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Secondary Research with Biospecimens and Data Under the Revised Common Rule

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Disclaimer

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Goals

- Explain key terms related to secondary research with information and biospecimens:
 - Secondary research
 - Human subjects research
 - Identifiable
- Describe the regulatory flexibilities for secondary research
- Explain the informed consent options for secondary research



Key Terms



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Secondary Research

The 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 drug being used for a *new* genetics study)

Consider the original purpose for which the materials were collected and whether the current research team was involved in the original collection



An investigator wants to see if there is a correlation between when IV fluids were started and treatment outcomes. She plans to review patient data that her mentor collected a few years ago for a now-completed research study.

Is the investigator conducting *secondary research*?

- A. Yes
- B. No
- C. It depends
- D. Undecided

For the purpose of the research, an investigator will study liver cancer tissue blocks obtained from the hospital's pathology lab after diagnosis is complete.

Is the investigator conducting *secondary research*?

- A. Yes
- B. No
- C. It depends
- D. Undecided



For the purpose of the research, an investigator will pay a commercial survey company for data on the food consumption behavior of pregnant women.

Is the investigator conducting *secondary research*?

- A. Yes
- B. No
- C. It depends
- D. Undecided



In a multi-institutional clinical trial, data and specimens will be collected from participants at one institution. Coded biospecimens will then be sent to researchers at another institution for analysis as part of the study.

Are the investigators at institution B conducting *secondary research*?

- A. Yes
- B. No
- C. It depends
- D. Undecided



Regulatory Definition of *Human Subject*

Human subject: a living individual about whom an investigator conducting research

- 1) Obtains information or biospecimens **through intervention or interaction** with the individual, and uses, studies, or analyzes the information or biospecimens;

In secondary research, there is no intervention or interaction with individuals specifically for the research.

or

- 1) Obtains, uses, studies, analyzes, or generates **identifiable private information or identifiable biospecimens**

Secondary research that uses non-identifiable materials is “not human subjects research”

§46.102(e)(1)



What *Identifiable* Means Under the Common Rule

Definition for “Identifiable”:

Identifiable private information or identifiable biospecimens refers to private information/biospecimens ***for which the identity of the subject is or may readily be ascertained by the investigator or associated with*** the information or biospecimens

- The Common Rule does not define other associated terms, such as, *coded, de-identified, or anonymized*
 - It does not have a list like the “HIPAA identifiers”
 - Unique identifiers may not necessarily be “identifiable” under the Common Rule
- Common Rule agencies will revisit this definition every 4 years



An investigator will be doing research using only coded private information and coded biospecimens collected for routine clinical care.

This is ***not human subjects research*** and is outside the Common Rule.

True or False?

- A. True
- B. False
- C. It depends
- D. Undecided



Research with **Coded** Materials: When is it Outside the Common Rule?

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

- 1) Investigators do not interact or intervene with subjects to collect the materials for the purpose of this research, **AND**
- 2) Investigator(s) cannot readily ascertain the identity of the individual(s) to whom data/specimens pertain

Then investigators are doing secondary research with non-identifiable materials.

This is **not human subjects research**, it is outside the Common Rule, and it does not require IRB review and approval.



An investigator conducting a longitudinal observational study obtains data from the medical records of the study population for analysis. The data is routinely collected for the subjects' medical care. The investigator maintains identifiers to the data.

Is the investigator conducting **secondary** research?

- A. Yes
- B. No
- C. It depends
- D. Undecided

An investigator conducting a longitudinal observational study obtains data from the medical records of the study population for analysis. The data is routinely collected for the subjects' medical care. The investigator maintains identifiers to the data.

Is the secondary research ***human subjects research*** according to the regulations?

- A. Yes
- B. No
- C. It depends
- D. Undecided

Regulatory Flexibilities for Secondary Human Subjects Research



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Exemptions for Secondary Human Subjects Research

When is secondary research with **identifiable private information** or **identifiable biospecimens** exempt?

- Ask if the research can be conducted under one of these **exemptions** in the revised Common Rule
 - Exemptions 4, (5,) 7, or 8 at §46.104(b)
 - If not, it is **non-exempt human subjects research** for which IRB review and approval is required according to the regulations



Remember:

Secondary research with non-identifiable materials is **not human subjects research** and does not require IRB review and approval under the regulations



What Does It Mean That Research is *Exempt*?

- Research activities that meet the conditions for an exemption category are exempt from the typical requirements of the Common Rule (i.e., IRB review and approval according to the regulations)
 - Institutions may elect to review these projects based on institutional policy
- Institutions generally designate experienced individuals (on IRB or in the IRB office) to make exemption determinations
 - Making exemption determinations \neq IRB review and approval
- The revised Common Rule introduces the new concept of *limited IRB review*, which is usually a one-off IRB determination
 - It differs operationally from the regular IRB review and approval process



Exemption 4: Main Exemption for Secondary Research Use of Identifiable Information or Identifiable Biospecimens

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

Note: The data/specimens no longer need to be existing when the research starts



Exemption 4 (cont'd)

- iii. Investigator's use is regulated under HIPAA as "health care operations," "research," or "public health,"
 - Note - HIPAA only applies to information, not biospecimens

OR

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



As long as the proposed secondary research satisfies the conditions for one of the provisions in exemption 4 under the Common Rule, no IRB review and approval is required.

True or False?

- A. True
- B. False
- C. It depends
- D. Undecided

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:

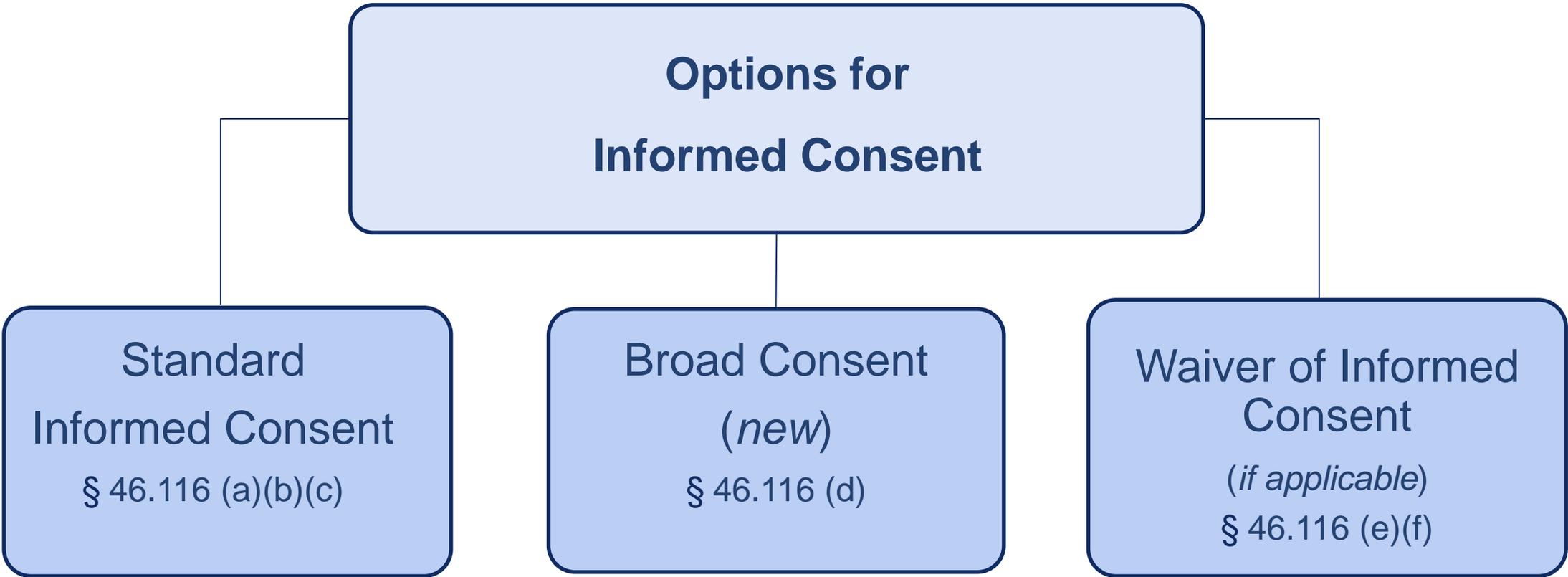
- Broad consent
- Limited IRB review for privacy and confidentiality protection, and some aspects of broad consent



Informed Consent Options & Requirements for Secondary Research



Informed Consent Options for *Non-exempt Secondary Human Subjects Research*



IRB Waiver or Alteration of Informed Consent

- i. No more than minimal risk to the subjects;*
- ii. Could not practicably be carried out without the waiver;*
- iii. If research involves using identifiable private information or identifiable biospecimens, the IRB must determine that the research could not practicably be carried out without using such [materials] in an identifiable format***
- iv. Will not adversely affect the rights and welfare of subjects; AND*
- v. Whenever appropriate, the subjects will be debriefed*

§46.116(f)(3)



Non-identifiable information should be used whenever possible



NEW! Broad Consent in the Revised Common Rule

- A new option permissible **only for secondary research** using identifiable private information or identifiable biospecimens
- A means to enable subjects to agree to a broad range of secondary research studies in the future when details of such future research may not be available
- Broad consent may be obtained:
 - When standard informed consent is obtained for a research study, **or**
 - In non-research settings, when information or biospecimens are collected for non-research purposes (e.g., clinical care, classroom activities), **or**
 - When re-consenting subjects for secondary research that is not exempt (and did not qualify for a waiver of informed consent)



Use of Broad Consent

- It may be used with non-exempt studies, or to qualify for the new exemptions 7, 8
- **If used, all of the elements for broad consent must be included, including, amongst others:**
 - a general description of the types of research that may be conducted,
 - the types of institutions or researchers who might conduct research with the subject's information or biospecimens

No flexibility for alteration is allowed!



Limitations of Broad Consent

- If individuals were asked and refused to provide broad consent, the IRB cannot waive informed consent for the secondary research use of the subject's identifiable private information or identifiable biospecimens
 - **Use of non-identifiable materials is still allowed**
- NOTE: use of broad consent will involve some mechanism for tracking the affected information or biospecimens; the cost and logistical difficulties involved may limit its use

For some researchers, it is possible that using other options for doing secondary research may be preferable to using broad consent.



Investigators for a clinical trial studying a new diabetes drug plan to **retain the research data and leftover biological samples with their identifiers** for future unspecified research after the trial is completed.

How might they be able to do this? (Choose all that apply)

- A. If they obtain standard informed consent for the future use at the time the participants consent to participate in the clinical trial
- B. If they obtain the (new) broad consent for the future use at the time the participants consent to participate in the clinical trial
- C. If they obtain IRB approval for a waiver of informed consent for future use at the time of the clinical trial
- D. None of the above options can be used
- E. Undecided

Investigators want to study the correlation between gene mutations in cancer cells and cancer progression. They will obtain cancer specimens leftover from diagnosis and access patient medical records to link individuals' disease progression with the gene mutations found in the specimens.

How can investigators do this under the revised Common Rule? (Choose all that apply)

- A. They can re-contact the patients to obtain their informed consent for the secondary research
- B. They can obtain IRB approval for a waiver of informed consent if all the conditions for the waiver are met
- C. If they are a HIPAA-covered entity, they can utilize the new provision iii under exemption 4
- D. They don't need informed consent because this is not human subjects research
- E. Undecided

Reminder: Options for Secondary Research Using Information or Biospecimens *with Identifiers*

- 1) Obtain standard informed consent
- 2) Obtain waiver of consent from IRB if waiver conditions are satisfied
- 3) Obtain broad consent as described in the revised Common Rule for unspecified secondary use
 - May be able to use with exemptions 7, 8
- 4) Secondary research involving information only, exemption 4 “HIPAA provision” or “government use provision” may apply

***Secondary research with information or biospecimens that cannot be linked back to individuals is generally either not human subjects research or exempt under the Common Rule**



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



