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RECORD OF TELEPHONE CONVERSATION

Submission Type: BLA Submission ID: 125432/0 Office: OCTGT

Product:
HPC, Cord Blood

Applicant:
LifeSouth Community Blood Centers, Inc.

Telecon Date/Time: 02-Oct-2012 12:30 PM Initiated by FDA? Yes

Telephone Number: ----(b)(4)---------

----------(b)(4)----------

Communication Categorie(s):
1. Information Request

Author: KAROLL CORTEZ

Telecon Summary:
FDA requested a t-con with the sponsor to discuss issues regarding collection of CBU's and Donor eligibility determination.

FDA Participants: Mohammed Heidaran, Ph.D., Biologist (CBER/OCTGT/DCGT)
Eric Dollins, Ph.D., Biologist (CBER/OCTGT/DCGT)
Karoll Cortez, Ph.D., Medical Officer (CBER/OCTGT/DHT)
Safa Karandish, Ph.D., Medical Officer (CBER/OCTGT/DHT)

Non-FDA Participants: Kathleen Sazama (Medical Officer)
Jill Evans, (Vice President of Quality)
Amy Lambert, (Manager Cellular Therapies)
Tammy Lawson, (Validation Coordinator)

Trans-BLA Group: No

Related STNs: None

Related PMCs: None

Telecon Body:
FDA requested a t-con with the sponsor to discuss issues regarding collection of CBU's and Donor eligibility determination.

Follow-up Comments regarding the responses received to the FDA Letter dated 7/16/2012

1. *Item #11: Donor Eligibility- Please submit SOPs that describe the relevant risk factors considered during the review of the donor's medical records (birth mother and baby) and the physical examination reports?*

   You have submitted the revised SOP CB-MO.1.4: Review CBU Lot Records. The revised SOP does not adequately define all the risk factors that should be considered during the review of the medical and physical examination records. You have only added few examples to the SOP. Your SOP should include detailed list for the:

   - Clinical evidence (signs/symptoms) for HIV, hepatitis, syphilis, vacccinia,WNV and sepsis
   - Physical evidence or high risk behavior associated with HIV, syphilis, sexually transmitted diseases, hepatitis B and C and vaccinia for the following RCDADs

   As indicated in our prior letter, we suggest that you refer to sections IV.F and IV.G in the Guidance for Industry: Eligibility Determination for Donors of Human Cell, Tissues, and Cellular and Tissue-Based Product (HCT/Ps).
   http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Tissue/ucm073964.htm

   LifeSouth response:
   The sponsor will send a revised SOP CB-MO.1.4 to include the review of medical records from the birth mother and address the risk factor for RCDADs

2. *Item #14: Donor Eligibility- We are not able to determine whether you finalize the donor eligibility determination based on the results of the donor screening and test results before the HPC, Cord Blood units get listed in the registry and who is responsible for making the final DE determination. Please provide applicable SOPs that describe the final DE determination process.*

   In your response, you have explained that the medical director is responsible for determining the final donor eligibility (DE); however, that is not stated in your revised SOP CB-MO.1.4. Furthermore, the revised SOP refers to a list of "suitability" criteria for banking but does not specify the process for donor eligibility determination based on the results of the donor screening and the infectious disease tests. There is also no documentation of the final donor eligibility on the CBU File Review Checklist C-Medical Director form that is signed by the medical director.

   The SOP should specify the following:

   - The final donor eligibility is determined by the Medical Director based on the donor screening (including donor medical history interview, review of medical and physical examination records) and infectious disease test results.
   - Whether donors with any risk factors identified during the review of the medical and physical examination records are determined to be ineligible or deferred. We note that on the Cord Blood Maternal Risk Questionnaire Action Guide, you have identified the donor eligibility criteria during the interview with the birth mother.

LifeSouth response:
Sponsor committed to send a new SOP to address the issues on final Donor eligibility determination.

Additional comments regarding SOP CB-MO.1.4 and the CBU File Review Checklist C-Medical Director form:

a. The SOP states that the medical director determines whether the CBU should be listed with notations about "variances" from criteria. Please clarify what you mean by "variances" and how they would impact the final donor eligibility determination and the acceptability criteria of the CBU for licensure.

b. The SOP states that vCJD risk should be documented in the "variations box" on the File Review Checklist C-Medical Director form. Please clarify whether donors with vCJD risk factors are determined to be ineligible or deferred.

c. On Checklist C, the medical director documents whether the unit is acceptable for "banking" but there is no documentation of the final donor eligibility determination and whether the unit is accepted for licensure or use under IND.

LifeSouth response:
The sponsor will send revised check lists including what the medical director considers a unit to be bankable, final donor eligibility determination and whether the units is acceptable for licensure vs. use under IND.

3. *Item #15: Donor Eligibility- We suggest that you add your final DE determination to the Certificate of Analysis. Please note that only units from eligible donors are qualified for licensure.*

   You submitted a revised COA that includes a section for the DE determination but you state that the DE determination is based on medical history only. Please note that the final DE determination must be based on the results for the donor screening (including donor medical history interview, review of medical and physical examination records) and the infectious disease test results. Please submit the revised form.

LifeSouth response:
Will submit a revised COA form.

4. *Item #16: Donor Eligibility- In the BLA summary, on pages 14, 17, and 45, for several infectious disease tests (e.g. ---------(b)(4)----------), you have listed the incorrect manufacturer's name. Please verify the manufacturer of all test kits used and submit the corrected information*

   The document entitled "letter of accreditation" (Attachment C) that you submitted includes a list of the donor tests performed by ----------(b)(4)---------- for blood and apheresis platelet donor specimens. Also multiple manufacturers are listed for several of the donor tests (e.g. ----------(b)(4)----------). Please submit the revised document that specifies the tests that are performed on the cord blood maternal specimens and the kit manufacturers used for testing.

LifeSouth response:
The sponsor explained that for some infectious disease tests, the contract testing lab has multiple assays but they are all FDA-approved, licensed or cleared tests. This is to ensure that appropriate tests are available. Therefore, the sponsor can't specify which specific tests are available at any given time to run the birth mother specimen. The sponsor agreed to provide the explanation in writing and will submit the revised document clearly stating that the listed tests are to be used on the specimens from the birth mother for Cord Blood donor eligibility determination.

5. *Item 18(d): CBU Collection Validation- You listed acceptable contamination rate for collected CBU in the protocol but you did not provide results of the sterility tests performed for this validation.*

   In your response, you stated that only 11 "bankable units" were tested for sterility post-processing but you did not provide the sterility results. Please refer to the additional comments below regarding the collection validation.

LifeSouth response:
The sponsor will provide the data on the 11 CBU collected and tested for sterility.

Addition Comments

Collection validation:

6. *Based on the validation report, you did not conduct the validation according to your own approved validation protocol. Specifically, the validation report did not provide any information regarding the following acceptability criteria defined in the plan:*

   - Collected units expected to be received within 24 hours of collection
   - Acceptable temperature on arrival at the processing lab: (b)(4)
   - Microbial contamination (b)(4)
   - (b)(4) of units meet minimum volume requirement

   Furthermore, the validation report states that minor documentation issues related to the transportation were noted and there were variances with packing/shipping but you did not provide any information regarding the variances, the investigation and the corrective actions.

   The validation is not acceptable unless you submit a revised validation report that includes the data for all the defined acceptability criteria.

LifeSouth response:
The sponsor agreed to submit the collection validation data.

Cord Blood Collection:

7. *Please address the following in SOP CB.2.2: Obtain Mother's Consent, Medical History, and Medical Records and submit the revised document(s):*

a) SOP states that the fact-to-face meeting with the birth mother post- delivery is arranged after a "bankable" unit has been identified. SOP does not define the criteria for a "bankable" unit.

b) SOP states that the full consent and the maternal and family medical history interview are conducted at mother's earliest convenience. Please clarify the following:

   1. What is the maximum time-limit for completing the consent form and the donor questionnaires?
   2. Can collected units be shipped to the processing facility without a signed consent? If yes, how are the signed consent forms and the completed donor questionnaires stored and tracked at the collection facility, and when are the documents sent to the processing facility?
   3. Is infectious disease testing completed prior to obtaining the full donor consent (according to the Pre-collection Nursing procedures, specimens may be collected prior to obtaining consent)?

c) According to SOP CB.7.1.2, the volume of collected units is determined in the laboratory; however, the SOP does not specify the minimum acceptable collection volume prior to processing. Please submit the revised SOP.

LifeSouth response:
The sponsor agreed to submit a revised SOP CB.7.1.2

Storage and Transportation

8. Please address the following in SOP CB.2.4 and submit the revised document:

a) SOP states that in case of temperature excursion during the storage of the collection kits, the affected components would be replaced and the kit returned to the inventory. The SOP doesn't define the parameters used for determining the affects on the kits components as the result of any temperature excursion.

b) Clarify whether the refrigerators at the collection hospitals are dedicated to storage of cord blood units.

c) When units are stored at room temperature, are they placed in a designated container prior to being placed in the transport box for shipment?

d) The SOP does not describe the process for investigating the temperature excursion events and whether the collected units that were affected by the temperature excursion are discarded.

9. Based on SOPs CB.5.3 and CB.6.1, we understand that the maternal specimens are not shipped from the collection hospitals with the collected units. Please submit SOP(s) that describes storage, shipping and transportation of the maternal specimens from the collection sites to the testing laboratory.

10. Based on SOPs CB.6.1 and CB.6.2, we understand that cold or room temperature gel packs for shipping are selected by on the "outside anticipated temperature" (---------(b)(4)----------

----------). Please explain how you ensure that the appropriate gelpack was chosen based on anticipated outside temperatures.

LifeSouth response:
The sponsor confirmed that a transportation validation will be conducted as indicated during the inspection. The sponsor is also considering to use a min-max (range) temperature monitoring device for transportation of CBU from the collection to the processing facility. The sponsor will also submit the SOPs for transportation of maternal specimens.

Donor Eligibility

11. The CBU File Review Checklists D & E do not include the final donor eligibility determination and whether the unit is acceptable for licensure or use under IND. Please submit the revised forms.

LifeSouth response:
The sponsor agreed to submit revised CBU file review checklists.

ISBT 128 Labeling and Donor Tracking

12. Please describe in detail the process for assigning the Donor Identification number (DIN) to the collected units and the maternal specimens starting from the collection hospitals and address the following SOP discrepancy:

a) SOP CB.6.1 states that DIN stickers must be removed from the CBU kit bag but, DIN stickers are not included in the pre-assembled collection kits SOP CB.5.1. The revised SOP(s) must be submitted.

LifeSouth response:
The sponsor agreed to submit revised SOPs CB.5.1.and CB.6.1.

13. Based on the batch records of 3 manufactured lots that you have submitted, we understand that different DINs are assigned to the cord blood unit and the maternal specimens. For example:

Local CBU: ---------(b)(6)-------
Maternal local #:-----(b)(6)---------7

a) Please explain how you maintain linkage between the cord blood unit and the birth mother.

b) Please address the following:

1. According to SOP CB.9.1, the birth mother information, maternal specimen and cord blood collection date and time is entered in the (b)(4). Is this system used at the collection hospital to generate DIN?

LifeSouth response:

The DIN is generated using the (b)(4) system which is at the cord bank. The DIN stickers are included with the collection kits.

2. Explain why the ISBT 128 Facility Identification Number (FID) assigned to the CBU differs from the FID assigned to the maternal specimens. (example above: Local CBU FID: (b)(6), Maternal FID: (b)(6))

LifeSouth response:
The sponsor stated that the Local CBU FID: (b)(6) is to identify the Cord Blood at LifeSouth; whereas the Maternal FID: (b)(6) is to identify the birth mother in LifeSouth Blood Bank. The FID used for the maternal specimens is identical to the FID used for the blood donor testing samples in the blood bank.

3. The Request for Serological Testing form that is sent to the testing laboratory and the Lab Testing Report only include the DIN # that is assigned to the birth mother. Describe how you determine the corresponding CBU for the test result report that you have received.

LifeSouth response:
The sponsor agreed to provide a description for the generation and assignment of the unqiue DIN and how the linkage is maintained between the birth mother and the corresponding CBU.

Note: The following additional comments were communicated to the sponsor:

- FDA suggested the sponsor to send in an example of an updated NMDP report (as an addendum) to the original application as labeling section is outdated.
- During the inspection, the sponsor had indicated that CBUs from birth mothers who had received antibiotics at the time of delivery would be excluded. The sponsor was informed that such criterion was not listed in any of their submitted SOPs. The sponsor will submit revised SOPs.