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

IN REPLY REFER TO
BUMEDINST 6300.21A
BUMED-M3
31 Dec 2018

BUMED INSTRUCTION 6300.21A

From: Chief, Bureau of Medicine and Surgery

Subj: HUMAN CELLS, TISSUES, AND CELLULAR AND TISSUE-BASED PRODUCTS MANAGEMENT PROGRAM

Ref: (a) BUMEDINST 6300.8A
(b) 21 CFR
(c) ASD(HA) memo of 26 Jul 2012
(d) NAVMED P-5101
(e) NAVMED P-5120
(f) TJC Comprehensive Accreditation Manual for Hospitals

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

1. Purpose. To establish updated policy for a human cellular and tissue product (HCT/P) and 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). This instruction is a complete revision and should be read in its entirety.

2. Cancellation. BUMEDINST 6320.20.

3. Scope and Applicability. This instruction applies to all medical centers, dental centers, hospitals, clinics, and tenant commands using tissue. This instruction does not reflect the process for retrieving living organ donations or vascularized composite allografts for transplantation. Refer to reference (a) for retrieving living organ donations or vascularized composite allografts for transplantation. References (b), part 1270 and part 1271, through (f) amplify regulatory requirements for management of HCT/Ps. Accreditation requirements for management of HCT/Ps can be found in reference (f) (available at https://www.jcrinc.com/2018-comprehensive-accreditation-manual-for-hospitals-camh-/cah18/), the American Association of Blood Banks (AABB) Guidelines for Managing Tissue Allografts in Hospitals (available at http://www.aabb.org), American Association for Tissue Banking Standards for Tissue Banking (available at https://www.aatb.org), and the Standards of the College of American Pathologists (available at http://www.cap.org).

4. Background. The Navy Blood Program Office (NBPO) and Bureau of Medicine and Surgery (BUMED) Quality Assurance and Risk Management Program have identified the need for a standardized process for safe tissue acquisition, receipt, storage, handling, distribution, and tracking throughout Navy Medicine (NAVMED), according to regulatory requirements. To address this risk, it is prudent to establish a well-defined and formal mechanism for tissue management. Reference (c) is the Assistant Secretary of Defense for Health Affairs (ASD(HA)) memorandum directing establishment of policy for HCT/Ps in compliance with regulatory standards. Enclosure (1) contains a list of definitions.

4. Policy. Procedures for the use of tissue(s) will be consistent throughout NAVMED 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. Reference (d) and the AABB Guidelines for Managing Tissue Allografts in Hospitals provide process guidelines. The American Association for Tissue Banking Standards for Tissue Banking, the Standards of the College of American Pathologists, and reference (e) provide 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, ophthalmology 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 and time 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 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 the electronic health record or Essentris® under implants, to include the following information:

(a) Identity of the staff member accepting the tissue and identity of the staff member 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 or implant.

(b) Recipient's name and identification.

(c) Surgeon's name.

(d) Surgical procedure.

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

(f) 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 in the medical record procedure note in the patient health record as stated in subparagraph 4d of this instruction, 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. Reference (d) and the AABB Guidelines for Managing Tissue Allografts in Hospitals provides guidelines while references (c), (e), and (f), the Standards of the College of American Pathologists, the American Association for Tissue Banking Standards for Tissue Banking, and the AABB Guidelines for Managing Tissue Allografts in Hospitals 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 must 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 or destroyed based on guidance provided by the FDA or the tissue establishment. Affected recipients of tissues that are subject to a recall will be contacted by the responsible 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 will be reviewed by the healthcare provider who transplanted or infused the tissue.

(6) A copy of the final report will then be sent via NAVMED East and NAVMED West to the BUMED Risk Manager and the NBPO at Healthcare Operations (BUMED-M3). Reference (d) and the AABB Guidelines for Managing Tissue Allografts in Hospitals provide guidelines for reporting of adverse events. The American Association for Tissue Banking Standards for Tissue Banking, the Standards of the College of American Pathologists, references (e) and (f) 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 will be implemented by individual commands per state law, when applicable, and in conjunction with legal review. Command policy must require mothers be educated about placentas, including the potential for disease and the risks associated with placental ingestion, and be required to sign the NAVMED 6300/19, Liability Waiver for Release of Placenta agreement, indicating they understand the hazards involved to include the risks of ingestion, the placenta is no longer suitable for further testing, and they agree not to 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. Policy for releasing placentas by request of mothers is outlined in enclosure (2).

5. Responsibilities. The AABB Guidelines for Managing Tissue Allografts in Hospitals provides guidelines for oversight responsibility while reference (f) requires organizations assign oversight responsibility for a HCT/Ps management program.

a. Medical Treatment Facility (MTF) and Navy Medicine Readiness and Training Command (NMRTC) Commanding Officers (CO) or Officers in Charge (OIC) must:

(1) Appoint a privileged provider as the command tissue manager to oversee the tissue management program throughout the command. Directors or COs of large facilities may elect to also have service area tissue managers 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 must:

(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) 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 and areas used to store tissues. Also ensures refrigerators, freezers, nitrogen tanks, and other storage equipment and 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 (SOP).

(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. Service Area Leadership. Must appoint 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.

(1) Ensures 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.

(2) Ensures 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

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.

(3) 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 or 9123, of any recall or lookback, and assist NAVMED 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.

d. 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 medical executive committee. 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 NAVMED 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

a. Records created as a result of this instruction, regardless of format or media, must be maintained and dispositioned for the standard subject identification codes (SSIC) 1000 through 13000 series per the records disposition schedules located on the Department of the Navy/Assistant for Administration (DON/AA), Directives and Records Management Division (DRMD) portal page at https://portal.secnav.navy.mil/orgs/DUSNM/DONAA/DRM/Records-and-Information-Management/Approved%20Record%20Schedules/Forms/AllItems.aspx.

b. For questions concerning the management of records related to this instruction or the records disposition schedules, please contact your local records manager or the DON/AA DRMD program office.

8. Review and Effective Date. Per OPNAVINST 5215.17A, BUMED-M3 will review this instruction annually around the anniversary of its issuance date to ensure applicability, currency, and consistency with Federal, Department of Defense, Secretary of the Navy, and Navy policy and statutory authority using OPNAV 5215/40 Review of Instruction. This instruction will be in effect for 10 years, unless revised or cancelled in the interim, and will be reissued by the 10-year

anniversary date if it is still required, unless it meets one of the exceptions in OPNAVINST 5215.17A, paragraph 9. Otherwise, if the instruction is no longer required, it will be processed for cancellation as soon as the need for cancellation is known following the guidance in OPNAV Manual 5215.1 of May 2016.

9. Information Management Control. Reports required in paragraphs 4 and 5 of this instruction are exempt from reports control per Secretary of the Navy Manual 5214.1 of December 2005, part IV, subparagraph 7k.

10. Form. NAVMED 6300/19, Liability Waiver for Release of Placenta is available at: http://www.med.navy.mil/directives/Pages/NAVMEDForms.aspx.

TERRY J. MOULTON
Acting

Releasability and distribution:
This instruction is cleared for public release and is available electronically only via the Navy Medicine Web site, 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 and 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 and 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, dura mater, embryo, fascia, veins, hematopoietic or umbilical stem cells, leukocytes, lymphocytes, meniscus, nerves, oocyte cells, ovarian cells, pancreatic islet cells, parathyroid, pericardium, periostium,

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.

POLICY FOR RELEASING PLACENTA

1. MTFs and NMRTCs must develop and implement written policy and procedure relating to a patient's right to retain and take home placental tissue upon request, consistent with paragraph 4f of this instruction and Federal regulations; State law when applicable; local laws of foreign countries; hospital regulations when applicable; and accreditation standards. Release of healthy placental tissue to the patient varies by States that have implemented laws or is controlled by hospitals in States that have no laws. As of this update, there are four States with laws (Hawaii, Oregon, Texas, and New York). Command policy must incorporate at a minimum, education on the following risks:

a. Written authorization by the healthcare provider and documented consent by the mother to receive the placental tissue. Use NAVMED 6300/19 to establish agreement the mother understands the hazards involved, to include the risks of ingestion, the placenta is no longer suitable for further testing, and they agree not to sell the placental tissue.

b. Placental tissue to be removed from the facility must be clearly identified as not being medical waste.

c. Requirement that placental tissue must be properly handled and transported in an appropriate, properly labeled, secured, and leak-proof container (e.g., Defense Medical Logistics Standard Support Item ID 81283, "BUCKET, 169OZ PLACENTA BUCKET W LID"). The MTF will not provide refrigeration of the placenta prior to transporting home; however, it may provide a plastic basin and ice to facilitate safe transport home.

d. Implementation of control measures to ensure absence of putrescence during and after transport. Advise the patient to bring a cooler to minimize ice melt and safely transport placental tissue. Upon arriving home, immediately refrigerate or freeze it.

e. Instructions concerning safe-handling of healthy placenta and protection of others include, at a minimum, the importance of washing hands thoroughly with soap and water after handling placenta.

f. Instructions for disposing of placenta at home in compliance with state or local law (for example, as biomedical waste or household trash). Disposal in household trash may be prohibited.

g. Instructions and education on the risks of placental ingestion including the risks of infection that can affect the mother and the baby. No guidelines or standards exist for processing the placenta for consumption. Placental encapsulation may not eradicate infectious pathogens. Therefore, placenta ingestion (including placenta capsules) is not encouraged. The following article and link is available from the Centers for Disease Control and Prevention (CDC):

(1) Buser GL, et.al. Notes from the Field: Late-Onset Infant Group B Streptococcus Infection Associated with Maternal Consumption of Capsules Containing Dehydrated Placenta – Oregon, 2016. MMWR Morb Mortal Wkly Rep 2017; 66:677-678.

(2) CDC: https://www.cdc.gov/mmwr/volumes/66/wr/mm6625a4.htm.

2. Counseling must be provided explaining the infectious risk in blood-borne diseases and the spread of communicable disease that prevents returning placental tissue to the mother if the following circumstances exist:

a. Mothers with documented or suspected intraamniotic infection, also known as chorioamionitis.

b. Mothers with documented or suspected active bacterial infection.

c. Mothers with documented blood-borne viral infections.

d. Placental tissue has been treated with hazardous chemicals such as formalin, formaldehyde, or other fixatives.

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

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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 6300.21A

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*) human cell, tissue, and cellular and tissue-based products 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 must 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

Copy to:
BUMED-M3