

**Guidelines for Collecting, Maintaining, Requesting, and
Using Specimens Stored in the
Department of Defense Serum Repository**

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Army Medical Surveillance Activity
Directorate of Epidemiology and Disease Surveillance
U.S. Army Center of Health Promotion and Preventive Medicine

1. REFERENCES

- a. Public Law 105-85 sec. 765, 18 Nov 1997
- b. 10 US Code section 1074f
- c. Department of Defense Directive 6490.2, 30 Aug 1997
- d. Department of Defense Instruction 6490.3, 7 Aug 1997
- e. Memorandum, Assistant Secretary of Defense (Health Affairs), 30 Sep 1999
- f. Memorandum, Assistant Secretary of Defense (Health Affairs), 6 Oct 1998
- g. Memorandum, Joint Chiefs of Staff, MCM-0006-02, 1 Feb 2002
- h. Title 45 CFR 164.512 (“HIPAA privacy regulations”)
- i. Title 45 CFR 46 (“Common rule”)
- j. Title 32 CFR 219
- k. Office of Human Subjects Research, National Institutes of Health, Information sheet #14, subject: Guidance on the research use of stored samples or data.
- l. Centers for Disease Control and Prevention, Guidelines for defining public health research and public health non-research.

2. BACKGROUND

- a. *Laws, regulations, and guidelines:*
 - i. References a and b direct the Secretary of Defense to establish a system (including blood samples maintained in a central location) to assess the medical conditions of servicemembers who deploy outside the United States.
 - ii. Reference c directs the establishment of a Department of Defense Serum Repository for medical surveillance, clinical diagnosis, and epidemiologic studies.
 - iii. Reference d directs the collection of sera from redeploying servicemembers for submission to a tri-service repository.
 - iv. Reference e directs the Army Medical Surveillance Activity, US Army Center for Health Promotion and Preventive Medicine, to provide the sole link between the DoD Serum Repository and other databases.
 - v. References f and g specify that sera collected for routine periodic or pre-deployment HIV-1 antibody testing fulfill the requirements for pre- and post-deployment serum samples.

vi. Reference h permits disclosures of health information by public health authorities authorized to collect such information for purposes of preventing and controlling disease through public health surveillance, investigations, and interventions.

vii. References i and j describe exemptions from federal policies regarding research involving human subjects, including studies of existing data or diagnostic specimens related to individuals who are not identified.

viii. Reference k states that research uses of existing unidentified or unlinked samples or data are generally exempt from requirements for prospective reviews by Institutional Review Boards.

ix. Reference l states that the primary intent of non-research in public health is to prevent or control a health problem in a population from which information is gathered; whereas the primary intent of research is to generate or contribute to generalizable knowledge.

b. *Current status*: In accordance with relevant laws, regulations, and guidelines, the Department of Defense maintains a repository of serum specimens collected prior to and during the military service of active and reserve component servicemembers. The primary purpose of the repository is to support force health protection, disease prevention, and public health programs of the Services, particularly related to operational deployments. However, the repository may also be used to support patient care, medical research, quality control programs within and outside the Department of Defense and other investigations when directed by the appropriate authority.

3. PURPOSE

This document establishes guidelines for collecting, maintaining, requesting, and using specimens stored in the Department of Defense Serum Repository (DoDSR).

4. RESPONSIBILITIES

a. The Army Medical Surveillance Activity is responsible for all aspects of operating the DoDSR.

b. The Chief, Army Medical Surveillance Activity, is the Director of the DoDSR.

5. PROCEDURES

a. *Initial specimens:* The first archived serum specimen of each servicemember will be collected during his/her pre-induction medical examination or as soon as possible after he/she begins military service.

b. *Follow-up specimens:* In general, follow-up specimens will consist of serum that remains after routine, periodic HIV-1 antibody testing (conducted in accordance with Department of Defense, regional combatant command, and Service-specific guidelines).

c. *Specimen and donor identification:*

- i. Specimens in the repository will be labeled with unique specimen identification numbers.
- ii. Linkages between specimen identification numbers and identities of specimen donors will be maintained exclusively in the Defense Medical Surveillance System.

d. *Processing, labeling, and shipping:*

- i. The Army Medical Surveillance Activity will develop and disseminate guidelines for processing, labeling, and shipping specimens to the DoDSR.
- ii. The Services will ensure that all specimens for archiving in the DoDSR are processed, labeled, and shipped to the repository in accordance with current guidelines.

e. *Shipping manifests:* On each day that serum specimens are shipped to the repository, the responsible Service or its contracted representative will provide the DoDSR with a manifest that documents:

- i. Date of shipment;
- ii. Source of shipment (e.g., Service, name and location of laboratory);
- iii. Point of contact (i.e., name, telephone number, email address);
- iv. Shipping information (e.g., Federal Express tracking number);
- v. Number of boxes included in the shipment;
- vi. Number of specimens included in the shipment;

f. *Specimen Data:* For each specimen sent to the repository, the responsible Service or its contracted representative will provide the DoDSR with an electronic file that includes, at a minimum, the following specimen information:

- i. Specimen identification number;
- ii. Social security number of donor;
- iii. Date specimen was drawn;
- iv. Location of specimen: box number, column, and row.

g. *Specimen handling:*

i. Other than during the preparation of serum/aliquots for shipment or use, the Services, the DoDSR, and their contracted representatives will ensure that specimens remain continuously frozen at approximately -30°C .

ii. All episodes of thawing/refreezing of specimens will be reported to and documented by the DoDSR (by date and specimen identification number).

h. *Authority to release specimens:*

i. The Director of the repository is solely responsible for authorizing releases of specimens from the repository.

ii. The Director may delegate authority to release specimens from the repository during his/her absence or unavailability. Delegation of authority to release specimens must specify individual(s), period(s) of time, and natures of contingency(ies) during which delegations of authority are in effect.

iii. The Director of the repository will adhere to all relevant laws, regulations, directives, and guidelines (including all specifications of this SOP) prior to authorizing releases of archived specimens.

iv. As a general rule, the last 0.5 milliliter of a specimen will not be released from the repository if:

- a) The specimen was collected within one year of the donor's deployment to or return from a major joint/unified command operation overseas;
- b) No other sera from the donor are archived in the DoDSR;
- c) The donor has been identified as a "case" in a current, previous, or known pending clinical or seroepidemiologic study.
- d) The donor has been identified as "exposed" to a known or hypothesized health risk in a current, previous, or known pending epidemiologic study.

i. *Physical security:*

i. Only individuals specifically authorized by the Director are permitted access to the repository.

ii. The DoDSR will comply with all applicable federal, state, local, Department of Defense, and Department of the Army laws and regulations regarding physical security.

j. Visits:

- i. Visits to the repository must be authorized in advance by the Director.
- ii. Requests to visit the repository must include:
 - a) Date and time of the requested visit;
 - b) Names, ranks/grades, and job titles of all visitors;
 - c) Specific reasons for/objectives of the requested visit;
 - d) Point of contact (i.e., name, voice telephone, e-mail).
- iii. Visitors must sign in, sign out, and be escorted throughout their visits.

6. REQUESTS FOR SPECIMENS

a. Requests for and limitations on uses of specimens, general:

- i. Requests for uses of specimens must indicate the following:
 - a) Specific objectives;
 - b) Serologic assays to be performed per objective;
 - c) Volume of serum required per assay to be performed;
 - d) Specific requirements of the DoDSR (e.g., number, volume, labeling, delivery of aliquots) and AMSA (e.g., identification of subjects/serum specimens with various characteristics).
- ii. Specimens from the DoDSR may be used only for purposes specifically requested and authorized prior to use.

b. Unused serum:

- i. Serum that remains after authorized uses may not be retained by users or used for purposes not specifically authorized.
- ii. The disposition of unused serum should be coordinated with the Director of the DoDSR.

c. Reimbursement, general:

- i. Users of specimens will reimburse the repository for costs associated with identifying appropriate specimens for intended uses; locating, retrieving, apportioning, and delivering required specimens (with appropriate documentation).

ii. The Director of the repository will determine costs associated with each use.
iii. In general, specimens will not be released until full reimbursement has been received.

d. *Responses to requests*: The timing and nature (e.g., estimated costs) of responses to requests to use serum will depend on multiple factors, including the following:

i. *Nature of intended use*: Requests specifically related to the evaluation, treatment, and/or protection of the health of current, former, or future U.S. servicemembers will have priority over other requests.

ii. *DoD versus non-DoD requestor*: Requests by individuals assigned to the Department of Defense will have priority over—and may be responded to more quickly than—requests from non-DoD requestors.

iii. *Magnitude of intended use*: In general, requests for small numbers of specimens will be responded to more quickly and will be less costly than requests for large numbers of specimens.

iv. *Method of selecting samples*: In general, requests that require complex sampling schemes (e.g., case-referent seroepidemiologic studies with multiple matching criteria) will be responded to less quickly and will be more costly than simpler requests.

e. *Non-research versus research use*:

i. Non-research: If the primary intention is to develop knowledge specific to the donors of specimens (e.g., evaluation/treatment of an illness or injury) or to populations/settings that donors specifically represent (e.g., outbreak investigation; detection or characterization of a current, emerging, or alleged health threat; assessment of the need for, the nature of, or the effect of a specific public health intervention in a specific population/setting), then the use is considered “non-research.”

ii. Research: If the primary intention is to create, extend, or validate generalizable knowledge—that is, knowledge that applies to individuals, populations, or settings external to and not directly associated with the donors of specimens from which the knowledge is generated—then the use is considered “research.”

iii. In general, non-research uses will be responded to more quickly than research uses.

iv. If there are questions regarding the research versus non-research nature of a requested use, the request should be referred by the requestor to his/her Institutional Review Board prior to its submission to the DoDSR.

v. At his/her discretion, the Director of the repository may defer responding to a request pending review by the requestor's Institutional Review Board.

f. *De-identified versus identified/identifiable specimens:*

i. If specimens are provided to users without information that identifies the donors *and* if all linkages between the specimens and donors are irreversibly destroyed, then the specimens are considered “de-identified”; otherwise, the specimens are considered “identified/identifiable.”

ii. In general, requests for “de-identified” specimens can be responded to more quickly than requests for “identified/identifiable” specimens.

7. SPECIFIC REQUIREMENTS, BY CATEGORIES OF INTENDED USE

a. *Research:*

i. General: The DoDSR will not release serum specimens for research use without a final protocol that includes all of the following:

- a) Details regarding the number, volume, and nature (e.g., labeling) of specimens required;
- b) Method(s) of selecting study subjects and serum specimens;
- c) Laboratory tests/assays to be conducted on each specimen/aliquot;
- d) Signatures of all investigators, coinvestigators, and collaborators;
- e) Written concurrences of all supporting individuals/organizations;
- f) Written approvals of all sponsoring/affiliated organizations;
- g) Written approvals of all cognizant institutional review boards/human use review committees.

h) Reimbursement.

ii. Modifications/amendments to previously approved research protocols: The DoDSR will not release specimens in support of modified/amended protocols without all of the following:

- a) A final copy of the modified/amended protocol;
- b) All previously listed requirements (section 7.a.i)

iii. Identities of serum donors/study subjects:

a) Linked/linkable identities of specimen donors: In general, studies that include or maintain links between serum specimens and the identities of their donors require the explicit informed consent of each donor.

b) Unlinkable identities of specimen donors: If links between serum specimens and the identities of their donors are irreversibly destroyed prior to the delivery of specimens to investigators (and if such links can never be reestablished), then the informed consent of each donor is generally not required.

iv. Relationship of investigators to the Department of Defense

a) Principal investigator(s) outside the Department of Defense: Serum specimens may be released to principal investigators outside the Department of Defense for purposes of medical research under the following conditions:

(1) Compliance with all applicable requirements in 6a(i-iii) of this document.

(2) The study has a coinvestigator who is assigned to the Department of Defense and is knowledgeable, responsible, and accountable for all aspects of the study's design and execution (including data management, analysis, interpretation, and reporting of results).

(3) The protocol includes written approvals of the cognizant Human Use Review Committees/Institutional Review Boards of the non-Department of Defense primary investigator and the Department of Defense coinvestigator.

b. *Patient care:*

i. Within the Military Health System:

a) Stored sera may be used by attending physicians in the Military Health System for the specific purposes of evaluating, treating, and/or following the clinical courses of individual patients (including assessment of immunologic susceptibility to vaccine preventable diseases/need for specific immunizations).

b) Sera used for patient care may be delivered to an attending physician without the explicit consent of the subject patients (in such cases, consent to use stored serum for one's own care is assumed).

c) Requests for uses of stored sera for patient care should be submitted by the attending physician to the Director of the DoDSR.

ii. Outside the Military Health System:

a) Stored sera may be used by attending physicians outside the Military Health System for the specific purposes of evaluating, treating, and/or following the clinical courses of individual patients (including the assessment of immunologic susceptibility to vaccine preventable diseases/need for specific immunizations).

b) In such cases, stored sera may be delivered to an attending physician only with the explicit signed informed consent of the subject patient (or an authorized representative of the patient if he/she is unable to provide consent).

c) Requests for stored sera for patient care outside the Military Health System should be submitted through a physician in the Military Health System in the same specialty as the requestor to the Director of the DoD Serum Repository.

d) A physician in the Military Health System in the same specialty as the requestor must validate the clinical relevance of the requested use prior to the release of any serum from the DoDSR.

c. Public health/force health protection: community and military preventive care

i. Specimens linked/linkable to the identities of donors: Linked specimens may be used without the explicit informed consent of the donors under the following conditions:

a) The use is non-research (by definition above).

b) The primary purpose is to characterize the nature, magnitude, and/or distribution of a specific and ongoing medical threat to individual US servicemembers, a defined military population, or a Military Health System beneficiary population (e.g., investigation of an outbreak); and/or to determine an intervention against a specific and ongoing medical threat to specific individuals or populations (e.g., public health response to an outbreak).

c) Prior to the release of linked/linkable specimens for public/force health protection purposes, there must be a plan for managing, reporting, and acting on all results (e.g., laboratory tests/assays) that are potentially relevant to the health care (e.g., indicative of a treatable illness) and/or the general welfare (e.g., evidence of a transmissible agent, genetic counseling) of the individual specimen donors;

d) Prior to the release of linked/linkable specimens for public/force health protection purposes, there must be approvals of all medical authority(ies) responsible for the health care of all individual donors.

ii. Specimens not linked and unlinkable to the identities of donors: De-identified specimens may be used for purposes of assessing and tracking the concentrations, distributions, and determinants of medically relevant conditions (e.g., susceptibility to vaccine-

preventable diseases) in defined military/other MHS beneficiary populations. Such uses are authorized when, for example, the primary *a priori* purpose is to develop or measure the effects of population based, military public health policies or interventions (e.g., deployment-specific immunizations, booster intervals for military vaccines, geographic -specific threat assessments).

d. Criminal investigations and prosecutions

Serum specimens linked to the identities of their donors shall be provided for use as evidence in criminal investigations and prosecutions when compelled by applicable law in cases in which all of the following conditions are present:

- i. The responsible DoD official has received a proper judge issued court order;
- ii. The serum sample is needed for the investigation or prosecution of a crime punishable by one year or more of confinement;
- iii. No reasonable alternative means for obtaining a serum sample is available;
- iv. The use is approved by the Assistant Secretary of Defense (Health Affairs) after consultation with the General Counsel of the Department of Defense.