Sponsor Telecon, July 13, 2011 - Hemacord

BLA #: 125397

Teleconference Date: July 13, 2011

FDA Participants: Bauer, Steven; McCright, Brenton; Przepiorka, Donna; Bross, Peter F

SPONSOR Participants:
Pablo Rubinstein, M.D. – Vice President, New York Blood Center (NYBC) and Director, National Cord Blood Program (NCBP)
Eva Quinley – Senior Vice President (NYBC), Quality & Regulatory Affairs
Andromachi Scaradavou, M.D. – Medical Director (NCBP)
Michael Zdanowski – Director of Operations (NCBP)
Rodica Ciubotariu, M.D., Ph.D. – Director of Donor Services (NCBP)
Ludy Dobrila, Ph.D. – Associate Director, Processing (NCBP)
Jay Valinsky, Ph.D. – Vice President (NYBC) & Director, Flow Cytometry Laboratory
Sarai Paradiso – Director, Clinical Laboratories (NYBC)
Donna Strauss – Executive Director, Core Operations (NYBC)
Kristin Keshishian – Quality Specialist, Cord Blood (NYBC)
Edwin W. Streun – Director, Regulatory Affairs (NYBC)

1. SOP CB37.0032.1 Follow-Up of Cord Blood Donors – FDA asked that BPD reporting be added to the SOP, and that the revision be submitted to the BLA.

2. SOP CB42.0004.1 Reporting of Infusion-Related Reactions – FDA recommended that the title be broadened to reporting all adverse experiences related to the product, not just infusion-related reactions, and clarified that the 15-days alert should be used for serious and reportable adverse experiences from NMDP, and that the listing of all infusion reactions from SCTOD can be submitted in the periodic reports unless they are serious and reportable. This is just an FYI for the applicant.

3. Outcomes Analysis Plan – FDA recommended that the analyses include aggregate SAE data, that benchmarks be established, and that the plan specify what will happen if a benchmark is reached for a safety event. This is just an FYI for the applicant.

4. Advisory Committee Meeting - FDA volunteered to have a separate telecon with sponsor to address any questions they have about the AC meeting. FDA also suggested that representatives from CIBMTR and NMDP attend the AC meeting with the sponsor to provide a brief overview of their activities and to answer questions from the committee.

5. Dataset – NYBC will be sending in the rest of the data corrections requested in the 7/8/2011 email. FDA also clarified that the dataset must include the actual lot numbers, not fantasy numbers, so that FDA can cross-check the information in the batch files and in the dataset. NYBC will submit a table with the actual CBI IDs and Patient IDs references to the UPNs in the original dataset.

We discussed items from the NCBP point-by-point responses to the FDA questions of June 15, 2011 and June 17, 2011, specifically numbers 12-20 relevant to flow cytometry assay validation.

These items refer to 3 major issues from review of Sections 2.2 and 4.3.2
Assay controls: positive/negative and isotype controls
SOPS: specific for CB
Validation: specific for CB, complete elements of validation as described in FDA guidance

Items 12 and 20 are related to SOPS and new instrument validation.
Sponsor agreed that accuracy, precision, and linearity tests will be used to qualify new instruments.
Item 13: Agreement on CB-specific SOP was not reached, but sponsor clarified the information and supplied arguments that the SOP does not need to be CB-specific. I will revisit this issue when after the telecon requested for next week.

Item 14: Sponsor clarified that the flow lab director is not involved in making the decision to use a CB unit. The flow lab director authorizes release of the data but the NYCB uses this data to make the decision regarding product quality, so the issue of possible use of out-of-specification units is resolved.

Item 15: regarding defective ------(b)(4)------, the sponsor will open an incident report pursuant to SOP 00.0005.7 (Incident Report Initiation – Tracking, Resolution and Reporting) if missing or degraded (b)(4) are detected. This issue is resolved.

Item 16. Sponsor clarified that only --(b)(4)-- mixtures of CD34/CD45 antibody would be used, this issue is resolved.

Item 17: SOPs will be reviewed for accuracy to other records and SOPS on a regular basis, this is resolved.

Item 18: Sponsor will modify the SOP to reflect the requirement for Quality review if there are template changes.
This resolves the issue.

Item 19. Sponsors validation studies do not completely accord with the VALIDATION OF ANALYTICAL PROCEDURES: METHODOLOGY FINAL GUIDANCE July 1999 Updated Oct 2010. In particular, there were no studies addressing limits of detection and limits of quantitation. Also, not all the studies for accuracy, precision, and

linearity were done with multiple lots, multiple operators, multiple machines. We sill discuss these issues in greater detail at a telecon next week. The sponsor believes that most of these issues are resolvable by presentation of existing data.
Regarding studies to support dilution, we discussed that the sponsor should include triggers to re-dilute and re-analyze data in the contingency that a sample had too many cells to count reliably. Sponsor agreed to add this to appropriate SOPs.

Item 20: resolved, see #12 above
Item 21: We agreed to discuss the issues of positive, negative, and isotype controls further at a telecon next week.