NIH HRPP SOP 6 v1

HRPP STANDARD OPERATING PROCEDURE/POLICY APPROVAL & IMPLEMENTATION

OFFICE OF HUMAN SUBJECTS RESEARCH PROTECTIONS

SOP Number: 6

SOP Title: DETERMINATIONS MADE BY THE OFFICE OF HUMAN SUBJECTS RESEARCH PROTECTIONS (OHSRP)

Distribution: Scientific Directors; Clinical Directors; Clinical Investigators, IRB Chairs, IRB Administrators, Protocol Navigators

Approval: Michael Gottesman — 9/17/13

Deputy Director for Intramural Research — **Date**

Date of Implementation: 9/17/2013

DHHS/NIH/OD/OIR/OHSRP

SOP 6. DETERMINATIONS MADE BY THE OFFICE OF HUMAN SUBJECTS RESEARCH PROTECTIONS (OHSRP)

TABLE OF CONTENTS

DHHS/NIH/OD/OIR/OHSRP

SOP 6. DETERMINATIONS MADE BY THE OFFICE OF HUMAN SUBJECTS RESEARCH PROTECTIONS (OHSRP)

6.1 PURPOSE

SOP 6 sets forth policies and procedures for OHSRP determinations of NIH research activities involving human subjects, and human specimens and/or data that do not require IRB approval. These determinations include exemptions under 45 CFR 46.101(b) (1)-(6), as well as OHSRP determinations that IRB review is not needed under NIH policy. (Collectively these two categories are referred to as research "excluded from IRB review.") For activities regulated also by FDA, as applicable, please refer to SOP 15, "Research Regulated by the FDA". Activities that may be IRB exempt under this policy may separately be subject to IRB review under applicable FDA regulations and policy**.**

6.2 POLICY

The Office of Human Subjects Research Protections (OHSRP) has sole NIH responsibility for making determinations to exclude research from IRB review under 45 CFR 46.101(b)(1)-(6) or NIH policy. Research may be excluded from the requirement for IRB review and approval if it involves only specimens/data without individually identifiable information, or if it meets 45 CFR 46 regulatory exemption criteria described below and the proposed research is not FDA-regulated. NIH researchers must follow the procedures set forth in this SOP.

6.3 DEFINITIONS

A. **Coded Data or Specimens**: For the purpose of this SOP, Coded Data or Specimens means that: 1. identifying information about specimens or data (such as name or social security number) that would enable the investigator to readily ascertain the identity of the individual to whom the private information or specimens pertain has been replaced with a number, letter, symbol, or combination thereof (i.e., the code); and 2. a key to decipher the code exists, enabling linkage of the identifying information to the private information or specimens.

B. **Data**: Information related to humans, including demographic, clinical, genetic and other individual information that may be derived from research with human subjects.

C. **Derivatives:** Materials produced by the modification of human specimens or isolation of a component(s) of samples originally obtained from humans. Examples include human stem cell lines, recombinant DNA clones of human genes, and isolated infectious agents from humans.

F**. Honest Broker**: A neutral intermediary (person or system) between the individual whose tissue and data are being studied, and the researcher. The honest broker collects and collates pertinent information regarding the tissue source, replaces identifiers with a code, and releases only coded information to the researcher.

G**. Human Subjects**: Means a living individual about whom an investigator (whether professional or student) conducting research obtains:

1. Data through intervention or interaction with the individual, or

2. Identifiable private information.

H. **Intervention** includes both physical procedures by which data are gathered (e.g., venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.

I. **Interaction** includes communication or interpersonal contact between investigator and subject.

J. **Private information** includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects.

K. **Individually Identifiable**: Individually identifiable means that the identity of the subject is or may readily be ascertained by the investigator or associated with the information (45 CFR 46.102)

L. **Material Transfer Agreement (MTA)**: a written document to facilitate the free transfer of materials between NIH scientists and other individuals or institutions. An MTA can be a model agreement such as the NIH Simple Letter Agreement ("SLA"), the Uniform Biological MTA ("UBMTA"), or one specifically developed for the transfer of materials from humans. There is a variety of templates (models) for MTAs at NIH, including the HM-MTA developed for the transfer of human materials from NIH intramural laboratories.

M. **Research:** A systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities that meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities.

N. **Research repository:** A collection of specimens or data for the overall purpose of sharing specimens and data for current and future research. Such research may be general and cover a wide array of diseases and topics, or may be more specific, focusing on a single disease or topic.

O. **Specimens**: A quantity of human tissue, blood, urine or other biologically derived material. A specimen can include everything from subcellular structures (DNA) to cells, tissue (bone, muscle, connective tissue), organs (e.g. liver, bladder, heart, kidney, skin), blood, gametes (sperm and ova), and waste (urine, feces, sweat, hair and nail clippings, shed epithelial cells, and placenta).

6.4 RESEARCH INVOLVING ONLY DATA/SPECIMENS, WITHOUT IDENTIFIABLE INFORMATION, THAT IS EXCLUDED FROM NIH IRB REVIEW

When an NIH research activity involves only the use of specimens and/or data that is either coded (and the NIH researcher/research team has no access to the code key) or is otherwise not individually identifiable, the research cannot begin until the PI has obtained a formal determination from OHSRP that the activity

does not require IRB review[1]. Such a request may involve de-identification of data/specimens by an "honest broker" as defined in this SOP. This requirement applies when data and/or specimens are coming to NIH researchers from outside collaborators, or repositories, as well as when NIH researchers send specimens or data that is either coded or otherwise not individually identifiable to individuals outside NIH.

A. Data and/or specimens received by NIH Researchers from collaborators and/or individuals outside NIH or from a different NIH laboratory.

    1. Data and/or specimens that are not individually identifiable: An NIH researcher who is using data and/or specimens that are not individually identifiable must obtain a determination from OHSRP that the research is excluded from IRB review.

    2. Coded data and/or specimens: An NIH researcher who is using data and/or specimens that are coded (and the NIH researcher/research team have no access to the code key) must obtain a determination from OHSRP that the research is excluded from IRB review.

B. OHSRP makes this determination, generally, when the following conditions are met:
    1. If the data or specimens were collected for research purposes, they must have been collected at a domestic or foreign institution with a Federalwide Assurance (FWA) or with certification that the specimens were collected under the laws and regulations of the foreign country for the protection of human subjects,

    2. The sending institution, if any, and as required by applicable law, has an IRB or Ethics Committee-approved research protocol that specifies what research activity will occur at NIH, and

[1] In this way, NIH exceeds the minimum requirements of 45 CFR 46, which do not expressly mandate OHSRP review in all cases. There are limited exceptions to this requirement (for OHSRP review), and they are set forth in Appendix 1 to SOP 5 describing activities with data and specimens that do not require IRB or OHSRP approval.

3. A written agreement specifies that the NIH researcher will not seek identifiable information or the key to the code linking the data or specimens to the human subjects. (See OHRP "Guidance on Research Involving Coded Private Information or Biological Specimens.") This agreement specifies that the sending institution will not share any identified data, identifiers, the code or means to determine the identities of individuals providing data and specimens with the researchers at the NIH. These terms may be included within a Material Transfer Agreement but can also be documented through e-mail communications.

4. Data and/or specimens provided by NIH researchers to collaborating researchers outside NIH[2] or to NIH researchers in a different NIH laboratory or Institute who are collaborating as part of the research team. Data must be:

    a. Not individually identifiable; or
    b. Not Identifiable through use of a code, i.e. the NIH researcher must not have access to a code key which identifies research subjects.

C. If NIH researchers collaborate with other researchers, pursuant to this SOP, the NIH researcher must not be able to identify the subject.

6.5 EXEMPT RESEARCH UNDER 45 CFR 46.101(b) THAT IS EXCLUDED FROM IRB REVIEW

OHSRP has sole NIH authority to make the determination that a research activity is exempt from the DHHS requirement for IRB review under 45 CFR 46.101(b) (see Appendix 2). Research involving tests, surveys, interviews or observations will not be granted exempt status if it represents a possible intrusion on the privacy of subjects. The OHSRP has discretion to refer a matter to an NIH IRB

[2] For more information about the NIH Office of Technology Transfer (OTT) requirements regarding the transfer of materials from NIH, contact your IC Technology Development Coordinator at http://www.ott.nih.gov/nih_staff/tdc.aspx. Also see the OTT Policy for the Transfer of Materials from NIH Intramural Laboratories at http://www.ott.nih.gov/PDFs/Policy-for-the-Transfer-of-Materials.pdf.

for ethical or policy reasons even if the research activity otherwise qualifies as IRB-exempt, see Section 6.12 below.

6.6 OTHER ACTIVITIES NOT SUBJECT TO THE REQUIREMENTS OF 45 CFR 46 AND THAT ARE EXCLUDED FROM IRB REVIEW

A. OHSRP has authority to determine that other activities involving human data and/or specimens fall outside of the purview of 45 CFR 46 and are excluded from IRB review when a researcher is uncertain about whether an activity is or is not human subjects research. These types of activities may include quality improvement/ assurance projects, case reports, program evaluation, and surveillance activities.

B. Research involving non-living individuals, data on these individuals, or specimens from these individuals is not subject to the requirements of 45 CFR 46, and does not require OHSRP or NIH IRB review. However, this type of research may be subject to other applicable laws and regulations. OHSRP encourages researchers working on research involving non-living individuals to contact their Institute or Center (IC) privacy coordinators prior to initiating this type of research.

Once it is determined that an activity falls into either of the above categories, research participant protection oversight is the responsibility of the IC.

6.7 ACTIVITIES NOT ELIGIBLE FOR EXEMPT RESEARCH AND CONSIDERATIONS FOR SPECIAL POPULATION GROUPS UNDER 45 CFR 46

A. All of the exemption categories in 45 CFR 46.101(b) are potentially applicable to research involving pregnant women, human fetuses and neonates (45 CFR 46, Subpart B).

B. None of the exemption categories of 45 CFR 46.101(b) apply to research when prisoners are research subjects, see (45 CFR 46, Subpart C).

C. Some exempt categories do not apply when children are research subjects, see Subpart D, 45 CFR 46, which states: Exemptions at §46.101(b)(1) and (b)(3) through (b)(6) are applicable to this subpart.

The exemption at §46.101(b)(2) regarding educational tests is also applicable to this subpart. However, the exemption at §46.101(b)(2), for research involving survey or interview procedures or observations of public behavior, does not apply to research with children (45 CFR 46, Subpart D), except for research involving observations of public behavior when the investigator(s) do not participate in the activities being observed. (Exemptions at §46.101(b)(1) and (b)(3) through (b)(6) may apply to research involving children.)

6.8 INVESTIGATOR RESPONSIBILITIES

A. NIH researchers must submit a form *Request for OHSRP Determination* (Attachments 1-3) to OHSRP to request a determination that the activity is exempt from IRB review.

B. Research activities may not begin until a final determination is issued by OHSRP. Studies that are determined to be exempt from IRB review must comply with the ethical criteria described in 6.12.A.

C.

6.9 OHSRP PROCEDURES FOR DETERMINING EXCLUDED STATUS

A. An OHSRP staff member will review each *Request for OHSRP Determination* form and communicate with the investigator if additional information is required. The investigator must respond to all requests for revisions or clarifications requested by OHSRP. After review, OHSRP will render a determination as follows:

   1. “Excluded from IRB Review” in which case applicable NIH institutional requirements may still apply.

   2. “Human Subjects Research Not Excluded from IRB Review”. The investigator must obtain IRB review and approval prior to initiating research.

B. If an activity is determined to be excluded, no further OHSRP action or oversight is required as long as the study is not amended. If the study is amended, the researcher needs to send an e-mail to OHSRP explaining the nature of the amendment and providing the original OHSRP approval number. The email should explain what new activity

ATTACHMENT 3 – HONEST BROKER AGREEMENT AND CERTIFICATION

Title of Research Project:
Senior Investigator Name:
OHSRP Determination Number:

Honest Broker Certification

By signing below, I agree/certify that:

1. I have reviewed this project with the Senior Investigator and agree to unlink, de-identify or code (select one) any data and/or specimens that will subsequently be used by the Investigator.

2. I will, under no circumstance, provide the Investigator or any member of the research team with identifying information about the subjects, information that would permit the re-identification of research subjects, or the key to the code (as applicable).

3. As applicable, I will not commence any research activities for this project until proof of IRB approval or an OHSRP Determination has been provided to me by the Investigator conducting the study.

4. I will not intervene or interact with human subjects during the conduct of this research project.

5. I will maintain the confidentiality of research subjects' identifiable information, records or specimens.

6. Once this project is complete I will destroy or return any identifiable information in my custody to its source, as appropriate and permitted by law and NIH policy. I understand that original copies of NIH data are not to be destroyed.

7. I will immediately inform OHSRP of any breaches to this agreement by calling 301-402-3444 or via e-mail at OHSR_NIH_DDIR@nih.gov.