

**US Army Medical Research and Materiel Command
Office of Research Protections
Human Research Protection Office
Guidance on HRPO Review Requirements for Research Involving the Secondary Use of
Data/Specimens**

All United States Army Medical Research and Materiel Command (USAMRMC) supported research involving the secondary use of human data, records, human tissue, or human specimens (hereafter referred as data/specimens) must be reviewed for compliance with Federal and Department of Defense (DoD) human subjects protection requirements and approved by the Office of Research Protections (ORP) prior to implementation. USAMRMC ORP Human Research Protection Office (HRPO) review includes assessing the source of the data/specimens and whether the initial manner and consent for the data/specimen collection permits use in the DoD funded research protocol. HRPO must review the use of post-mortem specimens for compliance with the Army Cadaver Use Policy.

For the purpose of this guidance, the term human specimens refers to the research use of any human anatomical substances or cell lines obtained or derived from humans, either living or post-mortem.

HRPO review, approvals, and determinations for specimen research are based upon the nature of the research, the source of the data/specimens, use and/or disclosure of identifiable health information, privacy and confidentiality protections, and whether the individual providing the data/specimens allowed the use of their data/specimens for research. Additional HRPO submission instructions and guidance are provided below.

HRPO Submission Form for Secondary Use.

For HRPO review of any DoD funded research activities involving access, use, and analysis of data/specimens, investigators should complete and submit the HRPO Submission Form for Secondary research found here: https://mrmc.amedd.army.mil/index.cfm?pageid=Research_Protections.hrpo

The Submission Form identifies the documents to include with the submission.

1. Secondary Research that Does Not Require HRPO Review Prior to Implementation.

A. HRPO review is not required for research conducted in its entirety using human cell lines obtained from commercially available repositories. If an investigator can purchase or obtain the cell lines from a vendor, the HRPO considers the cell lines commercially available. The vendor source could be a for-profit, not for profit, or academic entity. If the investigator has obtained/will obtain the cell lines from a collaborator and the collaborator purchased the cell lines from a commercial vendor, the cell lines are considered commercially available.

HRPO has determined the release of these samples to investigators does not meet the regulatory definition of human subjects research. Investigators/Program Management staff members are not required to forward this category of research to the HRPO for review and determination.

The following are examples commercial repositories/banks:

- American Type Culture Collection (ATCC)
- Cooperative Human Tissue Network (CHTN)
- Lonza
- National Center for Biotechnology Information (NCBI)
- National Disease Research Interchange (NDRI)

NOTE: If any cell lines from commercial sources were obtained post mortem the Army cadaver policy is applicable. NDRI, Lonza and International Institute for the Advancement of Medicine (IIAM) frequently obtain specimens post mortem, so investigators should be especially vigilant when either of these organizations is identified as the source. See Section F for HRPO requirements.

NOTE: This policy only applies to commercially available cell lines, and does not apply to other commercially available human anatomical substances (blood, saliva, tissue). HRPO will review use of other commercially available human anatomical substances per the guidance below.

B. HRPO review is not required when a DoD-funded organization is receiving samples to perform analyses as a commercial service to another organization. For example, Quest Diagnostic Laboratory providing serology support to a clinical trial through the receipt and analysis of samples does not require a separate HRPO review and determination.

2. Secondary Research that Requires HRPO Review Prior to Implementation.

A. Research on samples to be collected prospectively, explicitly, and solely for research.

DoD funded prospective collection of samples for research purposes requires both Institutional Review Board (IRB) and HRPO approval prior to implementation. These projects are not secondary use of samples. Investigators should complete the HRPO Submission Form for Human Subjects Research found on the HRPO website.

B. Secondary use of previously collected research samples.

HRPO review and determination is required for secondary use of existing human anatomical substances (specimens) for research. The consent form and protocol of the prior research activity must be reviewed by the institution to ensure that the proposed research use is not prohibited. The HRPO requires a copy of the consent form (and in some cases protocol) used to collect the data/specimens to determine whether the proposed research is consistent with any specific terms under which the specimens were collected and ensure the individual allowed the use of specimens for future research.

HRPO requires submission of an IRB office determination or IRB review of the DoD funded research activities. The institution/IRB can review the proposed DoD funded research through an amendment to an existing human subjects protocol to incorporate the proposed aims or a submission of a new protocol for IRB determination of human subjects research. Note that HRPO requires an IRB office/institutional review or determination specific to DoD funded research activities; a self-determination or self-certification process is not sufficient for HRPO review.

If the specimens originated outside the United States, HRPO will review the host nation oversight/approval of the collection activities and the collection consent form for prohibitions on export of samples out of country.

C. Research on excess clinical samples obtained/to be obtained from medical facility clinical departments/services (e.g. surgical discarded material obtained from clinical laboratories (including pathology) or clinical care areas, such as operating suites.)

HRPO review and determination is required for any DoD funded use of excess clinical samples, including pathology samples. The clinical samples may have been collected from patients who were given information (or signed a form) about storage and research use of excess samples. The

information (or signed form) may describe permissible storage and future use. The subjects may have specifically consented for use of their specimens for a specific research study.

HRPO requires submission of an IRB office review/determination of the DoD funded research activities and the institutional surgical/clinical consent form used for the consent to collection of the samples. The institution can review the proposed DoD funded research through an amendment to an existing protocol to incorporate the proposed aims or a submission of a new protocol.

If the specimens originated outside the United States, HRPO will review the host nation oversight/approval of the collection and the consent form for prohibitions on export of samples out of country.

If the proposed research is use of residual clinical specimens in support future US Food and Drug Administration (FDA) clearance of an in vitro diagnostic device, the FDA and HRPO requires prospective IRB review and approval of the research prior to implementation.

D. Research obtaining clinical specimens from established institutional clinical repositories, biobanks, or tumor banks.

Consent forms for material obtained from established institutional repositories, registries, or tissue banks are NOT required to be included in the submission for HRPO review. These entities have institutional procedures in place to ensure that the samples were collected with the appropriate consent of subjects and permitted release of data/specimens for research. If necessary during review, HRPO will request institutional procedures or confirm institution has oversight of the repository.

Example: A study will use existing and de-identified blood and liver samples obtained through the Pediatric Non-Alcoholic Fatty Liver Disease (NAFLD) Registry and the Tumor Bank of the University of Cincinnati. Both the registry and the bank are IRB approved and are considered to be institutional repositories. The surgical/clinical consent forms are not required to be submitted to HRPO.

HRPO requires submission of an IRB office review of the DoD funded research activities. In this case, the institution should review the proposed DoD funded research through a submission of a new protocol specific to the DoD funded research rather than an amendment to an established banking or collection protocol. Note that HRPO requires an IRB office/institutional determination for the DoD funded research activities; a self-determination or self-certification process is not sufficient for HRPO review.

E. Research on clinical or research specimens obtained from collaborators.

For this research, HRPO will review the submission and make a determination based upon the nature of the research, the source of the specimens, use and/or disclosure of identifiable health information, privacy and confidentiality protections, and whether informed consent/authorization of subjects should be required, among other factors as described in this guidance.

For HRPO review of specimens obtained from collaborators, investigators should complete and submit the HRPO Submission Form for Secondary research found on the HRPO website. The HRPO will require information on the source of specimens, the role of the collaborator, purposes of the collaboration, and the investigator access to identifiable data/specimens.

F. Research on cadavers and post-mortem human specimens.

HRPO reviews all projects involving cadavers in accordance with the 2012 Army Policy for Use of Human Cadavers for Research, Development, Test and Evaluation, Education or Training found here: https://mrmc.amedd.army.mil/index.cfm?pageid=research_protections.overview. In this policy, the term “cadaver” includes organs, tissue, bones, or other specimens obtained from an individual upon or after death.

HRPO requires an institutional approval from the organization performing work with cadaveric specimens. A determination, such as an “exempt” or “research not involving human subjects” determination, is not sufficient to document institutional approval. If there is no specific oversight committee at the performing institution for research with cadaveric specimens, a letter from the investigator’s department leadership, dean, environmental health office, or similar satisfies the requirement for institutional approval when the letter states that the investigator has met all institutional requirements to conduct the proposed project.

HRPO requires the investigator to identify the source of the cadaveric specimens and provide the template specimen donation form in use by that organization. This allows HRPO to confirm that the proposed research is reasonably consistent with donor intent.

HRPO also requires the investigator to provide basic information related to the physical security, safe handling, transportation, and disposition of cadaveric specimens.

Activities meeting the Army policy definition of “sensitive uses” (i.e. exposure of cadavers to destructive forces) have additional requirements, as well as a 15-day staffing period to the Office of the Surgeon General.

G. Use of unique or regulated sample types (human embryonic stem cell lines, fetal tissue)

HRPO submission and review is required when combining human specimens (e.g. cell lines, tissue) with non-human material to create a xenograft for research use. A xenograft is a surgical graft of tissue from one species to another species (for example, tissue from a patient’s cancerous tumor is implanted directly into a mouse). In addition to documentation of the institutional review and approval of the research, investigators should submit the consent form for the specimens used to create the xenograft for HRPO review and determination.

HRPO submission and review is required for research using fetal tissue and cell lines derived from fetal tissue. Note that use of cord blood or materials derived from a placenta are not considered fetal tissue. Due to state and federal laws that govern research use of fetal tissue, HRPO will confirm that the institutional review determined: the written consent of the mother was obtained; the fetus can be used for research; the use of fetal material is required for the research and other materials cannot be substituted; and the source of the materials are documented (institution, clinical providers, non-profit repositories, etc.).

HRPO adheres to the NIH policy requirements and requires submission and review of research on existing human embryonic stem cell lines and derivation of new human embryonic stem cell lines. Due to the ethical issues related to research use of embryonic stem cells, HRPO recommends investigators who plan to conduct research with embryonic stem cells consult HRPO for input during the proposal process. As part of the HRPO submission, investigators should provide the NIH registration numbers for the use of human embryonic stem cell lines.

3. HRPO Review and Determination. The HRPO will review the submission and request sufficient information to concur with the institutional review of the DoD funded activities. As required by DoD Instruction 3216.02, Encl 3, paragraph 4.c(1), when the institution determines either the activity is not research involving human subjects or is exempt research involving human subjects, the HRPO must concur with the performing institution's determination before the activity can begin. The HRPO will provide a written HRPO determination memorandum to the investigator and DoD funded institution and provide copies to the Science Officer and Contract Specialist. Investigators who do not have a designated institutional review board office at their institution (e.g. small business awardees) should consult HRPO for guidance on institutional review requirements.

4. If a clinical/surgical or research consent form is unavailable for HRPO submission and review: Institutional Certification Requirement

If an investigator proposes to use existing research data/specimens or excess samples from clinical care but the consent form is unavailable, HRPO requires that the researcher's institutional representative certify that the data/specimens can be used for the research contemplated. In order to do so, the institution must review how the data/specimens were originally obtained and what, if any, prohibitions were placed on the future use of the data/specimens. Note a statement that data/specimens are de-identified is not sufficient to support an allowable use of the data/specimens.

During the review of the HRPO submission, the HRPO may contact the institution to request an institutional certification that the data/specimens obtained for the DoD funded research are able to be ethically used given the scope/intent of the donor of the specimens.

Institutional certification is not required for data/specimens obtained from established institutional repositories, registries, or tissue banks because these entities have more procedures in place to ensure that release of samples/data is permissible.

An institutional representative can meet this requirement by providing a signed letter including the certification statement below to HRPO.

Institutional Certification:

The Principal Investigator (PI) [name of PI] for the research project [title of research] proposes to use existing [data and/or samples] from [description of source of data/samples, e.g., name of prior research project/PI/Institution, description of excess clinical samples].

The [name of PI's institution] has reviewed the [protocol and consent form of the prior research project or the relevant clinical care consent and/or policy] and determined that the proposed use of the [data/specimens] is not prohibited by the [protocol and consent form of the prior research project or the relevant clinical care consent and/or policy].

[Signature of Institutional Official]
