



FOOD AND DRUG ADMINISTRATION
CENTER FOR BIOLOGICS EVALUATION AND RESEARCH

MEMORANDUM

References for the Regulatory Process

Thank you for inquiring with the Center for Biologics Evaluation and Research (CBER), Office of Cellular Tissue and Gene Therapies (OCTGT) regarding your proposed product. In preparation for future communications please see the following references which may address some of your initial questions, and give you a better understanding of the regulatory process. After reviewing this information please contact the OCTGT Branch Chief, Regulatory Management Staff if you would like to set up a pre-Investigational New Drug application (IND) meeting.

GENERAL INFORMATION AND REFERENCES

1. OCTGT organization, mailing address, and contact numbers:

Food and Drug Administration
Center for Biologics Evaluation and Research
Office of Cellular Tissue, and Gene Therapies
Document Control Center, HFM-99, Suite 200N
1401 Rockville Pike
Rockville, MD 20852-1448

Phone Number: 301-827-5102
Fax Number: 301-827-9796

OCTGT is comprised of 3 Divisions in addition to the Office of the Director which includes the Regulatory Management Staff (RMS):

- Division of Cellular and Gene Therapies (DCGT)
- Division of Clinical Evaluation and Pharmacology/Toxicology (DCEPT)
- Division of Human Tissues (DHT)

These Divisions constitute the 3 main review disciplines of the regulatory process: Product, Preclinical (pharmacology/toxicology), and Clinical. For additional information about CBER please see

<http://www.fda.gov/cber/about.htm>.

2. **Formal Communications:** “Guidance for Industry: Formal Meetings With Sponsors and Applicants for PDUFA Products” found at: <http://www.fda.gov/cber/gdlns/mtpdufa.htm>. This document provides guidance regarding requesting and preparing for formal meetings with the FDA. The most common initial meeting with the FDA is a pre-IND meeting (21 CFR 312.82).

Please see SOPP 8101.1 – “Scheduling and Conduct of Regulatory Review Meetings with Sponsors and Applicants” found at <http://www.fda.gov/cber/regsopp/81011.htm> for additional information regarding the scheduling and conduct of formal meetings.

3. **Information on Submitting an Investigational New Drug Application for a Biological Product** found at <http://www.fda.gov/cber/ind/ind.htm>. You will find links to applicable regulations, including: the IND regulations contained in 21 CFR Part 312, which also address foreign clinical trials not conducted under IND; the informed consent regulations at 21 CFR Part 50, the Institutional Review Board regulations at 21 CFR Part 56 and other regulations. Please also see <http://www.fda.gov/cber/ind/indpubs.htm> which lists guidances related to submission of INDs.

Procedure for formatting document for submission is addressed in “**SOPP 8007 – DCC Binding Procedures for Regulatory Documents.**” It is available at <http://www.fda.gov/cber/regsopp/8007.htm>.

4. General information about **electronic submissions** is available at <http://www.fda.gov/cber/esub/esub.htm>. You may submit questions pertaining to the preparation of submissions in electronic format and the establishment of secure email accounts with CBER to ESUBPREP@CBER.fda.gov.
5. For **general information regarding the regulation of cellular and gene therapies** please see our website <http://www.fda.gov/cber/gene.htm>. This website includes a link to **Cellular & Gene Therapy Publications** found at <http://www.fda.gov/cber/genetherapy/gtpubs.htm>. This listing includes links to FDA Consumer Articles, Federal Register, Guidances, HHS News, Letters to Industry/Healthcare Professionals, and more.
6. **Manual of Regulatory Standard Operating Procedures and Policies** is available at <http://www.fda.gov/cber/regsopp/regsopp.htm>.
7. For information regarding the regulation of **Xenotransplantation** please see our website: at <http://www.fda.gov/cber/xap/xap.htm>. In addition to other references, the website contains: “**Guidance for Industry: Source Animal, Product, Preclinical, and Clinical Issues Concerning the Use of Xenotransplantation Products in Humans**” (Final, April 2003) <http://www.fda.gov/cber/gdlns/clinxeno.htm>.

8. The FDA has regulations on the exportation of investigational new drugs, including biological products [70 Federal Register at 70,720 (Nov. 2005)]. The final rule became effective on December 23, 2005. Please see “**Investigational New Drugs: Export Requirements for Unapproved New Drug Products**” found at <http://www.fda.gov/cber/rules/indexpreq.htm>
9. Several **Advisory Committee Meetings** discussed innovative investigational therapy approaches. The committee used for these advisories is the Cellular Tissue and Gene Therapy Advisory Committee (CTGTAC) formerly known as Biologics Response Modifiers Advisory Committee (BRMAC). Advisory committee information is available at <http://www.fda.gov/cber/advisory/advisory.html>

DEVICE REFERENCES

1. If you are requesting a pre-IDE, pre-510(k), or pre-PMA, meeting with OCTGT, it may be helpful to refer to the “**Guidance for Industry: Formal Meetings With Sponsors and Applicants for PDUFA Products**” found at: <http://www.fda.gov/cber/gdlns/mtpdufa.htm>, detailed above. Early stage device meetings are addressed in “**Early Collaboration Meetings Under the FDA Modernization Act (FDAMA), Final Guidance for Industry and CDRH Staff**” found at <http://www.fda.gov/cdrh/ode/guidance/310.pdf>.
2. For additional regulatory references regarding devices please see the following links:
 - <http://www.fda.gov/cdrh/devadvice/>.
 - <http://www.fda.gov/cber/devices.htm>.

Please note, all device submissions intended for OCTGT should be addressed to the address listed above.

TISSUE REFERENCES

For information regarding **human tissues** intended for implantation, transplantation, infusion, or transfer into a human recipient, please see <http://www.fda.gov/cber/tiss.htm>. In addition to other references, the website contains:

- **Draft Guidance for Industry: Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps)** (5/20/ 2004) found at <http://www.fda.gov/cber/gdlns/tissdonor.pdf>.

- **Final Rule: Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue -Based Products** (69 FR 29786, May 25, 2004) found at <http://www.fda.gov/cber/rules/suitdonor.pdf>.

PRODUCT REFERENCES

If you have questions regarding specific information to provide about your product in your pre-IND information package, please contact the OCTGT Branch Chief of Regulatory Management. Please also refer to the following guidances:

- **Draft Guidance for Reviewers: Instructions and Template for Chemistry, Manufacturing, and Control (CMC) Reviewers of Human Somatic Cell Therapy Investigational New Drug Applications (INDs)** (2003) found at <http://www.fda.gov/cber/gdlns/cmcsomcell.pdf>.
- **Guidance for Industry: Guidance for Human Somatic Cell Therapy and Gene Therapy** (3/30/1998) found at <http://www.fda.gov/cber/gdlns/somgene.pdf>.
- **Draft Guidance for FDA Review Staff and Sponsors: Content and Review of Chemistry, Manufacturing, and Control (CMC) Information for Human Gene Therapy Investigational New Drug Applications (INDs)** (11/8/04) found at <http://www.fda.gov/cber/gdlns/gtindcmc.htm>.
- **Points to Consider in the Characterization of Cell Lines Used to Produce Biologicals** (1993) (July 12, 1993) found at <http://www.fda.gov/cber/gdlns/ptccell.pdf>.
- **ICH Guidance on Quality of Biotechnological/Biological Products: Derivation and Characterization of Cell Substrates Used for Production of Biotechnological/Biological Products**, (63 FR 50244, September 21, 1998) found at www.fda.gov/cber/gdlns/qualbiot.pdf.
- **ICH Guideline Q5A. Guidance on Viral Safety Evaluation of Biotechnology Products Derived From Cell Lines of Human or Animal Origin**, (63 FR 51074, September 24, 1998) found at www.fda.gov/cber/gdlns/virsafe.pdf.
- **Guidance for Industry: Supplemental Guidance on Testing for Replication Competent Retrovirus in Retroviral Vector Based Gene Therapy Products and During Follow-up of Patients in Clinical Trials Using Retroviral Vectors** (10/8/2000) found at <http://www.fda.gov/cber/gdlns/retrogt1000.htm>.
- **Guidelines for Research Involving Recombinant DNA Molecules** (NIH Guidelines) found at <http://www4.od.nih.gov/oba/rac/guidelines/guidelines.html>.

- **Draft Guidance for Industry: Gene Therapy Clinical Trails- Observing Participants for Delayed Adverse Events** (8/23/2005) found at <http://www.fda.gov/cber/gdlns/gtclin.htm>.
- **Guidance for Industry: Source Animal, Product, Preclinical, and Clinical Issues Concerning the Use of Xenotransplantation Products in Humans** (Final, April 2003) found at <http://www.fda.gov/cber/gdlns/clinxeno.htm>.
- **Guidance for Industry: Pharmacogenomic Data Submissions** (March 2005) found at <http://www.fda.gov/cber/gdlns/pharmdtasub.htm>, with an attachment found at http://www.fda.gov/cber/gdlns/pharmdtasub_att.htm.

PHARMACOLOGY/TOXICOLOGY REFERENCES

If you have questions regarding what Pharmacology/Toxicology information to provide for OCTGT feedback, please contact the OCTGT Branch Chief of Regulatory Management. Please also refer to the following references:

- **ICH S6 Document: Preclinical Safety Evaluation of Biotechnology-Derived Pharmaceuticals**, (July 1997) found at www.fda.gov/cder/guidance/1859fnl.pdf.
- **Guidance for Industry: Source Animal, Product, Preclinical, and Clinical Issues Concerning the Use of Xenotransplantation Products in Humans** (Final, April 2003) found at <http://www.fda.gov/cber/gdlns/clinxeno.htm>.

CLINICAL REFERENCES

1. Please see the following website: **Guidances and Information Sheets on Good Clinical Practice in FDA-Regulated Clinical Trials** found at <http://www.fda.gov/oc/gcp/guidance.html>

For general questions regarding good clinical practice please see the following contact information found at <http://www.fda.gov/oc/gcp/contactogcp.html>. In addition, please see Clinical Investigator information found at <http://www.fda.gov/cber/clininv.htm>.

2. For information regarding use of **foreign clinical data**, please see “**ICH E5: Ethnic Factors in the Acceptability of Foreign Clinical Data**” found at <http://www.fda.gov/cber/gdlns/ichethnic.txt>.

Please also see “**Guidance for Industry: Acceptance of Foreign Clinical Studies**” found at <http://www.fda.gov/cder/guidance/fstud.htm>.

3. **References for Cardiac Indications:** The following link is to the meeting summary and transcripts from the Biological Response Modifiers Advisory Committee Meeting (BRMAC) from March 18-19, 2004, which discussed and made recommendations related to manufacturing, preclinical testing, and pilot clinical design questions for cellular therapies for cardiac indications. The summary provides a good resource for the type of data needed in this type of IND application (<http://www.fda.gov/ohrms/dockets/ac/04/minutes/4018m1.htm>). Transcripts and slides from the meeting are available at <http://www.fda.gov/ohrms/dockets/ac/cber04.html#BiologicalResponseModifiers>.

For additional information regarding cellular therapies for cardiac indications, please see CBER's website, "**Cellular Therapy: Potential Treatment for Heart Disease**" found at <http://www.fda.gov/cber/genetherapy/celltherapyheart.htm>.

4. **Guidance for Industry: Source Animal, Product, Preclinical, and Clinical Issues Concerning the Use of Xenotransplantation Products in Humans** (Final, April 2003) found at <http://www.fda.gov/cber/gdlns/clinxeno.htm>.
5. **Draft Guidance for Industry: Gene Therapy Clinical Trials- Observing Participants for Delayed Adverse Events** (8/23/2005) found at <http://www.fda.gov/cber/gdlns/gtclin.htm>.