

Telecon with MD Anderson Cord Blood Bank (December 14 and 19 2017 @ 2:00 pm)

MD Anderson Attendees: Elizabeth Shpall, MD; Jeffrey Wilson; Erin Eaton; Mil Fontenot; Ankita Desai

FDA Attendees 12/14: Virginia, Mercy, Heba, Shyh-Ching, Hanh, Safa, Brad

FDA Attendees 12/19: Mercy and Heba

The following information request was conveyed to sponsor:

Donor Eligibility and Collection:

1. Document P 054.001.002 includes SARS in the list of RCDADs but not Zika virus. The Maternal Risk Questionnaire W 081.092.003 includes screening questions for Zika but no mention of SARS. We request submission of updated documents.
2. For the following scenario: cord blood units that have been released and are available in the NMDP search registry but MDACBB obtained additional information that requires a change in the previously determined eligibility status, and hence licensure status, you state in the response to the 11/9 IR that the unit would be considered unlicensed per policy P 055.001.005. However, no process or procedure is in the submission. We request you submit an SOP to describe the procedure for changing the status of a cord blood unit, from eligible to ineligible.
3. Supplies used for cord blood collection at local collection sites are well controlled. However, at remote collection sites, you state the tissue cleaning solution is “standard” supply on the “delivery tables” at these remote collection site hospitals. We are unable to find where these supplies are qualified or documented at the time of use. You state on the 12/14 telecon that you are aware of this issue and is in the process of implementing procedural changes. Please submit the appropriate SOP.
4. Regarding labeling and tracking:
 - a. Based on documents submitted, it is unclear how many physical labels are printed for each CBID. Your SOPs state the CBID labels are pre-printed prior to distribution to the collection sites. You state the number of physical labels printed for each collection site varies, based on collection site requirements.
 - b. Based on documents submitted, it is unclear when the 13-digit ISBT 128 labels for the maternal blood samples (MBS) are printed and applied to the MBS tubes. SOP S 004.001.005 and S 016.012.002 state the tubes are labeled with CBID MBS-1-5. However, SOP S 007.011.003 state MBS are labelled with the ISBT 128 label with the 13-digit format. On the 12/14 telecon, you state the ISBT 128 labels are distributed to the collection sites. Please clarify the process for printing the ISBT 128 labels for the MBS and when these labels are applied to the MBS tubes.
 - c. Documents submitted do not show how the CBID labels are reconciled, to account for unused, missing, or discarded labels. On the 12/14 telecon, you state the labels are reconciled with each donor packet for which the CBID has been assigned. However, the procedure does not describe how labels are reconciled overall, such as end of year reconciliation. We request you submit SOP for CBID reconciliation.

5. We advised you to submit procedure to describe how new collection sites are qualified prior to collecting cord blood units for process at MDACBB. This addition to the submission packet is advantageous to the sponsor should the sponsor chooses to amend the BLA for addition of new collection sites.

Process Validation:

1. For your validation, you should have, a) a protocol that describes what will be done and also pre-specifies the criteria that will be met, and b) a report that contains the results after execution; you have submitted a report only. There are referenced steps, e.g. *Step 10.5.1, Step 10.4.2, Step 10.8.1*, in the report, but there are no SOPs with these references. Please clarify.
2. Please clarify if the cord blood units used for the validation were collected consecutively.
3. Please specify the reason (i.e. which specification was not met) some of the units did not advance in manufacturing. For example, only (b) (4) out of (b) (4) units collected advanced to pre-processing; and only (b) (4) of the (b) (4) advanced to processing.

Wash and Thaw:

1. Please provide information on the stability of cells after thaw and wash. In other words, under what conditions and for how long can you keep the washed cells prior to infusion into patient. For example, how long if kept at room temperature versus 4°C.
2. Please submit a list of all SOPs and their titles. There are references to SOPs that have not been submitted. For example, SOP 007.019 and others.
3. You calculate cell recoveries based on after wash cell counts that are compared to post thaw cell counts instead of comparing to pre-freeze cell counts. To properly evaluate your wash methods (b) (4) percent cell recovery after 'thaw and wash' should be compared to pre-freeze cell content.
4. Please clarify whether the (b) (4) viability reported is for TNC (b) (4) cells.
5. Please explain (b) (4) recovery for TNC-Post wash versus (b) (4) recovery for 'cells-Overall'.
6. Please

Stability Discussed 12/19:

1. Please explain whether the (b) cord blood units used for stability studies were randomly picked.
2. Please clarify how the cells were washed after thaw (b) (4) wash versus (b) (4) wash).
3. Please clarify whether the (b) (4) viability reported is for TNC (b) (4) cells.
4. Please explain the deviation report on (b) (4) unit with a post was cell recovery of (b) (4).

Flow Cytometry:

1. In your proposed (b) (4) linearity, please be advised that (b) (4) clinical software should be used and not (b) (4) viability template. Please be aware that you should use the same software that the 510(k) kit was cleared on to demonstrate instrument performance.
2. Please be aware that a minimum of (b) (4) data points / concentrations should be included in your linearity study. In addition, please clarify the discrepancy between the number of points

included as stated in V 013.096.001 Tabular Summary of Testing Plan (b) (4) points) and the response to agency request dated 10/11/2017, (b) (4) data points)

3. Please use cord blood samples and not mononuclear cell preparation in your 7AAD linearity study.
4. Please include an example of your (b) (4) strategy in your SOP.
5. You state that "acceptable linearity based on the obtained CD34+ counts from the control material and CBU derived samples (b) (4). However, you use (b) (4) and not percentage to demonstrate linearity between the expected and observed values. Please revise your SOP accordingly.
6. Please include the correct 510(k) number for (b) (4) in CBB V 013.096.001
7. Please include in detail steps to perform instrument QC/QA

Sterility Validation:

Please revise the sterility validation document to include the following specific statements:

- 1) In the protocol of validation studies, please specified the volume (e.g. (b) (4) of (b) (4) containing the specified (b) (4) of (b) (4) (CBB v013.041).
- 2) Please state specifically that no growth was observed in the (b) (4) of cord blood (b) (4) in all the validation studies conducted for the detection of test microorganisms with the required sensitivity using (b) (4)
- 3) Please include the statements that any HPC, Cord Blood unit that exhibits positive growth, either (b) (4), will be deferred and discarded in the section of sterility test protocol. Each (b) (4) tests positive will be sent out to a qualified reference laboratory for identification of the microbial contaminant(s). The records of test samples and microbial culture identifications and characterizations should be maintained for further review.