

OHRP Guidance on Research Involving Coded Private Information or Biological Specimens *October 16, 2008*

*Applies to research involving coded private information or human biological specimens that is conducted or supported by HHS.*

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*...obtaining identifiable private information or identifiable specimens for research purposes constitutes human subjects research.*

# OHRP Guidance on Research Involving Coded Private Information or Biological Specimens *October 16, 2008*

*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;*

- (1) have been provided to investigators from any source*
- (2) that were already in the possession of the investigator.*

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## *Private information or specimens*

- *are individually identifiable when they can be linked*
- *are not individually identifiable when they cannot be linked*

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*OHRP does not consider research involving **only** coded private information or specimens to involve human subjects if the following conditions are both met:*

- (1) the private information or specimens were not collected specifically for the currently proposed research project through an interaction or intervention with living individuals; and*
- (2) the investigator(s) cannot readily ascertain the identity of the individual(s) to whom the coded private information or specimens pertain because:*
  - (a) 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;*
  - (b) 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*
  - (c) there are other legal requirements prohibiting the release of the key to the investigators, until the individuals are deceased.*

# OHRP Guidance on Research Involving Coded Private Information or Biological Specimens *October 16, 2008*

*Guidance applies to:*

- *existing private information and specimens*
- *private information and specimens to be collected in the future for purposes other than the currently proposed research.*
  - *The following are examples of private information or specimens that will be collected in the future for purposes other than the currently proposed research:*
    - (1) medical records; and*
    - (2) ongoing collection of specimens for a tissue repository.*

# OHRP Guidance on Research Involving Coded Private Information or Biological Specimens *October 16, 2008*

## ***Research not Involving Human Subjects Versus Exempt Human Subjects Research***

*(1) Does the activity involve research? If yes, proceed to question (2). If no, 45 CFR part 46 does not apply to the activity.*

*(2) Does the activity involve human subjects? If yes, proceed to question (3). If no, 45 CFR part 46 does not apply to the activity.*

*If the investigators are not obtaining either data through intervention or interaction with living individuals, or identifiable private information, then the research activity does not involve human subjects.*

*(3) Is the activity exempt under HHS regulations at 45 CFR 46.101(b)? If yes, 45 CFR part 46 does not apply. If no, 45 CFR part 46 does apply.*

# OHRP Guidance on Research Involving Coded Private Information or Biological Specimens *October 16, 2008*

## *Research not Involving Human Subjects Versus Exempt Human Subjects Research*

*(3) Is the activity exempt under HHS regulations at 45 CFR 46.101(b)?*

*45 CFR 46.101(b)(4) 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.*

*If the investigators are obtaining identifiable private information or specimens, assessment under the exemption at 45 CFR 46.101(b)(4) focuses, in part, on:*

- (1) whether the data or specimens are **existing** at the time the research, and*
- (2) how the data or information is **recorded** by the investigators.*

# SECRETARY'S ADVISORY COMMITTEE ON HUMAN RESEARCH PROTECTIONS (SACHRP)

## PURPOSE

*...shall provide expert advice and recommendations ...on issues and topics pertaining to or associated with the protection of human research subjects.*

*...work to advise the Secretary as to how to improve the quality of the system of human research protection programs,*

# SACHRP Frequently Asked Question #18

## *research involving human subjects?*

*A tissue biopsy was obtained for clinical diagnostic purposes, which have now been satisfied. The hospital pathology department is willing to provide a portion of the remaining biopsy specimen to an investigator, who will perform research assays with no clinical relevance.*

*If the specimen is coded and identifying information is removed so that the identity of the patient cannot be readily ascertained by the investigator before it is provided to them (so that it is deidentified for the purposes of HIPAA), is the investigator conducting human subjects research under the purview of an IRB?*

**Response.** *No, this is not research involving human subjects, because the recipient investigator will not be able to readily ascertain the identity of patients from whom specimens were obtained.*

# SACHRP Frequently Asked Question #19

## *research involving human subjects?*

*A tissue biopsy was obtained for clinical diagnostic purposes, which have now been satisfied. The hospital pathology department is willing to send a portion of the remaining biopsy specimen to an investigator, who will perform research assays.*

*If the specimen will be provided to the researcher in an identifiable manner, is this considered to be human subjects research under the purview of an IRB?*

**Response.** *Yes, this is human subjects research. Because investigators will receive a specimen with identifiable information, the research is non-exempt human subjects research that is nevertheless potentially eligible for expedited review.*

# SACHRP Frequently Asked Question #5

## *Is consent or waiver of consent required?*

*When can informed consent be waived for use of previously-collected human specimens and data?*

**Response.** *The criteria for waiver of consent under 45 CFR 46.116(d) include that*

- *the research involves no more than minimal risk;*
- *the waiver would not adversely affect the rights and welfare of subjects;*
- *the research could not practicably be carried out without the waiver; and*
- *whenever appropriate, the subjects will be provided with pertinent information after participation.*

# SACHRP Frequently Asked Question #5

## *Is consent or waiver of consent required?*

*Points to consider in applying these criteria include*

- *the nature of the research;*
- *the protections in place to maintain privacy and confidentiality;*
- *the change in level of risk, if any;*
- *the ability to locate or contact subjects;*
- *risk of introducing bias into the research;*
- *potential anxiety or confusion for subjects;*
- *the number of subjects;*
- *the length of time since specimens were first collected; and*
- *the likelihood that subjects would object to the proposed secondary use, based on the nature of original collection.*

# SACHRP Frequently Asked Question #1

## *Is consent or waiver of consent required?*

*Tissue biopsies were obtained for clinical diagnostic purposes, which have now been satisfied.*

*The hospital pathology department is willing to provide a portion of the remaining biopsy specimens to an investigator who will perform research assays.*

*In order to allow matching with relevant clinical information, the specimens will be provided with identifiers such that the investigator can readily ascertain the identity of subjects.*

**Question** *Is consent of the patient from whom the biopsy was taken (or waiver of consent) required for the secondary research use?*

**Response** *Yes - because the samples are identifiable to the recipient investigator.*

**HIPAA Issues.** *The use or disclosure of patient identifiers for the research purpose would also require a HIPAA authorization from the patient or a waiver of authorization by an IRB or Privacy Board.*

# SACHRP Frequently Asked Questions #2

## *Is consent or waiver of consent required?*

*Tissue biopsies were obtained for clinical diagnostic purposes, which have now been satisfied.*

*The hospital pathology department is willing to provide a portion of the remaining biopsy specimens to an investigator who will perform research assays.*

*The specimens will be coded such that the investigator will not be able to readily ascertain the identity of individuals.*

**Question** *Is consent of the patient from whom the biopsy was taken (or waiver of consent) required for the secondary research use?*

**Response** . *No - not considered to be research involving human subjects.*

**HIPAA Issues** *If the information **associated with the specimen** is de-identified in accordance with the HIPAA Privacy Rule, neither authorization nor waiver of authorization is required*

# SACHRP Frequently Asked Question #23

## *consent or waiver?*

*Many hospitals have a sentence on the standard admission form to the effect that "This is a teaching and research institution, and any specimens remaining after your care is complete may be used for teaching or research purposes."*

*Is this sufficient to allow identifiable specimens to be used for research purposes, without any additional consent or waiver?*

**Response.** No, an additional consent or waiver should be required.

- *If the information provided to prospective subjects is limited to the above statement, this would not be sufficient to meet the requirements of informed consent for research under 45 CFR 46.*
- *The IRB could review each protocol that proposes to use such specimens and, as part of that review, consider whether the criteria for a waiver of informed consent have been met at 45 CFR 46.116(d).*

**HIPAA Issues.** *This approach (single sentence on the hospital admission form) would also not be sufficient for HIPAA authorization purposes.*

# SACHRP Frequently Asked Question #24

## *consent or waiver?*

*Many hospitals have a sentence on the standard admission form to the effect that "This is a teaching and research institution, and any specimens remaining after your care is complete may be used for teaching or research purposes."*

*Is this sufficient to allow identifiable specimens to be placed into a tissue bank, if they are coded and released to researchers through an honest broker mechanism?*

**Response.** *The plan to remove identifiers from the specimens and manage them through a bank might be factors the IRB considers when assessing the risks to subjects*

# SACHRP Frequently Asked Question #24

## *consent or waiver?*

*The creation of a bank containing identifiable specimens would be considered human subjects research and thus, subject to IRB review and informed consent.*

*However, the IRB could consider whether the criteria for waiving **or altering** informed consent have been met at 45 CFR 46.116(d).*

*The **subsequent** research use of specimens would not be considered human subjects research if the conditions of the OHRP guidance on coded private information or biological specimens have been met.*

# SACHRP Frequently Asked Questions #3

## *secondary use*

*Blood samples were obtained for research purposes, with informed consent of the subjects, and the original study has been completed.*

*The samples remain under the control of the original investigator.*

*Another investigator wants to use a portion of the remaining samples to perform research completely unrelated to the original study.*

**Question** *If the original consent stated that “. . .your sample will only be used for research on diabetes,” but the secondary user is interested in studying schizophrenia, can the samples still be used if provided to the secondary user in a coded fashion?*

**Response.** *The secondary use of de-identified or coded samples is not research involving human subjects under 45 CFR 46. Nevertheless, the original investigator and his/her institution have made an agreement with the subjects about use of their specimens, and have an obligation to honor that agreement.*

# SACHRP Frequently Asked Questions #3

## *secondary use*

*Coding should not be used as a means to circumvent the original terms of consent. This is ethically problematic, even if the original project is over and the secondary use is no longer considered to be research involving human subjects.*

*It is not, however, an enforceable regulatory violation, because the regulations do not extend in perpetuity beyond the point a given research activity involves human subjects.*

**HIPAA Issues** the original investigator would be required to get an authorization to use and disclose information for the research study. Unless the material is deidentified

# SACHRP Frequently Asked Question #6

## *secondary use*

*Blood samples were obtained for research purposes, with informed consent of the subjects, and the original study has been completed.*

*The samples remain under the control of the original investigator. Another investigator wants to use a portion of the remaining samples to perform research unrelated to the original study.*

**Question** *If the sample is identifiable to the secondary user, is this considered to be human subjects research under the purview of the IRB? If so, what are the consent considerations?*

**Response.** *Yes.*

**Points to Consider** *Whether the secondary use is compatible with the original terms of consent given by the subjects.*

**HIPAA Issues.** *A HIPAA authorization for research must be research-study specific.*

*If a HIPAA covered entity is involved, a new HIPAA authorization would be required for the subsequent unrelated research use or disclosure, or a waiver of authorization.*

# SACHRP Frequently Asked Question #7

## *secondary use*

*Blood samples were obtained for research purposes, with informed consent of the subjects, and the original study has been completed.*

*The samples remain under the control of the original investigator, who now wants to collaborate with another investigator to perform research unrelated to the original study.*

*If the original consent was silent on the question of subsequent uses, is informed consent (or waiver of consent) required before the sample can be used for other purposes?*

**Response.** *Yes.*

*If the samples are coded and identifying information is removed so that the identity of the subject cannot be readily ascertained by the secondary investigator before they are provided to him/her, is the secondary research considered to be human subjects research under the purview of an IRB?*

**Response.** *If the original investigator is not involved in the secondary analysis, NO*  
*If the original investigator is not involved in the secondary analysis, YES*

# SACHRP Frequently Asked Question #4

## *future unspecified research*

*It is increasingly common to collect and store specimens for future unspecified research.*

*How broad can this consent be without requiring investigators to obtain additional consent for specific uses? Alternatively, how specific must this consent be to allow for future use of biospecimens?*

**Response.** *There is a tension between the desire to be as specific as possible when informing subjects of what will be done, and the reality that specifics are, by definition, not known at the time of consent.*

# SACHRP Frequently Asked Question #4

## *future unspecified research*

- *be general enough in the consent form to give subjects a reasonable idea of the types of research that might be conducted in the future and the associated risks,*
- *without placing unreasonable restrictions on what the research might be.*
- *informed that future studies may involve*
  - *genetic research,*
  - *drug development*
  - *searching for links between genes and environmental factors or diseases.*
- *being overly-specific or restrictive in this regard may result in problems later,*
- *IRBs and investigators should consider the downstream implications before promising subjects that “your specimens will only be used for research on XYZ.”*

# SACHRP Frequently Asked Question #4

## *future unspecified research*

*Future uses of identifiable specimens should be reviewed by either*

- *the IRB which should determine whether the research is compatible with original terms of consent, or whether additional consent may be required.*
- *a repository oversight committee and “honest broker” mechanisms*
  - *that distribute specimens to investigators in coded fashion to the extent they no longer constitute human subjects research.*
  - *special attention should be given upfront to ensure that the repository is established with policies and procedures to effectively manage subsequent uses in keeping with what the IRB approved.*

# SACHRP Frequently Asked Question #4

## *future unspecified research*

**HIPAA Issues.** *This scenario raises a number of HIPAA-related issues for institutions that are covered entities under the Privacy Rule.*

*an authorization under the HIPAA Privacy Rule must be study-specific.*

- *How specific must that authorization be?*
- *How can health information associated with specimens be used and disclosed from a research repository when specific research uses are unknown at the time the information is collected?*

*There are two separate activities to consider when a HIPAA covered entity is collecting and storing identifiable health information in a research repository for future unspecified research:*

- *a covered entity's use or disclosure of protected health information (PHI) to create the repository; and*
- *the release of PHI from the repository for a future research purpose.*

# SACHRP Frequently Asked Question #4

## *future unspecified research*

- *An authorization for research use and disclosure of PHI under the HIPAA Privacy Rule must be study-specific.*
- *the authorization may state that the purpose of the authorization is to create a research repository or database.*
- *Health information can then be subsequently used and disclosed from the research repository in one of several ways:*
  - *With study-specific authorization*
  - *With waiver of authorization by an IRB or Privacy Board*
  - *Preparatory to research (with certain representations)*
  - *Use of a HIPAA De-identified Dataset\**
  - *Use of a Limited Data Set (with data use agreement)*
  - *Research solely on decedents (with certain representations)*

# SACHRP Frequently Asked Question #12

## *withdrawing specimens*

*A research participant agrees to allow extra blood to be stored for future research purposes. Blood samples will be stored in a repository with identifiers. The participant later changes his/her mind.*

**Question** *Do the samples need to be destroyed or removed from the repository?*

**Response.** *Yes. Subjects have the right to withdraw from research, and this extends to withdrawing their specimens from future research.*

*Subjects should be informed upfront about the procedures for withdrawing specimens from a repository.*

*The obligation to honor subjects' requests to withdraw does not extend to retrieving specimens already distributed to secondary users.*

*Analyses already completed will generally not be destroyed or removed from datasets. These practical limitations to withdrawal should be disclosed to subjects as part of the consent process.*

# SACHRP Frequently Asked Question #12

## *withdrawing specimens*

- OHRP Guidance on Withdrawal of Subjects from Research: Data Retention and Other Related Issues Date: September 21, 2010
- FDA Guidance for Sponsors, Clinical Investigators, and IRBs Data Retention When Subjects Withdraw from FDA-Regulated Clinical Trials October 2008
- HIPAA Privacy Rule (45 CFR part 160 and subparts A and E of 45 CFR part 164)

# SACHRP Frequently Asked Question #12

## *withdrawing specimens*

OHRP Guidance on Withdrawal of Subjects from Research: Data Retention and Other Related Issues Date: September 21, 2010

### **F. When seeking the informed consent of subjects, what should investigators tell subjects about data retention in the event the subjects withdraw?**

*OHRP recommends that when seeking the informed consent of subjects, investigators explain whether already collected data about the subjects will be retained and analyzed even if the subjects choose to withdraw from the research.*

*Following are some examples of what such an explanation might include, depending on whether the HHS-conducted or –supported research study is also subject to FDA regulations or the HIPAA Privacy Rule:*

# SACHRP Frequently Asked Question #12

## *withdrawing specimens*

OHRP Guidance on Withdrawal of Subjects from Research: Data Retention and Other Related Issues Date: September 21, 2010

*For HHS-conducted or –supported research that is also FDA-regulated, regardless of whether the research is subject to the HIPAA Privacy Rule,*

*The investigator should inform subjects that data collected about the subject up to the time of subject withdrawal will remain in the trial database and be included in the data analysis.*

# SACHRP Frequently Asked Question #12

## *withdrawing specimens*

OHRP Guidance on Withdrawal of Subjects from Research: Data Retention and Other Related Issues Date: September 21, 2010

*For HHS-conducted or –supported research that is not FDA-regulated but is covered by the HIPAA Privacy Rule,*

*If the investigator intends to retain and analyze already collected data about the subject after a subject chooses to withdraw from the research*

*the investigator should inform subjects that if a subject revokes authorization in writing for continued use or disclosure of his or her PHI that was already obtained in the research, analysis of that PHI will continue only to the extent necessary to protect the integrity of the research study.*

# SACHRP Frequently Asked Question #12

## *withdrawing specimens*

OHRP Guidance on Withdrawal of Subjects from Research: Data Retention and Other Related Issues Date: September 21, 2010

*For HHS-conducted or –supported research that is not subject to FDA regulations or the HIPAA Privacy Rule, the investigator should inform subjects whether the investigator intends to either:*

- (1) retain and analyze already collected data relating to the subject up to the time of subject withdrawal; or*
- (2) honor a research subject’s request that the investigator destroy the subject’s data or that the investigator exclude the subject’s data from any analysis.*

# SACHRP Frequently Asked Question #14

## *specimens from deceased individuals*

*An investigator collected specimens from a large number of cancer patients and stored them with identifiers. Some of the patient-subjects are now deceased.*

*Is research using the specimens of those subjects who died still considered to be human subjects research, and under the oversight of an IRB?*

**Response.** *No. 45 CFR 46.102 defines a human subject as a "living individual."*

*However, deceased individuals would still have protections under the HIPAA Privacy Rule.*

# SACHRP Frequently Asked Question #14

## *specimens from deceased individuals*

### **HIPAA Issues.**

*generally protects the Protected Health Information of decedents in the same manner as that of living individuals.*

*However, in the research context, the Privacy Rule allows the use or disclosure of decedent information without the authorization of a personal representative and without waiver of authorization by an IRB or Privacy Board if;*

- *the covered entity receives representations from the researcher that the decedents' protected health information is necessary for the research and*
- *is being sought solely for research on decedents (and not related living individuals) and,*
- *upon request of the covered entity, receives documentation of the deaths of the individuals.*

# SACHRP Frequently Asked Question #26

## *samples from minors*

*A 13-year-old child is enrolled by his/her parents in a tissue banking protocol that involves storage of specimens for future research. Is the child's assent required at the time of the original enrollment in the repository, in addition to parental permission?*

*Response.* Yes, if the IRB determines that the children are capable of providing assent

# SACHRP Frequently Asked Question #27

## *samples from minors*

*A child is enrolled by his/her parents in a tissue banking protocol that involves storage of specimens for future research.*

*Should there be a process in place for the child to give consent for continued storage and use of specimens when he/she turns 18?*

### **Response.**

*... it would be necessary for the investigator(s) to seek and obtain the legally effective informed consent of the now-adult subjects.*

The IRB may consider, if appropriate, *a waiver for obtaining informed consent in order for the subjects to continue their participation in the research.*

# SACHRP Frequently Asked Question #27

## **HIPAA Issues.**

*A valid HIPAA authorization signed by a parent, as the personal representative of a minor child at the time the authorization is signed, remains valid until it expires or is revoked, even if such time extends beyond the child's age of majority.*

*However, if the authorization expires on the date the minor reaches the age of majority, a new authorization (or other HIPAA permission) would be required at that time*