

Review of the Common Rule and Its Application in Human Research

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Disclaimer

The opinions expressed are those of the presenter and do not necessarily reflect the policy of the U.S. Department of Health and Human Services



Learning Objectives

- Discuss how the Federal regulations for human research protections came about
- Clarify the role of OHRP and its relationship with the NIH and the FDA
- Review how the Common Rule works, including what human subjects research and exemption means, and how you can use this knowledge in your NIH grant application process

Human Research: An Inherent Ethical Tension

- Research: *a systematic investigation... designed to develop or contribute to generalizable knowledge*
- Research is about promoting the common good
- Research subjects are the means to achieve this goal
 - In the pursuit of the common good, it is not always easy to manage competing interests and the rights and welfare of individual research subjects could easily be overlooked

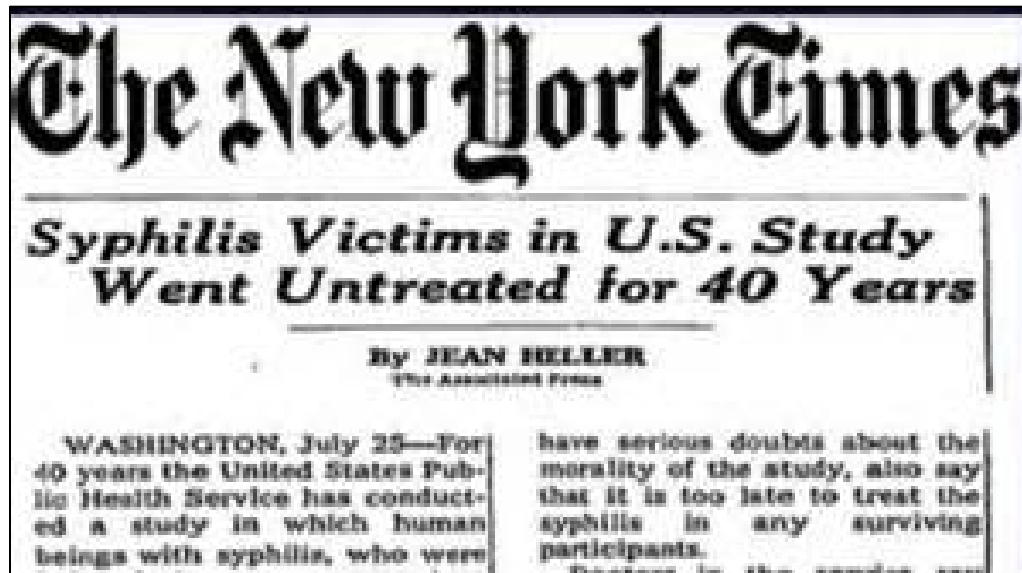


The Syphilis Study in Tuskegee, Alabama



- Began as an initiative to document the natural history of syphilis
- Researchers only told subjects that they were being treated for “bad blood,” did not tell them about the study, did not obtain consent
- When penicillin became available as an effective treatment, subjects:
 - Were not informed of its availability
 - Were not given the treatment
 - Were even prevented from finding out and accessing the treatment

How the Regulations for Human Research Protections Came About?



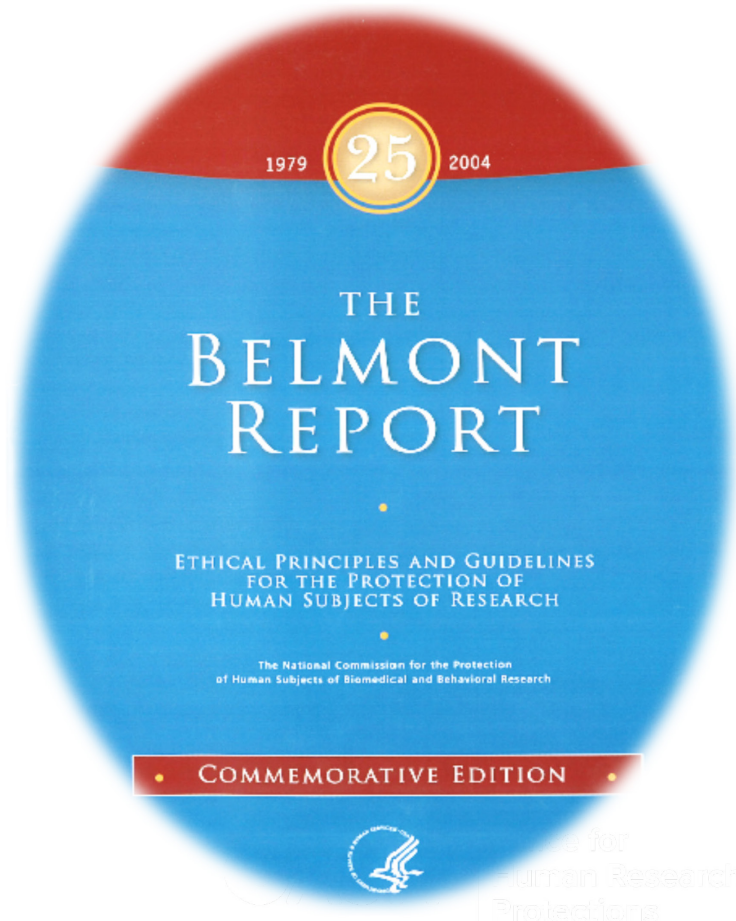
- 1974: National Research Act
- 1979: The Belmont Report
- 1991: The Common Rule

- 2018: The 2018 Requirements (Revised CR)

New York Times (July 26, 1972): Jean Heller exposes the syphilis experiment in Tuskegee



Regulations Developed on Ethical Principles



Principles of the Belmont Report

Regulatory Requirements

Respect for Persons



- Informed Consent (information, comprehension, & voluntariness)
- Provide information a reasonable person would want to make decision about participation

Beneficence



- Minimize risk of harm
- Favorable risk/benefit assessment

Justice



- Select individuals/groups of subjects equitably
- Link burdens to benefits

The Federal Regulatory Framework for Human Research Protections



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Striking a Balance

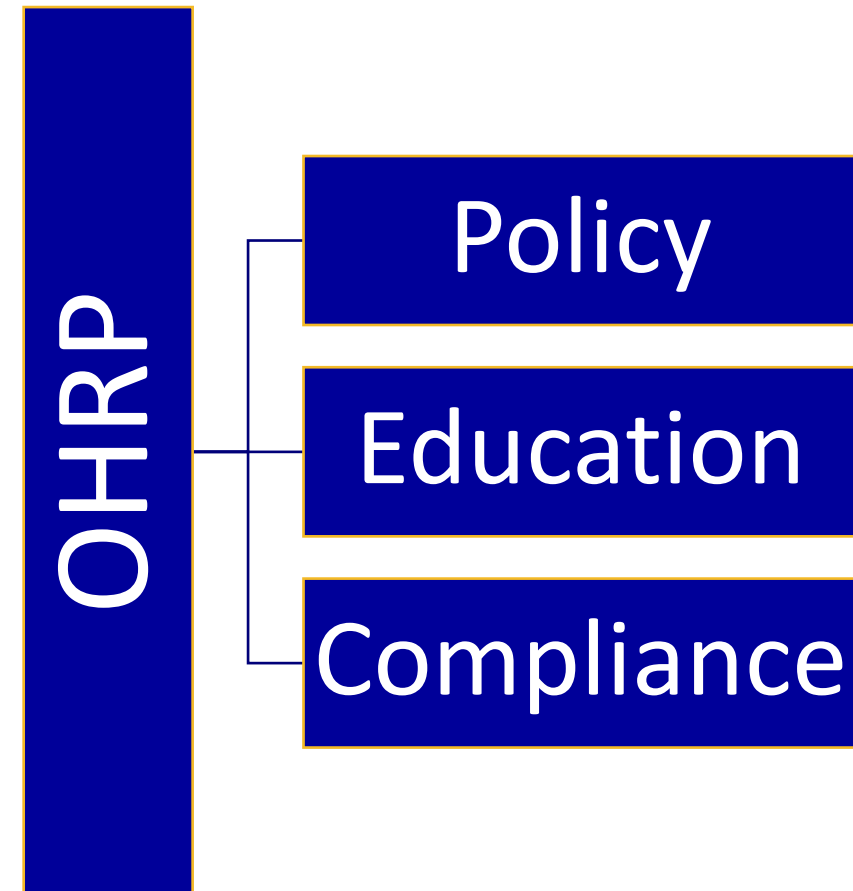
Protecting the rights & welfare of individual research subject

Furthering research interests to promote societal benefits



The Office for Human Research Protections (OHRP)

- OHRP holds the regulatory authority for **45 Code of Federal Regulation part 46** and provides leadership in protecting human subjects in research conducted or supported by the Department of Health and Human Services (HHS)
- Regulatory requirements for protections apply to **nonexempt human subjects** research that is **conducted or supported by HHS**



The HHS Regulations for Human Research Protections

45 CFR part 46

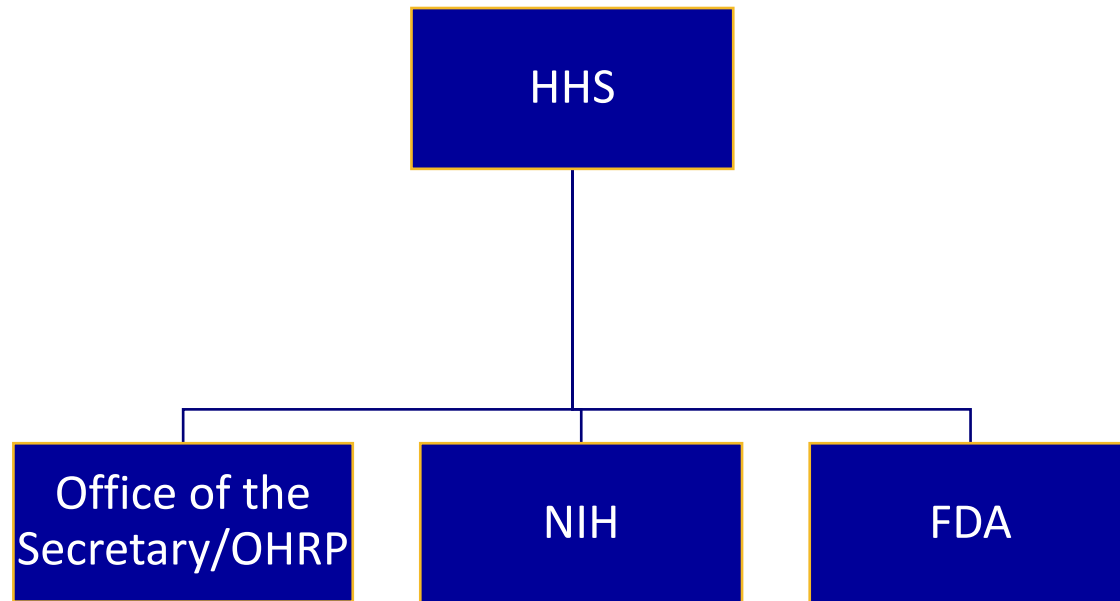
- **Subpart A – The Common Rule**
- Subpart B – Pregnant women & fetuses
- Subpart C – Prisoners
- Subpart D – Children
- Subpart E – IRB Registration

Note: The regulatory framework provides a baseline standard for human research protections. Compliance does NOT mean that the research study has no ethical concerns or presents no risks to participants!

CR Departments & Agencies



OHRP, NIH, and FDA



- **NIH** – Sponsors research
- **FDA** - Regulates clinical investigations involving drugs, devices, and biologics to make sure that they are safe for public use
- **OHRP** – Regulates HHS-conducted or supported human research
 - **All** NIH nonexempt human subjects research comes under OHRP’s oversight
 - NIH research that are also clinical investigations involving drugs, devices, and biologics will also come under FDA’s oversight

When Do Regulatory Requirements Apply and What Does That Mean ?

Regulatory Requirements Apply

When project is

Nonexempt Human Subjects Research

This means (among others):

- IRB review according to regulatory requirements & criteria
- Informed consent according to regulatory requirements (unless waived)
- Institution has active Federalwide Assurance (FWA), assures the government about ethical research, and provides certification of IRB approval

Requirements Typically Do NOT Apply

- When project is not *Research*, or
- When project is not *Human Subjects Research*, or
- When project is *Exempt Human Subjects Research*



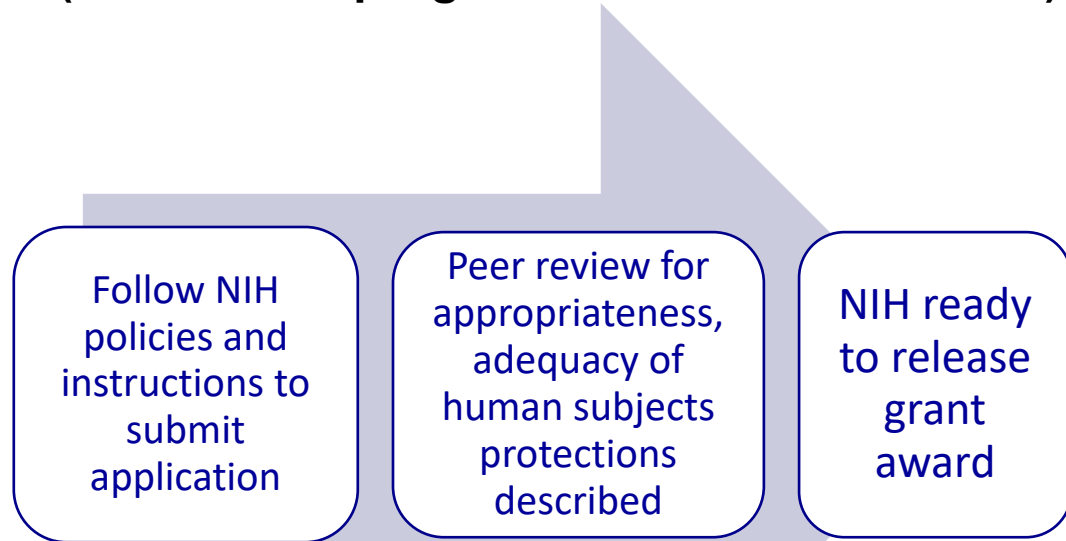
Investigators/Institutions have **Flexibility** outside the regulations

Ethical responsibilities for participants' rights & welfare remain!

Overview of the Human Subjects Review Process for NIH Grant Applications

NIH Peer Review

(contact NIH program officer for assistance)



Institutional IRB Process

(contact IRB office for assistance)

- Submit study to IRB office according to institutional policies
- IRB reviews, as appropriate
- IRB reviews and approves non-exempt human subjects research (HSR) according to regulatory criteria

Institution must provide certification of IRB review and approval for non-exempt HSR to NIH before federal money can be used to do human subjects research

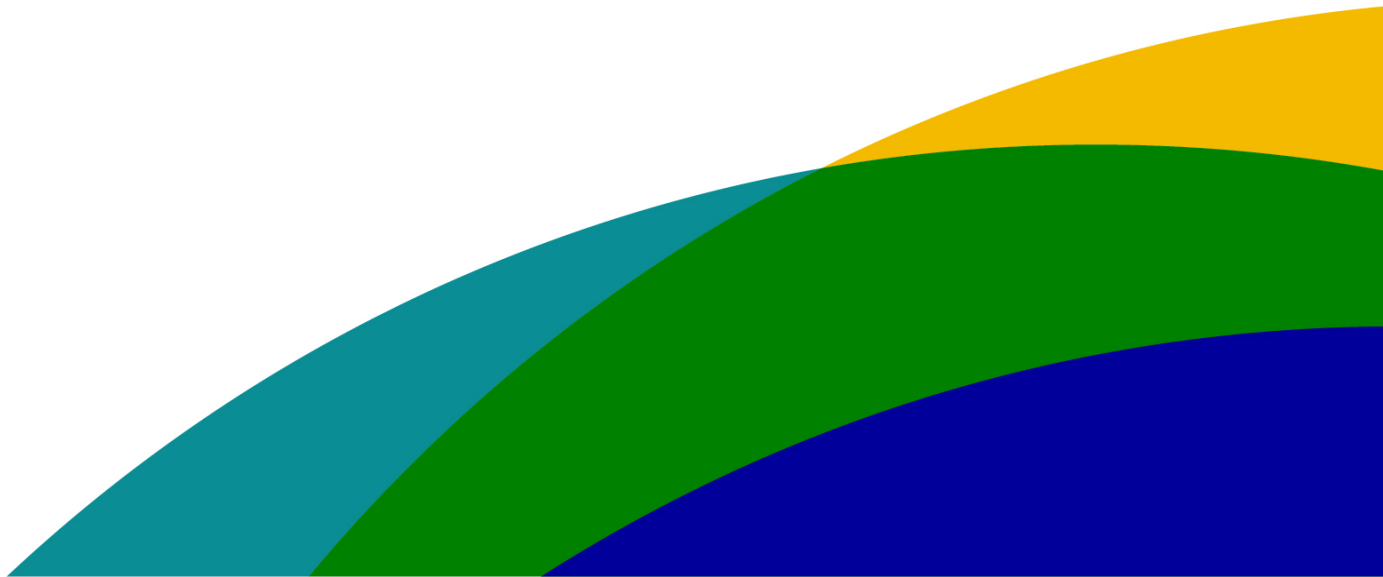
Start Here

Understanding Human Subjects Research and Exempt Research



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Determining If A Study is *Human Subjects Research* (1)

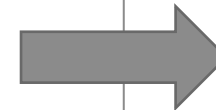
Review the regulatory definition for ***Human Subject***:

A living individual about whom an investigator conducting research

1) Obtains information or biospecimens ***through intervention or interaction*** with the individual...;

or

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



Human subj research
(Primary research)



May qualify for an exemption;
If not, follow regulatory requirements for IRB review and informed consent

On the NIH Grant Submission Form – Scenario 1



Yes, human subjects involved



Exempt Research

Entire study may fit one or more
exempt categories;

If checked yes, be prepared to provide
clear justification for your selection

Determining if Study is *Human Subjects Research* (2) – (Secondary Research with Identifiable Data/Biospecimens)

Consider the regulatory definition for ***Human Subject***:
a living individual about whom an investigator
conducting research

1) Obtains information or biospecimens ***through
intervention or interaction*** with the individual...;

OR

2) Obtains, uses, studies, analyzes, or generates
identifiable private information or identifiable
biospecimens

Human subj research
(Secondary research)



Materials identifiable
at time of access



Human subjects research:
May qualify for an exemption;
If not, follow regulatory
requirements for IRB review and
informed consent

On the NIH Grant Submission Form – Scenario 2



Yes, human subjects involved



Exempt Research

Entire study may fit one or more
exempt categories;

If checked yes, be prepared to provide
clear justification for your selection

What Does *Identifiable* Mean Under the Common Rule?

Definition for “Identifiable”:

Identifiable private information or identifiable biospecimens refers to private information or 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

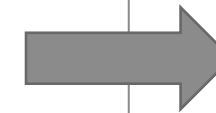
Determining if Study is *Human Subjects Research* (3) – (Secondary Research with Non-identifiable Data/Biospecimens)

Consider the regulatory definition for **Human Subject**: a living individual about whom an investigator conducting research

1) Obtains information or biospecimens **through intervention or interaction** with the individual...;

or

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



Only non-identifiable materials - Not human subjects research



No Common Rule requirements

On the NIH Grant Submission Form – Scenario 3



Research involves human specimens and/or data



Human subjects involved

No human subjects research (- no need to worry about exempt category because not applicable)

Be prepared to provide justification, such as:

- There is no interaction or intervention with human subjects to collect their information or biospecimens for the purpose of this research
- Nobody on the research team can readily link the data and biospecimens used in this research back to living individuals

What Does It Mean That *Research Is Exempt*?

- Study is **human subjects research**
- The entire study meets the conditions for one or more exempt categories described in the Common Rule
- Exempt studies are exempt from the typical requirements of the Common Rule, i.e., IRB review according to the criteria at 46.111 and the informed consent requirements at 46.116
 - There may be a special limited IRB review
- Institutions generally rely on experienced individuals in the IRB office to make exemption determinations instead of leaving this to investigators
 - Making exemption determinations ≠ IRB review and approval

Summary of the Eight Exempt Categories

Exemption 1: Normal educational practices in established educational settings

Exemption 2: Educational tests, surveys, interviews, or observation of public behavior

Exemption 3: Benign behavioral interventions

Exemption 4: Secondary research use of biospecimens or information for which informed consent is not required

Exemption 5: Evaluation of public benefit and service programs

Exemption 6: Tasted and food quality evaluation & customer acceptance studies

Exemption 7: Storage and maintenance of identifiable materials for unspecified secondary research with broad consent

Exemption 8: Secondary research use of stored identifiable materials with broad consent

Complexity of Exempt Categories – Example Exempt 3

Research involving **benign behavioral interventions** with **adults** who **prospectively agree** when **information collection is limited to** verbal or written responses (including data entry) or audiovisual recording, and:

- A. Information recorded in a manner that the identity of the subjects cannot be readily ascertained, **or**
- B. Not sensitive (i.e., low risk of harm if disclosed), **or**
- C. Identifiable and sensitive information with limited IRB review for privacy and confidentiality protections

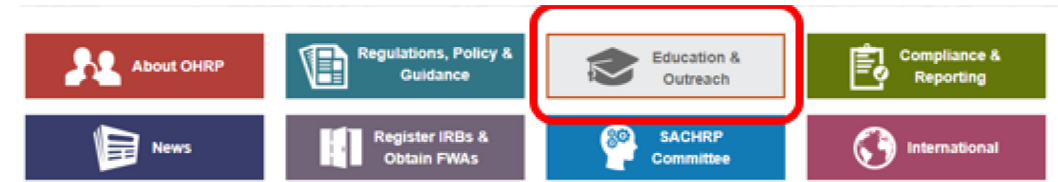


§46.104(d)(3)

OHRP's Human Research Protection Training

- Free training
- Satisfies the NIH requirements for training on human research protections for key personnel
- Five self-study lessons with completion certificate after each lesson:
 1. When HHS Regulations Apply
 2. What is Human Subjects Research?
 3. What are IRBs?
 4. IRB Review of Research
 5. Institutional Oversight of Human Research

Find it at OHRP website > Education & Outreach > Online Education
<https://www.hhs.gov/ohrp/education-and-outreach/online-education/human-research-protection-training/index.html>



[HHS Home](#) > [OHRP](#) > Education & Outreach

A screenshot of the OHRP Human Research Protection Training page. The page has a left sidebar with a list of links: 'About Research Participation', 'Upcoming Educational Events', 'Revised Common Rule', 'Online Education' (highlighted with a red box), 'Hot Topics', 'Human Research Protection Training', 'Mini-Tutorials', 'Videos', 'Exploratory Workshop', 'Luminaries Lecture Series', 'Human Research Protection Program Resources', 'Educational Collaboration with OHRP', and 'Education & Outreach Archived Materials'. The main content area is titled 'Human Research Protection Training' and includes an introductory paragraph, a note about a printable completion certificate, and five lesson cards: 'When HHS Regulations Apply', 'What is Human Subjects Research', 'What are IRBs', and 'IRB Review of Research'. Each lesson card features an icon, a title, a brief description, and a right-pointing arrow.

Contacts and Resources

- Contact us or submit your questions to OHRP@hhs.gov
- Visit OHRP website at www.hhs.gov/ohrp

