Lesson 1:
WHEN HHS REGULATIONS APPLY

Office for Human Research Protections

CONTENTS

OVERVIEW

Purpose of This Lesson

This lesson will introduce you to the Common Rule and the offices and agencies that are responsible for the regulatory oversight of human subjects research.

This lesson focuses on the Revised Common Rule (or 2018 Requirements) that became effective in 2018.

Lesson Overview

This lesson contains four parts:

- Part 1: Protecting People in Research
- Part 2: The Common Rule
- Part 3: HHS Offices and Agencies
- Part 4: Regulations and Institutional Policies

You will answer quiz questions throughout each part to test your knowledge.

Learning Objectives

After completing this lesson, you will be able to:

1. Identify the central ethical principles for protecting human research subjects.
2. Provide an overview of the Common Rule.
3. Describe the responsibilities of the HHS Office for Human Research Protections (OHRP) and other HHS offices and agencies.
4. Understand the relationship between the regulations and institutional policies.

PART 1: PROTECTING PEOPLE IN RESEARCH

Introduction

We encourage scientific research because all members of society stand to benefit from:

- A better understanding of human biology and behavior;
- New ways to improve health; and
- Better treatments or social programs.

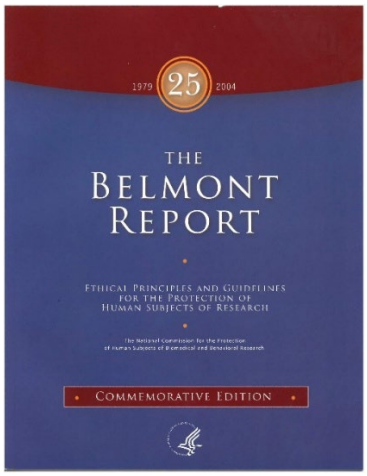
But in order for this to happen, the research community must earn and maintain the public's trust.

One way the research community accomplishes this is by following ethical guidelines and adhering to applicable research regulations.

Much of the biomedical and behavioral research that seeks to benefit individuals in our society involves human subjects — those individuals who participate in the research. **Without them, the research couldn't happen.**

The Belmont Report

The U.S. has regulations to protect research subjects that are based on a core set of ethical principles. Three principles — **respect for persons, beneficence, and justice** — were identified and explained in the 1979 Belmont Report.



Visit OHRP's webpage on the Belmont Report

These Belmont Principles became the ethical foundation of the first comprehensive set of federal regulations to protect human subjects in research, enacted shortly after the Belmont Report was published.

While the regulations have been updated since that time, their ethical foundation remains the same.

Respect for Persons

The principle of **respect for persons** acknowledges that individuals make decisions about how they want to live their lives, including if they want to volunteer for research studies.

The primary goal of research is to develop generalizable knowledge and not necessarily to further the individual interests of research participants. An important way the regulations support the ethical principle of respect for persons in research is, with some exceptions, the requirement for investigators to seek informed consent from prospective participants (or their legal representatives) before involving them in research. Apart from certain specific information about the research study, investigators must also provide information that a reasonable person would want to have to make an informed decision about whether to participate.

Hence, it's imperative that investigators strive to understand prospective participants and their perspectives to satisfy this requirement and fulfill the investigators' ethical responsibility.

Beneficence

The principle of **beneficence** acknowledges that research could bring about important contributions to public good. It calls for attention to the significance of the knowledge that may be gained from the research that the investigators propose.

Investigators should conduct research in a way that would not only maximize the benefits for all but also minimize the risks to individual participants. Separately, the regulations also require that the risks the research poses to participants are reasonable in relation to the overall anticipated benefits.

Justice

The principle of **justice** is concerned with the fair distribution of burdens and benefits. Investigators should strive for an equitable selection of subjects to participate in the research. This means they should maximize the inclusion of those individuals who would most likely benefit from the knowledge that may result, paying particular attention to those who may be under-represented in research.

Note: For more information on the Belmont Report, go to https://www.hhs.gov/ohrp/regulations-and-policy/belmont-report/index.html

Quiz 1: Protecting People in Research

Answer the following quiz questions to test your knowledge.

Question 1 of 5

How might society benefit from health and medical research? (Select all that apply)

A. Gain new ways to improve health
B. Investigators might achieve financial gain
C. Find better treatments/social programs
D. Take a break from work
E. Gain a better understanding of human biology and behavior

Question 2 of 5

Which of the following statements best represents the ethical goal of research?

A. Research is done to achieve global recognition for investigators
B. Research is done to achieve multiple grants for investigators
C. Research should uphold and maintain the public's trust
D. Researchers should only strive for HHS funding

Question 3 of 5

Which set of ethical principles provides the foundation for human research protections in the U.S.? (Select the best answer)

A. The Vermont Principles of Ethics
B. The Good Clinical Practice (GCP) Guidelines
C. The World Medical Association's Declaration of Helsinki
D. The Belmont Report
E. The International Ethical Guidelines for Biomedical Research

Question 4 of 5

Who wrote the Belmont Report?

A. University of Belmont professors
B. National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research
C. National Institutes of Health researchers
D. Office for Human Research Protections staff

Question 5 of 5

What are the main ethical principles from the Belmont Report that are integrated into the Common Rule? (Select all that apply)

A. Justice
B. Maleficence
C. Respect for persons
D. Right to privacy
E. Compassion
F. Beneficence
G. None of the above

Quiz 1 Answers

PART 2: THE COMMON RULE

Overview of the Common Rule

The Common Rule

The first Federal human subjects protection regulations were created in response to concerns about how some medical research was being conducted at the time. Since this research was primarily health-related, the Federal Health Department (what is now the Department of Health and Human Services, or HHS) oversaw the development of the regulations.

Currently, the **HHS Office for Human Research Protections (or OHRP)** is responsible for oversight of these regulations for HHS. The HHS regulations, which can be found in the Code of Federal Regulations at 45 C.F.R. Part 46, provide basic protections for people who participate in research that comes under HHS's purview.

There are five subparts to these regulations.

- Subpart A establishes basic protections for research subjects generally.
- Subparts B (pregnant women and fetuses), C (prisoners), and D (children) provide additional protections for certain vulnerable groups in research.
- Subpart E establishes requirements for registration of institutional review boards (IRBs).

Subpart A

Subpart A of the regulations is referred to as the **Common Rule** because many other Federal departments and agencies have also adopted it to protect participants in the research they conduct or fund. The Common Rule provides a broad set of protections for research subjects. These protections include review and approval of research protocols by IRBs and requirements for informed consent and privacy and confidentiality protection, among others.

Check out OHRP's infographics to find out how the regulations protect research participants: https://www.hhs.gov/ohrp/education-and-outreach/about-research-participation/protecting-research-volunteers/index.html.

OHRP infographic about protecting research participants

Common Rule Videos

Find out more about IRBs and informed consent by watching these short videos.

- How IRBs Protect Human Research Participants (6:45): https://youtu.be/U8fme1boEbE?si=5F_yPCiB_Co2Um4F
- Informed Consent for Research: What to Expect (8:09): https://youtu.be/Y7ul3sM9wtc?si=aOw2fS8aw4Ha88VF

Quiz 2: Overview of the Common Rule

Answer the following quiz questions to test your knowledge.

Question 1 of 5

Which of the following statements is true about the Code of Federal Regulation at 45 C.F.R. part 46?

A. It is referred as the Common Rule
B. It has 5 subparts including the Common Rule
C. It is the principal set of regulations regulating research misconduct
D. It applies to all research conducted in the United States

Question 2 of 5

What does Subpart A of the HHS regulations for the protection of human subjects in research entail?

A. Additional protections for pregnant women and fetuses, prisoners, and children in research
B. Baseline general protections for research subjects
C. Establishment of requirements for registration of IRBs
D. Requirements for managing financial conflict of interests

Question 3 of 5

What do Subparts B, C and D of the HHS regulations for the protection of human subjects in research entail?

A. Additional protections for pregnant women and fetuses, prisoners, and children in research
B. Baseline general protections for research subjects
C. Establishment of requirements for registration of IRBs
D. Requirements for managing financial conflict of interests

Question 4 of 5

What does Subpart E of the HHS regulations for the protection of human subjects in research entail?

A. Additional protections for pregnant women and fetuses, prisoners, and children in research
B. Baseline general protections for research subjects
C. Establishment of requirements for registration of IRBs
D. Requirements for managing financial conflict of interests

Question 5 of 5

Why is the main set of federal regulations for the protection of human subjects in research referred to as the Common Rule?

A. Because it applies to all common people who participate in research
B. Because it applies to all research involving human participants
C. Because it provides commonly accepted standards for the protection of research participants
D. Because it is adopted by many U.S. federal departments and agencies

Quiz 2 Answers

2018 Revisions to the Common Rule

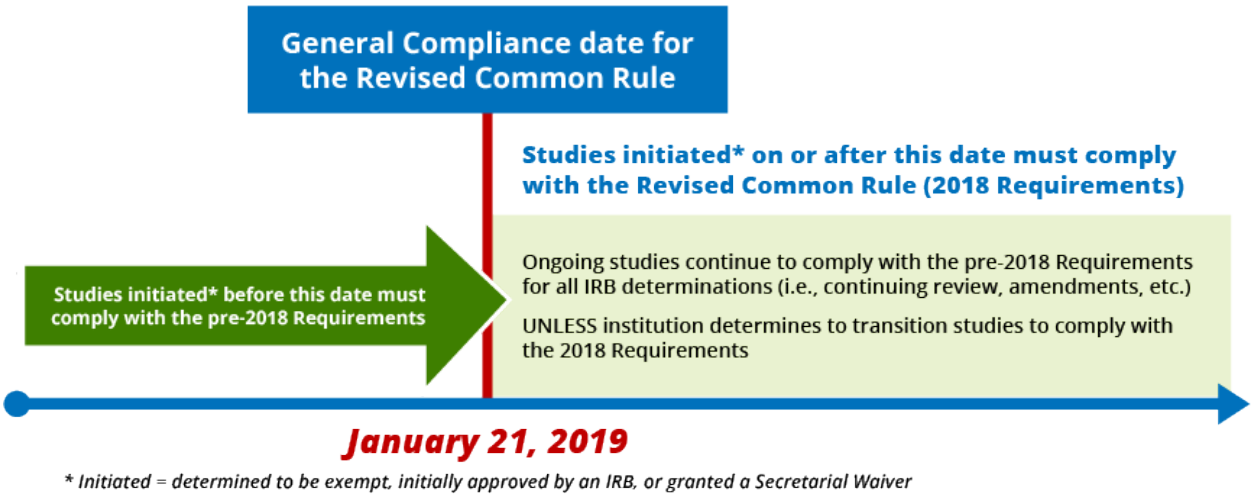
The Common Rule (subpart A of the HHS regulations) has been revised. These revisions became effective in 2018, but its compliance date was delayed until January 21, 2019. Nevertheless, the revised rule is officially called the "2018 Requirements," although many continue to refer to it as the "revised Common Rule," or simply the "new Rule."

In general:

- Research initiated on or after January 21, 2019 must comply with the revised Common Rule.
- Research initiated before this date must continue to comply with the pre-2018 Common Rule.
- Institutions may choose to transition the latter research to the revised Common Rule, but they are not required to do so.

Note: For now, at many institutions, both sets of regulations continue to be in operation for different research projects.

Because there are distinct differences between the two versions of the Common Rule, particularly with regard to the requirements for informed consent, exemptions, and continuing review, **it is vital that investigators and IRBs know which version of the Common Rule a research project is under.**



Quiz 3: 2018 Revisions to the Common Rule

Answer the following quiz questions to test your knowledge.

Question 1 of 2

In general, relevant research initiated on or after January 21, 2019, must comply with the revised Common Rule. True or false?

A. True
B. False

Question 2 of 2

It is possible that an institution may need to review and approve different federally funded research projects using different versions of the Common Rule. True or false?

A. True
B. False

Quiz 3 Answers

The Common Rule Departments and Agencies

As we mentioned, in addition to HHS, many Federal departments and agencies also follow the Common Rule. HHS-funded research must comply with both the Common Rule and the other subparts of the regulations. However, some of the other Federal departments and agencies have only adopted the Common Rule and not the other subparts of the HHS regulations.

Each Common Rule department or agency is responsible for oversight of the research that it supports or conducts.

Each of them may have its own policies or a slightly nuanced interpretation of certain provisions of the Common Rule that differs from HHS's interpretations.

The Common Rule departments and agencies — for the full list, visit https://www.hhs.gov/ohrp/education-and-outreach/revised-common-rule/common-rule-departments-agencies/index.html

For example, if you are receiving funding from the Department of Education for a research study, you would direct your questions about the Common Rule and protecting research participants to the program officers at the Department of Education.

Note: If you have a question or concern about human subjects protections, compliance, or oversight, it is important to ask the department or agency that is supporting your research.

Quiz 4: The Common Rule Departments and Agencies

Answer the following quiz questions to test your knowledge.

Question 1 of 3

An IRB has a question about how to apply the Common Rule for a research study funded by the U.S. Department of Energy, a Common Rule Department. Who should the IRB contact for more information?

A. The HHS Office for Human Research Protections (OHRP)
B. The U.S. Department of Energy (DOE)
C. The National Institutes of Health (NIH)
D. The U.S. Food and Drug Administration (FDA)
E. The Congressional Research Oversight Office

Question 2 of 3

Each Common Rule department or agency is responsible for oversight of the research that it supports or conducts. True or false?

A. True
B. False

Question 3 of 3

Each Common Rule department or agency may have its own policies or a slightly nuanced interpretation of certain provisions of the Common Rule that differs from HHS interpretation. True or false?

A. True
B. False

Quiz 4 Answers

PART 3: HHS OFFICES AND AGENCIES

The HHS Office for Human Research Protections (OHRP)

OHRP is responsible for the regulatory oversight of human subjects research that HHS supports or conducts.

OHRP:

- Develops guidance;
- Provides interpretation;
- Educates the regulated community; and
- Enforces compliance for the HHS regulations for human research protections at 45 C.F.R. part 46.

To preserve its independence in regulating HHS-funded research, OHRP is under the Office of the Assistant Secretary for Health (OASH) and separate from other HHS components that fund or conduct HHS-regulated research.

Other HHS Offices and Agencies

As a large federal department, HHS has numerous agencies and offices that serve different functions. For example, the **National Institutes of Health (NIH)** and the **Centers for Disease Control and Prevention (CDC)** are both part of HHS and they fund human subjects research to varying extents.

The **U.S. Food and Drug Administration (FDA)** is also a part of HHS. Part of FDA's broad mission includes ensuring the safety, efficacy, and security of drugs, biological products, and medical devices available to the American public.

The FDA has its own regulations that apply to the clinical investigations it oversees. These regulations align with the Common Rule but also differ in some important ways. **While there is an ongoing effort to harmonize them, it is important for investigators and IRBs to know which regulations are applicable for a particular research project.**

Sometimes, both sets of regulations may apply.

- For example, research funded by a private company to test a new drug may have to comply with the FDA regulations because it involves an FDA-regulated product, but not the Common Rule because it does not involve HHS support.
- However, an NIH-funded study that involves the research use of an FDA-regulated drug may need to comply with both sets of regulations — the FDA regulations because the drug is an FDA-regulated product, and the Common Rule and its subparts because the research is funded by NIH, which is part of HHS.
- Since the FDA is part of HHS, when it funds human subjects research, that research would be regulated by OHRP and must comply with the HHS regulations at 45 C.F.R. part 46, which includes the Common Rule.

Quiz 5: HHS Offices and Agencies

Answer the following quiz questions to test your knowledge.

Question 1 of 3

Which of the following are agencies within HHS? (Select all that apply)

A. National Institutes of Health (NIH)
B. Social Security Administration (SSA)
C. Department of Defense (DOD)
D. Food and Drug Administration (FDA)
E. Centers for Disease Control and Prevention (CDC)

Question 2 of 3

The Office for Human Research Protections (OHRP) is part of the National Institutes of Health (NIH). True or false?

A. True
B. False

Question 3 of 3

Investigators do not need to know which regulations are applicable for a research project. True or false?

A. True
B. False

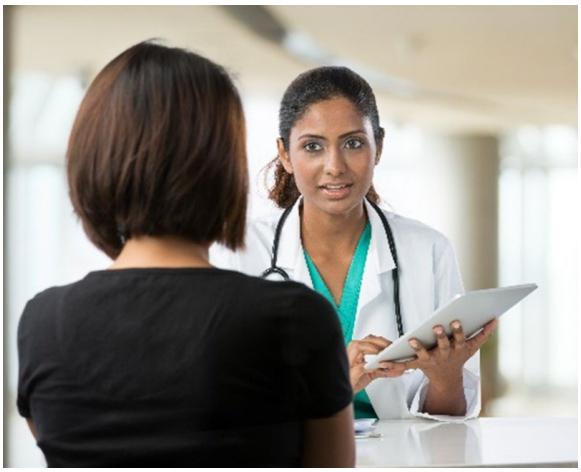
Quiz 5 Answers

PART 4: REGULATIONS AND INSTITUTIONAL POLICIES

The Relationship Between Regulations and Institutional Policies

The Common Rule applies to certain human subjects research that is supported or conducted by a Common Rule agency. However, not all research is supported by a Common Rule agency. For these studies, there is not a comprehensive set of regulations for the protection of research subjects.

However, many research institutions choose to apply the Common Rule to all of their human subjects research regardless of funding source.



They can adopt the Common Rule requirements as institutional policy, in which case the institution uses the Common Rule framework for the purpose of their internal oversight of research.

In addition, institutions implement their own institutional policies and procedures, which may be more protective than the regulatory requirements.

Institutions may have a mechanism to enforce their own requirements, even though the federal government may not have regulatory authority over research when it is not supported by a Common Rule agency.

Note: If you have questions about your institution's policies and procedures, contact your institution's human research protection program or IRB office to get more information.

Federalwide Assurances

In order to receive HHS funding to conduct certain human subjects research, institutions must have an active assurance on file with OHRP. This assurance is called an FWA, which stands for Federalwide Assurance.

Through the FWA, institutions commit to comply with the regulations, comply with additional human subjects regulations and policies as applicable, establish certain required written procedures, and support IRB activities and review. Filing an FWA is a straightforward process.

Note: You can find information on how to get started on OHRP's website at https://www.hhs.gov/ohrp/register-irbs-and-obtain-fwas/fwas/index.html. Contact OHRP at IRBorFWA@hhs.gov if you have questions about this.

For more information, you can watch the videos on the assurance process to learn about the requirements related to the FWA application and step-by-step instructions for the FWA submission process.

Other Common Rule agencies rely on FWAs; however, some require other types of assurances as well. Institutions or investigators should contact their funding agency to find out what type of assurance is required before research funding can be provided.

Watch the video "Nothing basic about it, but we'll try to make it so — Common Rule ABCs with OHRP" (34:23).

The required part of the video is from 15:12 to 19:19, although you can watch the whole video if you prefer.

Quiz 6: Regulations and Institutional Policies

Answer the following quiz questions to test your knowledge.

Question 1 of 4

Federal law requires that any research conducted in the U.S. must comply with the Common Rule. True or false?

A. True
B. False

Question 2 of 4

Many research institutions choose to apply the Common Rule regardless of funding source. True or false?

A. True
B. False

Question 3 of 4

What does FWA stand for?

A. Federalwide Applicability
B. Federalwide Assurance
C. Federalwide Access
D. Federalwide Acceptance

Question 4 of 4

Which of the following statements is true about FWAs? (Select all that apply)

A. An institution must have an active FWA before it can receive funds from NIH to conduct non-exempt human subjects research
B. When an institution files an FWA, it assures the federal government that it has the facility to conduct the research
C. When an institution files an FWA, it assures the federal government that it will comply with the Common Rule when applicable
D. All of the above

Quiz 6 Answers

CONCLUSION

Congratulations!

You've completed this module of OHRP's Human Research Protection Foundational Training, Lesson 1: When HHS Regulations Apply.

APPENDIX: QUIZ ANSWERS

Quiz 1 Answers: Protecting People in Research

Return to Quiz 1

Question 1 of 5

How might society benefit from health and medical research? (Select all that apply)

Answers: A. Gain new ways to improve health, C. Find better treatments/social programs, and E. Gain a better understanding of human biology and behavior

Question 2 of 5

Which of the following statements best represents the ethical goal of research?

Answer: C. Research should uphold and maintain the public's trust

Question 3 of 5

Which set of ethical principles provides the foundation for human research protections in the U.S.? (Select the best answer)

Answer: D. The Belmont Report

Question 4 of 5

Who wrote the Belmont Report?

Answer: B. National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research

Question 5 of 5

What are the main ethical principles from the Belmont Report that are integrated into the Common Rule? (Select all that apply)

Answers: A. Justice, C. Respect for persons, and F. Beneficence

Quiz 2 Answers: Overview of the Common Rule

Return to Quiz 2

Question 1 of 5

Which of the following statements is true about the Code of Federal Regulation at 45 C.F.R. part 46?

Answer: B. It has 5 subparts including the Common Rule

Question 2 of 5

What does Subpart A of the HHS regulations for the protection of human subjects in research entail?

Answer: B. Baseline general protections for research subjects

Question 3 of 5

What do Subparts B, C and D of the HHS regulations for the protection of human subjects in research entail?

Answer: A. Additional protections for pregnant women and fetuses, prisoners, and children in research

Question 4 of 5

What does Subpart E of the HHS regulations for the protection of human subjects in research entail?

Answer: C. Establishment of requirements for registration of IRBs

Question 5 of 5

Why is the main set of federal regulations for the protection of human subjects in research referred to as the Common Rule?

Answer: D. Because it is adopted by many U.S. federal departments and agencies

Quiz 3 Answers: 2018 Revisions to the Common Rule

Return to Quiz 3

Question 1 of 2

In general, relevant research initiated on or after January 21, 2019, must comply with the revised Common Rule. True or false?

Answer: A. True

Question 2 of 2

It is possible that an institution may need to review and approve different federally funded research projects using different versions of the Common Rule. True or false?

Answer: A. True

Quiz 4 Answers: The Common Rule Departments and Agencies

Return to Quiz 4

Question 1 of 3

An IRB has a question about how to apply the Common Rule for a research study funded by the U.S. Department of Energy, a Common Rule Department. Who should the IRB contact for more information?

Answer: B. The U.S. Department of Energy (DOE)

Question 2 of 3

Each Common Rule department or agency is responsible for oversight of the research that it supports or conducts. True or false?

Answer: A. True

Question 3 of 3

Each Common Rule department or agency may have its own policies or a slightly nuanced interpretation of certain provisions of the Common Rule that differs from HHS interpretation. True or false?

Answer: A. True

Quiz 5 Answers: HHS Offices and Agencies

Return to Quiz 5

Question 1 of 3

Which of the following are agencies within HHS? (Select all that apply)

Answers: A. National Institutes of Health (NIH), D. Food and Drug Administration (FDA), and E. Centers for Disease Control and Prevention (CDC)

Question 2 of 3

The Office for Human Research Protections (OHRP) is part of the National Institutes of Health (NIH). True or false?

Answer: B. False

Question 3 of 3

Investigators do not need to know which regulations are applicable for a research project. True or false?

Answer: B. False

Quiz 6 Answers: Regulations and Institutional Policies

Return to Quiz 6

Question 1 of 4

Federal law requires that any research conducted in the U.S. must comply with the Common Rule. True or false?

Answer: B. False

Question 2 of 4

Many research institutions choose to apply the Common Rule regardless of funding source. True or false?

Answer: A. True

Question 3 of 4

What does FWA stand for?

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Question 4 of 4

Which of the following statements is true about FWAs? (Select all that apply)

Answers: A. An institution must have an active FWA before it can receive funds from NIH to conduct non-exempt human subjects research and C. When an institution files an FWA, it assures the federal government that it will comply with the Common Rule when applicable