DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
1401 Rockville P ke
Rockville, MD 20852-1448

March 9, 2011

Our STN: BL 125397/0

New York Blood Center
Attention: Edwin W. Streun
Director, NYBC Regulatory Affairs
310 East 67th Street
New York, NY 10021

Dear Mr. Streun:

This letter is in regard to your biologics license application (BLA) submitted under section 351 of the Public Health Service Act.

We have completed an initial review of your application dated January 7, 2011 for Hematopoietic Progenitor Cells, Cord (HPC-C) to determine its acceptability for filing. Under 21 CFR 601.2(a) we have filed your application today. The review goal date is November 10, 2011. This acknowledgment of filing does not mean that we have issued a license nor does it represent any evaluation of the adequacy of the data submitted.

We will contact you regarding your proposed labeling no later than October 13, 2011. If post marketing study commitments (506B) are required, we will contact you no later than October 13, 2011.

While conducting our filing review, we identified the following potential review issues:

1. You have indicated in Section 4.1 of the original BLA submission that you propose for licensure all HPC-C manufactured according to Method 4 beginning in August of 2006. Please provide a detailed table indicating the following information for all HPC-Cs you propose to be licensed:

    a. Date of processing;

    b. Location/facility of processing (Long Island vs New York City);

    c. Methods of collection, processing and cryopreservation;

    d. Equipment or devices used in collection, processing, testing and cryopreservation (indicate if a non 510(k) cleared equipment/device is used);

    e. Testing methods.

    f. Demonstration of conformance to cGMPs

2. For any significant changes made during the timeframe proposed for licensure (for example, change to the new facility), please provide the protocols executed and the data obtained to demonstrate that there was no effect on the quality of HPC-C. For any changes that were not considered significant, please explain how you decided that the change would not impact product quality.

3. For the full time period of collections proposed for consideration for licensure, please submit all versions (including dates of implementation) of the following SOPs and all related forms:

   a. Maternal consent

   b. Maternal screening

   c. Maternal testing (including implementation date of each test)

   d. Donor eligibility determination

   e. Notification of mothers or their responsible physicians of positive or indeterminate test results according to local or national regulations

   f. Elicitation and handling of post donation information

4. In sections 4.1.5 and 4.1.6 of the CMC section, you have indicated that since July 8, 2009, you have been using [redacted] collection bags [redacted] The Collection of Cord Blood procedure (CB37.0001.1) and the NCBP Cord Blood Collection Validation (NCBP-VAL-10-021P) only describe use of the [redacted] collection bags. Please provide the following information:

   a. Clarify if the [redacted] collection bags are being used. If yes,

      i. Submit the collection procedure and validation for the [redacted] collection bags.

      ii. Define the criteria for using a specific bag size at the time of collection.

   b. SOPs for collection procedure(s) for HPC-Cs manufactured after August 2006 and prior to July 8, 2009.

5. In Collection of Cord Blood procedure (CB37.0001.1), you state that [redacted] anticoagulant is added to collected cord blood of [redacted] Please describe:

   a. The maximum allowable fill volume for the collection bags.

b. How is the [redacted] anticoagulant volume factored in to your calculation for the cord blood volume? Based on the information in the Accessioning of Cord Blood Units for Processing procedure (CB38.0001.1, step, 6.4.11.16), we note that [redacted] of anticoagulant [redacted (b)(4)]

6. You indicate that cord blood will be collected from multiple birth placenta(s). Please provide the following:

   a. Detailed information on donor identification, labeling and traceability, starting from the delivery room. We note that multiple ID numbers are assigned after placenta(s) has been retrieved from the delivery room (SOP CB37.0001.1).

   b. A description of the process in place to prevent cord blood unit mix-ups in cases of multiple births.

7. We understand that the donor eligibility determination is completed after HPC-Cs are entered into the search inventory. Please provide the following information:

   a. How are HPC-Cs identified and kept in quarantine prior to the completion of the donor eligibility determination (21 CFR 1271.60)?

   b. How are HPC-Cs from donors that are determined to be ineligible identified and stored to prevent improper release (21 CFR 1271.65)?

8. Please provide the descriptions and results of studies validating the specificity, sensitivity, and variability of your HLA and ABO/Rh tests. Please include any descriptions of reference standards and their validation.

9. You have indicated in Section 4.1.3.1 that all testing laboratories are CLIA certified. Please provide the CLIA certification numbers for each laboratory used for maternal infectious disease testing since August of 2006.

10. Please provide a list of major equipment and/or devices used in cord blood processing, testing and storage, including those single-used, disposable, reusable, dedicated and shared, if applicable. Please also provide a summary report on the major equipment and/or device qualifications.

11. Please provide the plans and summary reports of qualifications/validations for clean rooms, HVAC system, environmental monitoring and EMPQ of the clean rooms.

12. Please provide SOPs for line/room clearance and changeover.

13. Please provide a detailed summary for cleaning validation for the NCBP facility and equipment including Biological Safety Cabinets.

14. Please provide the following SOPs:

    a. SOP CB38.0014.1 – Maintenance and Monitoring Equipment;

    b. SOP CB00.0004.1 – Cleaning of the NCBP GMP Process Area;

    c. SOP CB38.0009.1 – Aseptic Process Simulation (Media Fill) of Cord Blood Processing;

    d. SOP CB38.004.1 – [redacted] Sterile Tubing Welder;

    e. SOP CB29.0002.1 – Validation of Cord Blood Processing as an Aseptic Process, using Media Fill;

    f. SOP for spillage cleaning.

15. After a preliminary review of your BLA for the indications as defined in Guidance for Industry Minimally Manipulated, Unrelated Allogeneic Placental/Umbilical Cord Blood Intended for Hematopoietic Reconstitution for Specified Indications" available at: http://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Blood/UCM187144.pdf, we believe that a full pharmacovigilance plan (PVP) as described in "Guidance for Industry: E2E Pharmacovigilance Planning" will not be necessary. Please note, however, that if you submit a supplement for a new indication not covered by the cord blood BLA guidance, a PVP will be necessary.

    For the current BLA for HPC-C, you are expected to comply with the postmarketing safety activities described in the cord blood BLA guidance. Please submit revised SOPs that comply with the outcomes analysis and serious adverse event reporting as described in the guidance. We will be happy to discuss proposed revisions with you prior to submission.

    Please also note that if we identify any new safety issue(s) with your product upon further review, additional postmarketing requirements may be imposed as discussed in "Guidance for Industry Postmarketing Studies and Clinical Trials — Implementation of Section 505(o) of the Federal Food, Drug, and Cosmetic Act."

16. You have provided a dataset with your current outcomes information, but the dataset does not include gender and race as variables. Please submit a revised dataset that includes gender and race for each subject.

17. You have provided in the outcomes dataset the processing date, processing method, TNC and storage time for the HPC-Cs released. Please also identify for each HPC-C, any deviation from the required product characteristics and donor eligibility requirements indicated in the cord blood BLA and in the donor eligibility guidances.

18. You have provided a letter of cross reference to IND 6637. Please clarify if the clinical outcomes and safety data submitted in this BLA was collected on a protocol conducted under that IND.

19. Regarding your February 22, 2011 submission, we were not able to access the prior submissions through the hyperlinks in the table of contents. Please note that in the table of contents, the hyperlinks to all submissions must be accessible; if not, in the future, the new submission will be rejected. For assistance on how to accomplish this in the roadmap format for BLAs, please contact Yudha Rustaman (FDA/CBER Electronic Submissions Team) at Yudha.Rustaman@fda.hhs.gov or call 301-827-1381.

We are providing the above comments to give you preliminary notice of potential review issues. Our filing review is only a preliminary evaluation of the application and is not indicative of deficiencies that may be identified during our complete review. Issues may be added, deleted, expanded upon, or modified as we review the application. If you respond to these issues during this review cycle, we may not consider your response before we take an action on your application. Following a review of the application, we shall advise you in writing of any action we have taken and request additional information if needed.

If you have any questions, please contact the Regulatory Project Manager, Terrolyn Thomas, M.S., M.B.A at (301) 827-6536

Sincerely yours,

Raj K. Puri, M.D., Ph.D.
Director
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