Center for Biologics Evaluation and Research
TISSUE SAFETY TEAM

Ruth Solomon, M.D.
Director, Division of Human Tissues
Office of Cell, Tissue and Gene Therapies

ADVISORY COMMITTEE ON BLOOD SAFETY AND AVAILABILITY
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CBER's Tissue Safety Team

- **Objectives**
  - **Purpose of TST**
  - **Background**
  - **Composition**
  - **Procedures**
  - **Accomplishments**
  - **Challenges**

Purpose

- **Provide a coordinated approach to the receipt, routing, investigation, evaluation, documentation and trending of reported adverse reactions involving human cells, tissues, and cellular and tissue-based products (HCT/Ps) across 5 Offices and beyond the Center**
- **Communicate—one voice**
- **Give guidance to industry on how and when to report adverse reactions**
- **Provide outreach/education to industry, healthcare professionals and the public about tissue donation and transplantation**

Background--Definitions

- **HCT/P**
  - **An article containing or consisting of human cells or tissues that is intended for implantation, transplantation, infusion, or transfer into a human recipient**
  - ***Examples*: bone, tendon, cornea, skin, heart valve, dura mater, vascular grafts, hematopoietic stem cells, islet cells**
  - **HCT/Ps can be regulated as:**
    - **"Tissues"—to prevent the introduction, transmission, or spread of communicable disease ; no pre-market review,**
    - **Biological products—to ensure safety and effectiveness, or**
    - **Medical devices—to ensure safety and effectiveness**
- **Adverse Reaction**
  - **A noxious and unintended response to an HCT/P for which there is a reasonable possibility that the HCT/P caused the response**

Reporting Requirements

- **3 HCT/P rules—all in effect May 25, 2005**
  - **Registration and Listing**
  - **Donor Eligibility**
  - **Current Good Tissue Practice**

- **CGTP rule—Adverse reaction reports for tissues**
  - **You must investigate any adverse reaction involving a communicable disease related to an HCT/P that you made available for distribution.**
  - **You must report to FDA (within 15 days) an adverse reaction involving a communicable disease if it fatal, life-threatening, results in permanent impairment or damage or necessitates medical or surgical intervention**
  - **MedWatch : Form FDA 3500A—mandatory reporting; Form FDA 3500—voluntary reporting**

Composition of TST

- **Five offices within CBER**
  - **Office of Biostatistics and Epidemiology**
  - **Office of Cell, Tissue and Gene Therapies**
  - **Office of Communication, Training and Manufacturers Assistance**
  - **Office of Compliance and Biologics Quality**
  - **Office of the Director**
  - **Points of contact within each office**
- **Outside of CBER**
  - **Center for Devices and Radiological Health**
  - **Office of Regulatory Affairs**
  - **Office of Criminal Investigations**
- **Outside of FDA**
  - **CDC, HRSA, CMS**

Procedures—SOPP 8508

- **Responsibilities and procedures for TST and each office**
- **Reports received from various sources**
  - **MedWatch reports→OBE**
  - **Directly from hospital, physician or recipient→OCTMA**
  - **Directly from tissue bank→OCTGT or OCBQ**
  - **Other agencies—CDC, HRSA→OCTGT or OCBQ**
- **Proper routing and database entry**
  - **Contractor forwards appropriate MedWatch reports to Centers**
  - **Entered into Center database; for CBER—AERS; forwarded to OBE**
  - **Entered into OBE database; e-mail alert to other points of contact who access database**
- **Initial information**
  - **Is adverse event related to communicable disease? Yes→F/U**

Procedures, cont.

- **Additional information**
  - **OBE contacts reporter—standard set of questions; description of the event; physician's impression**
  - **OCBQ contacts tissue bank—standard set of questions; request and review tissue bank's investigation (review donor records; processing records; pre- and post processing culture results; complaints from other consignees)**
  - **ORA for cause inspection**
- **Discussion / evaluation**
  - **notify senior management, CDC, etc. (at any point)**
- **Conclusion**
  - **Classify as: possibly; probably; or definitely related to the tissue**

Procedures, cont.

- **Further action**
  - **Notification of consignees**
  - **Recall**
  - **Order**
  - **Public notification; press release**
- **Decision to close case if no further action indicated**

Communication

- **TST points of contact—meet bi-weekly**
- **TST meets monthly**
- **Center senior management is briefed quarterly**

Adverse Reaction Reports Statistics—Nov. ’05 to July ‘06

- **Total Reports= 152**
- **Product Type**
  - **Tissues—108 (71%)**
  - **Cells---------44 (29%)**
- **Tissue Type**
  - **Bone—39 (36%)**
  - **Eye ----26 (24%)**
  - **Skin----23 (21%)**
  - **Soft Tissue—9 (8%)**
  - **Cardiac—8 (7%)**
- **Reports from**
  - **Manufacturers---------54%**
  - **Healthcare workers—46%**
- **Infectious/Non-infectious----80%/20%**

TST Accomplishments

- **Routing of MedWatch reports**
  - **List of HCT/Ps and establishments to contractor**
  - **Access to CDRH database**
- **SOPP 8508**
- **Revised MedWatch Form**
  - **More user friendly**
- **Guidance for completing MedWatch Form**
- **Improvement of database**
- **Additional information entered into database for easy access**
- **Improved training and communication with FDA field**

Challenges/Future Goals

- **Reports**
  - **When to follow-up**
  - **How to classify**
  - **When to close**
  - **How to trend**
- **Outreach to consumer and health care providers**
- **ACTIVE surveillance**
  - **MedSUN project with CDRH**
  - **CDC NHSN: in hospital infection surveillance—tissue module under development**
  - **Stimulate reporting--electronic**

Helpful Websites

- www.fda.gov/cber/tiss.htm
- www.fda.gov/cber/reqsopp/8508.htm
- www.fda.gov/medwatch
- www.fda.gov/cber/biodev/biodevsub.htm

Ruth Solomon, M.D.
Division of Human Tissues
HFM-770
1401 Rockville Pike
Rockville, MD 20852

Ruth.solomon@fda.hhs.gov
301-827-5363