



DEPARTMENT OF THE NAVY
BUREAU OF MEDICINE AND SURGERY
7700 ARLINGTON BOULEVARD
FALLS CHURCH, VA 22042

IN REPLY REFER TO
BUMEDINST 6300.21
BUMED-M3
27 Jul 2015

BUMED INSTRUCTION 6300.21

From: Chief, Bureau of Medicine and Surgery

Subj: ESTABLISHMENT OF A HUMAN CELL, TISSUE, AND CELLULAR AND
TISSUE-BASED PRODUCTS MANAGEMENT PROGRAM

Ref: (a) BUMEDINST 6300.8A
(b) 21 CFR 1270
(c) 21 CFR 1271
(d) American Association of Blood Banks (AABB) Guidelines for Managing Tissue
Allografts in Hospitals
(e) Standards for Blood Banks and Transfusion Services
(f) AABB Technical Manual
(g) American Association for Tissue Banking Standards for Tissue Banking
(h) The Joint Commission Comprehensive Accreditation Manual for Hospitals
(i) Standards of the College of American Pathologists
(j) ASD(HA) Policy Memo 00-Memo-2012-07-26 of 26 Jul 2012

Encl: (1) Definitions
(2) General Guidelines for Releasing Placenta
(3) Human Cell, Tissue, and Cellular and Tissue-Based Products Manager Appointment
Letter Template

1. Purpose. To provide a human cell, tissue, and cellular and tissue-based products (HCT/Ps) management program and requirements for safe acquisition, receipt, storage, distribution, and tracking, per regulatory requirements. To define the management process regarding audits, recalls, and investigation of adverse events or infectious complications related to tissue(s).

2. Scope. This instruction applies to all medical centers, dental centers, hospitals, clinics, and tenant commands that use tissue. This instruction does not reflect the process for retrieving living organ donations or vascularized composite allografts for transplantation. Refer to reference (a) for those processes. References (b) through (i) amplify regulatory requirements for management of HCT/Ps.

3. Background. The Navy Blood Program Office (NBPO) and Bureau of Medicine and Surgery (BUMED) Quality Assurance/Risk Management Program have identified the need for a standardized process for safe tissue acquisition, receipt, storage, handling, distribution, and tracking throughout Navy Medicine, according to regulatory requirements. To address this risk,

it is prudent to establish a well-defined and formal mechanism for tissue management. Reference (j) is the Assistant Secretary of Defense for Health Affairs (HA) memorandum directing establishment of policy for HCT/Ps that complies with regulatory standards. Enclosure (1) contains a list of definitions.

4. Policy. Procedures for the use of tissue(s) will be consistent throughout Navy Medicine and will be per the tissue(s) supplier's instructions and regulatory requirements. Medical or dental treatment facilities must have written procedures for all functions pertaining to the acquisition, receipt, storage, issuance, and tracking and tracing of tissues. References (d) and (f) provide process guidelines while references (e), and (g) through (i) provide required accreditation standards for management of HCT/Ps.

a. Inventory and Acquisition

(1) All tissue(s) will be managed, stored, and distributed by a tissue manager.

(2) All tissue(s) ordered by main operating room or individual service (i.e., dental clinic, dermatology clinic, wound care clinic, orthopedic clinic, and vascular clinic) supply officers, will be tracked by a service or area tissue manager.

b. Receipt and storage of tissue(s). Reference (e) provides specific requirements for receipt and storage of HCT/Ps

(1) Tissue(s) received will be logged and placed in appropriate storage, according to manufacturer instructions.

(2) Tissue Manager, or designee, will ensure tissues are logged using a tissue tracking log until a suitable electronic tracking system is available. The following information will be included in the log:

(a) Date received and name of staff member documenting arrival.

(b) Tissue description as listed on the package label.

(c) Tissue identification number, unique lot number, or serial number.

(d) Expiration date.

(e) Documentation of inspection of tissue container and contents (i.e., tissue).

(f) Temperature of the tissue upon arrival, and temperature of device or area used to store the tissue (i.e., refrigerator, freezer, or room temperature, according to manufacturer storage instructions).

(g) Location of storage device or area (i.e., freezer, refrigerator, or room temperature storage). A chart recorder or electronic measuring device will be used to continuously monitor the temperature of all tissue(s) storage areas, freezers, and refrigerators. An explanation for deviations from acceptable storage temperatures (i.e., freezer door open to perform inventory count) must be documented. Refrigerators and freezers used to store tissues will have an emergency power source. In the event of a power failure, tissue(s) will be managed per manufacturer recommendations and regulatory requirements.

c. Compromised Tissue(s). Tissues must not be used if any of the following conditions exist:

- (1) The container seal is damaged or otherwise not intact.
- (2) The container is physically damaged.
- (3) The container label or identifying barcode is severely damaged, not readable, or is missing.
- (4) The vacuum inside the freeze-dried container is not intact when the reconstitution procedure is started.
- (5) The freeze-dried container has been damaged by moisture or other environmental factors.
- (6) The freeze-dried graft has been hydrated for more than 24 hours.
- (7) The frozen graft has not been used within 24 hours of thawing or has been stored at temperatures outside the recommended storage temperatures.
- (8) The expiration date shown on the package label has been exceeded.
- (9) There is evidence that the appropriate storage temperature for the tissue has not been maintained.
- (10) Storage or handling of the tissue violates the manufacturer's specifications.

d. Documentation

(1) For tissue used in the operating room, perioperative personnel will enter appropriate information in the perioperative nursing note in Essentris® under implants, to include the information below:

(a) Identity of the staff member accepting the tissue, and issuing to surgical team for implantation (if separate staff members, document all staff member names).

(b) Date and time of receipt.

(c) Tissue description as listed on the package label.

(d) Tissue identification, unique lot, serial, or other identification number.

(e) Documentation of inspection of tissue container.

(f) Recipient's name and identification.

(g) Surgeon's name.

(h) Surgical procedure.

(i) Disposition of tissue(s) if not used (i.e., returned to refrigerator), or not used in its entirety.

(j) Preparation solutions and or medications (description, amount, dose, expiration date, manufacturer, lot number, name of clinical staff preparing tissue).

(2) For implanted tissue(s), the service area tissue manager, or designee, will ensure the following additional information is documented on the tissue tracking log or suitable electronic tracking system when available:

(a) Date, time, and staff member(s) who retrieved tissue for transplant/implant.

(b) Recipient's name and identification.

(d) Surgeon's name.

(e) Surgical procedure.

(f) Preparation solution and or medications used (description, name, manufacturer, lot number, dose, amount, expiration date, and name of clinical staff who prepared tissue).

(g) Document all parameters met for integrity and temperature (if applicable).

(3) For tissue used in a clinic or outpatient setting, the surgeon or designated staff member(s) will complete the documentation as stated above in the medical record procedure note in the patient health record, in addition to completing the tissue tracking log or suitable electronic tracking system.

(4) For tissue(s) or portions of tissue(s) not used, the tissue manager or designee will log the following additional information on the tissue tracking log or suitable electronic tracking system when available:

- (a) Other disposition, whether destroyed, discarded, or returned to manufacturer.
- (b) Reason for other disposition.

(5) Completed tissue tracking log, with the tissue establishment reply card(s), for return to the tissue establishment. References (d) and (f) provides guidelines while references (e), and (g) through (i) provides record-keeping requirements for an HCT/Ps program.

e. Report of Adverse Events

(1) Commands must have procedures for investigating adverse events and handling recalls. Adverse events must be communicated to the command tissue manager to ensure the adverse event is reported to the command via a patient safety report. The report will be submitted to include the following information:

- (a) Date of surgery.
- (b) Patient name, prefix, and patient identification number.
- (c) Surgeon(s) name.
- (d) Type of surgery.
- (e) Tissue identification number, unique lot number, or serial number.
- (f) Description of the adverse event and any other pertinent information regarding the event.

(2) Leadership, as assigned in the command's quality assurance program, will review the report and forward pertinent information to the respective tissue manager, or designee, and throughout the organization as appropriate.

(3) The command tissue manager shall notify the tissue(s) supplier by telephone and, in writing, document the response, or other pertinent information obtained from the supplier. The tissue supplier, if a tissue distribution intermediary, will contact the appropriate tissue processor and follow up with the surgeon or healthcare provider via the medical or dental treatment facility of the recipient per Food and Drug Administration (FDA) regulations for tissue establishment. All related records and correspondence must be maintained for at least 10 years per reference (e).

(4) When a look-back or recall is received on a tissue product, the tissue(s) will be quarantined and/or destroyed based on guidance provided by the FDA or the tissue establishment. Affected recipients of tissues, at any establishment that are subject to a recall, will be contacted by their healthcare provider to discuss possible illness or adverse reactions the recipient may experience.

(5) After the investigation is completed, a written report identifying the results and any corrective actions should be reviewed by the healthcare provider who transplanted or infused the tissue.

(6) A copy of the final report will then be sent to the BUMED Risk Manager and to the NBPO at the Office of Deputy Director, Healthcare Delivery (BUMED-M3). References (d) and (f) provide guidelines for reporting of adverse events. References (e), and (g) through (i) provide specific requirements for reporting adverse events associated with HCT/Ps.

f. Placenta Disposition

(1) Human placenta tissue designated for return to the patient is classified as HCT/Ps. Some state laws stipulate mothers can take their placenta home. Policy should be implemented by individual commands per state law and in conjunction with their legal departments. Command policy should require mothers be educated about placentas, including the potential for disease, and be required to sign the NAVMED Form 6300/19 (06-2015), Liability Waiver for Release of Placenta agreement indicating they understand the hazards involved, the placenta is no longer suitable for further testing, and to not sell the placental tissue.

(2) Requests by mothers to take possession of their placenta will be honored to the extent possible except in instances where the placenta has been sent for laboratory testing. Requests cannot be honored if the placenta has been treated with hazardous chemicals such as formaldehyde, or when the placenta carries the risk of transmitting blood-borne diseases such as human immunodeficiency virus (HIV) or Hepatitis C. General considerations for returning placentas to requesting mothers are given in enclosure (2).

5. Responsibilities. Reference (d) provides guidelines for oversight responsibility while reference (h) requires organizations assign oversight responsibility for a HCT/Ps management program.

a. Commanding Officers or Officers in Charge

(1) Appoint a privileged provider as the command tissue manager to oversee the tissue management program throughout the command. Commanding officers of large facilities may elect to also have service area tissue managers and/or tenant command tissue managers. Enclosure (3) is provided as a template appointment letter.

(2) Establish a tissue oversight committee or function whose purpose is to monitor the safety, effectiveness, and availability of tissue allografts and to provide peer review of their clinical use.

b. Command Tissue Manager

(1) Ensure the command maintains records of tissue acquisition, receipt, storage, distribution, surgeon and recipient identification, implantation information, final disposition, or expiration (whichever is later) are retained for a minimum of 10 years per reference (e).

(2) Ensure the command writes and maintains records of procedure manuals and publications pertaining to tissue handling, preparation, and use for a minimum of 10 years per reference (e). Records will allow bi-directional traceability and tracking of tissue(s) in the event of tissue recall or an adverse event.

(3) Ensure the command provides point of contact information to tissue source facilities for notification in the event of tissue recall or adverse events. Contacts source facilities for copies of appropriate documentation regarding the handling, storage, and preparation of tissue(s) if not provided with tissue(s) upon receipt. Ensures the tissue usage information cards supplied by the distributor are completed and returned to the distributor in order to assist with maintaining traceability.

(4) Ensure the command maintains records to demonstrate tissues requiring a controlled environment are stored at the required temperatures, depending on the manufacturer storage requirements. Records are maintained for a minimum of 10 years per reference (e). Ensures systems are in place for continuous temperature monitoring of refrigerators, freezers, nitrogen tanks, and other storage equipment/areas used to store tissues. Also ensures refrigerators, freezers, nitrogen tanks, and other storage equipment/areas used to store tissues at a controlled temperature have functional audible alarms and emergency back-up systems.

(5) Annually review tissue source facilities licensure and assures vendor registration with the FDA as an approved tissue establishment, as required by regulations.

(6) Ensure all personnel who handle, prepare, and dispense transplantable tissue are initially trained on the appropriate standard operating procedures (SOPs).

(7) Ensure personnel who handle, prepare, and dispense transplantable tissue review the appropriate SOPs annually to maintain full understanding of the process and requirements of this instruction.

(8) Ensure updated training documentation is maintained for all personnel who handle, prepare, and dispense transplantable tissue to reflect they have met their initial and annual training requirements.

(9) Ensure service area tissue managers and tenant command tissue managers have read this instruction and are familiar with its references.

(10) Liaise with service area tissue managers and tenant command tissue managers to ensure command compliance with the tissue management program.

(11) Maintain full responsibility for the program, but may delegate duties to service area tissue managers and tenant command tissue managers, as necessary, to meet compliance requirements of this instruction and its references.

c. Tenant Command Leadership. Appoint a tenant command tissue manager and ensure the tenant command's clinical use of tissue complies with this instruction.

d. Service Area Tissue Manager. Appoint a service area tissue manager to assist the command tissue manager with ensuring specific service areas such as the main operating room, dental clinic, orthopedic clinic policies, procedures, training, and program are in compliance with accrediting agencies.

e. Tenant Command Tissue Manager. Assist the command tissue manager as outlined above in subparagraphs 5b(1) through 5b(11) for tissue stored or used in the tenant command.

f. Head of Quality/Risk Management Department. Provide appropriate support to assist tissue manager(s) in adverse event investigations according to the hospital's patient safety reporting system.

g. Head of Logistics

(1) Ensures tissue vendors are registered with the FDA. The vendor will provide a copy of the FDA registration, state license, and other accrediting license, if any, to determine qualification of the supplier. Tissue suppliers should be selected based on their ability to reliably provide high quality tissues that meet expectations for tissue availability, safety, and effectiveness.

(2) Ensure logistics personnel receiving tissue products log the items and notify the service area tissue manager or designated representative at the earliest opportunity. If there is a delay in transporting tissues, logistics personnel will annotate the date and time of its receipt, as well as, the tissue's package integrity on a tissue tracking log or a designated electronic tracking system.

(3) Ensure contracts for tissue acquisition include a requirement for suppliers to provide a quarterly written report to the command that outlines and identifies all tissue by type, date ordered, date shipped, tissue identifier, serial number, lot number, and expiration date of products that were shipped to the facility so the facility can cross-reference and account for all

27 Jul 2015

tissue procured and received. This information will be cross-referenced with tissue usage information cards provided to the suppliers after implantation. This information provides the ability to track the tissue from donation to implantation.

(4) Contracts for tissue procurement include a requirement for the suppliers to notify the contract medical and dental treatment facility, BUMED Risk Manager at (703) 681-9187, and NBPO at (703) 681-5541/9123, of any recall or lookback, and assist Navy Medicine facilities and BUMED by providing any requested information in a timely manner. All information will be centrally requested by the command involved or the NBPO.

h. Oversight Committee

(1) Commands will establish a tissue oversight committee similar to the blood utilization review committee, to oversee and report any adverse events to the executive committee of the medical staff. Enclosure (3) is provided as a template appointment letter for committee chair and members.

(2) The command tissue manager will report to, and hold a seat on, the tissue oversight committee.

6. Summary. Adherence to this standardized policy across Navy Medicine supports a safe environment to patients receiving implanted tissues and tissue products. Meticulous auditing and tracking of compliance with this instruction is essential to ensuring a quality process, while maintaining all regulatory compliance.

7. Records Management. Records created as a result of this instruction, regardless of media and format, shall be managed according to SECNAV Manual 5210.1 of January 2012.

8. Reports. The reports required in instruction are exempt from reports control per SECNAV M-5214.1 of December 2005, Part IV, Paragraph 7k.

9. Form. NAVMED 6300/19 (06-2015), Liability Waiver for Release of Placenta is available at: <http://www.med.navy.mil/directives/Pages/NAVMEDForms.aspx>



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Distribution is electronic only via the Navy Medicine Web site at:
<http://www.med.navy.mil/directives/Pages/BUMEDInstructions.aspx>

DEFINITIONS

1. American Association of Blood Banks. An organization that accredits blood banks and transfusion services.
2. Authorized User. Any person granted express, implied, or apparent authority to complete an assigned task.
3. Blood Utilization Review Committee. A committee appointed by the command to oversee the appropriate use of blood and blood products.
4. Designated Personnel. Any person selected, or assigned by executive management, as being qualified to perform specific duties.
5. Essentris®. A comprehensive Military Health System computer platform utilized for inpatient clinical documentation.
6. HCT/Ps. Include, but may not be limited to: bone, cornea, skin, heart valves/conduits, tendons, fascia, dura, bone marrow, veins, arteries, cartilage, sperm, embryos, eggs, stem cells, placenta, cord blood, synthetic tissue (artificially prepared, human and nonhuman based), and other cellular and tissue-based transplant or implant products.
7. Lookback. After recognition of a newly infected tissue recipient, the identification and evaluation of other recipients from the common donor for the presence or absence of disease.
8. Quality Assurance/Risk Management Unit. Any person or organization element designated by executive management to perform the duties related to quality assurance.
9. Quarantine. The identification of tissue(s) deemed unsuitable for transplantation. Quarantine includes storage of tissue(s) in a physically separate and clearly identified area, for such use, or through use of other procedures, such as automated or manual designation, to prevent improper release for transplantation.
10. Recall. The tracking and removal of tissue(s) from active inventory that are identified by the FDA, or the tissue establishment, as posing potential health risks.
11. Tissue(s). Human (allograft and autograft) and nonhuman (xenograft) cellular based implantable, transplantable, or infusible products. Examples include tendon, ligament, amnion membrane, placental stem cells, heart valves, arteries, bone-derived products (paste, powder, putty, slurry, cancellous chips), cartilage, conjunctivae, cornea, skin/dermis, duramater, embryo, fascia, veins, hematopoietic or umbilical stem cells, leukocytes/lymphocytes, meniscus, nerves, oocyte/ovarian cells, pancreatic islet cells, parathyroid, pericardium, periosteum, sclera, semen,

or others that are classified as tissue(s) by federal law and regulation. Collagen or certain synthetic tissue(s), such as those derived from plastics and polymers, are not considered cellular based products.

12. Traceability. The ability to follow the history, location, receipt, storage, application, and final disposition of a product by means of recorded documentation.

GENERAL GUIDELINES FOR RELEASING PLACENTA

(DATE)

1. Medical treatment facilities should have a written policy for releasing placental tissue, which incorporates the following guidelines:

- a. Written authorization and documented consent by the mother to receive the placental tissue.
- b. Placental tissue to be removed from the facility is clearly identified as not being medical waste.
- c. Ensuring the placental tissue is transported in an appropriate, properly labeled, secured, and leak-proof container.
- d. Implementation of control measures to ensure absence of putrescence during transport.
- e. Instructions concerning safe-handling of the placenta and protection of others.
- f. Instructions for disposing of the placenta at home by normal means such as utilizing a biological waste service.

2. Counseling should be provided explaining that infectious risk prevents returning the placenta. Placental tissue should not be released if the following circumstances exist:

- a. Mothers with documented and/or suspected chorioamionitis.
- b. Mothers with documented and/or suspected active bacterial infection.
- c. Mothers with documented blood borne viral infections, such as HIV, hepatitis B or C.
- d. Treatment of placental tissue with hazardous chemicals such as formaline, formaldehyde or other fixatives, may preclude tissue release.

HUMAN CELL, TISSUE, AND CELLULAR AND TISSUE-BASED PRODUCTS
MANAGER APPOINTMENT LETTER TEMPLATE

6000
Ser 00/
Date

From: Commanding Officer, (facility/area/tenant command)

To: (Name of Appointee)

Subj: APPOINTMENT AS HUMAN CELL, TISSUE, AND CELLULAR AND TISSUE
BASED PRODUCTS PROGRAM MANAGER FOR (FACILITY, AREA, OR TENANT
COMMAND)

Ref: (a) ASD(HA) Memo of 26 Jul 2012

(b) BUMEDINST 6300.21

1. Effective this date, you are hereby appointed as (*facility tissue manager, service area tissue manager, tenant command tissue manager*) for (*facility/area/tenant command*) HCT/Ps per reference (a). This appointment is effective immediately and is in addition to your primary assigned duty. In carrying out your responsibilities as (*facility tissue manager, service area tissue manager, tenant command tissue manager*), you must ensure performance of the functions as described in reference (b) and compliance with the most current versions of its listed references.
2. If, at any time you anticipate a change in your availability for the responsibilities of this appointment, you should notify your commanding officer at the earliest opportunity. In such circumstances, you are expected to provide your recommendation for an appropriate interim replacement or successor.
3. Your appointment as (*facility tissue manager, service area tissue manager, tenant command tissue manager*) reflects your commitment to quality patient care and the highest standards of Navy Medicine.

A. B. COMMAND