Telecon, October 3, 2011 - HPC Cord Blood

RECORD OF TELEPHONE CONVERSATION

Submission Type: BLA Submission ID: 125391/0 Office: OCTGT
Product:
Hematopoietic Progenitor Cells,Cord (HPC-C)
Applicant:
Clinimmune Labs
Telecon Date/Time: 03-October-2011 11:30 AM Initiated by FDA? Yes
Telephone Number: ------(b)(4)------
Communication Categorie(s):
1. Advice – 483 responses, ICF, DE and product clarifications

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Telecon Summary:
Clarification: 483 responses, ICF, DE and product clarifications
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Trans-BLA Group: No
Related STNs: None
Related PMCs: None

Telecon Body: Inspection related items have been recorded in a separate document filed under IRL and are therefore grayed out.

DMPQ – 483 responses

The Sponsor had submitted their responses to FDA issues 483 when the Sponsor's facilities were inspected in August. FDA provided feedback on the items from the 483

and informed the Sponsor if the item was adequately addressed or needed additional information.

Item 1a: Quality Unit. FDA stated that the information presented was a marked improvement, the titles of SOPs are well defined, but there is still comingling of other information. A quality management plan will suffice. For example SOP B100.5 defined the roles and responsibilities of personnel, but also included information on validation which should be limited to validation SOP. The sponsor stated that they included the information, that they felt was useful and was easy to refer back if need be. FDA then suggested titling the SOP as “Quality Management Overview” and then subtitling the SOP, to which the Sponsor agreed.

Regarding the SOP on signatory authority, the SOP has to be more specific since it was not clear who would sign off. The Sponsor stated that they have another SOP for signatory authority, which FDA requested to see. FDA asked the Sponsor to explain the schematics of 5014. FDA also stated that the signatory SOP is very useful to keep handy in the event of future inspections, since the inspectors are used to seeing this information in other facilities they would expect the Sponsor to have it too.

FDA advised the Sponsor to improve their Quality Management SOPs, to specifically define the roles of each quality unit, - process improvement, design control, and change control, and specifically state what they are doing. The Sponsor stated that they have set up a cord blood quality unit that reviews every aspect of production; they have all the adequate documentation that they could stratify in to the three quality units.

FDA advised the Sponsor to better define their quality unit, go through all their appropriate SOPs and have one document to review with some overview information rather than having a Quality Unit subheading and cross referencing another SOP. It was also beneficial to have the signatory authority information in the quality unit.

The Sponsor asked if they can send the updated document via email to the DMPQ team, to which the FDA agreed.

Item 1b-d: Sponsor responses are acceptable.

Item 2: Batch production records are a huge improvement and are acceptable

Item 3: Aseptic Technology was addressed by Dr. Yong Fan, correction is acceptable

Item 4: Has been addressed and the SOP is acceptable

Item 5: Sponsor committed to provide the information in November, this plan is acceptable.

Item 6 a&b: Responses are adequate.

Item 7 a, b & c: Responses are adequate

Item 7d: Freezer validation is not adequate.
Sponsor stated that they are almost ready to invalidate the prefill with ----------(b)(4)----------. FDA requested the Sponsor to include CD34 cells too. The Sponsor stated they were ready to invalidate the (b)(4) and TNC assay, but were unsure how to proceed with these assays. FDA's product chair, Dr.Fan offered to speak with the Sponsor at a later time to provide more information. The Sponsor stated they would submit all the information in November.

Item 8: a. Addressed and complete
b. Will be completed by November

Item 9: a. Response acceptable
b. Discussed
c. Submit a summary report.

Item 10: Will be completed in November, which is acceptable.

Summary of pending items from 483

1a – Quality Plan
5 – Complete summary report for growth promotion
7 – Freezer validation to be completed
9c – Validation submitted, summary report will be submitted when completed
10 – Complete summary report will be submitted when completed

Donor Eligibility (DE)

The DE reviewer informed the Sponsor that she will be reviewing the donor eligibility, donor testing and tracking of information from donor to recipient aspects of the BLA application and requested clarification regarding the number of collection sites the Sponsor planned to use. The Sponsor reviewed some of the sites they used. The DE reviewer stated that there were several SOPs that were submitted in the application and it would help in the review if the Sponsor clarified in tabular form which SOP belonged to a particular site or statewide program, to which the Sponsor agreed.

Regarding SOP C1.200.4, the Sponsor was requested to clarify their definition of ineligible donor versus non conforming unit. The Sponsor stated that DE is based on infectious disease testing. Non conforming is when there is a deviation in the procedure, where potency, purity is not affected, quality control testing process is not completed as it should have been. The unit is distributed via a IND after consulting the physician if they want it. The product will be distributed via BLA if it conforms to all processes exactly.

FDA explained that DE determination must be based on donor screening as well as donor testing. Sponsor was informed that SOP C1.200.4 does not define the criteria for quarantine, non conforming or ineligible donor and there is not adequate documentation of DE determination. FDA asked the Sponsor to address donor eligibility issues in their SOPs, add details regarding the assessment of risk factors during the review of medical and physical exam records. Sponsor was referred to the DE guidance for additional information. Sponsor agreed to revise SOPs.

FDA asked the Sponsor regarding their ineligible units. The Sponsor replied that all units are quarantined till they pass a full DE review, requiring the medical director and quality unit review and the donor ineligible due to history are not released. Units collected between 9/9/07 to 1/08 with RPR testing are discarded or used for research only. FDA asked the Sponsor to update their SOPs to clearly state this information.

FDA also stated that details regarding the assessment of plasma dilution in mothers should be included in the procedures. The Sponsor agreed.

Clinical

Clinical requested some clarifications regarding the Sponsor's submitted SOPs and an update regarding the requested individual informed consent forms for each center the Sponsor has listed.

Product Discussion

FDA asked the Sponsor regarding their collection bags. The Sponsor stated that the collection bags used currently are from (b)(4) which are under a 510k. They have also validated a back up system in case they need it. The back up is -(b)(4)-. The Sponsor stated that the freeze mix with DMSO has a expiration date of ---(b)(4)---, they are working on collecting data for beyond this time period and will update FDA at later date.