Comparability of Cord Blood Units

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Survey

- Draft Guidance document allows the CBB to present comparability data for units previously collected by different methods
- Snapshot of practices that have been used by CBB for some of their inventory
  - Asked questions about numbers of different procedures
  - Asked questions about "GMP" compliance

Survey

- Number of centers: 21
- Number of responses: 9

- Note: Last minute request

	# Different Procedures Used
Collection	1(2), 2(5), 4(2) - in utero vs ex utero - different collection bags - donor screening
Processing	
Cryopreservation	
Quality Control	

	# Different Procedures Used
Collection	
Processing	1 (5), 2 (4) - Manual vs automated - RBC depletion
Cryopreservation	
Quality Control	

	# Different Procedures Used
Collection	
Processing	
Cryopreservation	1 (7), 2 (2) - CRF vs Mechanical B/U
Quality Control	

	# Different Procedures Used
Collection	
Processing	
Cryopreservation	
Quality Control	1 (4), 2 (1), ? (4) - TNC/CFU only - NAT Testing - Anaerobic bottles - Missing data (CFU, CD34)

GMP Documentation p.1

Complete documentation of procedure	1) Always.....8 2) Never 3) Past __ years.....1
Cleaning documentation (instruments and work area) between products	1) Always 2) Never 3) Past __ years
Cleaning documentation (instruments and work area) daily, weekly, monthly	1) Always 2) Never 3) Past __ years

GMP Documentation p.1

Complete documentation of procedure	1) Always.....7 2) Never 3) Past __ years.....1
Cleaning documentation (instruments and work area) between products	1) Always.....4 2) Never.....3 3) Past __ years.....2
Cleaning documentation (instruments and work area) daily, weekly, monthly	1) Always 2) Never 3) Past __ years

GMP Documentation p.1

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Cleaning documentation (instruments and work area) daily, weekly, monthly	1) Always.....7 2) Never 3) Past __ years.....1

GMP Documentation p.2

Materials management (Quarantine, Release specifications, etc)	1) Always.....6 2) Never 3) Past __ years.....3
Environmental Monitoring of NON VIABLE particles in the Cell Processing Lab	1) Always 2) Never 3) Past __ years
Environmental Monitoring of VIABLE particles in the Cell Processing Lab	1) Always 2) Never 3) Past __ years

GMP Documentation p.2

Materials management (Quarantine, Release specifications, etc)	1) Always.....6 2) Never 3) Past __ years.....3
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GMP Documentation p.2

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GMP Documentation p.3

Training documentation of all personnel involved with CBB	1) Always.....9 2) Never 3) Past __ years
Quality review of all deviations	1) Always 2) Never 3) Past __ years
Two person sign-off of critical steps of procedure (i.e. addition of starch)	1) Always 2) Never 3) Past __ years

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GMP Documentation p.3

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Two person sign-off of critical steps of procedure (i.e. addition of starch)	1) Always.....5 2) Never.....4 3) Past __ years

Cord Blood Technology
(And HPC-A)

- Different than other therapeutic products
  - Half life is 50 years (?)
  - Not end stage differentiation
  - Take 20 – 40 days to detect in the periphery
  - Non-engraftment
    - Maybe due to poor Stem Cell Product
    - Double cord transplantation
    - Conditioning regimen
    - Clinical course during engraftment
    - Previous chemotherapy

Comparability

- Based on Clinical utility
  - Difficult if not impossible
    - Similar to drug study requirements
    - Large numbers of infusions dilute out the clinical factors
  - What is the endpoint
    - Engraftment
      - 30d, 6mo, 1, 2 5 year engraftment
  - Inhibit new technology
    - 1-3% of inventory is used on a yearly basis
  - Inhibit others from entering the field

Comparability

- Based on in vitro data
  - Goal is to have the maximum number of CB units available for clinical use balanced with protecting the safety of the patients receiving the product
  - **Less data is better** (within reason)
  - What are the minimum requirements to accomplish this goal

Choosing a Cord Blood Unit

- HLA: 6, then 5, then 4
- TNC
- Bank
- CD34 Numbers

- All other factors are reviewed but usually at time of CB arrival

Comparability Suggested Parameters

- TNC
- HLA
- Sterility

- CFU (growth) OR
- Viable CD34 (presence)

Collection	1(2), 2(5), 4(2) - in utero vs ex utero - different collection bags - donor screening

- In utero vs ex utero
  - Published studies showing no difference in vitro or in vivo
- Collection bags
  - Qualification/validation runs of the different bags
    - Viability and sterility of cells
- Donor screening
  - License products as is with requirement of a callback at time of CT. If unreachable, then label appropriately

Processing	1 (5), 2 (4) - Manual vs automated - RBC depletion

- Manual vs automated
  - In vitro split runs comparing products
    - Sterility, viability, CFU
  - Minimum number - ???
- RBC depletion vs no depletion
  - Same comparison

Cryopreservation	1 (7), 2 (2) - CRF vs Mechanical B/U

- Validate your method
  - Viability and yield
  - Sterility….yes but how?
- Two methods
  - Split runs and compare viability and yield

Quality Control	1 (4), 2 (1), ? (4) - TNC/CFU only - NAT Testing - Anaerobic bottles - Missing data (CFU, CD34)

- Minimum QC of TNC, HLA, Sterility and either CFU or CD34
- NAT testing/Anaerobic micro
  - Products licensed with requirement that NAT (or Sterility) be done at time of CT
    - NAT and Cord Blood
- Missing data
  - Product licensed with requirement that test be performed on segment (vial) at time of CT

Comparability
GMP Manufacturing Conditions

- Require analysis for all of the "GMP" requirements that have not been performed
  - Quality review of the effect of this deficiency on the potential safety of the product as part of Licensure submission
  - Example: No documentation of cleaning between products
    - Overall contamination rate before and after implementing this documentation
    - Review all positives and look upstream and downstream in manufacturing process to see if any other contamination
    - Viral screening on products processed in the same time period

Comparability
Additional Information (if available)

- Engraftment
- Chimerism for single CB infusions

Questions for discussion

- Back-up procedures
- New technologies
- Donor History