Secondary Research and the Revised Common Rule

Dr. Yvonne Lau, MBBS, MBHL, PhD
Director, Division of Education and Development Office for Human Research Protections (OHRP)

May 1, 2018
Overview

• The concepts of secondary research and identifiability
• Secondary research with nonidentifiable materials
• Secondary research with identifiable materials
  • Exempt research
  • Nonexempt research
THE CONCEPTS OF SECONDARY RESEARCH AND IDENTIFIABILITY
What is Secondary Research?

Research use of information or biospecimens originally collected for:

• **Non-research purposes**  
  (e.g., leftover blood from routine clinical tests, general information collected for the census)

  OR

• **Research studies other than the proposed one**  
  (e.g., blood samples left over from a study evaluating a new diabetes drug obtained for a new study on genetic predisposition of diabetic patients to Alzheimer’s disease)
Test Your Knowledge

For the purpose of the research, an investigator will obtain tissue blocks from a biobank.

Is the investigator conducting secondary research?

A. Yes
B. No
C. It depends
D. I don’t know
An investigator conducting a longitudinal observational study will obtain data from medical records. The data are all routinely collected as part of clinical care. The dataset include patients’ identifiers.

Is the investigator conducting secondary research?

A. Yes
B. No
C. It depends
D. I don’t know
For the purpose of the research, an investigator will contract with an institution to collect research data from people. The data will be anonymized before being provided to the investigator for analysis.

Is the investigator conducting secondary research?

A. Yes
B. No
C. It depends
D. I don’t know
What is **Not** Secondary Research?

It is *not* secondary research when investigators interact or intervene with living individuals to obtain their data or biospecimens *specifically for the proposed research*.
Concept of Identifiable

- No change in the definition of identifiable

- [...] information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the [...] 

- Specify definitions for “identifiable biospecimen” and “identifiable private information” for clarity
SECONDARY RESEARCH WITH NONIDENTIFIABLE INFORMATION AND BIOSPECIMENS
Secondary Research with Nonidentifiable Materials

• Secondary research use of nonidentifiable private information or nonidentifiable biospecimens:
  • Does not involve human subjects, and therefore,
  • Does not require IRB review and approval under the regulations

• No change under the revised Common Rule
Research with Coded Biospecimens or Coded Private Information

If research involves **only** coded biospecimens or coded private information **and** meets both of the following:

1) **is not collected specifically for the research in question,**
   **AND**

2) investigator(s) **cannot readily ascertain identity of the individual(s) to whom data/specimens pertain,**

then it is **not human subjects research**

- **No change under the revised Common Rule**
SECONDARY RESEARCH WITH IDENTIFIABLE INFORMATION AND BIOSPECIMENS
Regulatory Options for Secondary Research with Identifiable Private Information or Identifiable Biospecimens

- Apply **exemptions** 4, 7, or 8 if conditions are met, OR

- Conduct **nonexempt** research with
  - Standard informed consent, or
  - Waiver of informed consent if applicable, or
  - Broad consent under the revised Common Rule
Exemption 4: Secondary Research Use of Identifiable Private Information or Identifiable Biospecimens

Materials no longer need to be “existing”

Exempt if:

i. Identifiable materials are publicly available, OR

ii. Information, which may include information about biospecimens, is recorded by the investigator in such a manner that the identity of the human subjects cannot be readily ascertained directly or through identifiers linked to the subjects, and the investigator does not contact the subjects or re-identify subjects, OR
Exemption 4 (cont’d)

iii. Investigator’s use is regulated under HIPAA as “health care operations,” “research,” or “public health,”

• Note - HIPAA does not apply to biospecimens

OR

iv. Research is conducted by, or on behalf of, a Federal agency using data collected or generated by the government for nonresearch purposes, and the information is protected by federal privacy standards
Exemptions 7 and 8

- **Exemption 7**: Storage or maintenance of identifiable private information or identifiable biospecimens for secondary research
- **Exemption 8**: Secondary research using identifiable private information or identifiable biospecimens
  - Investigator does not include returning individual research results to subjects as part of the study plan except when required by law

Both require:

- Broad consent
- Limited IRB review for privacy and confidentiality protection, and some aspects of broad consent
Limited IRB Review for Exemptions 7 and 8

• IRB review limited to certain determinations specified for the exemptions
• Can be done using the expedited review mechanism (i.e., by a designated experienced IRB member)
• Annual continuing review is not required
Determining When the Common Rule Applies to Secondary Research

- Is it research? Yes → Does it involve human subjects? Yes → Is it exempt? No
- Non-exempt HS research that requires IRB review
- Require limited IRB review that necessary conditions are satisfied

- Is it research? No or Activities deemed not to be research No IRB Review
- Does it involve human subjects? No (e.g., secondary research with nonidentifiable materials) No IRB Review
- Does it involve exemptions 7, or 8? No

Legend: New to the revised Common Rule
Nonexempt Secondary Research with Identifiable Materials Requires Informed Consent or Waiver

Options for Informed Consent

- Standard informed consent
- Waiver of informed consent (if applicable)
- Broad consent (New)
Conditions for Waiver or Alteration of Informed Consent Relevant to Secondary Research with Identifiable Materials

i. No more than minimal risk to the subjects;
ii. Could not practicably be carried out without the waiver;
iii. The IRB must determine that the research could not *practically* be carried out without using the materials in an identifiable manner
iv. Will not adversely affect the rights and welfare of subjects; **AND**
v. Whenever appropriate, the subjects will be debriefed
Broad Consent is a New Option in the Revised Common Rule

• Broad consent is a new option for doing secondary research

• Existing options for doing secondary research remain, are expanded, and include, e.g.,
  • Using nonidentifiable materials
  • Using the expanded exemption 4
  • Getting IRB waiver of informed consent
  • Getting standard informed consent

• For many researchers, using the existing options may be preferable to using broad consent
Broad Consent

• Permissible option only for secondary research i.e.,
  • Research using identifiable private information or identifiable biospecimens collected for either research studies other than the proposed research or nonresearch purposes

• Can facilitate storage, maintenance, and future secondary research with identifiable materials when details of such future research may not be available
  • Used to qualify for exemptions 7, 8
  • May be used for nonexempt studies
Use of Broad Consent

• Envisioned that broad consent for future secondary use may be obtained:
  • At the time when standard informed consent is obtained through research interaction or intervention with subjects, or
  • In the nonresearch setting where information or biospecimens are collected
• If used, all of the elements for broad consent must be included
Limitations of Broad Consent

• If individuals were asked, and refused, to provide broad consent, the IRB cannot waive informed consent to the use of the subject’s identifiable private information or identifiable biospecimens in a secondary study that falls within the scope of research described in the broad consent. (Use of nonidentifiable materials is still allowed.)

• Use of broad consent will require tracking of affected information or biospecimens; the cost and logistical difficulties involved are likely to limit its use
As long as the proposed secondary research fits into the criteria of one of the provisions in exemption 4 under the revised Common Rule, no IRB review is required

**True or False?**

A. True  
B. False  
C. It depends  
D. I don’t know
As long as there is broad consent for secondary research use of the subjects’ identifiable private information or identifiable biospecimens, researchers can use exemption 8 without any IRB oversight.

True or False?

A. True
B. False
C. It depends
D. I don’t know
Your institution decides to make use of the new exemptions 7 and 8 to facilitate future secondary research where investigators will need access to identifiable patient information. Every patient is now asked to provide broad consent for future secondary use of their clinical samples. For the few who decline, the IRB will be allowed to waive informed consent if their use is vital to the scientific validity of the research.

True or False?

A. True  
B. False  
C. It depends  
D. I don’t know
Please refer to the text of the revised Common Rule available on OHRP’s website for a complete and accurate description of the regulatory requirements.

For this presentation, please review the revised rule at sections 46.102(e), 46.104(d) & 46.116
Questions About the Revisions?

- Submit your questions to OHRP@hhs.gov
- Check out the OHRP website at www.hhs.gov/ohrp for resources on the revised Common Rule