RESEARCH USING CODED PRIVATE INFORMATION OR BIOSPECIMENS

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Research that uses coded specimens or coded identifiable private information, including protected health information, can be determined to be research not involving a human subject, and therefore not subject to IRB review, and to comply with the regulations of the Office of Human Research Protections (OHRP) and the Health Insurance Portability and Accountability Act (HIPAA) if all of the requirements detailed in this policy are met. This policy applies only to specimens or data not collected specifically for the current proposed research project through an interaction or intervention with living individuals, such as specimens or data collected primarily for clinical and/or quality improvement (QI) purposes or a previously approved research study, whether the specimens or information were collected in the past or will be collected in the future.

Investigators conducting human subject research in the DUHS must apply for a determination of exemption by completing a new protocol submission using the electronic e-IRB system. In his/her submission, the investigator will describe the proposed research in detail and the methods that will be used to protect the privacy of the subjects and the confidentiality of the specimens or identifiable private information, such as protected health information. These methods must include those outlined in this policy statement.

Only the IRB can declare a research activity exempt. Even if a project is declared exempt by the IRB, all key personnel must still meet institutional requirements for education on the protection of human subjects research.

The PI must notify the IRB if during the course of this research any changes are proposed in the research study. At that time, the IRB will decide whether or not the status of the research as not involving a human subject can continue. Similarly, continued HIPAA compliance will be evaluated.

A. Definitions

Code. This is a linking field as defined by HIPAA for re-identification [45 CFR 164.514(c)]. According to the federal regulation, the code cannot be “derived from or related to information about the individual and is not otherwise capable of being translated so as to identify the individual" (This language makes it impossible to use an encrypted identifier, or such combinations as Initials and Date of Birth as the code.). To comply with both OHRP and HIPAA regulations, the code cannot be part of the source specimen data or information database.

Data Use Agreement (DUA). This is the written assurance required by HIPAA that “the limited data set recipient will only use or disclose the protected health information for limited purposes” (45 CFR 164.514(e)(4)).

Honest Broker (HB). 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. This person has access to the source specimens and/or data that retain an identifier. When requests are made to use specimens from the repository or data from the database for research purposes, the HB is responsible for extracting, coding, and creating the limited data set from the source specimens and/or data and following the other procedures required by the IRB, as explained below under the heading Process. The HB must not be involved in the research being proposed (beyond creating the limited data set for use by the PI and other key personnel). If the HB is using PHI only for creating the limited data set and is not participating in the research, under HIPAA his/her activities are considered part of health care operations (45 CFR 164.501(6)(v), thereby permitting his/her use or disclosure of the PHI without waiver of authorization (45 CFR 164.502(a)(1)(ii)). The HB is the only person who has long-term access to the full subject identifiers and health information from the source specimens or information database.

**Identifiable Private Information.** OHRP regulations define identifiable private information as follows:

“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.”

45 CFR 46.102(f)(2)

**Limited Data Set.** This is the coded data set created by the IK by removing sufficient identification from the source specimen data or information database to meet the HIPAA definition of limited data set [45 CFR 164.514(e)]. The principal investigator (PI) must document for the IRB how creation of the limited data set is to be done.

**Principal Investigator (PI).** This person is responsible for conducting the research study in compliance with the terms of the IRB determination that the study is not human subject research. The PI and other key personnel are the only people who have long-term access to the limited data set for research purposes.

**Protected Health Information (PHI).** HIPAA privacy regulations define PHI, i.e., individually identifiable health information, as follows:

“Individually identifiable health information is information that is a subset of health information, including demographic information collected from an individual, and: (1) Is created or received by a health care provider, health plan, employer, or health care clearinghouse; and (2) Relates to the past, present, or future physical or mental health or condition of an individual; the provision of health care to an individual; or the past, present, or future payment for the provision of health care to an individual; and (i) That identifies the individual; or (ii) With respect to which there is a reasonable basis to believe the information can be used to identify the individual.”

(45CFR160.103)

**Source Specimen Data or Information Database.** These are the PHI data that are collected for clinical or research purposes, from which limited data sets are extracted for specific research projects.
Unique Identifier(s). These are the identifiers, unique to an individual subject, that are used by the Identity Keeper (IK), who is defined below in Section B, to link the code to the subject and, in turn, extract the subject’s specimen or data record. For example, it could be the medical record number (MRN), a combination of the MRN and account number, or an identifier internal to the source specimen data or information database.

B. IRB Submission and Review Process
The PI/study team are responsible for submitting the research protocol to obtain IRB determination of research not involving human subjects under 45 CFR 46.102(f), which declares that research involves human subjects only if the private information is "...individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information.)."

1. The Principal Investigator (PI) verifies that s/he:
   (a) Will not attempt or direct others to attempt to identify subjects in the research specimen/data set or ask the HB to do so,
   (b) Does not oversee the work of the designated HB for the proposed study
   (c) Will notify the IRB if any changes are proposed in the research study that might alter the IRB’s determination or HIPAA compliance related to the study.

2. The Honest Broker (HB) verifies that s/he:
   (a) Has or will possess the coded limited data set and/or biospecimens derived from the code together with the unique identifier(s) for subjects in the extracted data for the PI, initially or subsequently,
   (b) Will not reveal the code together with the unique identifiers to the PI or other key personnel for the proposed study unless approved by the IRB under special circumstances that ensure that the interests of human subjects involved in the research or to anyone outside DUHS, and
   (c) Does not work with or directly report to the PI or other key personnel for the proposed study and will not be involved in the proposed research study

3. IRB Review and Determination
An IRB Chair/Vice Chair will review the proposed research and assurances from the PI and HB to ensure the proposed research does not involve human subjects. If not covered by an existing grant or research agreement, the Chair/Vice Chair may also request or identify the need for a data use agreement (DUA) to ensure compliance with HIPAA requirements or a maternal transfer agreement (MTA) to govern the provision or receipt of biospecimens. The PI/study team will be directed to work with Duke’s Office of Corporate Research Collaborations (OCRC) to obtain the appropriate agreements (https://medschool.duke.edu/research/research-support-offices/office-corporate-research-collaborations). DUAs and MTAs must be submitted to the IRB following full execution.

C. Study Conduct
1. The Honest Brokers will:
   (a) Extract from the source specimens or information database that portion of the data/specimens that has been requested by the Principal Investigator (PI) for a given study, plus unique identifiers for each subject
   (b) Add a code for each subject to the extracted data, if not already assigned (e.g. barcode-labeled specimens)
(c) Create the limited data set (if applicable) from the extracted data according to HIPAA [45 CFR 164.514(e)] and retains the code
(d) Send the coded limited data set and/or biospecimens to the PI
(e) If 1) additional specimens or data for subjects in the original limited data set or 2) additional subjects with a limited data set/specimens are requested by the PI after the initial request has been fulfilled, the HB will extract the additional specimens or data, create a new coded limited data set, and send the new coded limited data set and/or biospecimens to the PI.

2. **The Principal Investigator (PI)** will conduct the study using only the coded limited data set and/or biospecimens obtained through the process described above. The PI will notify the IRB if any changes arise during the conduct of the study that might alter the IRB’s determination or HIPAA compliance related to the study.

Reference: FAQs, Terms and Recommendations on Informed Consent and Research Use of Biospecimens The Secretary’s Advisory Committee on Human Research Protections (SACHRP) July 20, 2011

Previous Version Dates: 05/15/2008