



Our STN: BL 125594/0

BLA FILING NOTIFICATION
August 7, 2015

Cleveland Cord Blood Center
Attention: Wouter Van't Hof, PhD
25001 Emery Road
Suite 150
Warrensville Heights, OH 44128

Dear Dr. Van't Hof:

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 June 9, 2015 for HPC, Cord Blood to determine its acceptability for filing. Under 21 CFR 601.2(a) we have filed your application today. The review goal date is June 9, 2016. 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.

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

Donor Eligibility and Collection

1. Please clarify whether you are using a treponemal or non-treponemal screening test for syphilis. In section 3.1.4A, Table 4A-3 and in SOP-L0025, you have listed (b) (4) (non-treponemal test), but in Table 4-A-8, you have listed (b) (4) (treponemal test). In SOP-L008, you refer to both tests. Furthermore, if you are using a non-treponemal screening test (b) (4), please provide the test kit manufacturer information and explain how you determine the donor eligibility for donors who test reactive with the non-treponemal screening test.
2. Please submit the following documents:
 - a. Maternal Medical and Family History questionnaires and any associated decision or action guides.
 - b. Forms used for documentation of maternal consent and pre-screening, medical record review, labor and delivery information, maternal and infant donor linkage, and cord blood collection.

3. Please submit the SOP(s) that describes how findings related to the clinical and physical evidence of communicable diseases are factored in to the final donor eligibility determination. In SOP-H0012 you only describe the information that you document.
4. Please submit the SOP (including the training materials) that you use to train the cord blood collectors and the staff responsible for screening the birth mothers and the infant donors for relevant communicable diseases.
5. It appears that you intend to use ISBT 128 system. Please note that BLA applicants, who wish to use ISBT 128 identification and labeling standards in lieu of an NDC number, may submit an exemption request from the barcode labeling requirements. The agency will consider the exemption request if the BLA applicant has fully implemented the ISBT 128 labeling systems.

Sterility Test Method Validation:

6. We note that you have cross-referenced the (b) (4) in your application for the sterility test method validation.
 - a. Please specify the sections of the MF that you are cross-referencing by submitting a table indicating the titles of the MF chapters/sections with the respective submission dates, volumes and page numbers.
 - b. Please clarify if you are cross-referencing this MF for the validation of specificity, limit of detection, ruggedness and robustness of both the sterility test incubation/detection instrument (b) (4) and your used media (b) (4). If so, specify the respective sections of the MF as explained under the previous bullet-point.
7. Please provide the following details on your actual incubation/detection instrument (b) (4).
 - a. Model number
 - b. Software version currently loaded and a clarification on if the same version of the software was used during the actual validation studies.
 - c. The installation qualification (IQ), operation qualification (OQ) and performance qualification (PQ) documents/data and a clarification on if (b) (4) has performed those studies.

Flow Cytometry

8. Please explain your back up plan to determine CD34 count for lot release in the case of malfunction of the (b) (4) flow cytometer.

9. Please provide validation data for your viability test.

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, Lori Tull, at (240) 402-8361.

Sincerely yours,

Raj K. Puri, MD, PhD
Director
Division of Cellular and Gene Therapies
Center for Biologics Evaluation and Research