Post Mid-Cycle Telecon, February 22, 2012 - Ducord

BLA 125407
Minutes: Telecon with Duke: February 22, 2012 11 AM
Duke: Amanda Parrish, Bruce Burnett, Joanne Kurtzberg…
FDA: Mark Davidson, Safa Karandish, Mercy Quagraine, Cheng-Hong Wei, Joydeep Ghosh, Denise Gavin
RE: The FDA set up the teleconference to discuss outstanding CMC issues and to get clarification of some CMC issues prior to PLI scheduled for Feb 27-March 2, 2012.

1) Sponsor was reminded that official information submitted via email should be submitted
as hard copies to the file.

a. Duke stated that they had submitted Am 5 on Tuesday, 2-21-12.

2) Sterility validation studies are ongoing- no additional discussion.
3) Clarification was requested regarding who performs Quality control testing for release and how Quality control system is structured since several different labs are involved in testing at various stages of processing

a. Dr. Kurtzberg stated that Duke does not have a distinct quality control laboratory; that the

1. processing technicians perform in process tests (e.g. volume, cell counts, sterility), some quality control tests (CMV (b)(4))
2. contract labs such as the Duke Stem Cell Laboratory perforem post processing tests[e.g. (b)(4), viability, CD34+ for listing] and
3. Robertson Clinical Translation Laboratory tests thawed segments for potency prior to transplant: (b)(4), viable CD34+/viable (b)(4), TNCC.

ii. Duke agreed to submit additional information regarding the testing structure (who does what, when and where) and responsibilities of personnel in each laboratory (e.g. technician, QA).

b. FDA stated that a quality control system must be in place with SOPs and specific processes for determining release of products. And, that we would evaluate these processes in more detail at the inspection.

4) FDA inquired about the progress on Stability protocol revision.

a. Duke discussed revised program and stated that revised protocol has been submitted. They are working on validation and comparability analysis of assays used in the protocol.

i. Still discussing the use of units at transplant to determine stability, but only those units transplanted at Duke ("Duke to Duke" comparison).

b. FDA indicated that products should meet specified acceptance criteria and we can discuss further after we review the revised protocol.

5) Thawing/washing procedure that accompanies units was discussed.

a. SOP was fairly clear, but validation (manuscript) inadequate

i. Prospective validation with preset criteria

ii. Include method descriptions and information on method suitability

iii. Should include % viability

b. Duke stated they will submit thaw/wash validation procedure for review

6) CD34+ validations studies were discussed:

a. Duke was reminded to submit details and SOPs of the (b)(4) strategy for ------(b)(4)---------- info submitted), text description and sample -(b)(4)- showing the ----------(b)(4)---------- and strategy as well as standard template should be provided;

b. Validation plan for validation studies of the CD34+ cell enumeration and viability assay and CD34/----(b)(4)------ enumeration and viability assay: accuracy, specificity, precision, linearity, limits of detection

c. SOP for ----(b)(4)----- reagent qualification

d. SOP for instrument quality control and maintenance

e. Information on ----(b)(4)----- instrument comparability studies

f. SOP for new ----(b)(4)----- instrument validation

- **Duke stated that they are working on validation of a new method to replace --(b)(4)--- CD34+ method and that they will submit this information when it is available.**

7) Donor Eligibility and Collection of CB (please see attached request for additional information):

a. FDA inquired about the status of collection validation. Duke stated that they were developing the validation plan.

b. FDA inquired about the status of the process for review of birth mother's medical, physical examination records at fixed and non-fixed sites, and assessing the birth mothers for possibility of

plasma dilution prior to the collection of the infectious disease test samples. Duke stated that the review and documentation has been incoporated into their screening procedures. Revised SOPs will be submitted.

c. FDA inquired about the references to "--(b)(4)-- collection sites" and shipment of -(b)(4)- in several SOPs. Duke explained that the references were related to research studies and confirmed that the -(b)(4)- were not packaged and shipped with the collected cord units. Sponsor agreed to remove references to "--(b)(4)-- collection sites" and shipment of -(b)(4)- from the SOPs and forms.

d. FDA discussed sponsor's response to the filing letter regarding the donor eligibility determination. FDA explained that the DE determination must be based on the donor screening and test results and SOPs should define the criteria for eligibility and ineligibility. Also DE must be completed prior to listing the units in the search inventory. Duke stated that they will be revising the process and SOPs.

e. FDA requested clarification regarding shipment of maternal specimens from the collection sites to the CCBB. Duke confirmed that the specimens are shipped in the same shipping container with the collected cord units. They will make the clarifications in the SOP(s) and form(s) and submit the revised documents.

f. FDA informed the sponsor that they will receive a list of comments and questions.

8) Cord Blood processing: additional information was provided late last week, and has not been thoroughly reviewed at the time of the call.

a. FDA inquired about the plan to license only units manufactured by the --(b)(4)-- process (--(b)(4)-- collection) and had they considered options for licensing the larger units that are processed by the -(b)(4)- method. One suggestion was ---------- (b)(4) ------.

b. Dr. Kurtzberg stated that yes, their plan is to license the (b)(4) processed units, and they are working on options for processing the (b)(4) units

https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ApprovedProducts/default.htm

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