What is Research and What it isn't? And Who is Human Subject Anyway? – Explaining the Common Rule in Plain Language

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

- Review and explain the regulatory definitions for “research” and “human subject”
- Provide examples to demonstrate what does and does not constitute research and who is and who is not a human subject
- Describe when the regulatory requirements apply and when they do not

The Office for Human Research Protections (OHRP) and How the Common Rule Works

- OHRP holds the regulatory authority for 45 CFR 46 and provides leadership in protecting human subjects in research conducted or supported by HHS
  - 45 CFR 46 has 5 subparts: **Subpart A – The Common Rule**
    Subpart B, C, D – Additional requirements for selected vulnerable populations;

- Regulatory requirements for protections apply to **Nonexempt human subjects research** that is **funded by HHS** (or other Common Rule agencies and departments)

***Note*: The regulatory framework provides a baseline standard for human research protections. Mere compliance does NOT mean that the research study is necessarily protective or free from ethical concerns!**

When Do Regulatory Requirements Apply and When Don't They?

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)

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!

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…

Question #1: Does the Activity Involve Research?

*Research refers to a **systematic investigation**, including research development, testing, and evaluation, **designed to develop or contribute to generalizable knowledge** …*

§46.102(l)

Is This Research?

A team of physicians sees a patient with an unusual constellation of symptoms. They run a variety of diagnostic tests and procedures. Results of the test do not yield a known diagnosis.

They write a case summary of their observations and submit it to a medical journal for publication.

Answer: No

Is This Research?

The same group of physicians identified several case reports in the medical literature of patients with similar disease presentations. They have a hypothesis, that these patients suffer from the same disease. They want to systematically review these cases to identify characteristics and commonalities that would help them better understand this disease – thus contributing to generalizable knowledge about the disease.

Answer: Yes

Activities Deemed Not to be Research

There are **4 types of activities deemed not to be research**

1) Scholarly and journalistic activities

[*Government functions with separately mandated protections*]

2) Public health surveillance activities
3) Information collection for criminal justice purposes
4) Operational activities for national security purposes

§46.102(l)

Scholarly and Journalistic Activities

Collection and use of information focused directly on the specific individuals about whom the information is collected

- In the fields of oral history, journalism, biography, literary criticism, legal research, and historical scholarship, a lot of the activities directly concern specific individuals. Hence, many of these wouldn't come under the Common Rule definition of *research*

- Excludes certain **activities**, not entire academic fields

Is This Research?

A journalism professor wants to write about the specific experiences of a group of first responders to the 9/11/2001 attacks on the World Trade Center to create a record of the events of that day.

Answer: No

Is This Research?

A group of psychologists hypothesized that certain characteristics may render a group of people to be more susceptible to PTSD following a traumatic event, like 9/11.To investigate their hypothesis, they conducted interviews and surveyed 9/11 survivors. They then analyzed the data, drew conclusions from it, and published the findings in a scientific journal to contribute to the academic literature on PTSD.

Answer: Yes

Public Health Surveillance Activities (1)

*Limited to activities conducted, supported, requested, ordered, required or authorized by a **"public health authority"***

Defined as: agency or authority of the United Sates, a state, territory, political subdivision of a state or territory, Indian tribe, foreign government, or a person/entity acting under the authority of such an agency, including employees or agents of the public agency or its contractors, or granted authority responsible for public health matters by official mandate

Public Health Surveillance Activities (2)

Limited to activities conducted by a public health authority and:

- Are necessary to allow a public health authority to **identify, monitor, assess, or investigate** potential public health signals, onsets of disease outbreaks, or conditions of public health importance, including **trends, signals, risk factors, patterns of diseases, or increases in injuries** from consumer products
- Provide **timely situational awareness and priority setting** during the course of an event or crisis that threatens public health

§46.102(l))

Is This Research?

State public health practitioners observe that certain young children who had COVID presented with inflammatory reactions affecting different systems in the body. They begin to track the symptom progression to determine how soon after initial infection inflammatory reactions may occur. They write their observations as case reports of what was seen and what was done and submit these reports to journals for publication. As COVID is a crisis that threatens public health, the public health practitioners report their observations to help identify, monitor, assess, and investigate the patters of COVID infection.

Answer: No

Is This Research?

A physician reports what appears to be an outbreak of an unusual type of meningitis. A public health authority in the area plans to collect the patients' medical and demographic information to document trends and identify signals and risk factors to better manage this potential public health crisis.

Answer: No

Is This Research?

A public health authority has a hypothesis that certain environmental exposures and lifestyles may result in an unusual form of meningitis infection. To test this hypothesis, they plan to collect medical, demographic, family history, and behavioral information from patients who present at the local hospitals with the unusual form of meningitis to look for a potential relationship between environmental exposures, the patients' lifestyles and behaviors, and the resulting infection.

Answer: Probably Yes

Questions #2: Does the Research Involve Human Subjects?

Human subject:

a **living** individual **about whom** an investigator conducting research

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

or

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

§46.102(e)(1)

Associated Terms & Concepts (1)

- **Intervention**: includes physical procedures by which **information or biospecimens** are gathered and manipulations of the subject or subject's environment for research purposes.

- **Interaction:** includes communication or interpersonal contact between investigator and subject.

Associated Terms & Concepts (2)

- **Private information:** Includes information about behavior that occurs in a context in which **an individual can reasonably expect that no observation or recording is taking place**, and information that has been provided for specific purposes by an individual and that the individual can reasonably expect will not be made public (e.g., a medical record).

- **Identifiable private information:** Private information for which the identity of the subject is or **may readily be ascertained** by the investigator or associated with the information.

- **Identifiable biospecimen:** A biospecimen for which **the identity of the subject is or may readily be ascertained** by the investigator or associated with the biospecimen.

Is This Human Subjects Research?

A researcher hypothesizes that some middle-aged women who died from COVID-19 had undiagnosed or untreated underlying heart disease. To investigate the hypothesis, the researcher plans to systematically review identifiable medical records of 400 deceased women ages 45-65 who were hospitalized with COVID-19 to look for commonalities like high blood pressure, high LDL, etc.

Answer: No

Is This Human Subjects Research?

A researcher hypothesizes that children who attend pre-kindergarten with rigorous academic instruction present with behavioral issues and attention deficit by first grade. To investigate this hypothesis, the researcher plans to interview 250 pre-kindergarten, kindergarten, and first grade teachers across the country.

Answer: Yes

Is This Human Subjects Research?

A genetic researcher is studying a possible correlation between environmental exposures and the development of rare forms of pancreatic cancer. Researcher has reviewed patient medical records and identified 30 individuals with documented environmental exposure to toxic dust who are being treated for a rare form of pancreatic cancer at her medical center. Researcher hypothesizes that toxic dust exposure has caused genetic mutations in the pancreas. To perform genetic sequencing, the researcher obtains pancreatic tissue samples leftover from clinical procedures performed on the 30 qualifying patients. Samples are provided to the researcher with patient identifying information.

Answer: Yes

Is This Human Subjects Research?

A researcher is studying pancreatic cancer. She arranges to receive pancreatic tumor samples that are leftover from routine clinical procedures. The researcher will receive these samples without any identifying information, and the clinical team that provides the samples to her will not keep track of what sample come from which patient. There will be no link between the samples and the patients from whom they were collected.

Answer: No

Are Quality Improvement or Quality Assurance (QI/QA) Activities Human Subjects Research?

The Common Rule does not define QI/QA

The Common Rule defines the terms *research* and *human subject*

- Often, the question is whether QI/QA activities meet the regulatory definitions of **research**
- So, for QI/QA activities, always ask the same question - is it a ***systematic investigation*** designed to contribute to ***generalizable knowledge***
- Calling something QI/QA or using words like “evaluation”, etc., does not make a project NOT research. The terms are not mutually exclusive.

QI/QA That Is NOT Also "Research"

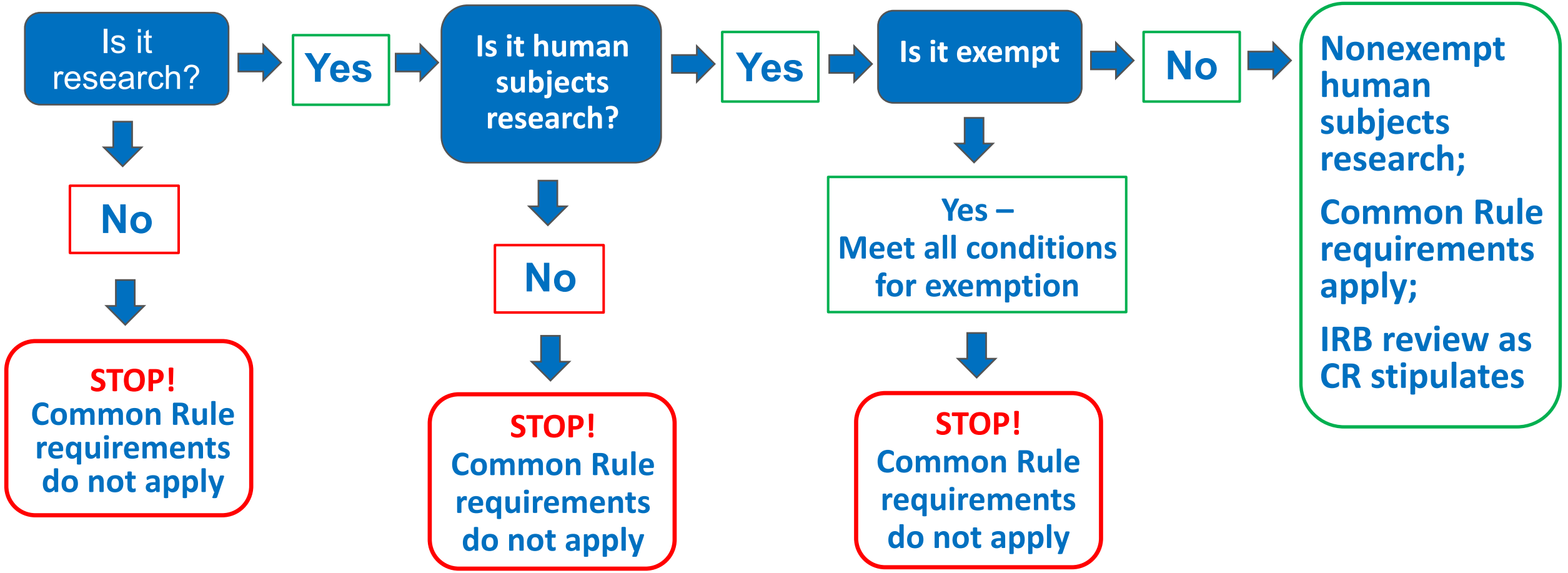
- OHRP **QI FAQs**
  - If *purpose is* limited to the following ONLY, this could be a QI activity that does not also involve research:
    - ✓implementing a practice to improve quality of patient care, and
    - ✓collecting data (on the practice) for clinical/practical/admin purpose
  - If *purpose* includes establish scientific evidence = research
  - Intent to publish not sufficient to determine if QI involves HSR

Is This QI/QA That Does Not Also Involve "Research"?

A hospital administrator wants to collect data on the incidence of 7-day infection rate of patients who underwent surgery at their hospital to monitor the quality of disinfection and staff adherence to hygiene protocols with the goal of determining budget needs for additional training.

Answer: This is QI/QA that does not involve research

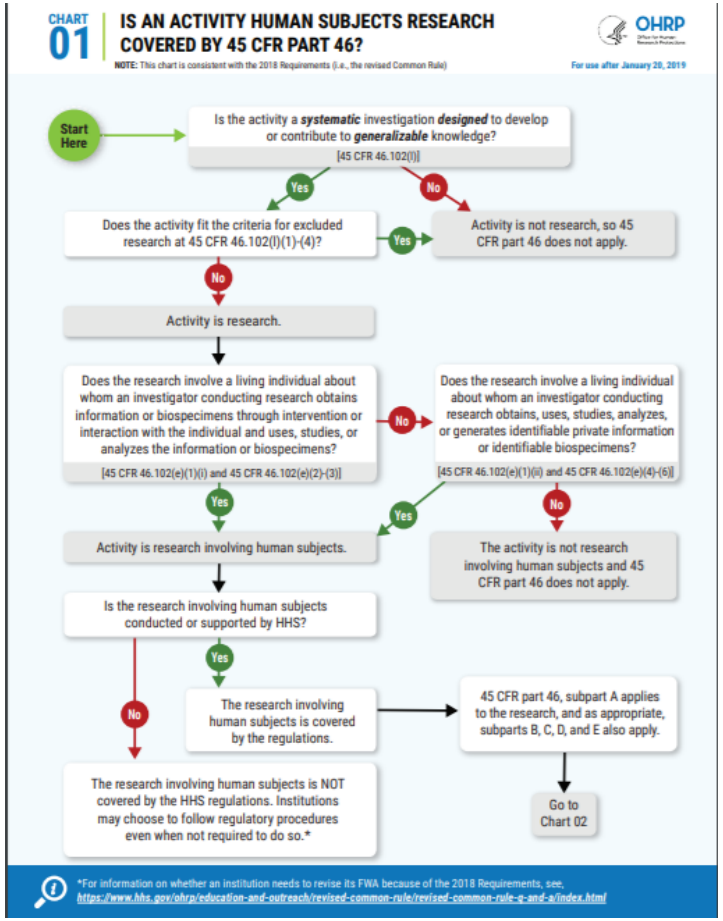
Question 3: Is the Human Subjects Research Exempt?



Human Subject Regulations Decision Charts

Visit the OHRP website to view graphic charts intended to aid those who need to decide if an activity is research involving human subjects that must be reviewed by an IRB!

Human Subject Regulations Decision Charts



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
- Two interactive trainings on IRB review criteria considerations

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!