an inspector.

enables users to create a personal profile for updating demographic information, participating in FACT education, and managing downloads.

factweb
Cellular Therapy Community Portal

fact FOUNDATION FOR THE ACCREDITATION OF CELLULAR THERAPY
AT THE UNIVERSITY OF NEBRASKA MEDICAL CENTER

International Accreditation

- FACT International Task Force
  - Establishes key contacts in other regions of the world
  - Identifies barriers to accreditation
  - Educates members of regional BMT societies
- Promising conclusions so far:
  - People and programs outside US are very interested in accreditation and motivated to give their patients the best care possible
  - International programs are able to meet the FACT Standards
  - Variances or relaxed versions of the Standards are not necessary
  - Communication enhances understanding of geographical and cultural differences and identifies needed education

New FACT Accreditation Goals

- Collection

  (Apheresis) For Research, Clinical Trials, or manufacturing IND or licensed products

- Processing

  More than minimal manipulation; usually IND-related

New FACT Accreditation Goals

- Collection for Research and IND Products Only
  - Traditional collection accreditation requires use of a processing facility that meets the FACT Standards
  - Some collected products go to third-party manufacturers
- Requests from facilities that only collect cell products for research
  - Desire to perform in accordance with established standards promotes the field
  - Emphasizes FACT supports research following good scientific research principles, required regulatory pathways, and IRB oversight

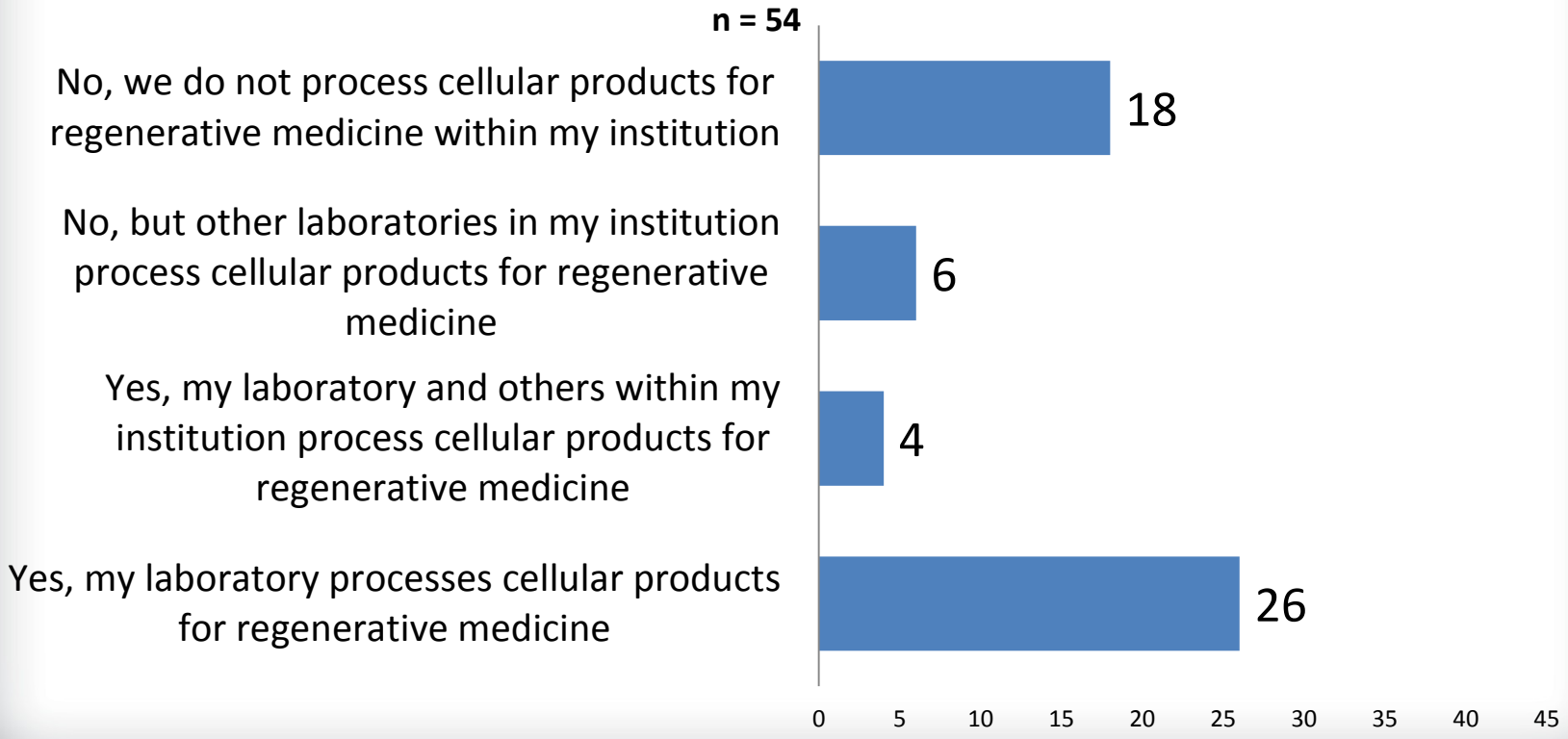
“More than Minimal”

- 4th edition of FACT-JACIE Cellular Therapy Standards broadened to include Therapeutic Cells in addition to HPCs
- Four non-HPC facilities previously accredited:
  - cGMP Cell Processing Facility Diabetes Research Institute
    University of Miami Miller School of Medicine
  - The Cell Manufacturing Program Laboratory
    University of Miami
  - Immunologic Monitoring and Cellular Products Laboratory
    University of Pittsburgh
  - Clinical Cell and Vaccine Production Facility - Philadelphia

Regenerative Medicine Questionnaire

- Purpose: Determine what cellular products for regenerative medicine are being processed
  - in FACT-accredited facilities
  - in those facilities' institutions
- Distributed in May 2011
- 54 Respondents

Does your laboratory process cellular products for regenerative medicine?



Benefits of FACT Accreditation

- Provides evidence of external validation for use in applications to funding organizations
- Demonstrates to clinical trial sponsors that the facility meets requirements published by experts in the field of cellular therapy
- Facilitates the establishment of quality management and process control to minimize liabilities and regulatory noncompliance

New FACT Accreditation Goals

- Processing facilities may choose to be accredited for:
  - Minimal manipulation
  - More than minimal manipulation
  - Both
- If accredited for both, the designation of facility accreditation, inspection teams, and fees depend on:
  - If minimal and more than minimal manipulation are performed in the same facility
  - If minimal manipulation activities are already accredited (or vice versa)
  - If the facility's director and/or QM Program is the same or different between the two

Creation of Core Standards

- Initiated by special study group of Board of Directors in 2010
- Task force charged with creating draft
- Line-by-line review
  - Removed requirements specific only to HPC transplants
  - Generalized terminology
  - Created more flexibility

Overview of Core Standards

- Based on Cellular Therapy Standards; some ideas from Cord Blood Standards
- Apply to cellular therapy products intended for human administration
- Broad enough to include most types of cellular therapy products
  - Does not include all requirements necessary to adequately determine quality processes

How Outcome Analysis Standards Would be Applied

- Typical HPC processing:
  - Time to engraftment for HPC products
  - Product efficacy and/or clinical outcome
- Processing under IND:
  - Safety
  - Product efficacy and/or clinical outcome *as applicable* should be reviewed regularly
  - Depends on stage of research

Core Standards

- Illustrate FACT's relevance to other cell therapies
- Useful in assessing complex laboratories and potentially regenerative medicine products
- Starting point for discussions with other fields (e.g., cardiology) Discussion has begun.
- Foundation for future sets of standards to include additional relevant specific points

Bringing Transplant Centers Together to Determine...

Practices for Testing Cord Blood Units and Preparing Units for Administration

AN INTER-ORGANIZATIONAL SURVEY

FACT Professional Relations Committee

- NMDP
- ASHI

Transplant Center Practices for Cord Blood Units 1

- Demographics
  - Part of the world; size of transplant program (# of CB units)
- Matching:
  - Consider NIMA (non-inherited maternal haplotype) if not 6/6 match?
- Standard testing at Tx Ctr after receipt, prior to administration
  - Asks both: 1) sample taken 2) results required
  - TNC; WBC diff; CD34+; ABO, Plt ct; HCT; HLA; HLA antibody; CFU; other
  - Viability method
- Standard testing after administration to confirm identity
  - HLA, ABO

Transplant Center Practices for Cord Blood Units 2

- Three scenarios: identity testing questions
  1) CBU confirmatory typing was performed via registry or CBB on an attached segment prior to shipment
     - Which tests would you do? HLA; ABO; Neither
       - HLA – Which loci; What method
     - What sample? Segment; Anything available; None
  2) CBU confirmatory typing performed on ancillary material, attached sample not tested but available
  3) CBU extended typing performed on ancillary material but not on attached segment; ancillary material available, no segment
     - If best match and dose, would you accept it?
     - What post-administration testing would be done o confirm identity?

Transplant Center Practices for Cord Blood Units 3

- Scenario: CBU extended typing done on ancillary material, no segments available or tested; no further material available
  - Would you accept the CBU?
  - Are tests performed prior to administration? (Aliquot of thawed unit)
    - ABO
    - HLA – which loci / testing methodology
  - Which tests are performed after administration to confirm identity?
- When does your center perform post-administration testing?
  - All CBUs / if no segment prior / if not done pre / never
- When post-administration testing is done, what is done?
  - ABO / HLA / HLA methods

Transplant Center Practices for Cord Blood Units 3

- Scenario: CBU extended typing done on ancillary material, no segments available or tested; no further material available
  - Would you accept the CBU?
  - Are tests performed prior to administration? (Aliquot of thawed unit)
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    - HLA – which loci / testing methodology
  - Which tests are performed after administration to confirm identity?
- When does your center perform post-administration testing?
  - All CBUs / if no segment prior / if not done pre / never
- When post-administration testing is done, what is done?
  - ABO / HLA / HLA methods

Transplant Center Practices for Cord Blood Units 4

Thawing, Washing, and Dilution

- When do you thaw CBUs?
  - In the lab / At bedside / Either
- For double CB transplants, do you wait to thaw the second until after the first has been administered?
  - Always / Usually/ Occasionally / Never
- Preparative method for each type of CBU (thaw, infuse/ thaw, dilute / thaw, wash):
  - RBC-replete CBU / CBU containing dextran / RBC-deplete unit – small / RBC-deplete CBU – large > 30 mL
- What is your method of washing and/or dilution?

THANK YOU