# Guide For Determining When Protocols Involving Coded Private Information or Biological Specimens Meet the Federal Definition of "Human Research"

**Does the activity involve research?**

*Research* means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities which 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.

**Does the research involve human subjects?**

*Human subject* 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 (the identity of the subject is or may readily be ascertained by the investigator or associated with the information).

*Note: Under the definition of human subject at 45 CFR 46.102(f), obtaining identifiable private information or identifiable specimens for research purposes constitutes human subjects research. Obtaining identifiable private information or identifiable specimens includes, but is not limited to:*

- *using, studying, or analyzing for research purposes identifiable private information or identifiable specimens that have been provided to investigators from any source; and*
- *using, studying, or analyzing for research purposes identifiable private information or identifiable specimens that were already in the possession of the investigator.*

**Does the research involve coded information?**

Identifying information (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** a key to decipher the code exists, enabling linkage of the identifying information to the private information or specimens.

**Does the researcher (or any of the research staff listed on the protocol) have access to the code (possibility of re-identifying subjects or readily ascertain the identity of the individual)?**

OHRP considers private information or specimens **not** to be individually identifiable when they cannot be linked to specific individuals by the investigator(s) either directly or indirectly through coding systems. **For example, OHRP does not consider research involving only coded private information or specimens to involve human subjects as defined under 45 CFR 46.102(f) IF the following conditions are BOTH met:**

I. the private information or specimens were not collected specifically for the currently proposed research project through an interaction or intervention with living individuals; **and**

# Guide For Determining When Protocols Involving Coded Private Information or Biological Specimens Meet the Federal Definition of "Human Research"

II. the investigator(s) cannot readily ascertain the identity of the individual(s) to whom the coded private information or specimens pertain because, for example:

- the investigators and the holder of the key enter into an agreement prohibiting the release of the key to the investigators under any circumstances, until the individuals are deceased (note that the HHS regulations do not require the IRB to review and approve this agreement);
- there are IRB-approved written policies and operating procedures for a repository or data management center that prohibit the release of the key to the investigators under any circumstances, until the individuals are deceased; or
- there are other legal requirements prohibiting the release of the key to the investigators, until the individuals are deceased.

**What if the individual providing the specimen is involved in the conduct, analysis or reporting of the research?**

*If the individuals who provide coded information or specimens collaborate on other activities related to the conduct of this research with the recipient investigators, then OHRP would consider such additional activities to constitute involvement in the conduct of the research (ex. the study, interpretation, or analysis of the data resulting from the coded information or specimens; authorship of presentations or manuscripts related to the research).*

**What if the investigator unexpectedly learns or believes it is necessary to learn the identity of individuals to whom the previously obtained private information or specimens pertain?**

*If an investigator who obtains coded private information or specimens about living individuals unexpectedly learns the identity of one or more living individuals, or is able to readily ascertain, the identity of the individuals to whom the previously obtained private information or specimens pertain, then the research activity now would involve human subjects under the HHS regulations. Unless this human subjects research is determined to be exempt under HHS regulations at 45 CFR 46.101(b), IRB review of the research would be required. Informed consent of the subjects also would be required unless the IRB approved a waiver of informed consent under HHS regulations at 45 CFR part 46.116(c) or (d).*

**What if testing requires analysis of fresh tissue?**

*For procurement of fresh tissue, it may be necessary to have prior knowledge of specific procedures in order to obtain excess tissue in time to conduct analysis that is sensitive to tissue decay. However, if knowledge of surgical procedures results in the researcher's ability to ascertain a patient's identity, then the research activity involves human subjects and would require IRB review. Research personnel showing up at the operating room to collect a sample indicates prior awareness of the individual patient. Doing so would only be allowed under an IRB approved research protocol and with informed consent.*

*In such cases, it is recommended to consult with an organized specimen bank that can perform rapid identification of tissue availability and serve as an honest broker* to promptly provide the specimen to researchers without identifiers. Organized biospecimen repositories that provide such procurement services generally operate under an IRB approved protocol in which donors have provided informed consent and authorization for research use and/or sharing of excess or leftover specimens for research purposes.*

**An honest broker is 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.*

# Guide For Determining When Protocols Involving Coded Private Information or Biological Specimens Meet the Federal Definition of "Human Research"

*Access the following links for information on biospecmen repositories:*
*http://www.ccts.uky.edu/ccts/BIOCCTS or http://ukhealthcare.uky.edu/markey/biospecimen/*

**What if the research is NIH-funded and generates large-scale genomic data?**

The NIH Genomic Data Sharing (GDS) Policy requires informed consent for future research and broad data sharing be obtained **even if the cell lines or clinical specimens are de-identified.** The NIH GDS policy applies to all NIH-funded research that generates large-scale genomic data. Large-scale data include genome-wide association studies (GWAS), single nucleotide polymorphisms (SNP) arrays, and genome sequence, transcriptomic, metagenomic, epigenomic, and gene expression data. Examples can be found in the Supplemental Information to the NIH Genomic Data Sharing Policy.

**What if the research is federally-funded and includes use newborn dried blood spots?**

The Newborn Screening Saves Lives Reauthorization Act of 2014 includes two significant changes to the human subjects regulations as they apply to research with newborn dried blood spots. First, the law requires that all research funded pursuant to the Public Health Service Act using newborn dried spots be considered human subjects research **regardless of whether the specimens are identifiable**. This means that such research will require IRB review. Second, the law eliminates the ability of the IRB to waive informed consent under 45 CFR 46.116(c) and 116(d) for research involving newborn dried blood spots. Therefore, parental permission must be obtained to conduct this research.

**Could the research be exempt under HHS regulation 45 CFR 46.101(b)?**

"Research involving the collection or study of **existing** data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is **recorded** by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects."

*Note: This exemption would not apply if the investigators, having obtained identifiable private information or specimens from existing records or specimens, record the data or information in a coded manner, since the code would enable subjects to be identified through identifiers linked to the subjects.*

References:

OHRP - Guidance on Research Involving Coded Private Information or Biological Specimens (2008) http://www.hhs.gov/ohrp/policy/cdebiol.html

Attachment D: FAQ's Terms and Recommendations on Informed Consent and Research Use of Biospecimens https://www.hhs.gov/ohrp/sachrp-committee/recommendations/2011-october-13-letter-attachment-d/#

NIH Genomic Data Sharing Policy (2014) https://gds.nih.gov/

Newborn Screening Saves Lives Reauthorization Act (2014) https://www.congress.gov/bill/113th-congress/house-bill/1281