Nothing Basic About It, But We'll Try to Make It So – Common Rule ABCs with OHRP

HHS Office for Human Research Protections (OHRP)
Division of Education and Development (DED)

OASH | Office for Human Research Protections

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.

For a complete and accurate description of the regulatory requirements, please refer to the text of the revised Common Rule available on OHRP's website.

Learning Objectives

- Discuss how the U.S. federal regulations for human research protections came about
- Describe the ethical and regulatory framework for human research protections
- Review the basics about how the Common Rule works

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 (1932-1972)

- 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?

The New York Times

Syphilis Victims in U.S. Study Went Untreated for 40 Years

By JEAN HELLER

WASHINGTON, July 25—For 40 years the United States Public Health Service has conducted a study in which human beings with syphilis, who were

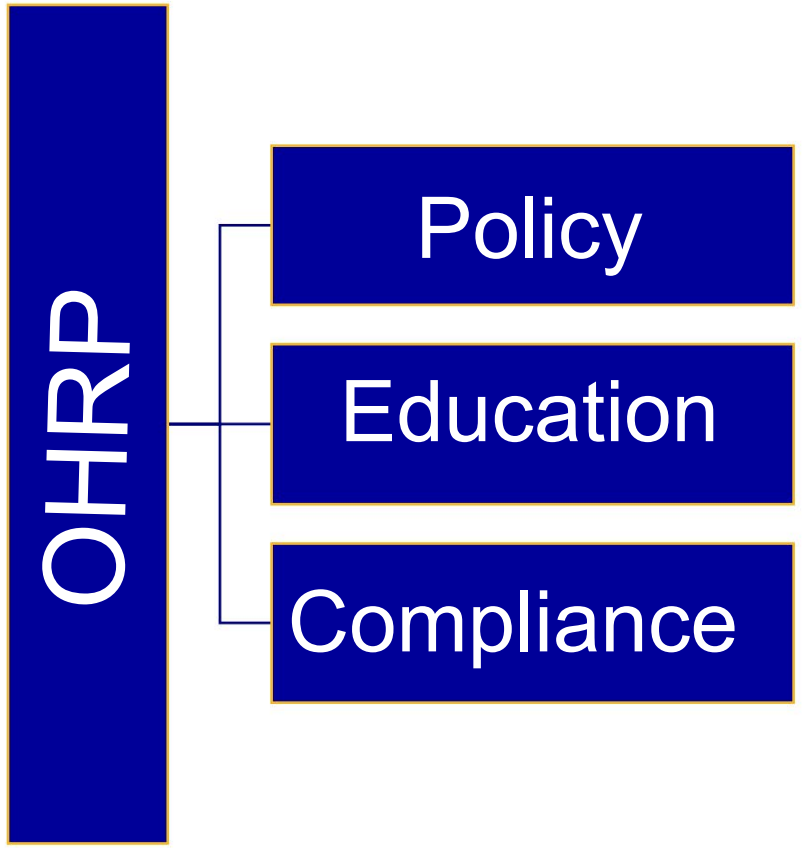
have serious doubts about the morality of the study, also say that it is too late to treat the syphilis in any surviving participants.

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

- 1974: National Research Act
- 1979: The Belmont Report
- 1991: The Common Rule (CR)
- 2018: The 2018 Requirements (Revised CR)

The Office for Human Research Protections (OHRP)

- Within the U.S. Federal Department of Health and Human Services (HHS)
- OHRP holds the regulatory authority for the HHS regulations at **45 Code of Federal Regulation part 46** and provides leadership in protecting human subjects in HHS-conducted or supported research



HHS Regulations at 45 CFR 46

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

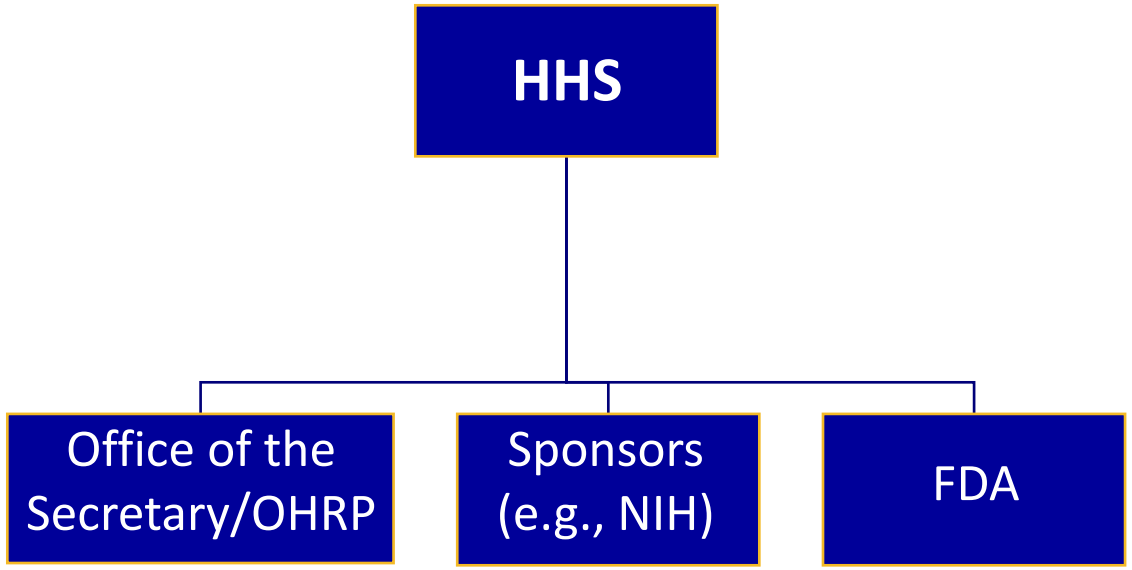
The regulatory framework provides a baseline standard for human research protections. Compliance does NOT mean that the research study has no ethical concerns or presents no risks to participants!

What is "Common" About the Common Rule?

- Followed across the U.S. Federal government (by 20 Federal Departments and Agencies through various mechanisms) for human subjects research that they fund
- Provides the foundational framework for human research protections
- **Each CR department or agency is responsible for oversight of the research that it supports or conducts**

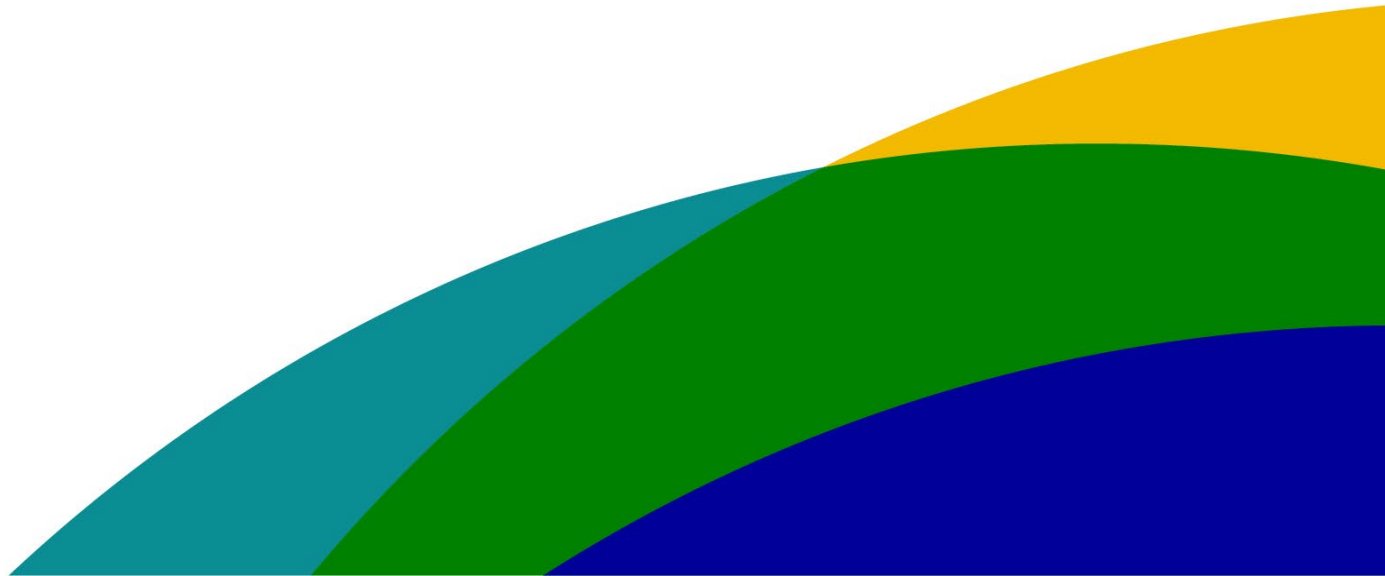
CR Departments & Agencies

Who Does What: FDA, OHRP, & HHS Sponsors of Research



- **HHS sponsors** of research (e.g., NIH) – Funds and administers research grants
- **FDA** - Regulates clinical investigations involving drugs, devices, and biologics (regardless of funding source) to make sure that they are safe for public use
- **OHRP** – Regulates HHS-conducted or supported human research, e.g.,
  - ***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

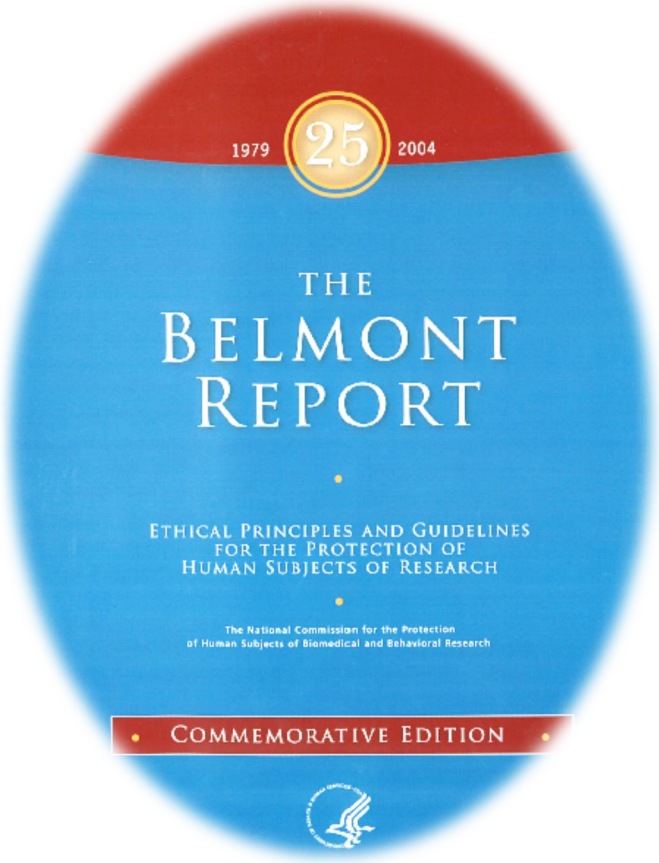
How Does the Common Rule Work?



Protecting the rights & welfare of individual research subject

Furthering research interests to promote societal benefits

Regulations Developed on Ethical Principles



Principles of the Belmont Report	Regulatory Requirements
Respect for Persons	• Provide information a reasonable person would want to make decision about participation • Informed Consent from subjects/LAR
Beneficence	• Minimize risk of harm • Favorable risk/benefit assessment
Justice	• Select individuals/groups of subjects equitably • Link burdens to benefits

What is in the Common Rule?

- Nuts & Bolts
  - Assurances, definitions, exemptions
- Institutional Review Board (IRB) Provisions
  - Membership, functions, operations, and records
- IRB Review and Approval of Research
  - Mechanisms and review criteria
- Informed Consent
  - Requirements and documentation
- Other Stipulations

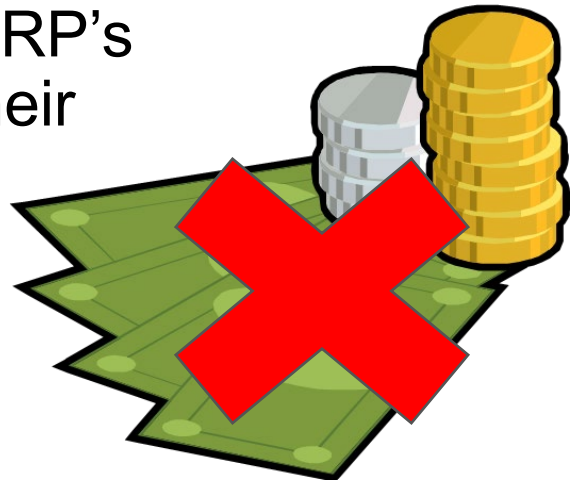
How Does the Common Rule Work?

- The Common Rule (CR) regulatory requirements generally apply to **nonexempt human subjects research funded** by HHS or the other Common Rule agencies and departments
  - Institutions must assure their compliance (usually through a Federalwide Assurance (FWA)) before receiving federal funds for nonexempt human research
- The CR department or agency is responsible for compliance oversight of the research that it supports or conducts
  - OHRP has the responsibility for compliance oversight for all HHS-funded human subjects research, including NIH, CDC, HRSA, etc.

What If Research is NOT Funded by a CR Agency?

What is the relevance of CR? There are several possibilities:

- Institutions may still be compelled to comply with the Common Rule by another authority, such as their state government
- Institutions may have voluntarily selected to come under OHRP's compliance oversight by "checking the box" when they file their FWA with OHRP
  - OHRP has no expectation for institutions to do so
  - OHRP will be removing this option soon
- Institutions may voluntarily adopt the Common Rule as a framework of relevance for themselves **using their own institutional policies for oversight** of the research they conduct
- Institutions may disregard the Common Rule



OK, There is CR Agency Funding – Now What?

Regulatory requirements apply when project is

***Nonexempt* Human Subjects Research**

This generally means (among others):

- **IRB review** according to regulatory requirements & criteria
- **Informed consent** according to regulatory requirements (unless waived)
- Institution has an active **FWA** and provides certification of IRB approval

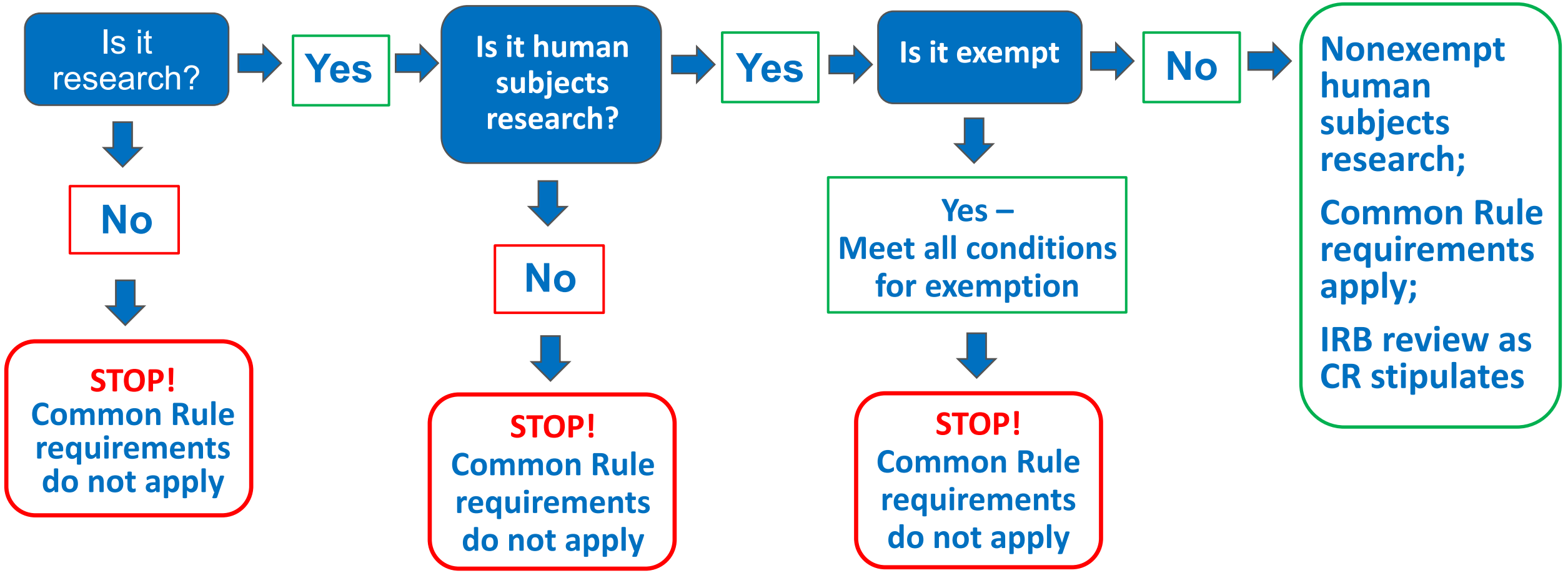
What Activities are *Nonexempt Human Subjects Research*?

To determine if your project is ***nonexempt human subjects research***, ask these questions in this order:

1. Does the activity involve ***Research***?
2. Does the research involve ***Human Subjects***?
3. Is the human subjects research ***Exempt***?

According to the regulatory definitions…

Flowchart Showing How to Determine if a Project is *Nonexempt Human Subjects Research*



Regulatory Requirements Typically Do NOT Apply

When the project is

1. **<u>not</u> *Research***, or
2. **<u>not</u> *Human Subjects Research***, or
3. ***Exempt Human Subjects Research***

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

- No need for standard IRB review **as prescribed by the regulations**
- No need for informed consent **as prescribed by the regulations**

Ethical responsibilities for participants' rights & welfare remain!

Who Makes the Determination for *Nonexempt Human Subjects Research*?

- CR does not stipulate who should make these determinations
- OHRP does not recommend investigators making these determinations
- It is recommended that institutions designate someone with knowledge and experience about the regulations and ethics for human research protections to make the determinations (e.g., an IRB professional working in the institution's IRB/research administration office), for the following reasons:
  - Ensuring consistency and fairness in the determination
  - Ensuring that the determinations are made correctly to protect the institution from having a compliance issue with the federal government
  - For research projects that do not require IRB review under CR, an institutional determination could be used to meet the independent review for ethics and protections that reputable journals often require for publication submissions

IRB Professionals

- The role of an IRB professional is crucial considering how a lot of projects investigators submit aren't going to be *nonexempt human subjects research* requiring IRB review per CR.
- For many institutions, IRB professionals may have a bigger role to play than IRB members. A professional can also be a member of the IRB.
  - Train them well!
  - Give them the necessary support!
  - Both investigators and IRB members will appreciate knowledgeable and helpful IRB professionals!
  - IRB professionals help develop, apply, and uphold institutional policies, thus protecting the institution's reputation and integrity in human research.

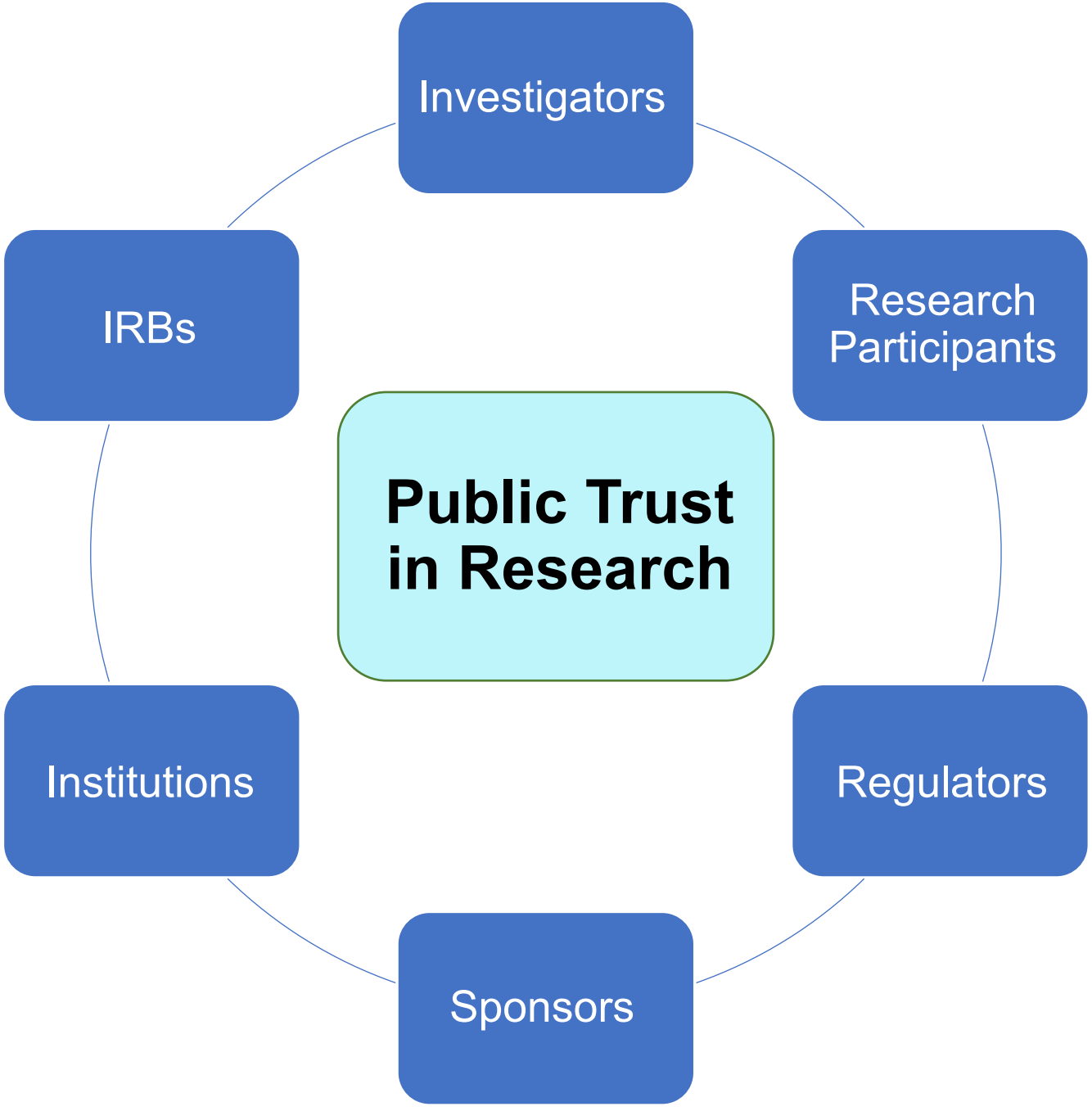
IRBs Under the Common Rule

- A formalized structure with regulatory requirements that include, among others,
  - IRB membership (46.107)
  - Functions and operations (46.108)
  - Review, meeting, voting… (46.109, 46.110, 46.111)

- IRB options for institutions:
  - Set up and use their own
  - Rely on an external IRB, of another research institution, commercial IRBs, or otherwise

  Decision would likely depend on the volume of research requiring IRB reviews, and the anticipated administrative burden and costs

A Connected Framework of Partnerships and Commitment to Protect Research Participants



OHRP's Human Research Protection Training

- Free comprehensive foundational training on the Common Rule framework
- Five self-study lessons with completion certificate after each lesson
- Satisfies the NIH requirements for training on human research protections for key personnel

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

When HHS Regulations Apply (Lesson 1)

This lesson introduces human research protections, the Common Rule, and the offices and agencies that oversee of human subjects research. It takes approximately 35 min to complete.

What is Human Subjects Research (Lesson 2)

This lesson explains how the Common Rule regulations define "research" and "human subjects" and explains what it means to be exempt from the regulations. It takes approximately 1hr and 35 min to complete.

What are IRBs (Lesson 3)

This lesson explains the purpose and membership requirements of Institutional Review Boards, or IRBs. It takes approximately 45 min to complete.

IRB Review of Research (Lesson 4)

This lesson will describe the regulatory requirements for IRB Review and the criteria for IRB review and approval under the Common Rule. It takes approximately 1hr and 40 min to complete.

Institutional Oversight of Human Research (Lesson 5)

This lesson explains the requirements for research institutions and IRBs for ensuring regulatory compliance and oversight of research to protect human participants. It takes approximately 45 min to complete.

Contacts and Resources

- Contact us or submit your questions to **OHRP@hhs.gov**
- Visit OHRP website at **www.hhs.gov/ohrp**, particularly the educational offerings under Education & Outreach
- Check out OHRP's ***About Research Participation*** informational resources for the public


Thank
You