



Advancing Transfusion and
Cellular Therapies Worldwide

**Statement of AABB before the
Cellular, Tissue and Gene Therapies Advisory Committee
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AABB is an international association dedicated to advancing transfusion and cellular therapies worldwide. Our members include 1800 hospital and community blood centers, transfusion and transplantation services and 8000 individuals involved in activities related to transfusion and transplantation medicine. For over 50 years, AABB has established voluntary standards and inspected and accredited institutions. Our members are responsible for virtually all of the blood collected and more than 80 percent of the blood transfused in this country. AABB's highest priority is to maintain and enhance the safety and availability of the nation's blood supply.

AABB thanks the Food and Drug Administration (FDA) for the opportunity to provide a statement on the draft guidance, *Minimally Manipulated, Unrelated, Allogeneic Placental/Umbilical Cord Blood Intended for Hematopoietic Reconstitution in Patients with Hematological Malignancies*. We would like to acknowledge the time and effort that was expended in drafting this guidance document. During the review of the draft document, we noticed a few areas that we believe should be revisited to provide clarity for the personnel that will ultimately have to implement the guidance.

The guidance document does an excellent job of outlining what required and recommended tests should be performed for the licensed products but not for the products previously manufactured. We are pleased that the committee has been asked to discuss the types of data that could be submitted to demonstrate comparability between the previously manufactured HPC-C and HPC-C manufactured currently. There are thousands of products that are in inventory which are acceptable but may not have had the recommended tests performed. Test kits currently in use do not list umbilical cord blood as an appropriate sample for testing. We would also ask that FDA consider what mechanisms might be available to release these products for transplant in the event they cannot be demonstrated to be comparable for purposes of licensure. Another issue that has not been addressed is products imported from Europe. Approximately 20% of the cord blood products that are transplanted in the United States originate from Europe. Products that are collected in Europe may not have had the required and recommended tests performed, and the products may not be licensed by the FDA. It is of great concern that European facilities will not

want to pursue FDA licensure for the products. If this becomes the situation, how does FDA envision the continued use of imported products?

We applaud FDA for the flexibility that they have allowed in the draft document in areas that permit flexibility. However, in review of the draft document, we did find two areas where flexibility should be incorporated.

- The results of hemoglobinopathy testing is not dependent on when the cord blood sample is collected (i.e., pre- or post-volume reduction) but according to the draft guidance only the pre-volume reduction sample is acceptable. Therefore, we recommend that the appropriate sample type be modified to include the use of a post-volume reduction sample.
- In the draft document, it is recommended that the validation summary include data from the manufacture, as well as the thawing and cryoprotectant removal. While we agree that processes to be performed must be validated, not all facilities will perform the process of cryoprotectant removal. Different protocols/procedures for administration of HPC-Cs may or may not require the removal of cryoprotectant prior to administration. There is usually very little DMSO in an umbilical cord blood unit and only patients under approximately 15kg would potentially need to have the product washed. Therefore, the requirement to validate the process to remove cryoprotectant should be clarified so that the process is validated only if the procedure is performed.

The draft guidance document states that sterility of these products must be performed using the testing methodology defined in 21 CFR part 610.12. As the committee is aware, many of the cord blood banks are using one of the automated methods for sterility testing. Please comment on the necessity for validating the automated method vs the CFR method. If required, please comment on the validity of submitting a collaborative validation study from multiple banks which could then be used by all banks for justification for not doing the CFR method.

The proposed requirement for the labeling of these products with a National Drug Code (NDC) number raises serious risk-benefit concerns. This has been previously addressed with comments to the docket in response to the August 29, 2006, draft guidance document, *"Requirements for Foreign and Domestic Establishment Registration and Listing for Human Drugs, Including Drugs that are Regulated Under a Biologics License Application, and Animal Drugs."* It is our position that the NDC system is not a good fit for placental/umbilical cord blood products or other therapeutic cells and that manufacturer and consignee's worldwide receiving them for patient infusion and/or transplantation are already implementing a system that was developed specifically for them. The system that has been voluntarily accepted by the international cellular therapy community is the ISBT 128 standard. The community has invested much time and money in developing the system as well as implementation plans. A careful review of the facts indicate that use of the NDC numbering system in addition to the already existing ISBT 128 system does not offer any increase in patient safety. In fact, we would argue that implementing NDC codes for placental/umbilical cord blood products or other therapeutic cells will hinder the progress of implementing the superior ISBT 128 information standard for these products.

We request that FDA carefully consider patient safety issues when evaluating the requirement for NDC codes on these products, for ultimately having to utilize two different labeling systems will negatively impact patient safety and provide opportunity for increased errors during the manufacturing process. If the primary purpose for the use of NDCs on cord blood products is to maintain a list of manufacturers and their products, we propose that the information could be captured more efficiently and economically via a modified facility registration form. We believe that the NDC system is not a reasonable option for improving the safety of cord blood products and that these products should be exempt from requirements found in 21 CFR Part 201 and 207 for the use of the NDC system.

Regarding the final question to the committee today – we believe that a set of recommendations for HPC-A similar to what has been proposed for HPC-C is appropriate to demonstrate safety and efficacy of HPC-A products.

The majority of the comments presented today are the result of an interorganizational work group consisting of AABB, International Society for Cellular Therapies (ISCT) and National Marrow Donor Program (NMDP). Overall, the work group believes this is a comprehensive and well prepared guidance document. The work group's comments on the draft guidance document will be submitted to the docket by the April 17, 2007, closeout date.

Again, we thank the committee for the opportunity to make this presentation today. To the Executive Secretary, we wish to comment on the draft *Guidance for Industry: Advisory Committee Meetings — Preparation and Public Availability of Information Given to Advisory Committee Members* that was issued in February. We commend FDA for drafting these recommendations as we believe it is important for information to be publicly released as early as possible. The ability to prepare a focused presentation for today's Open Public Hearing was dependent on knowing what the committee is being asked to consider. In cases, such as today, where information that would be considered to be exempt from disclosure under the Freedom of Information Act is to be discussed, release of the Briefing Information and Questions to the Committee prior to 48 hours would have been beneficial to the committee's consideration of all applicable information.