Use of Automated Separation Device for Cord Blood Processing

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Objectives

- Background
- Review of product and processing method
- Device information
- Regulatory steps taken for use of a device not approved by FDA
- Device installation and validation
- Manufacturer designated study site for 510k application submission to FDA
MD Anderson Cord Blood Bank (CBB) Background

- Public CBB established in April 2005
- IRB approved protocol for cord blood collection, processing and banking
- NMDP member bank-
  - NMDP is IND holder for phase II clinical protocol: A centralized cord blood registry to facilitate allogeneic, unrelated donor umbilical cord blood transplantation
Product and Processing Method

- Cord blood collected from volunteer donors

- Existing processing method
  - Buffy coat separation using hydroxyethyl starch (HES) and manual centrifugation
  - Controlled-rate cryopreservation (Bioarchive system, Thermogenesis) in Pall bags
  - Storage in liquid nitrogen storage tank-liquid phase (Bioarchive)
Is there a way to use an automated device that has not been approved by FDA to process our cord blood units for public banking?
Device Information

- Biosafe Sepax: Commercially available in Europe for over 3 years (*CE mark*)
- Published data available
- In use at public cord banks outside the United States
- Automated buffy coat separation
- Functionally closed system
- Single-use, sterile tubing set
MANUAL METHOD

1st Centrifugation

Plasma and Buffy Coat Collection

2nd Centrifugation

Plasma Removal & Buffy Coat Collection

Addition of Cryoprotectant

Cryopreservation & Storage

AUTOMATED METHOD

HES Addition

Automated Device

Tubing Set

Addition of Cryoprotectant

Cryopreservation & Storage
Regulatory Steps Followed

1. Dialogue with FDA
   • Moratorium on cord blood regulatory pathway- IND or IDE not required
   • IRB approval needed
   • Validation needed
Regulatory Steps Followed

2. IRB approval obtained

3. Verbal discussion followed by notification letter sent to FDA by the manufacturer prior to shipment of device to U.S.

4. Material Transfer Agreement and Letter of Intent signed

5. Validation runs performed

6. Discussed evaluation with NDMP prior to receiving final membership approval
Device Installation and Validation

Provided by Manufacturer

- Installation and Operation Qualification (IQ/OQ)
- ISO Certification
- Certificate of Analysis for Tubing Set
- Training
- Operator’s Manual
Device Installation and Validation

Procedure Validation (n=5)
- Developed Standard Operating Procedures (SOP)
- Cord blood units collected following existing SOPs
- Used existing cryopreservation and storage method
Device Installation and Validation

Procedure Validation

- Post-processing parameters:
  - TNC and CD34 recovery
  - TNC and CD34 viability
  - Colony forming unit assay
  - Sterility
Device Installation and Validation

Procedure Validation

- Post-thaw parameters:
  - TNC recovery
  - TNC and CD34 viability
  - Colony forming unit assay
Device Installation and Validation

Additional data evaluation

- Data compared to the validation data for the existing manual processing method
- 30 additional procedures performed and data was compared to the available data from over 300 runs performed using the manual processing method
Study Site for 510k Submission

- Evaluation protocol developed by manufacturer
- Reviewed and accepted by FDA
- Device and tubing set function evaluation was included in the plan
Part 1

- 10 split runs comparing manual to automated method

Part 2

- 75 runs, evaluating the following parameters:
  - TNC, CD45, CD34 and CD3 recovery
  - Viability
  - RBC depletion
  - CFU
  - Sterility
  - Endotoxin
Study Site for 510k Submission Evaluation Protocol

Part 3

- 60 runs using manual method, performed concurrently with the automated runs for comparison

*Note*: With IRB approved protocol, other than products used for the split runs, all units processed with the device were acceptable for clinical banking if all standard release criteria were met.
Summary

- Discuss plan with FDA early on.
- Various regulatory pathway may be available depending on the type of device or product and the status of existing regulations pertaining to them.
- Consider if use of device may affect other existing protocols or INDs (NMDP in our case).
- Discuss with manufacturer and ensure appropriate contracts and documentation are in place.
- Monitor data closely.