

## Current Issues for Investigators: Human Subjects Research

Valery M. Gordon, Ph.D., M.P.H.  
Extramural Human Subjects Research Policy Officer  
Office of Extramural Research, OD  
National Institutes of Health  
(301) 435-0945  
[vg10w@nih.gov](mailto:vg10w@nih.gov)



NIH Regional Seminar, 2006

1

## Outline

- ❑ Research Involving Human Data or Specimens  
(<http://www.hhs.gov/ohrp/humansubjects/guidance/cdebiol.pdf>)
- ❑ Definitions
- ❑ NIH implementation of requirements
  - Get ready for the SF 424 R&R!
- ❑ Case Studies
- ❑ Other issues

2

## OHRP "Guidance on Research Involving Human Data or Specimens"

Directed toward **IRBs**, **investigators**, and **funding agencies**

- ❑ Provides clarification of terms in HHS regulations  
<http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm>
- ❑ Describes when research with coded data or specimens **is** or **is not** human subjects research
- ❑ Effective date: August 10, 2004
- ❑ Implemented by NIH: January 10, 2005  
<http://www.hhs.gov/ohrp/humansubjects/guidance/cdebiol.pdf>

3

## Specific Information in Guidance

- ❑ Research with coded human data/specimens does not involve human subjects if:
  - Data/specimens not collected specifically for proposed study; and
  - Investigators cannot readily ascertain identities of donors because:
    - Key to code destroyed before research begins; or
    - Non-disclosure agreement between provider and investigator (no requirement for IRB approval); or
    - IRB policies prohibit release of key to code; or
    - "Other legal requirements" prohibit release of key to code

4

## Recommendations in Guidance

- ❑ Institutions have policies designating the individual or entity authorized to determine whether research with coded data/specimens is human subjects research
- ❑ Investigators should not be given authority to make independent determination whether their proposed studies with coded data/specimens involve human subjects

5

## Definition of *Human Subject*

- ❑ ... a living individual
- ❑ about whom an investigator... conducting research *obtains*
  - 1) Data through intervention or interaction with the individual,  
or
  - 2) Identifiable private information

<http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm#46.102>

6

## Definition of *Obtain*

- ❑ To receive or access individually identifiable human data or specimens
  - Includes an investigator's use, study, or analysis of human data or specimens already in investigator's possession

<http://www.hhs.gov/ohrp/humansubjects/guidance/cdebiol.pdf>

7

## Case Study #1: **Research with autopsy specimens**

- ❑ An application describes the following proposed research activities:
  - An investigator receives autopsy specimens from a pathologist at the same institution.
  - The investigator will receive and record identifiable private information about the individuals from medical records

8

## Case #1: **Is the investigator conducting human subjects research?**

- ❑ **No:** Research involving only specimens and data from deceased individuals is not human subjects research
  - Investigator is neither interacting nor intervening with living individuals for research;
    - ❑ Definition of "human subject" is not met

9

## Case #1: **What information should appear in Human Subjects section?**

- ❑ "No human subjects research is proposed in the application"
  - Required for PHS 398 applications
  - Will not be required for SF 424 R&R

10

## Definition of *Investigator*

- ❑ Includes anyone involved in conducting the research  
For example:  
Individuals who
  - Provide coded human data or specimens and collaborate on other activities related to conducting the research are involved in HS research
  - "Solely provide" previously-collected coded human data or specimens without a key to code are not involved in HS research

11

## Case Study #2: **Research using human blood**

- ❑ An application describes the following proposed research activities:
  - An investigator will obtain blood from the Red Cross for basic research
- ❑ Is the investigator conducting human subjects research?
  - **No:** Data/specimens not collected specifically for proposed study; and investigators cannot readily ascertain identities of donors because:
    - ❑ Red Cross is prohibited by law from disclosing identities of donors

12

## Case #2: **What information should appear in Human Subjects section?**

- ❑ "No human subjects research is proposed in the application"

13

## Definition of *Coded*

- ❑ Identifying information that enables the investigator to readily ascertain the identity of the individual has been replaced with a
  - number,
  - symbol, and/or
  - letter; **and**
- ❑ A key to the code exists, enabling linkage of information to an individual

14

## Definition of *Research*

- ❑ ... a systematic investigation
    - research development
    - testing, and
    - evaluation
  - ❑ designed to develop or contribute to generalizable knowledge
- <http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm#46.102>

15

## NIH Human Subjects section requirements

- ❑ Human Subjects
  - "Yes" or "No" must be checked
- ❑ Research Plan: Human Subjects Section
  - No proposed Human Subjects Research; or
  - Justification for Exemption; or
  - Protections for Human Subjects

16

## Case Study #3: **Discarded Surgical Specimens**

- ❑ An application describes the following proposed research activities:
  - Investigators will obtain human specimens for basic research from a surgeon.
  - The surgeon will collect surgical specimens, at the request of the investigators, that would otherwise be discarded and provide them in a coded fashion.
  - The surgeon will have no other involvement in the proposed research.

17

## Case #3: **Is the surgeon involved in human subjects research?**

- ❑ **Yes:** The surgeon is involved in human subjects research because he is interacting with living individuals and collecting specimens for the proposed research.
  - The surgeon meets the definition of an *investigator*.
    - ❑ "OHRP considers the term *investigator* to include anyone involved in conducting the research."
    - ❑ The surgeon's involvement may be limited to collecting, coding, and providing the specimens, however, this activity is conducted specifically for this study.

18

### Case #3: Is the recipient investigator conducting human subjects research?

- ❑ **Yes:** The recipient investigator is conducting human subjects research, because
  - an *investigator* involved in the research (the surgeon) is collecting specimens from living individuals for the specific study, and
  - An *investigator* can readily link the specimens to the living individuals.

19

### Case Study #4: Discarded Human Specimens

- ❑ An application describes the following proposed research activities:
  - Investigators will obtain human specimens for basic research from a surgeon.
  - The surgeon has IRB approval to collect specimens that would otherwise be discarded and provides them, in coded fashion, to any investigator upon request.
  - The surgeon requires that recipient investigators enter into a written agreement prohibiting the release of the key to the codes to the investigators under any circumstances.
  - The only involvement of the surgeon in the proposed research is to provide the specimens to the investigator.

20

### Case #4: Is the surgeon involved in human subjects research?

- ❑ **Yes:** The surgeon is involved in human subjects research insofar as the surgeon is creating a research repository of human specimens
    - Human Tissue Repositories “collect, store, and distribute human tissue materials for research purposes.”
      - Require IRB-approved written policies that prohibit release of key to codes
- <http://www.hhs.gov/ohrp/humansubjects/guidance/reposit.htm>

21

### Case #4: Is the surgeon involved in human subjects research with respect to the investigator's study?

- ❑ **No:** The surgeon is not involved in the recipient's research, however, because the surgeon is
  - “solely providing coded private information or specimens (for example, by a tissue repository)” and, therefore,
  - The surgeon is not an *investigator* in the recipient's study.

22

### Case #4: Is the recipient investigator conducting human subjects research?

- ❑ **No:** The investigator is not conducting human subjects research because:
    - 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 cannot readily ascertain the identity of the individuals to whom the coded private information or specimens pertain because:
      - the investigator and the holder of the key enter into an agreement prohibiting the release of the key to the investigators under any circumstances,...
      - 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,...
- <http://www.hhs.gov/ohrp/policy/index.html#databases>

23

### Case #4: What information should appear in Human Subjects section?

- ❑ “No human subjects research is proposed in the application”

24

### Case Study #5: **Retrospective Record Review**

- ❑ An application describes the following proposed research activities:
  - An investigator obtains individually identifiable information on treatment outcomes of patients treated with two different FDA-approved drugs by accessing medical records.
  - The investigator records the treatment outcomes in a coded manner.

25

### Case #5: **Is the investigator conducting human subjects research?**

- ❑ **Yes:** the investigator is conducting human subjects research because
  - the investigator obtains individually identifiable private information about living individuals; and
  - The investigator records the data in a coded manner allowing the subjects to be identified via the code.

26

### Case #5: **What information should appear in Human Subjects Section?**

- ❑ Description of:
  - Risks
  - Protections against risks
  - Benefits to human subjects and others
  - Importance of knowledge to be gained
- ❑ Inclusion of women and minorities
- ❑ Inclusion of children or justification for exclusion; and
- ❑ Proposed/targeted enrollment tables

27

### Case Study #6: **Archived Human Specimens**

- ❑ An application describes the following proposed research activities:
  - An investigator is using archived, individually identifiable specimens from an NIH-funded clinical trial.
  - The investigator removes identifiers from the specimens and does not maintain links to identifiers.
  - The investigator then conducts research on the anonymized specimens.

28

### Case #6: **Is the investigator conducting human subjects research?**

- ❑ **Yes:** If the individuals from whom the specimens were obtained are living, then obtaining individually identifiable specimens is human subjects research.

29

### Case #6: **Does the study involve exempt human subjects research?**

- ❑ Exemption 4:
  - Research involving the collection or study of **existing**
    - ❑ data,
    - ❑ documents,
    - ❑ records,
    - ❑ pathological specimens, or
    - ❑ diagnostic specimens,
  - from publicly available sources or
  - if information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.
- OHRP recommends that institutions adopt clear procedures under which the IRB (or some authority other than the investigator) determines whether proposed research is exempt from the human subjects regulations [45 CFR 46.101(b)].

30

### Case #6: Does removing identifiers from existing specimens meet the criteria for Exemption 4?

- ❑ **Yes:** If all specimens are existing at the time the research is proposed to an institutional official or IRB for a determination of whether or not the research is exempt; and
- ❑ If the investigator collects the specimens and then removes links to identifiers from the specimens; then

➤ This research activity meets the criteria for Exemption 4.

<http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm#46.101>

31

### Case #6: Does the research with anonymized specimens involve human subjects?

- ❑ **No:** Conducting research using anonymized specimens is not human subjects research because the specimens cannot be linked to individually identifiable living individuals.

■ Criteria for "human subject" not met

32

### Case #6: What information should appear in Human Subjects section?

- ❑ Description of:
  - Risks
  - protections against risks
  - benefits to human subjects and others
  - Importance of knowledge to be gained
- ❑ Inclusion of women and minorities
- ❑ Inclusion of children or justification for exclusion; and
- ❑ Proposed/targeted enrollment tables

33

### Summary: Case study analyses

- ❑ In order to determine whether research with coded data/specimens is human subjects research, consider:
  - Role of data/specimen provider
    - ❑ Is the provider an *investigator*?
  - Role of recipient investigator
    - ❑ What is being *obtained*?
      - Data through interaction or intervention with living individuals?
      - Identifiable private information about living individuals?
      - Identifiable data or specimens for the proposed study?

34

### Non-competing Progress Reports

- ❑ If institutions re-interpret ongoing research to conform to OHRP Guidance:
  - Involvement of human subjects has not changed
- ❑ Research classified as not involving human subjects will change to involve human subjects if investigators:
  - "Unexpectedly learn" identities of individuals; or
  - "For previously unforeseen reasons now believe that it is important to identify the individual(s)."

35

### Other Issues or Questions?

NIH OER Human Subjects Website:

<http://grants.nih.gov/grants/policy/hs/index.htm>

36