Regulatory Compliance and Tissue Tracking

Presented by:
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Background

- Overall, tissue transplantation is a safe practice in the U.S.
- Infections
  - 2001- musculoskeletal graft-associated infection lead to a 23 year-old's death
    - Recovery processes violated national standards
  - 14 other patients with allograft-related clostridium infections
    - Deviations from national standards

Recall of Human Tissue

DATE RECALL INITIATED:

October 13, 2005

PRODUCT:

Human Tissue for Transplantation

MANUFACTURER:

Biomedical Tissue Services, Ltd
Fort Lee, New Jersey

REASON:

Biomedical Tissue Services (BTS) was recently made aware that there is the possibility that tissue has been procured from donors without proper medical/social histories. BTS is performing a voluntary recall of any unused tissue from its consignees.

Body parts harvested in N.C. are recalled FDA won't say how many tainted parts sent to hospitals for transplant

AP Aug 23, 2006
WASHINGTON - A leading medical firm has quietly recalled hundreds of human tissue products destined for transplants around the nation that were supplied by a North Carolina body parts broker believed to have a tainted history. The broker used an unsterile embalming room to carve up dozens of corpses to procure tissue, a Raleigh funeral home director said Tuesday. The U.S. Food and Drug Administration shut down the body broker on Friday, but refuses to say how many people may have received potentially risky tissue.

Regulations and Standards

Current FDA Regulations

- FDA 21 CFR 1270 Human Tissue Intended for Transplantation
  - Screening and testing rules donors for hepatitis B and HIV
  - Rules for record keeping
  - Authority to inspect
  - Authority to recall/ destroy tissues

40444 **Federal Register** / Vol. 62, No. 145 / Tuesday, July 29, 1997 / Rules and Regulations

List of Subjects

21 CFR Part 16

Administrative practice and procedure.

21 CFR Part 1270

Communicable diseases, HIV/AIDS, Reporting and recordkeeping requirements.

Therefore, under the Public Health Service Act, and under authority delegated to the Commissioner of Food and Drugs, 21 CFR parts 16 and 1270 are amended as follows:

PART 16—REGULATORY HEARING BEFORE THE FOOD AND DRUG ADMINISTRATION

1. The authority citation for 21 CFR part 16 continues to read as follows:

Authority: Secs. 201–903 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321–394); 21 U.S.C. 41–50, 141–149, 467f, 679, 821, 1034; secs. 2, 351, 361 of the Public Health Service Act (42 U.S.C. 201, 262, 264); secs. 2–12 of the Fair Packaging and Labeling Act (15 U.S.C. 1451–1461); 28 U.S.C. 2112.

2. Section 16.1 is amended in paragraph (b)(2) by revising the entry for "§ 1270.15(e) * * *" to read as follows:

§ 16.1 Scope.

* * * * *

(b) * * *

(2) * * *

§ 1270.15(e), relating to the retention, recall, and destruction of human tissue.

3. Part 1270 is revised to read as follows:

PART 1270—HUMAN TISSUE INTENDED FOR TRANSPLANTATION

Subpart A—General Provisions

Sec.

1270.1 Scope.
1270.3 Definitions.

Subpart B—Donor Screening and Testing

1270.21 Determination of donor suitability for human tissue intended for transplantation.

Subpart C—Procedures and Records

1270.31 Written procedures.
1270.33 Records, general requirements.
1270.35 Specific records.

Subpart D—Inspection of Tissue Establishments

1270.41 Inspections.
1270.42 Human tissue offered for import.
1270.43 Retention, recall, and destruction of human tissue.

Authority: Secs. 215, 311, 361, 368 of the Public Health Service Act (42 U.S.C. 216, 243, 264, 271).

Subpart A—General Provisions

§ 1270.1 Scope.

(a) The regulations in this part apply to human tissue and to establishments or persons engaged in the recovery, screening, testing, processing, storage, or distribution of human tissue.

(b) Regulations in this chapter as they apply to drugs, biologics, devices, or other FDA-regulated commodities do not apply to human tissue, except as specified in this part.

(c) Regulations in this chapter do not apply to autologous human tissue.

(d) Regulations in this chapter do not apply to hospitals or other clinical facilities that receive and store human tissue only for transplantation within the same facility.

§ 1270.3 Definitions.

(a) *Act* for the purpose of this part means the Public Health Service Act, section 361 (42 U.S.C. 264).

(b) *Blood component* means any part of a single-donor unit of blood separated by physical or mechanical means.

(c) *Colloid* means a protein or polysaccharide solution that can be used to increase or maintain osmotic (oncotic) pressure in the intravascular compartment such as albumin, dextran, hetastarch; or certain blood components, such as plasma and platelets.

(d) *Contract services* are those functions pertaining to the recovery, screening, testing, processing, storage, or distribution of human tissue that another establishment agrees to perform for a tissue establishment.

(e) *Crystalloid* means a balanced salt and/or glucose solution used for electrolyte replacement or to increase intravascular volume such as saline, Ringer's lactate solution, or 5 percent dextrose in water.

(f) *Distribution* includes any transfer or shipment of human tissue (including importation or exportation), whether or not such transfer or shipment is entirely intrastate and whether or not possession of the tissue is taken.

(g) *Donor* means a human being, living or dead, who is the source of tissue for transplantion.

(h) *Donor medical history interview* means a documented dialogue with an individual or individuals who would be knowledgeable of the donor's relevant medical history and social behavior; such as the donor if living, the next of kin, the nearest available relative, a member of the donor's household, other individual with an affinity relationship, and/or the primary treating physician. The relevant social history includes questions to elicit whether or not the donor met certain descriptions or engaged in certain activities or behaviors considered to place such an individual at increased risk for HIV and hepatitis.

(i) *Establishment* means any facility under one management including all locations, that engages in the recovery, screening, testing, processing, storage, or distribution of human tissue intended for transplantation.

(j) *Human tissue* means any tissue derived from a human body, which:

(1) Is intended for transplantation to another human for the diagnosis, cure, mitigation, treatment, or prevention of any condition or disease;

(2) Is recovered, processed, stored, or distributed by methods that do not change tissue function or characteristics;

(3) Is not currently regulated as a human drug, biological product, or medical device;

(4) Excludes kidney, liver, heart, lung, pancreas, or any other vascularized human organ; and

(5) Excludes semen or other reproductive tissue, human milk, and bone marrow.

(k) *Importer of record* means the person, establishment or their representative responsible for making entry of imported goods in accordance with all laws affecting such importation.

(l) *Legislative consent* means relating to any of the laws of the various States that allow the medical examiner or coroner to procure corneal tissue in the absence of consent of the donor's next-of-kin.

(m) *Person* includes an individual, partnership, corporation, association, or other legal entity.

(n) *Physical assessment* means a limited autopsy or recent antemortem or postmortem physical examination of the donor to assess for any signs of HIV and hepatitis infection or signs suggestive of any risk factor for such infections.

(o) *Plasma dilution* means a decrease in the concentration of the donor's plasma proteins and circulating antigens or antibodies resulting from the transfusion of blood or blood components and/or infusion of fluids.

(p) *Processing* means any activity performed on tissue, other than tissue recovery, including preparation, preservation for storage, and/or removal from storage to assure the quality and/or sterility of human tissue. Processing includes steps to inactivate and remove adventitious agents.

(q) *Quarantine* means the identification of human tissue as not suitable for transplantation, including human tissue that has not yet been characterized as being suitable for

State Regulations

- New York
- California
- Florida
- Maryland

Tissue is Not a Surgical Supply

First Step: Determine Oversight

- Medical director
- Administrator
- Personnel
- Descriptions
  - Responsibilities
  - Training/competencies

Personnel

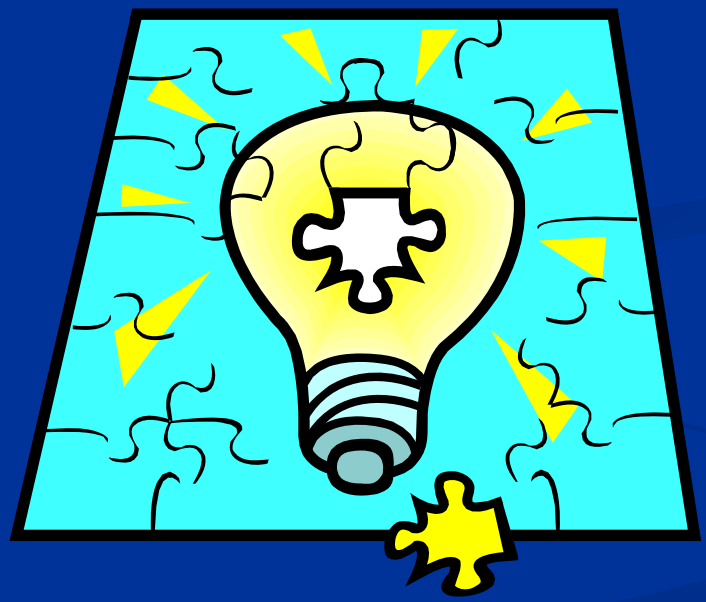
- Surgical tissue bank personnel must be knowledgeable about the aspects of tissue banking in which they participate.
  - Ongoing and continuing education provided
  - Focus on responsibilities
    - Ordering tissue
    - Receiving tissue
    - Storage of tissue
    - Release of tissue from tissue bank
    - Dispensing tissue onto sterile field
    - Preparing tissue for use
    - Return to tissue bank or disposal
    - Documentation/tracking

Registration with FDA

- Facilities procuring, processing, and/or preserving tissue, and facilities storing tissue for potential transfer to different facility, must register as tissue banks with the FDA.
- Exemptions
  - Cranial bone flaps
  - Autograft skin
  - Only purchased tissue

Tissue Bank Selection Criteria

- Develop criteria for selecting a vendor of tissue

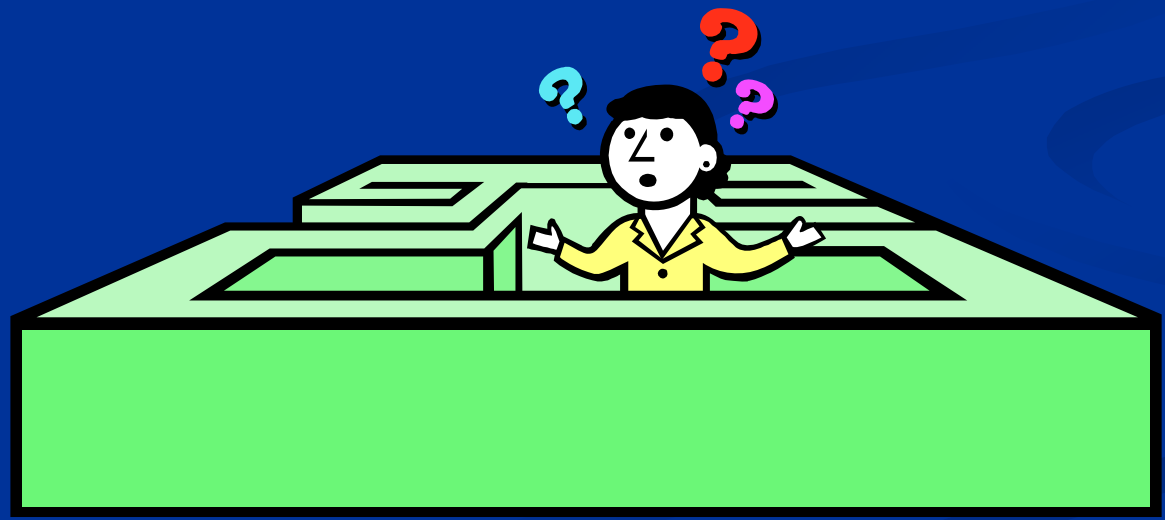


Selecting a Tissue Bank

- AATB accreditation status
- FDA registration
- State registration
- ISO certification
- Surgeon preference
- Type of processing
- Quality of tissue
- Availability of tissue
- Safety track record
- Clinical results
- Processing fees
- Packaging
- Customer service

Tissue Tracking

- From donor to recipient
- From donor to disposition



Receipt of Tissue

- Record receipt, including unique identifiers, expiration date, identification of person accepting tissue, date & time.
- Verify that the package integrity was maintained during transport & that the expiration date has not been not been exceeded.
- Document the recommended temperature.
- For tissue requiring controlled storage, verify that the recommended temperature was maintained during transport.
  - Validated shipping container is undamaged and within the validated timeframe.
  - Presence of any remaining regular or dry ice
  - Taking the temperature in the center of the product, or using a commercial shipping temperature indicator.
  - Not required for ambient temperature

Storage

- Transfer to storage in a manner consistent with the source facility's written instructions.
- Tissue stored in a secure area, with access restricted to authorized personnel.
- AATB recommendations for storage temperatures, durations
  - Monitored for refrigerated, frozen, or if manufacturer gives a temperature range
  - TJC does not require for ambient temperature
- Freezers- monitor & alarm
- Have a backup plan for freezer failure/cleaning

Storage Temperatures

- Lyophilized or dehydrated musculoskeletal tissue
  - ambient temperature or cooler (but not frozen) 68-77 ° F
- Refrigerated musculoskeletal and osteoarticular tissue
  - 33.8° F (1° C) to 50° F (10° C).
- Refrigerated skin:
  - 33.8° F (1° C) to 50° F (10° C).
- Frozen musculoskeletal & osteoarticular tissue:
  - –40° F (–40° C) or colder for long-term storage
  - –20° C to –40° C for short-term storage (less than 6 months).
- Frozen or cryopreserved skin
  - –40° F (–40° C) or colder.

Transportation

- Tissue is transported and stored in a manner to minimize the risk of compromise or contamination.
  - Containers for transportation must protect tissue from contamination
  - Maintain temperature of frozen and refrigerated tissue- validated containers

Recipient Rights

- Potential recipients of tissue should be treated with respect, dignity, and sensitivity, and their rights should be protected.
  - Discussion of risks, benefits, and alternatives
  - Informed consent

Preprocedural Time Out

Verify the availability of

- Relevant documents, such as the history and physical, pre-anesthesia assessment
- Accurate, complete, and signed procedure consent form*
- Correct and properly labeled diagnostic and radiology test results
- Any required blood products, implants, devices or special equipment

Reconstitution

- Allograft tissue obtained from an outside tissue bank should be handled in a manner consistent with the source facility's or manufacturer's written instructions.
- Written instructions should be maintained for each tissue implanted.

Policies and Procedures

- Readily available in the practice setting.
- Reviewed annually
  - Authority, accountability, oversight
  - Criteria for selection of tissue banks
  - All steps of process
  - Approval of release of tissue for implantation by responsible authority
  - Receiving, storing, and handling tissue
  - Criteria for returning tissue to storage
  - Adverse tissue reactions and recall procedures

Adverse Tissue Reaction Policies

- Reporting: Facility to the patient
- Reporting: Patient to donor source
- The Joint Commission. Adverse tissue reaction policies (12/24/08)
  - http://www.jointcommission.org/AccreditationPrograms/Office-BasedSurgery/Standards/09_FAQs/PC/Adverse_Tissue_Reaction.htm

Recordkeeping

- Each tissue bank must maintain donor, tissue, and recipient records to ensure that pertinent data are retrievable.
  - Log of all tissues ordered, received, stored, implanted, discarded
  - Ordering
  - Receipt
    - Packaging integrity, temperature controlled & acceptable, instructions, date, time, person accepting
  - Dates, times of issuing from the tissue bank
  - Dates, time, methods, and person overseeing preparation of tissue for use
    - Source manufacturer's instructions
  - Patient identification
  - Disposal of tissue
- Maintain for 10 years

Quality Management

- Must be in place to evaluate the structure, processes, and outcomes of tissue bank services.
  - Structure
    - Training and competencies of personnel
    - Criteria for selection of tissue banks
    - Copies of registration, certifications of sources
  - Records
    - Traceability from source to donor
    - All steps of processes used
    - Package integrity verified upon receipt
    - Transport temperature controlled and acceptable
  - Adverse tissue reactions and recalls

Managing a tissue recall in a large academic hospital

Victoria M. Steelman and Annette J. Schlueter

BACKGROUND: In October 2005, a recall of human tissue for implantation was initiated because one recovery center obtained tissues from donors who were not screened properly for infectious diseases. The Food and Drug Administration (FDA) and Centers for Disease Control (CDC) recommended notifying affected patients and offering access to infectious disease testing.
STUDY DESIGN AND METHODS: A multidisciplinary team was established to provide a framework for responding to the recall. The plan was designed to meet six goals. Steps included patient identification, surgeon and patient notification, patient education and testing, communication of test results, and information for the public.
RESULTS: The institution received 55 recalled tissues, of which 48 had been implanted into 30 patients undergoing neurosurgical, orthopedic, and general surgical procedures. Patients were identified and sent notification letters within 2 weeks of the FDA and CDC recommendations. Twenty-seven patients underwent testing, which was performed at the convenience of the patients at no cost to them. One patient had evidence of previous (but not current) hepatitis B infection. Overall, patients were appreciative of the processes used. Media coverage was positive.
CONCLUSION: The response plan was generally successful in achieving the established goals. Potential improvements were identified in several areas, including initial patient notification and coordination of test result communication. It is critical to allow flexibility to meet each patient's needs. The plan may serve as a template for use in future tissue recalls by other hospital-based tissue banks.

The transplantation of human tissue carries with it inherent risk of infectious disease (ID) transmission. This risk is minimized through regulations of the Food and Drug Administration (FDA), including registration of tissue banks,[1] donor suitability criteria,[2] and good tissue practices[3] and by standards of the Joint Commission for Accreditation of Hospital Organizations[4] and American Association of Tissue Banks.[5] These regulations and standards, however, may be violated. When errors are identified, the potentially compromised tissue is recalled. Hospital-based tissue banks must rapidly respond to these recalls. This article describes a complex tissue recall process in a large academic hospital and the lessons learned from this process.

In October 2005, hospitals across the United States were notified that tissue procured by Biomedical Tissue Services (BTS) was being recalled. The recall initially involved skin procured by BTS that was subsequently processed and distributed by LifeCell Corp. (Branchburg, NJ) and was based on concern about the authenticity of donor screening records supplied by BTS (letter from B. Lamb, Senior Vice President of LifeCell, to LifeCell customers, October 12, 2005, and *Recall of Human Tissue Products*[6]). Ten to twelve days later, three other tissue banks that distributed tissue obtained from BTS also initiated recalls. These were Lost Mountain Tissue Bank,[7] The Blood and Tissue Center of Central Texas,[8] and Tutogen.[9] On October 13, BTS initiated a recall[10] followed the next day by a recall from a major distributor of musculoskeletal tissue,

ABBREVIATIONS: APN = Perioperative Nursing Division; BTS = Biomedical Tissue Services; ID = infectious disease.

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Summary

- Tissue is not a medical supply!
- Tissue banking includes use of purchased tissue.
- Implement a structure with clear accountability to maximize safety.
- Follow the manufacturer's instructions for storage, handling, and preparation of tissue.
- Maintain adequate records of ordering, receipt, storage, transplant, and disposal.
- Include a quality management program with adverse tissue reaction policies.

References

- AORN Recommended Practices Committee. (2009). Recommended practices for surgical tissue banking. In *2009 Perioperative Standards and Recommended Practices*, AORN, Denver, CO.
- American Association of Tissue Banks, *Standards for Tissue Banking,* 10th ed *(McLean, VA:* American Association of Tissue Banks, April 2002).
- Steelman, V.M., Schlueter, A.J, (2007). Managing a Tissue Recall in a Large Academic Hospital. *Transfusion 47*(5), 927-34.
- The Joint Commission. Adverse tissue reaction policies. http://www.jointcommission.org/AccreditationPrograms/Office-BasedSurgery/Standards/09_FAQs/PC/Adverse_Tissue_Reaction.htm (accessed 4/16/09).
- US Food and Drug Administration. "Current good tissue practice for human cell, tissue, and cellular and tissue-based product establishments; Inspection and enforcement; Proposed rule". *Federal Register 66*(January 8, 2001) 1507-1559.
- US Food and Drug Administration. "Human cells, tissues, and cellular and tissue-based products; Establishment registration and listing: Final rule," *Federal Register 66*(Jan 19, 2001) 5447-69.