Updates to *Standards* - Cellular Tissue (CT)
(with amendments)
relevant parts only

INTRODUCTION

…
The format of this edition of *Standards* is that of general requirements applicable to all tissue with subsections delineating *Donor* and *Tissue* standards for:

(A) autologous tissue,
(C) cardiac tissue,
(CT) cellular tissue,
(DM) dura mater,
…

A2.000 DEFINITIONS OF TERMS

CELLULAR TISSUE (CT) *– cells that are autologous or allogeneic, committed or uncommitted, and non-expanded.*

D1.000 GENERAL POLICIES FOR TISSUE RECOVERY OR COLLECTION ORGANIZATIONS

In addition to the requirements at the series of standards at B1.500 Multi-Facility Tissue Banking, all referral arrangements with organ procurement organizations, Donor Referral Sources, and other tissue banks shall be documented.

(~~A,~~*LD*) *Except for a Reproductive* ~~The~~ *Tissue Bank*, ~~shall establish~~ written ~~or verbal~~ procedures for interacting with operating room staff, the patient's physician, or other sources/facilities shall *be established* ~~prior to *Recovery*, for autologous tissue donation~~.

D4.000 DONOR SUITABILITY

D4.100 General

Donor suitability criteria shall be established by the Medical Director and shall not conflict with these *Standards*. Each donor shall be evaluated according to established criteria. The suitability of each donor shall be determined by the Medical Director or licensed physician designee upon review of all records as specified in ~~Section~~ F1.100 and in accordance with the *SOPM*.

(LD) Criteria for accepting Living Donors shall be established by the Medical Director or licensed physician designee.

D4.350 Blood Tests

D4.354 Required Infectious Disease Tests

Excluding autologous tissue, oocytes and embryos, all human tissue intended for

transplantation shall be from donors who are tested and found to be negative for:

1) antibodies to the human immunodeficiency virus, type 1 and type 2 (anti- HIV-1 and anti-HIV-2);

2) nucleic acid test (NAT) for HIV-1;

3) hepatitis B surface antigen (HBsAg);

4) total antibodies to hepatitis B core antigen (anti-HBc—total, meaning IgG and IgM);

5) antibodies to the hepatitis C virus (anti-HCV);

6) nucleic acid test (NAT) for HCV; and

7) syphilis (a non-treponemal or treponemal-specific assay may be performed).

Donors of viable leukocyte-rich tissue (e.g., semen*, certain (CT)*) shall also be tested and found to be negative for antibodies to human T-lymphotropic virus type I and type II (anti-HTLV-I and anti-HTLV-II). Note: HTLV testing of donors of other tissue types may be required by law and/or regulation, including, where applicable, foreign laws and/or regulations.

All test results shall be documented in the donor's record.

D5.300 Tissue Recovery and Collection — General

(~~A~~ *LD*) Methods for ~~perioperative autologous tissue~~ *Recovery* ~~and transplantation~~ *of perioperative tissue* shall be safe, aseptic, and ensure accurate identification of ~~autologous~~ tissue.

D5.400 Time Limits for ***Postmortem*** Tissue Recovery

D5.900 Transportation of Tissue Following Recovery

Following tissue *Recovery*, tissue shall be packaged in a manner that permits required environmental conditions to be maintained for the duration of transportation. Transportation temperatures do not require monitoring if the packaging and transport conditions have been validated to maintain the required environmental conditions, including temperatures. The transportation receptacle must indicate that "*DONATED HUMAN TISSUE*" is enclosed as well as include the name and address of the *Recovery* agency and *Processing* center (if different) in accordance with applicable laws and regulations. All human tissue processed or shipped prior to determination of donor suitability must be under *Quarantine*, accompanied by records assuring identification of the donor and indicating that the tissue has not been determined to be suitable for transplantation (e.g., "*Quarantine*"; *"Donor Eligibility Has Not Been Completed"*; and "Not Suitable for Transplant in its Current Form").

(LD, CT)
When Wet Ice Temperatures would be injurious to the tissue recovered, it may be transported at appropriate temperatures and within time limits that maintain the

integrity of the tissue for its intended use.

E1.000 PROCESSING, PRESERVATION, QUARANTINE, AND STORAGE—GENERAL

E1.020 Processing Environment

(C, V, *CT*)

Processing, which includes dissection, *Disinfection* and packaging of *cellular,* cardiac and vascular tissues, shall be performed in a certified and qualified ISO 5 (Grade A, Class 100) or cleaner laminar flow environment. Tissue shall be processed in an aseptic fashion using *Sterile* drapes, packs, solutions, instruments, and packaging material.

(MS, OA)

~~Musculoskeletal t~~*Ti*ssue shall be processed in a bacteriologically and climate- controlled environment.

E1.030 Processing Methods

E1.035 Additives

~~(C, V, OA, R, S)~~

When applicable, the type, amount, concentration, and method of incorporation/addition of all media, *Cryoprotectants*, and any other additives used in ~~the freezing solution/media~~ *Processing* shall be specified in the *SOPM*. This information about the *Allograft* shall be made available to the implanting/transplanting physician, upon request.

E1.040 Sterilization/Disinfection of Tissue

Individual *Processing* facilities shall establish, validate, and document disinfection or sterilization regimens and microbial surveillance methods. The *SOPM* shall establish a list of organisms ~~which~~ *that* necessitate discard, *Sterilization* and/or *Disinfection* of tissue. The list shall be based upon not only the category type of tissue but also the method by which the tissue was processed (e.g., *Cryopreserved* MS tissues that cannot be ‘‘sterilized’’ and can only be ‘‘disinfected’’).

(C, V, *CT*)

The following are considered to be pathogenic, highly virulent *Microorganisms* that result in tissue discard:

1) fungi (yeasts, molds);

2) *Clostridium*; and

3) *Streptococcus pyogenes* (group A strep.).

E1.050 Tissue Evaluation

Written criteria for evaluation and assessment of tissue Quality must be established.

~~*(R) Reproductive Tissue Banks engaged in embryo Cryopreservation shall establish written criteria for evaluation/assessment of embryo quality.*~~

(C, V, OA)

Standardized evaluation and classification system is required (e.g., valve with no visible abnormalities or aberrations, implantable Allograft with some imperfection(s), and discard/non-implantable Allograft). The Allograft evaluation system shall be made available to the implanting surgeon.

E1.060 Tissue Preservation/Cryopreservation

E1.061 Techniques

(CT) If tissue is to be preserved using any method, appropriate protocols shall be validated with respect to cell Quality.

E1.067 Freezing Tissue

(CT) If tissue is to be frozen/cryopreserved, a specific freezing rate to a predetermined specific end-point must be selected. When applicable, procedures for freezing shall be established and the method controlled to maintain cell Quality.

E1.068 Cryopreservation

(OA, MS, *CT*)

Procedures for the *Cryopreservation* of ~~musculoskeletal~~ tissue shall be established and documented. Documentation of the concentrations of *Cryoprotectant* and, nutrient or isotonic solutions in the cryopreservative solution shall be maintained.

E1.300 Reagents, Supplies, Materials, and Equipment

(C, V, MS, OA, S, *CT*)

All non-disposable surgical instruments and mechanical/electrical equipment used in tissue *Processing* shall be cleaned, disinfected, and *Sterilized* between use for tissue from different donors according to written procedures. For non-disposable surgical instruments and mechanical/electrical equipment deemed *Critical,* written procedures must be prepared and should be *Validated* to prevent contamination or *Cross-Contamination* during *Processing*.

E4.000 STORAGE

E4.100 Storage Temperatures

(CT) Procedures for storing cells should be established and methods controlled to maintain or preserve cell Quality.

E4.140 Monitoring Storage Temperatures

E4.141 Storage Conditions for Commonly Transplanted Human Tissue

Storage Conditions for Commonly Transplanted Human Tissue

Human Tissue	Storage Conditions	Temperature (°C) *
Cardiac, Vascular	Frozen, *Cryopreserved*	-100°C or colder
Cellular	*Refrigerated*	*Above freezing (0°C) to 10°C*
	Frozen, Cryopreserved	*Established by tissue bank*
Musculoskeletal	Refrigerated	Above freezing (0°C) to 10°C
	Frozen, *Cryopreserved* and non-cryopreserved (temporary storage for 6 months or less)	-20°C to -40°C
	Frozen, *Cryopreserved* and non-cryopreserved (long term storage)	-40°C or colder
	Lyophilized	Ambient **
Reproductive	Frozen, *Cryopreserved*	LN_2 (Liquid or Vapor Phase)
Skin	Refrigerated	Above freezing (0°C) to 10°C
	Frozen, *Cryopreserved*	-40°C or colder
	Lyophilized	Ambient **

* Warmest target temperature unless noted to be a range
**Ambient temperature monitoring not required for lyophilized tissue

E4.200 Expiration Date/Storage Period

The maximum storage period for tissue shall be appropriate to the type of tissue, *required storage temperature*, packaging, and *Processing*, as well as to its intended application. Expiration dates should be qualified to demonstrate that the packaging is suitable to maintain product integrity (e.g., sterility, moisture content) for the entire shelf life.

G3.000 LABELING INFORMATION

G3.100 Container Labels

G3.120 Content

Container labels shall include the *Tissue Identification Number.*

The ~~F~~*f*ollowing information shall be included on *the* container label unless space limitations require use of a corresponding insert:

1) Descriptive name of the tissue;

2) Name(s) and address(es) of tissue bank(s) responsible for determining donor suitability, *Processing* and *Distribution*. Should more than two banks be involved, the name of all banks are required but the address is only required for the bank determining donor suitability;

3) Expiration date (if applicable), including the month and year;

4) Acceptable storage conditions, including recommended storage temperature and/or acceptable storage temperature range;

5) *Disinfection* or *Sterilization* procedure utilized (if applicable);

6) Preservative (if utilized) and/or method of *Preservation* (if applicable);

7) Quantity *or other characteristics* of tissue expressed as *applicable (e.g.,* volume, weight, dimensions*, cell density, number of viable cells,* or a combination of these*)* ~~units of measure, if applicable~~;

8) Potential residues of *Processing* agents/solutions (e.g., antibiotics, ethanol, ethylene oxide, dimethylsulfoxide); and

9) A reference to the *Package Insert*.

G3.200 Summary of Records and Package Insert

G3.220 Package Insert Content

The *Summary of Records* may be included in the *Package Insert*. The *Package Insert* shall contain the following information:

1) A statement limiting use to specific health professionals (e.g., physicians, dentists, and/ or podiatrists);

2) A statement that the tissue is intended for use in one patient, on a single occasion only, or as is applicable for *Reproductive Tissue*;

3) Known contraindications (if any) to the use of the tissue;

4) Warnings and list of known possible significant adverse reactions;

5) A statement that *Adverse Outcomes* potentially attributable to the tissue must be reported promptly to the tissue supplier;

6) Presence of known sensitizing agents (if any);

7) A statement that indicates that the tissue may transmit infectious agents;

8) A statement, if applicable, that the tissue may not be *Sterilized* or re-sterilized.

9) Dosage information (if applicable);

10) Description of how the tissue was supplied (e.g., frozen, lyophilized, irradiated);

11) Type of antibiotics present (if applicable);

12) Concentration of preservative(s) and/or cryoprotectant(s) in final package solution(if applicable);

13) Instructions for opening the *Package* and/or *Container*;

14) Instructions for preparation of tissue for transplantation;

15) Expiration time of tissue following reconstitution *(upon preparation for use)*;

16) Instructions indicating that once a *Container* seal has been compromised, the tissue shall be either transplanted, if appropriate, or otherwise discarded;

17) ~~Recommended a~~*A*cceptable storage conditions and *Tolerance Limits*;

18) Special instructions required for the particular tissue*, when applicable* (e.g., ‘‘DO NOT FREEZE,’’ *“DO NOT X-RAY,” “DO NOT IRRADIATE”*);

19) A statement that it is the responsibility of the *Tissue Dispensing Service, Tissue Distribution Intermediary,* and/or *End-User* clinician to maintain tissue intended for transplantation in appropriate storage conditions prior to further *Distribution* or transplant and that *Recipient* records must be maintained for the purpose of tracing tissue post-transplantation;

20) A statement that the tissue is ‘‘DONATED HUMAN TISSUE,’’ when applicable; and

21) Effective date or other traceable version identifier.

G3.300 Transport Package Label Content

G3.310 Domestic Shipments

The transport package label shall include the following information:

1) Name, address and telephone number of the *Distribution* facility;

2) Name and address of the destination;

3) Unless the shipment contains reproductive tissue, prominent identification of contents as ‘‘DONATED HUMAN TISSUE;’’

4) Recommended storage conditions and transport expiration date (if applicable);

5) Type and quantity of refrigerant or other hazardous materials enclosed in the transport package; and

6) Any special handling instructions*, when applicable (e.g., "DO NOT FREEZE," "DO NOT X-RAY," "DO NOT IRRADIATE").*

H1.000 DISTRIBUTION AND DISPENSING—GENERAL

There shall be SOPs for the following: receipt of tissue orders, unit selection, final *Container*, and/or package inspection, shipping, and transportation of tissue for transplantation.

H1.010 Solutions

(S*, CT*) Any specifically required solutions needed to prepare the ~~*Allograft* skin~~ tissue ~~and/or cells~~ for use shall be made available to the utilizing facility.

(V) Any specially required solutions (not readily available in an operating room) needed to complete the vascular *Allograft* operative preparation procedure shall be made available to the utilizing facility. Each tissue bank should have procedures detailing proper storage, handling, and return of any required solutions.

H1.300 Requests for Donor Status and Tissue Processing Information

Donor risk assessment, tissue-related information, and tissue *Processing* details shall be made available to the ~~transplanting physician~~ *End-User* upon request, except such information that may infringe upon the confidentiality of donor information.

H4.000 RETURN OF TISSUE

H4.100 Temperature Records

~~(C, V, OA)~~
For tissue that requires controlled environmental temperatures, at a minimum, ~~D~~*d*ocumentation *is required* that *attests* the tissue was ~~continuously~~ maintained at ~~the~~ required storage temperatures ~~shall be maintained~~.

K1.000 QUALITY ASSURANCE PROGRAM

K1.200 Qualification, Verification, and Validation Requirements

Protocols shall be developed, implemented, and documented for the *Qualification*, *Verification*, or *Validation* of significant components of facilities, processes, equipment, reagents, labels, *Containers*, packaging materials, and electronic systems. Process validations shall be performed where the results of a process cannot be fully verified by subsequent inspection and test. *Validations shall be assessed when process changes are made and revalidation performed as indicated.* Determination of *the frequency and* which elements or

items are to be qualified, verified, or validated shall be made by individuals responsible for *Quality Assurance* and regulatory compliance. Evaluation of parameters tested shall be performed and adequacy of the study to demonstrate necessary outcomes shall be determined.

K1.210 Validation of Shipping Containers

(C, V, *CT*)
Qualification studies of the transportation devices and methods for temporary storage ~~of *Cryopreserved* cardiac, and vascular tissue~~ shall demonstrate maintenance of the temperature *and appropriate characteristics* of the ~~frozen~~ tissue at required storage temperatures for the entire requisite time.

K1.220 Validation Procedures—Packaging and Freezing Protocols

(C, V, *CT*)
~~Individual *Processing* facilities shall establish and document validated p~~*P*ackaging and freezing protocols*, to meet pre-specified tissue characteristics, shall be established and documented.*

K2.200 Microbiological Tissue Cultures

K2.210 Pre-Sterilization/Pre-Disinfection Cultures

(C, V, *CT*)
Standard E1.040 Sterilization/Disinfection of Tissue (C, V, *CT*) applies.

(S) Pre-processing skin cultures from representative anatomical areas shall be obtained prior to exposure of the tissue to antibiotic-containing *Processing* solutions or other disinfecting/sterilization methods. Culture results shall be documented in the donor's record. Individual anatomic areas yielding cultures positive for *Microorganisms* considered ~~being~~ pathogenic, highly virulent must be discarded unless the tissue can be disinfected/sterilized with a validated process (See E1.040 Sterilization/Disinfection of Tissue). The Medical Director or designee shall review all available pre-processing skin culture results prior to releasing the tissue for transplantation. Skin *Recovery* shall be performed as a separate zone from other tissue types so that culture results can be independently reviewed.

K2.220 Final/Pre-Packaging

(MS, OA, SB, C, V, *CT*)
Microbiologic testing of processed tissue, which includes testing to detect bacteria and fungi, shall be performed on each donor *Lot*.