Department of Health and Human Services Human Subject Protection Regulations:

How Does 45 CFR part 46 Apply to Research Involving Data?

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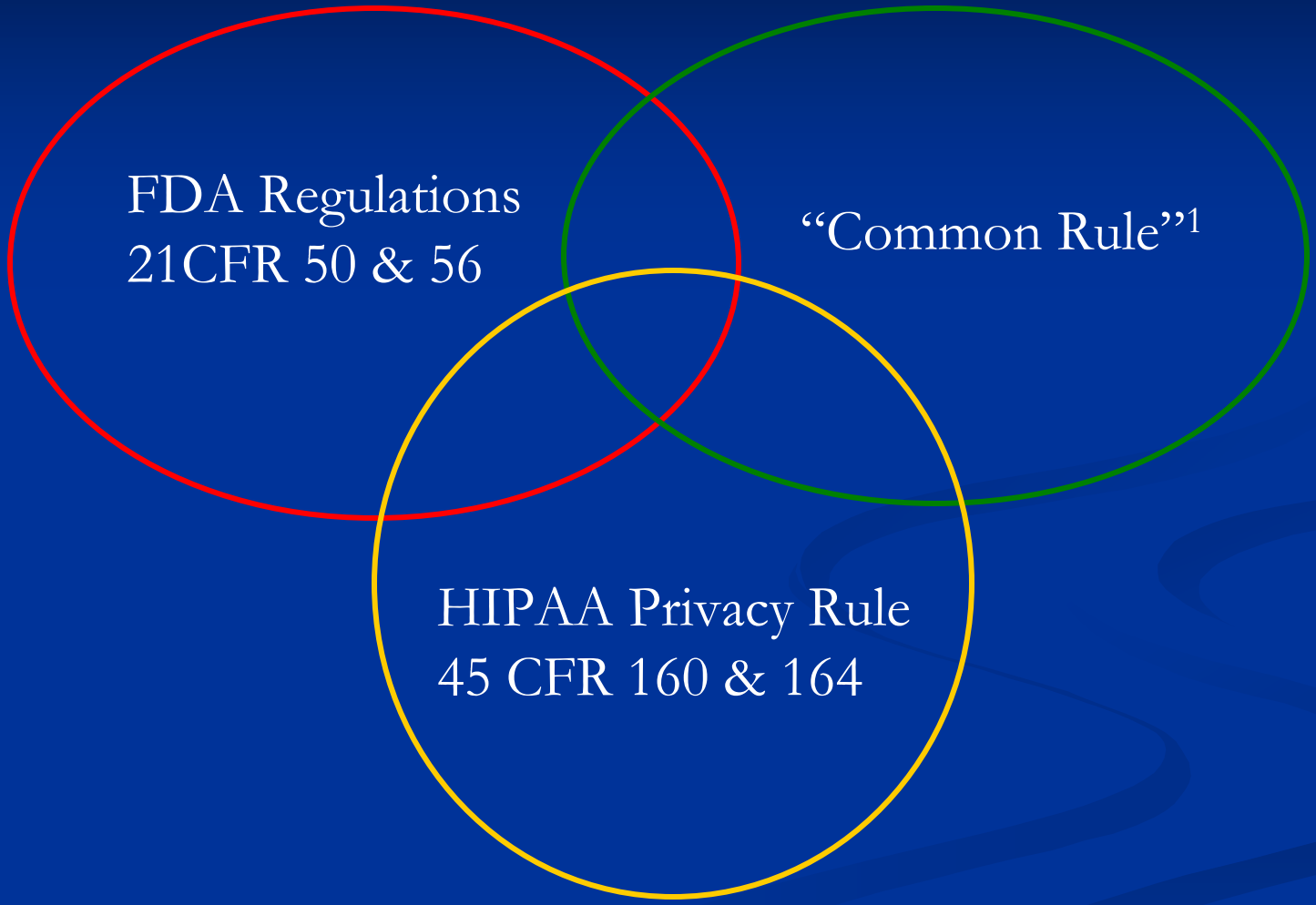
Topics

- What U.S. federal regulations govern human subjects research?
- What is the scope of the Common Rule?
- How does 45 CFR 46 relate to the "Common Rule"?
- How does an institution/investigator determine if the regulations apply?
- What are the basic features of protection?
- When can informed consent be waived?

Three Key U.S. Federal Regulations



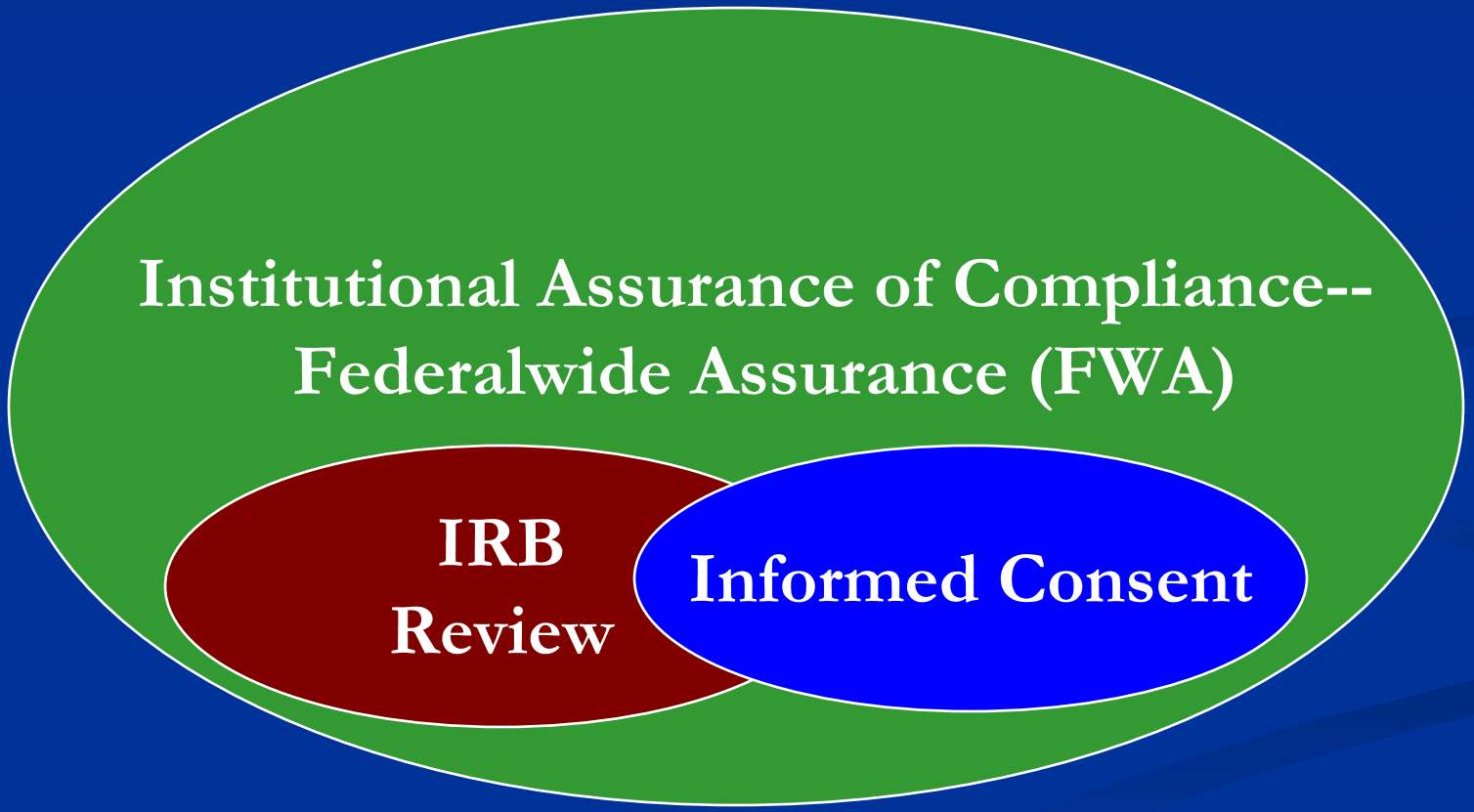
[1]Department of Health and Human Services (HHS) has additional regulatory requirements for certain "vulnerable" populations

What's the Scope of the "Common Rule"?

- Apply to human subject research conducted or supported by Common Rule department/agency—that is not exempt.

- If U.S. institution chooses to apply to all human subjects research—apply regardless of source of support

45 CFR 46:
Scope: What are the Basic Regulatory Protections for Human Subjects?



Common Rule Departments & Agencies

Additional HHS Human Subject Protections (45 CFR 46)

- Subpart B - Pregnant Women, Human Fetuses, and Neonates
- Subpart C - Prisoners
- Subpart D - Children

Scope of Regulations

- FDA human subject protection regulations:
  - Apply to clinical investigations regulated by FDA
  - Contains requirements that are nearly identical to the Common rule

- HIPAA Privacy Rule:
  - Applies to "covered entities"
  - Contains requirements for the use and disclosure of certain individually identifiable health information

Applicability of the HHS Regulations

Research?

Human Subject?

Exempt?

What is "Research"?

A systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. [45 CFR 46.102(d)]

Activities with Research and/Or Other Purposes

What is a "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.

[45 CFR 46.102(f)]

Identifiable Private Information

Individually identifiable: The identity of the subject is or may readily be ascertained by the investigator or associated with the information.

[45 CFR 46.102(f)]

Research Using Coded Private Data/Biologic Samples

- Private information or samples that retain a link to individually identifying information is ordinarily considered by OHRP to be individually identifiable to the investigator.

- But, there are exceptions…

Research involving only coded private information/specimens is not human subjects research if:

1. The private information or specimens were not collected specifically for the currently proposed research project through an intervention or interaction 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, for example:

Example:

- The investigator 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.

OHRP GUIDANCE ON RESEARCH INVOLVING CODED PRIVATE INFORMATION OR BIOLOGICAL SPECIMENS (2004)

Research Databases:
3 Paths to Human Subjects Research

- Creating a research repository/database **through intervention or interaction with individual**
- Creating a research repository/database by **obtaining identifiable private information**
- Obtaining identifiable private information **from a research repository/database.**

Applicability of the HHS Regulations

Research?

Human Subject?

Exempt?

Exemption 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.

  [45 CFR 46.101(b)(4)]

What's meant by "existing"?

- Specimens and data are existing at the time the research is proposed to an institutional official for a determination of whether the research is exempt

- Since research repositories and databases often continually accrue new specimens/data, Exemption 4 may not apply

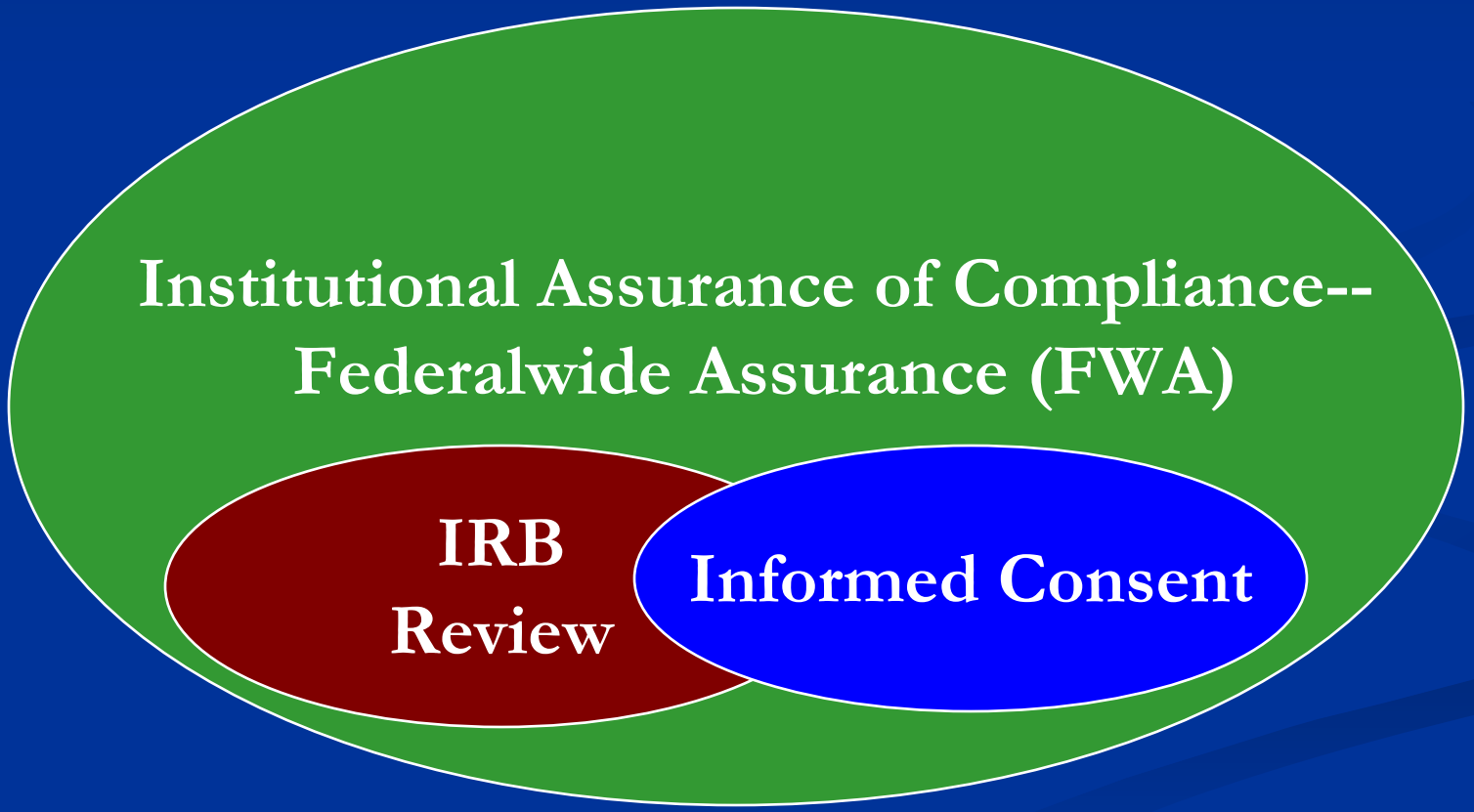
What's meant by "publicly available"?

- In general, available without restrictions or conditions (can include a fee).
- Since research repositories and databases often impose restrictions or conditions on access, Exemption 4 may not apply.

What's meant by "recorded by the investigator in such a manner that subjects cannot be identified directly or through identifiers"

- Information recorded is not directly or indirectly identifiable
- Information cannot be coded

45 CFR 46: What are the Basic Regulatory Protections for Human Subjects?



45 CFR 46: What is an Institutional Assurance of Compliance (FWA)?

- Documents institution's commitment to comply with Common Rule and/or 45 CFR 46 and all of its subparts
  - Note: Regulations include provision for substitute foreign procedures if HHS determines they are at least equivalent to 45 CFR 46
- Generally recognized by other Common rule Departments/Agencies

45 CFR 46: What are Some Key Features of IRB Review?

- IRB: A committee charged with review of human subjects research to assure that subjects' rights and welfare are adequately protected
- Review by IRB designated in assurance/FWA
- IRB membership requirements
- Criteria for IRB approval

45 CFR 46: What are Some Key Features of IRB Review?

- When required :
  - Initial review
  - Proposed protocol change
  - Continuing review
- Method of review:
  - Convened IRB
  - Expedited Review

45 CFR 46: What is Informed Consent?

- Consent each prospective subject or legally authorized representative

- In accordance with 45 CFR 46.116
  - Unless waived in accordance with §46.116(c) or (d), § 46.408(c), or §46.101(i)

Basic Elements of Informed Consent

- Research
  - Purpose
  - Duration
  - Procedures
- Risks
- Benefits
- Alternatives
- Confidentiality
- Compensation for Injury
- Whom to Contact
- Right to Refuse or Withdraw

[45 CFR 46.116(a)]

Additional Elements

- Risks related to pregnancy
- Anticipated reasons for termination from the study
- Costs
- Consequences of withdrawal
- New Findings
- Number of subjects

[45 CFR 46.116(b)]

Voluntary Participation

- Informed Consent may be sought only under circumstances that:
  - provide the prospective subject, or representative, sufficient opportunity to consider whether or not to participate, and
  - minimize the possibility of coercion or undue influence

[45 CFR 46.116]

When Can Informed Consent be Waived/Altered?

If IRB finds and documents that:

- Research is no greater than minimal risk,
- Waiver/alteration will not adversely affect rights & welfare of subjects,
- Research could not practicably be carried out without the waiver or alteration, AND
- When appropriate, subjects will be "debriefed" after participation

[45 CFR 46.116(d)]

OHRP Resources

- Web site: www.hhs.gov/ohrp
- Email: ohrp@hhs.gov
- Telephone: (866) 447-4777 (toll-free)
  (240) 453-6900
- Join news distribution list:
  www.hhs.gov/ohrp/news/index.html

OHRP Resources

- OHRP guidance on repositories and databases: http://www.hhs.gov/ohrp/humansubjects/guidance/reposit.htm

- OHRP guidance on coded private information: http://www.hhs.gov/ohrp/humansubjects/guidance/cdebiol.pdf