

Guidance for Industry and FDA Staff

Investigational New Drug Applications for Minimally Manipulated, Unrelated Allogeneic Placental/Umbilical Cord Blood Intended for Hematopoietic and Immunologic Reconstitution in Patients with Disorders Affecting the Hematopoietic System

Additional copies of this guidance are available from the Office of Communication, Outreach and Development (OCOD), (HFM-40), 1401 Rockville Pike, Suite 200N, Rockville, MD 20852-1448, or by calling 1-800-835-4709 or 301-827-1800, or e-mail ocod@fda.hhs.gov, or from the Internet at

<http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>.

For questions on the content of this guidance, contact OCOD at the phone numbers or e-mail address listed above.

**U.S. Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research
March 2014**

Contains Nonbinding Recommendations

Table of Contents

I.	INTRODUCTION.....	1
II.	BACKGROUND	2
III.	SCOPE OF THIS GUIDANCE	3
IV.	SPONSORS AND INVESTIGATORS	4
V.	PREPARING INDS FOR CERTAIN HPC, CORD BLOOD UNITS	5
VI.	ADDITIONAL INFORMATION.....	11
VII.	REFERENCE.....	12

Guidance for Industry and FDA Staff

Investigational New Drug Applications for Minimally Manipulated, Unrelated Allogeneic Placental/Umbilical Cord Blood Intended for Hematopoietic and Immunologic Reconstitution in Patients with Disorders Affecting the Hematopoietic System

This guidance represents the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the appropriate FDA staff. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

I. INTRODUCTION

We, the Center for Biologics Evaluation and Research (CBER), FDA, are providing advice to you, potential sponsors (e.g., cord blood banks, registries, transplant centers, or individual physicians serving as sponsor-investigators), to assist in the submission of an Investigational New Drug Application (IND) for certain hematopoietic progenitor cells from placental/umbilical cord blood (HPC, Cord Blood)¹, when such HPC, Cord Blood units are not licensed in accordance with Title 21 of the Code of Federal Regulations Part 601 (21 CFR Part 601), and when a suitable human leukocyte antigen (HLA) matched cord blood transplant is needed for hematopoietic and immunologic reconstitution in patients with disorders affecting the hematopoietic system that are inherited, acquired, or result from myeloablative treatment and there is no satisfactory alternative treatment available. If unlicensed HPC, Cord Blood units are made available for clinical use, they must be distributed under an IND meeting the applicable requirements in 21 CFR Part 312.

This guidance finalizes the draft guidance of the same title dated June 2013, (78 FR 36194) and supersedes the guidance entitled “Guidance for Industry and FDA Staff: Investigational New Drug Applications (INDs) for Minimally Manipulated, Unrelated Allogeneic Placental/Umbilical Cord Blood Intended for Hematopoietic Reconstitution for Specified Indications” dated June 2011 (August 2, 2011, 76 FR 46303) (2011 IND guidance). The changes from the 2011 IND guidance include replacing the term “HPC-C” with the term “HPC, Cord Blood,” which is the proper name for these products, expanding the clinical indication, and clarifying the applicability of the requirement for a table of contents in the IND submission.

¹ For the purposes of this guidance, the term “HPC, Cord Blood” refers to the final drug product (cryopreserved or thawed) of minimally manipulated hematopoietic stem/progenitor cells from placental/umbilical cord blood, sourced from an unrelated allogeneic cord blood donor and intended for hematopoietic and immunologic reconstitution in patients with disorders affecting the hematopoietic system that are inherited, acquired, or result from myeloablative treatment.

Contains Nonbinding Recommendations

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe FDA's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in FDA's guidances means that something is suggested or recommended, but not required.

II. BACKGROUND

In the *Federal Register* notice dated January 17, 2007 (72 FR 1999), FDA announced the availability of the draft guidance for licensure of minimally manipulated cord blood entitled "Guidance for Industry: Minimally Manipulated, Unrelated, Allogeneic Placental/Umbilical Cord Blood Intended for Hematopoietic Reconstitution in Patients with Hematological Malignancies" dated December 2006 (2006 draft licensure guidance). FDA received comments on the 2006 draft licensure guidance, those comments were considered, and the guidance was finalized.

In the *Federal Register* notice dated October 20, 2009 (74 FR 53753), FDA announced the availability of the finalized guidance entitled "Guidance for Industry: Minimally Manipulated, Unrelated Allogeneic Placental/Umbilical Cord Blood Intended for Hematopoietic Reconstitution for Specified Indications" dated October 2009 (2009 licensure guidance). The 2009 licensure guidance provided recommendations to cord blood manufacturers applying for licensure of their HPC, Cord Blood units for specified indications.

Some of the comments received by FDA on the 2006 draft licensure guidance expressed the importance of access and availability of HPC, Cord Blood units that do not meet standards for licensure and therefore cannot be licensed. FDA acknowledged that there would be situations in which there will not be a licensed cord blood unit that provides an appropriate match for a patient and that an unlicensed cord blood unit may be the best match. Because we recognized the importance of these products, we published the companion draft IND guidance in October 2009 to address IND submissions for unlicensed HPC, Cord Blood. FDA finalized the draft IND guidance in August 2011 (2011 IND guidance).

In addition to issuing this guidance, which supersedes the 2011 IND guidance, we are also issuing a guidance which supersedes the 2009 licensure guidance, entitled "Guidance for Industry: Biologics License Applications for Minimally Manipulated, Unrelated Allogeneic Placental/Umbilical Cord Blood Intended for Hematopoietic and Immunologic Reconstitution in Patients with Disorders Affecting the Hematopoietic System" dated March 2014 (2014 licensure guidance). As discussed therein, the 2014 licensure guidance expands the clinical indication that was in the 2009 licensure guidance and makes additional clarifying changes.

The clinical indications contained in this guidance differ from the indications listed in the scope of the 2011 IND guidance and the 2009 licensure guidance. This difference is a result of the Agency's re-examination of the legacy docket data and the Agency's consideration of the

Contains Nonbinding Recommendations

proceedings of the September 2011 meeting of the Cellular, Tissue, and Gene Therapies Advisory Committee (Ref. 1).

III. SCOPE OF THIS GUIDANCE

This guidance document is applicable to certain unlicensed HPC, Cord Blood units that are made available for transplantation in cases when no satisfactory alternative treatments are available.

Thus, this guidance applies to HPC, Cord Blood units that are:

- Manipulated minimally; and
- Intended for use in unrelated donor hematopoietic progenitor cell transplantation procedures in conjunction with an appropriate preparative regimen for hematopoietic and immunologic reconstitution in patients with disorders affecting the hematopoietic system that are inherited, acquired, or result from myeloablative treatment.

This guidance does not apply to the use of unlicensed HPC, Cord Blood for indications other than described above. In addition, this guidance does not apply to any use of licensed HPC, Cord Blood.

There are a variety of reasons why an HPC, Cord Blood unit may not be licensed. For example, these reasons may include:

- The HPC, Cord Blood unit does not meet the standards for licensure. This could be the case for units that were placed in inventory either before or after the cord blood bank received a biologics license. HPC, Cord Blood units that do not meet all licensure criteria may be banked or maintained to enhance diversity of HLA phenotypes of units in inventory to increase the likelihood that individuals with less common HLA types will be able to find suitably matched HPC, Cord Blood units for transplantation. Examples of units that do not meet licensure criteria include:
 - HPC, Cord Blood unit with a cell dose smaller than the value of the licensed product; however, the smaller cell dose unit may be appropriate for use in some pediatric patients.
 - HPC, Cord Blood unit from an ineligible donor or from a donor who did not undergo complete screening and testing. For example, in donors with a complete donor eligibility determination, an ineligible donor is one who has an identified risk factor or a reactive/positive test result. In the event that the HPC, Cord Blood unit is from an ineligible donor, the HPC, Cord Blood unit may only be used if there is a documented urgent medical need as defined in 21 CFR 1271.3(u) and the requirements described in 21 CFR 1271.65 are met. Similarly, an HPC, Cord Blood unit from a donor for whom the donor eligibility determination is not complete may only be used, if there is a documented urgent medical need as defined in 21 CFR 1271.3(u) and the requirements in 21 CFR 1271.60 are met.

Contains Nonbinding Recommendations

- HPC, Cord Blood units that are not comparable to licensed inventory. For example, HPC, Cord Blood release criteria are different from those in the product license and insufficient information is available to demonstrate their comparability, e.g., lower total nucleated cell count (TNC), or the CD34⁺ cell count was not performed.
- HPC, Cord Blood units that were manufactured prior to licensure that do not conform to current good manufacturing practices (CGMPs).
- The HPC, Cord Blood unit was manufactured in a cord blood establishment that does not hold an approved Biologics License Application (BLA) for manufacturing HPC, Cord Blood units.
 - The HPC, Cord Blood unit is in a bank where a license application has not yet been submitted or is pending.
 - The HPC, Cord Blood unit is in a non-United States bank without a license and is listed in an international cord blood registry.

IV. SPONSORS AND INVESTIGATORS

The HPC, Cord Blood units described in section III of this guidance, may be made available for clinical use when an IND is submitted to FDA and the IND goes into effect under 21 CFR 312.40(b). The individual or entity that submits an IND is considered a sponsor (21 CFR 312.3(b)). The sponsor of the IND may be the manufacturer (generally a cord blood bank), a transplant center, or a national or international cord blood registry involved in coordinating the distribution of HPC, Cord Blood units from participating cord blood banks.

A physician seeking to transplant an unlicensed HPC, Cord Blood unit may serve as an investigator under the IND, but a physician also can be a sponsor-investigator (21 CFR 312.3(b)). A licensed physician under whose immediate direction an investigational drug is administered or dispensed is considered an investigator. A licensed physician under whose immediate direction an investigational drug is administered or dispensed, and who also submits an IND as described in this guidance, is considered a sponsor-investigator, and must comply with the requirements applicable to a sponsor and investigator set forth in 21 CFR Part 312 Subpart D to the extent they are applicable to the IND (21 CFR 312.3(b)).

Sponsors are responsible for:

- Submitting IND safety reports and annual reports (when the IND or protocol continues for one year or longer) to FDA as required by 21 CFR 312.32 and 21 CFR 312.33.
- Obtaining a curriculum vitae or other statement of qualifications of the licensed physician(s) in order to ensure that the physician is qualified to administer the investigational drug (21 CFR 312.53(c)(2)).
- Providing licensed physicians who will be administering the investigational drug with an investigator brochure, as well as information about new observations, particularly

Contains Nonbinding Recommendations

with respect to adverse effects (21 CFR 312.55) in order to minimize the risk and maximize the potential benefits of the investigational drug. (Note: A sponsor-investigator is not required to prepare an investigator brochure.) (21 CFR 312.55).

- Maintaining an effective IND with respect to the investigations (as set forth in the IND regulations in 21 CFR 312.50).
- Maintaining adequate drug disposition records, and other required records in a manner consistent with the requirements of 21 CFR 312.57.

Investigators are responsible for:

- Reporting adverse drug events to the sponsor (21 CFR 312.64(b)).
- Ensuring that the informed consent requirements of 21 CFR Part 50 are met.
- Ensuring that Institutional Review Board (IRB) review of the use of the HPC, Cord Blood units under the IND is obtained in a manner consistent with the requirements of 21 CFR Part 56.
- Maintaining accurate case histories and drug disposition records and retaining records in a manner consistent with the requirements of 21 CFR 312.62.

V. PREPARING INDs FOR CERTAIN HPC, CORD BLOOD UNITS

This guidance document outlines the minimum information that should be included in an IND for the HPC, Cord Blood units described in this guidance. Sponsors who follow this guidance may choose to either submit one IND to cover the use of multiple cord blood units, or submit a separate IND for each single-patient use. The general content and format of information to be included in the submission of an IND can be found in 21 CFR 312.23. The minimal information that should be included in the IND for the HPC, Cord Blood units for which this guidance is applicable is summarized in Table A. Note that the requirements listed in Table A are not meant to be an exhaustive list. Additional regulatory requirements in 21 CFR Part 312 may be applicable.

Contains Nonbinding Recommendations

TABLE A: MINIMAL INFORMATION TO BE INCLUDED IN THE IND²

A. Cover Sheet (21 CFR 312.23(a)(1))	Form FDA-1571
B. Table of Contents (21 CFR 312.23(a)(2))	All applications must include a table of contents; we expect that a table of contents for requests for treatment of a single patient will be brief.
C. Introductory Statement (21 CFR 312.23(a)(3))	Description of intended use and reason(s) why HPC, Cord Blood units cannot be licensed.
D. Investigator’s Brochure (21 CFR 312.23(a)(5))	Product description and instructions for use.
E. Protocol (21 CFR 312.23(a)(6))	Include treatment plan, safety monitoring, outcomes assessment, safety reporting plan, and model consent form.
F. Donor Eligibility (21 CFR Part 1271 Subpart C)	Include description of donor eligibility determination.
G. Manufacturing, Release Testing and Specifications (21 CFR 312.23(a)(7))	Summary of manufacturing information. Summary of product testing: <ul style="list-style-type: none"> • Sterility (no evidence of contamination) • Total Nucleated Cell (TNC) count • Cell viability • HLA • ABO/Rh • Hemoglobin testing

² The information in the right column reflects certain regulatory requirements and/or what FDA considers current best practices.

Contains Nonbinding Recommendations

<p>H. Labeling (21 CFR 312.23(a)(7), 21 CFR 1271.55, 21 CFR 1271.60(d)(2), 21 CFR 1271.65(b)(2))</p>	<p>Container label and English language supplemental labeling (if applicable) as described in the regulations, including:</p> <ul style="list-style-type: none"> • Donor eligibility summary of records (for HPC, Cord Blood units manufactured on or after May 25, 2005) • Directions for use • Caution statement for IND use • Warning of communicable disease risk
<p>I. Pharmacology/Toxicology (21 CFR 312.23(a)(8))</p>	<p>It is unlikely that this requirement would be applicable.</p>
<p>J. Prior Human Experience (21 CFR 312.23(a)(9))</p>	<p>It is unlikely that this requirement would be applicable.</p>
<p>K. Charging for Investigational Drugs under an IND (21 CFR 312.8)</p>	<p>A request to charge, in accordance with the regulation, may be included.</p>

A. Cover Sheet – The cover sheet must include: the sponsor’s name, address, and telephone number; date of the application; commitment that an IRB will be responsible for review and approval of the study; name and title of the person responsible for monitoring the clinical investigation; and signature of the sponsor. A Form FDA-1571 is used to convey this information, available at <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083533.pdf>.

B. Table of Contents – As indicated above, all applications must include a table of contents. We expect that a table of contents for requests for treatment of a single patient will be brief.

C. Introductory Statement – The cover letter should plainly indicate that the IND is being submitted in accordance with this guidance. The cover letter should also indicate the reason(s) why the HPC, Cord Blood unit(s) to be used cannot be licensed (see section III of this guidance for applicable indications).

D. Investigator’s Brochure (IB) – An IB is required when the sponsor is distributing an HPC, Cord Blood unit to an investigator. A sponsor-investigator is not required to prepare an IB. The recommended format for an IB is outlined in Chapter 7 of the ICH E6 document “Good Clinical Practice: Consolidated Guidance” dated April 1996, available at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM073122.pdf>. At a minimum, the IB must describe the product and its formulation (cell content and additives), and contain a description of possible risks. Instructions for HPC, Cord

Contains Nonbinding Recommendations

Blood handling, thawing and administration, and instructions for reporting a serious adverse event related to the product should also be included.

E. Protocol – A request to treat a single patient should include in the cover letter, or an additional separate document, the patient’s diagnosis, treatment history and relevant comorbidities, the treatment plan (including minimum HPC, Cord Blood cell dose), safety monitoring schedule, safety reporting plan, and consent form. For a request to treat multiple patients, the protocol should include the subject eligibility requirements, treatment plan, safety monitoring, outcomes assessment, safety reporting plan, and model consent form (21 CFR 312.23(a)(6)(iii)). The details in the protocol may be limited to use of the HPC, Cord Blood units alone. The outcome assessment should include a plan for data review to determine whether any adverse experience (e.g., seroconversion or other evidence of relevant communicable disease agent or disease transmission, failure to engraft) or other serious or unexpected outcomes identified may be due to problems with product manufacture. Alternatively, a conventional protocol with scientific objectives may be submitted. In all cases, the diagnoses for eligibility are limited to those listed in section III of this guidance.

F. Donor Eligibility – For HPC, Cord Blood units manufactured on or after May 25, 2005, you must follow 21 CFR Part 1271 Subpart C (Donor Eligibility Regulations) including the requirement that a donor eligibility determination must be made for each allogeneic HPC, Cord Blood donor. For a request to treat a single patient, the IND should include the results of the donor eligibility determination (See 21 CFR 1271.55(b) Summary of records). For a multiple patient protocol, the IND should describe procedures used for making a donor eligibility determination. Additional information about the donor eligibility determination is available in the FDA guidance entitled “Guidance for Industry: Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps)” dated August 2007, available at <http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/CellularandGeneTherapy/ucm072929.htm>. For HPC, Cord Blood units manufactured before May 25, 2005, describe the donor screening and testing performed to prevent the spread of communicable disease. In the event that the HPC, Cord Blood is from an ineligible donor, the HPC, Cord Blood unit may only be used if there is a documented urgent medical need as defined in 21 CFR 1271.3(u) and the requirements described in 21 CFR 1271.65 are met. Similarly, an HPC, Cord Blood unit from a donor for whom the donor eligibility determination is not complete may only be used, if there is a documented urgent medical need as defined in 21 CFR 1271.3(u) and the requirements in 21 CFR 1271.60 are met. See Section H of this guidance, for additional labeling requirements for HPC, Cord Blood units from ineligible or incompletely screened and tested donors.

G. Manufacturing, Release Testing and Specifications – In this section of the IND, you should provide a summary of the manufacturing of the HPC, Cord Blood, which includes a description of the processing, testing performed on the unit, test methods used, and the acceptance criteria for test results that should be obtained before the unit is released for use in patients. The description of processing should include information on volume reduction such as plasma reduction, red cell depletion, or other nucleated cell concentrating methods that were

Contains Nonbinding Recommendations

used. The manufacturing information should also include the description of the cryopreservation procedure and storage.

FDA acknowledges that there will be circumstances in which the IND sponsor may not be able to obtain all of the information on processing and testing of the various HPC, Cord Blood units. In particular, this may be true if the HPC, Cord Blood units that are used under the IND are from a wide range of manufacturers where different procedures, test methods, and acceptance criteria are used. In such cases, an IND sponsor should describe the criteria they will use to select an HPC, Cord Blood unit and what, if any, additional testing will be performed prior to transplantation (e.g., confirmation of HLA). This description should include how you will review accompanying manufacturing records and testing results, donor records, labels and labeling, and what criteria you will use to make decisions on the acceptability of the HPC, Cord Blood. You should obtain as much information as possible from the manufacturer and submit that information to the IND. We also recommend that you provide in each annual report a cumulative list of the manufacturers that provided the HPC, Cord Blood units and the information on how the HPC, Cord Blood was manipulated before cryopreservation (e.g., volume reduction).

We suggest that the minimum acceptance criteria for an HPC, Cord Blood unit meet the release criteria recommended in the 2014 licensure guidance. For pre-cryopreservation testing, this would include:

- Sterility testing: No evidence of microbial contamination.
- TNC count: $\geq 5.0 \times 10^8$ TNC/unit HPC, Cord Blood (based on 20 kg recipient, a target dose of $\geq 2.5 \times 10^7$ nucleated cells/kg and $\geq 70\%$ post-thaw recovery = 1.7×10^7 nucleated cells/kg).
- Viable CD34⁺ cell number: 1.25×10^6 viable CD34⁺ cells/unit HPC, Cord Blood (based on CD34⁺ cells $\geq 0.25\%$ of TNC prior to freezing).
- Cell viability: $\geq 85\%$ viable nucleated cells.
- Identity (HLA, ABO/Rh): Report.
- Hemoglobin testing: Report.

We understand that failure to meet these criteria may be one of the reasons that a unit will need to be used under IND. Therefore, alternative specifications and the conditions where the alternative would be justified should be clearly defined and supported in the IND submission. Results of other tests used to evaluate the HPC, Cord Blood should be reported. For example, results of such testing may include nucleated red blood cell content, colony forming unit assay (CFU), and other phenotyping analysis.

If the IND sponsor is also the manufacturer, the IND should include instructions for the transplant center or end user regarding how the HPC, Cord Blood should be prepared for administration. Such instructions may include procedures for: thawing; washing to remove cryoprotectant; dilution; and reformulating for administration. If the IND sponsor is not the manufacturer, we recommend that the instructions from the manufacturer be followed for thawing and preparation of the unit.

Contains Nonbinding Recommendations

Manufacturing information may be incorporated by reference from another regulatory file, such as another IND or a drug master file. This allows FDA to use information in that referenced regulatory file to support the review of your IND. To reference another regulatory file, you must obtain and include in your IND application a signed letter of cross reference stating that FDA has permission to access this information (21 CFR 312.420(b)). This authorization letter must specify the information to be referenced and where the information is located in the referenced file (21 CFR 312.420(b)). See 21 CFR 314.420 for information on drug master files.

H. Labeling – Labeling includes the container label and all documents that accompany the HPC, Cord Blood. A representative copy of all container labels and English language supplemental labeling (if applicable), as described in the regulations, should be submitted in the IND. In addition, a description of how the immediate package label will be attached to the HPC, Cord Blood unit should be submitted in the IND. For example, the sponsor may propose and justify the use of tie-tags, a second overwrap, or other means at the time of distribution.

The immediate package label must include the statements, “Caution: New Drug - Limited by Federal (or United States) law to investigational use” (21 CFR 312.6(a)).

The donor eligibility summary of records must accompany the HPC, Cord Blood at all times (for HPC, Cord Blood units manufactured on or after May 25, 2005 (21 CFR 1271.55)). You should also provide instructions for preparation and administration of the HPC, Cord Blood with the HPC, Cord Blood unit.

Additional labeling requirements may also be applicable. If the requirements in 21 CFR 1271.75, 21 CFR 1271.80 and 21 CFR 1271.85 have not been fully satisfied, the HPC, Cord Blood unit must be labeled according to the requirements in 21 CFR 1271.65(b)(2) or 21 CFR 1271.60(d)(2), whichever applies.

If, upon completion of all required donor screening and testing, the donor is determined to be ineligible, the HPC, Cord Blood unit must be labeled with the Biohazard legend and with the statement “WARNING: Advise patient of communicable disease risks.” (21 CFR 1271.65(b)(2)); and the risk factor must be listed in the summary of records (21 CFR 1271.55(b)(4)). If, on completion of all required donor screening and testing, the donor is determined to be ineligible because the donor has a positive test result, the HPC, Cord Blood unit must additionally be labeled with the statement “WARNING: Reactive test results for (name of disease agent or disease).” (21 CFR 1271.65(b)(2)).

The labeling requirements for HPC, Cord Blood units from donors who have not been completely screened and tested and that are to be used under conditions of urgent medical need (21 CFR 1271.60(d)(1)) are different from the labeling requirements described above. If the donor eligibility determination has not been completed, the HPC, Cord Blood unit must be labeled, “NOT EVALUATED FOR INFECTIOUS SUBSTANCES” and “WARNING: Advise patient of communicable disease risks.” The results of any required donor screening and testing that have been completed, as well as a list of any required screening or testing that have not yet been completed, must accompany the HPC, Cord Blood unit (21 CFR 1271.60(d)(2)).

Contains Nonbinding Recommendations

In situations where the HPC, Cord Blood units are obtained from various manufacturers that do not use similar labeling procedures, the IND should describe your proposed approach to complying with the applicable regulations.

I. Pharmacology/Toxicology – No pharmacology or toxicology information is required for INDs submitted in accordance with this guidance. If the product is such that additional information is needed to demonstrate that the product is safe to use in humans in the dose and route planned, then it is likely this guidance does not apply.

J. Prior Human Experience – No summary of prior human experience is required for the INDs submitted in accordance with this guidance. A description of the prior human experience is available at www.regulations.gov under Docket numbers FDA-1997-N-0010 (Legacy Docket number 1997N-0497) and FDA-2006-D-0157 (Legacy Docket number 2006D-0514), which contain the data used to develop this guidance and the 2013 draft licensure guidance. If additional information about prior human experience is needed to support the proposed protocol, then it is likely this guidance does not apply.

K. Charging for Investigational Drugs under an IND – You must obtain prior written authorization from FDA to charge for an investigational drug used under an IND (21 CFR 312.8(a)(3)). For INDs submitted in accordance with this guidance, a request to charge may be included. The request must comply with the requirements set forth by 21 CFR 312.8, and include the amount to be charged and the documentation for the calculation of that amount.

VI. ADDITIONAL INFORMATION

Although an IND sponsor may not be the manufacturer of an HPC, Cord Blood unit, the sponsor is responsible for the chemistry, manufacturing and control (CMC) information as well as the labeling information as described in this guidance, in addition to the clinical protocol. You may request a pre-IND meeting with FDA during which you can pose specific questions to the FDA review team. For information on requesting pre-IND meetings, please see the following “Guidance for Industry: Formal Meetings With Sponsors and Applicants for PDUFA Products” dated February 2000, available at: <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM079744.pdf>, which addresses how to request a pre-IND meeting.

Contains Nonbinding Recommendations

VII. REFERENCE

1. Cellular, Tissue and Gene Therapies Advisory Committee (CTGTAC) Meeting #53 September 22-23, 2011. Transcripts available at <http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/BloodVaccinesandOtherBiologics/CellularTissueandGeneTherapiesAdvisoryCommittee/ucm280554.htm>.