Lesson 4:

INDEPENDENT REVIEW OF RESEARCH

Office for Human Research Protections

CONTENTS

OVERVIEW

Purpose of This Lesson

This lesson will describe the regulatory requirements for IRB Review and the criteria for IRB review and approval under the Common Rule.

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

Lesson Overview

This lesson contains five parts:

- Part 1: HRPP or IRB Office
- Part 2: IRB Review
- Part 3: Criteria for IRB Review and Approval
- Part 4: Initial and Continuing IRB Reviews
- Part 5: Other Common Rule Requirements

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 role of HRPP or IRB Offices.
2. Identify the regulatory requirements for IRB review and expedited IRB review.
3. Identify the criteria for IRB review and approval under the Common Rule.
4. Define initial and continuing IRB reviews.
5. Describe other Common Rule requirements for ongoing oversight of research activities.

PART 1: HRPP OR IRB OFFICE

Background

Anyone interested in conducting research involving humans or using their data or biospecimens should get to know the Human Research Protection Program (HRPP) or Institutional Review Board (IRB) office that will be processing their human research application.

The professionals in HRPP or IRB offices help to make sure that the research complies with:

- Applicable regulations;
- Relevant ethical standards; and
- Any legal and institutional requirements.

In Lesson 2, this training explained that the Common Rule requirements only apply to federally funded research that qualifies as "human subjects research" under the regulations and that does not qualify for an exemption.

Generally, only "non-exempt human subjects research" needs to undergo IRB review and approval under the Common Rule.

Quiz 1: HRPP or IRB Office

Answer the following quiz questions to test your knowledge.

Question 1 of 3

The Common Rule requires that ***all*** federally funded research be reviewed by an IRB. True or false?

A. True
B. False

Question 2 of 3

The Common Rule requires that the IRB Chair make determinations about whether a research study is non-exempt human subjects research. True or false?

A. True
B. False

Question 3 of 3

An HRPP or IRB office is responsible for the following:

A. Making sure that research complies with applicable regulations, relevant ethical standards, and institutional requirements
B. Publishing research
C. Interviewing potential research participants
D. All the above

Quiz 1 Answers

Role of HRPP or IRB Offices

The determination of whether a research study is non-exempt human subjects research is usually made by the HRPP or IRB office.

This determination can be complicated and requires a thorough understanding of regulatory terms and definitions, as well as how to apply them.

This is why institutions usually rely on staff in the HRPP or IRB office with the knowledge and experience to make this kind of determination.

Most research institutions do not let their investigators make the determination themselves because some investigators are not as familiar with the regulatory terms, and, if they make an incorrect determination, the institution can face consequences for being non-compliant with the regulations.

Investigators should follow institutional procedures to submit their research protocols to the HRPP or IRB office for consideration.

There is another good reason for researchers to seek input from their HRPP or IRB office before the research begins. Many journals require proof that research studies involving humans had some kind of independent review for ethics and human research protections. This is something an HRPP or IRB office can assist with.

To understand what the determinations entail and how they are made, please review the earlier training **"Lesson 2: What is Human Subjects Research?"** either on OHRP's website or through your institution's learning platform.

Finally, for a research study that has been determined to be non-exempt human subjects research that requires IRB review, staff in the HRPP or IRB office will be able to advise the investigators and help them gather all the information needed to be submitted to the IRB for review and approval as required by the Common Rule and institutional policy.

Quiz 2: Role of HRPP or IRB Offices

Answer the following quiz questions to test your knowledge.

Question 1 of 4

It is best practice to allow investigators to make the determination regarding whether their research is non-exempt human subjects research. True or false?

A. True
B. False

Question 2 of 4

Some journals require proof that research involving humans had undergone an independent review for ethics and human research protections. True or false?

A. True
B. False

Question 3 of 4

What are some common activities of an HRPP or IRB office? (Select all that apply)

A. Make determinations about whether a research study can be exempt from the Common Rule
B. Assist investigators with submitting protocols to the IRB for review
C. Conduct audits of research data
D. Provide administrative support for IRB full board meetings
E. Help ensure that research submitted by investigators complies with applicable regulations, institutional policies, and ethical standards

Question 4 of 4

The Common Rule prohibits communications between IRBs and investigators in order to preserve the IRBs' independence. True or false?

A. True
B. False

Quiz 2 Answers

PART 2: IRB REVIEW

Regulatory Requirements

IRB review under the Common Rule is a process directed by regulatory requirements.

For example,

- The regulations require a convened IRB meeting to review research, with an expedited review alternative for some research;
- The IRB must review the study according to a set of criteria laid out in the regulations; and
- Apart from the initial review and approval of a research study, there are regulatory requirements for ongoing oversight of the research, including the subsequent "continuing" review of some research.

This training will explain these elements of the process in more detail.

IRB Full Board Review

Typically, IRB review takes place at a convened meeting of IRB members. This is often referred to as "**full board review**."

For a full board review to proceed, it must meet **quorum** requirements, which means that a majority of the total number of voting members on a given IRB are present, including at least one "non-scientist."

At a full board review, IRB reviewers will deliberate and decide whether the research study satisfies the criteria for approval.

The IRB may approve, require changes to, or disapprove the research. The Common Rule includes specific requirements for IRB committee membership, quorum, voting, and documentation of IRB actions.

For details, please review OHRP's mini-tutorial on Quorum and Voting "Membership Requirements for Institutional Review Boards (IRB)" (13:02).

Next, watch "Quorum and Voting in IRB Meetings" (22:16).

Investigators should make sure to submit all necessary information to the IRB. The IRB cannot make the required determinations when essential information is missing, and approval of the research could be delayed. The most common reason for delayed IRB approval is incomplete protocol submissions.

Researchers and HRPP or IRB office staff should work together to ensure that submissions to the IRB contain all the necessary information for an adequate review of the ethics and human research protections.

Expedited IRB Review

In addition to IRB full board review, the Common Rule provides for another review mechanism that relies on one or more IRB members to conduct the review instead of the full IRB at a convened meeting. This is commonly referred to as "**expedited review**."

Expedited review is a flexibility available only to research that meets certain required conditions. Because there are fewer people reviewing the study, often just one reviewer, expedited review can be arranged more readily than full board review.

The reviewer can be the IRB Chair or another experienced IRB member whom the Chair designates.

However, the designated reviewer must review the study according to the same set of criteria that the full board is required to apply.

The expedited reviewer may approve or require changes to the research but cannot disapprove research. If the reviewer does not think the research is approvable according to the criteria, they may pass it on to the full board for consideration.

Quiz 3: IRB Review

Answer the following quiz questions to test your knowledge.

Question 1 of 6

For a convened or full board IRB review meeting, the Common Rule includes specific requirements for which of the following?

A. IRB committee membership
B. Quorum
C. Voting
D. Documentation of IRB actions
E. All of the above

Question 2 of 6

IRB decisions include which of the following potential outcomes? (Select all that apply)

A. Approve
B. Disapprove
C. Require changes

Question 3 of 6

In order to proceed with a meeting, IRBs require a majority of their voting members to be present, including at least one “non-scientist.” True or false?

A. True
B. False

Question 4 of 6

A common reason for delays in approval of research is protocol submissions that are missing required information. True or false?

A. True
B. False

Question 5 of 6

Which actions can a reviewer conducting an expedited review of research take about a research protocol? (Select all that apply)

A. Approve the research
B. Disapprove the research
C. Request changes to the research
D. Request changes to the informed consent form
E. All of the above

Question 6 of 6

Which of the following statements is true?

A. Expedited review requires complying with a simpler set of review criteria
B. Expedited review can be done by one designated IRB member
C. Full board committees review only high-risk research
D. Full board review can only be done with all IRB members present

Quiz 3 Answers

PART 3: CRITERIA FOR IRB REVIEW AND APPROVAL

Criteria for IRB Review and Approval Under the Common Rule

Before approving a research study under the Common Rule, IRB reviewers must make sure that the study satisfies a number of requirements and see that there are additional safeguards to protect potentially vulnerable subjects. Investigators should be careful to include enough information in their research protocol submissions so that the IRB can apply these criteria.

Criteria for IRB Review and Approval of Research (Refer to §46.111 for full details)

- Risks to subjects are minimized
- Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of knowledge that may reasonably be expected to result
- Selection of subjects is equitable
- Informed consent will be obtained and documented (unless waived) accordingly
- There are adequate provisions for data monitoring to ensure safety of subjects if appropriate
- There are adequate provisions to protect the privacy of subjects and to maintain confidentiality of the data if appropriate
- There are additional safeguards to protect the rights and welfare of subjects likely to be vulnerable to coercion or undue influence

For more information, watch "Unlocking the Mysteries of the §46.111 Criteria for IRB Approval of Research" (1:01:29). (Optional)

Considerations for Reviewing Human Subjects Research

Click here to complete interactive programs designed to enhance your understanding and knowledge of what IRBs consider when they review and approve protections for research participants. Learn what is meant by minimizing risks to research subjects and the concept of equitable selection of subjects in research among others.

Watch the video from the late Dr. Edmund Pellegrino of the Kennedy Institute of Ethics explaining the IRB review process and criteria, "Balancing Society's Mandates: I.R.B. Review Criteria" (34:18).

HHS-Funded Non-Exempt Human Subjects Research

For HHS-funded non-exempt human subjects research, IRB reviewers must also ensure that the research satisfies, as appropriate, the additional protections for certain populations required in subparts B, C, and D of the regulations before they approve the research.

Quiz 4: Criteria for IRB Review and Approval

Answer the following quiz questions to test your knowledge.

Question 1 of 2

Expedited reviews can be “expedited” because the review criteria are fewer and less stringent. True or false?

A. True
B. False

Question 2 of 2

The Common Rule requires the IRB to review research using which of the following criteria? (Select all that apply)

A. Risks to subjects are minimized
B. Target enrollment numbers
C. Investigators’ conflict of interest
D. Selection of subjects is equitable
E. Additional protections for vulnerable populations

Quiz 4 Answers

PART 4: INITIAL AND CONTINUING IRB REVIEWS

Initial IRB Reviews

Initial review refers to the first official IRB review of a non-exempt human subjects research protocol. This occurs before any research activities involving human subjects, including recruitment, are allowed to begin.

During initial review, the IRB examines the proposed research and reviews the protocol and other associated documents and information to ensure that all regulatory criteria for approval are satisfied.

To ensure that the IRB has all the information necessary to approve the research, many HRPP or IRB offices work closely with investigators and research teams to address any preliminary concerns and provide all necessary documentation and information prior to initial review.

During initial review, IRBs may also request certain changes to the research and consent documents as a condition for approval. Investigators can only begin the human subjects research activities after they receive IRB approval.

Continuing IRB Reviews

Following approval of the research, IRBs also conduct periodic continuing review of the ongoing research for some studies. Generally, research that was originally reviewed at a full board meeting will be reviewed at least once a year, or more frequently depending on the level of risk the study presents to participants.

Under the revised Common Rule, unless the IRB determines otherwise, once the research progresses to the point where all that is left to do is data analysis or accessing some follow-up data, continuing review may no longer be required.

Similarly, research that qualifies for expedited review is not generally required by the regulations to undergo continuing review, although many institutions require some kind of periodic “check-in” with their HRPP or IRB office.

Lesson 4: Independent Review of Research

During continuing review, IRBs review and evaluate whether the research continues to satisfy the criteria for IRB approval of research. They consider the progress of the study, the risks of research, and whether the risk and benefit assessment has changed. They review the adequacy of the informed consent process and other study specific factors.

Check out OHRP's (2010) Continuing Review Guidance for details and watch the OHRP webinar "How Do I Review Thee? Let Me Count the Ways: The Types and Manners of IRB Review" (47:25). (Optional)

Quiz 5: Initial and Continuing IRB Reviews

Answer the following quiz questions to test your knowledge.

Question 1 of 4

Recruitment of human participants can begin prior to IRB approval. True or false?

A. True
B. False

Question 2 of 4

After an IRB administrator confirmed to the investigator that her protocol submission package was complete, the investigator began consenting people to participate in her NIH-funded study. This is:

A. Consistent with the regulations because the investigator is only consenting people to participate; research activities have not begun yet
B. Consistent with the regulations because the IRB administrator confirmed completeness of the submission, so IRB approval is imminent
C. Inconsistent with the regulations because the investigator must complete a human subjects protection training first
D. Inconsistent with the regulations because consenting people to participate is considered a human subjects research activity and may not begin prior to IRB approval

Question 3 of 4

IRBs are not allowed to request changes to research and consent documents. True or false?

A. True
B. False

Question 4 of 4

For research that was approved under an expedited category, which of the following statements is true?

A. Continuing review is required once a year
B. Continuing review is required if the research is more than minimal risk
C. Continuing review is required every two years
D. Continuing review is not required under the revised Common Rule, unless the IRB determines otherwise

Quiz 5 Answers

PART 5: OTHER COMMON RULE REQUIREMENTS

Protocol Amendments

Beyond IRB review and approval of research, the Common Rule imposes certain obligations for ongoing oversight of research activities.

For example, IRBs are required to have procedures to ensure that investigators conduct research according to the IRB-approved protocol. IRBs must also approve proposed changes to an approved study before such changes are implemented, except when the changes are necessary to eliminate apparent immediate hazards to subjects. These requirements apply to research reviewed either by the full board or through the expedited mechanism.

For exempt research studies, because they are generally "exempt" from the Common Rule requirements, there is no regulatory requirement for reviewing changes to a protocol. However, many institutions have policies requiring that changes to exempt research be reported to the HRPP or IRB office to make sure that the exemption still applies.

If the proposed changes cause the research study to no longer meet the criteria for exemption, then the research would no longer be exempt and would need to comply with the regulatory requirements and undergo IRB review.

Quiz 6: Protocol Amendments

Answer the following quiz question to test your knowledge.

Question 1 of 1

During the onset of the COVID-19 pandemic, an investigator conducting a series of in-person interviews at the hospital quickly switched to online interviews to avoid unnecessary exposure to the novel coronavirus. The investigator also added a supplemental research survey. They will notify the IRB of these changes in the near future. Which is true about the two changes to the protocol:

A. The new survey could be implemented without prior IRB approval, but the switch to online interviews requires prior IRB approval
B. The switch to online interviews could be implemented without prior IRB approval to eliminate apparent immediate hazards to subjects, but the new survey requires prior IRB approval
C. Both the switch to online interviews and the new survey require prior IRB approval
D. Both the switch to online interviews and the new survey could be implemented without prior IRB approval

Quiz 6 Answer

Reporting to IRBs

The Common Rule also requires prompt reporting to the IRB, OHRP, and other relevant officials of any unanticipated problems involving risks to subjects or others, serious or continuing noncompliance, and suspensions or terminations of IRB approval. In addition, adverse events that also meet the criteria for unanticipated problems involving risks to subjects or others are reportable to OHRP.

- Click here to learn more about reporting to OHRP.
- Visit OHRP Mini-Tutorials for short videos discussing reporting requirements.

These reporting requirements allow IRBs to stay informed regarding issues that may affect the risk level of the research during the course of the research.

Additionally, investigators may have reporting responsibilities to the IRB or other entities resulting from, for example:

- Institutional policies;
- Research sponsors;
- Data and safety monitoring boards; and
- Other federal, state, or local regulations.

It is important that investigators and IRBs are aware of the Common Rule's requirements with regard to oversight of research to ensure sustaining protections for the health and welfare of research participants and continued compliance with the regulations.

Quiz 7: Reporting to IRBs

Answer the following quiz question to test your knowledge.

Question 1 of 1

Which of the following statements about what investigators should do is true? (Select the best answer)

A. Report all adverse events to OHRP
B. Obtain IRB approval before making changes to approved research, unless there are immediate hazards to subjects
C. Report monthly enrollment numbers to the IRB
D. Report serious unanticipated problems to the IRB only at the annual continuing review
E. All of the above

Quiz 7 Answer

CONCLUSION

Congratulations!

You've completed this module of OHRP's Human Research Protection Foundational Training, Lesson 4: Independent Review of Research.

APPENDIX: QUIZ ANSWERS

Quiz 1 Answers: HRPP or IRB Office

Return to Quiz 1

Question 1 of 3

The Common Rule requires that *all* federally funded research be reviewed by an IRB. True or false?

Answer: B. False

Question 2 of 3

The Common Rule requires that the IRB Chair make determinations about whether a research study is non-exempt human subjects research. True or false?

Answer: B. False

Question 3 of 3

An HRPP or IRB office is responsible for the following:

Answer: A. Making sure that research complies with applicable regulations, relevant ethical standards, and institutional requirements

Quiz 2 Answers: Role of HRPP or IRB Offices

Return to Quiz 2

Question 1 of 4

It is best practice to allow investigators to make the determination regarding whether their research is non-exempt human subjects research. True or false?

Answer: B. False

Question 2 of 4

Some journals require proof that research involving humans had undergone an independent review for ethics and human research protections. True or false?

Answer: A. True

Question 3 of 4

What are some common activities of an HRPP or IRB office? (Select all that apply)

Answers: A. Make determinations about whether a research study can be exempt from the Common Rule, B. Assist investigators with submitting protocols to the IRB for review, D. Provide administrative support for IRB full board meetings, E. Help ensure that research submitted by investigators complies with applicable regulations, institutional policies, and ethical standards

Question 4 of 4

The Common Rule prohibits communications between IRBs and investigators in order to preserve the IRBs' independence. True or false?

Answer: B. False

Quiz 3 Answers: IRB Review

Return to Quiz 3

Question 1 of 6

For a convened or full board IRB review meeting, the Common Rule includes specific requirements for which of the following?

Answer: E. All of the above

Question 2 of 6

IRB decisions include which of the following potential outcomes? (Select all that apply)

Answers: A. Approve, B. Disapprove, C. Require changes

Question 3 of 6

In order to proceed with a meeting, IRBs require a majority of their voting members to be present, including at least one "non-scientist." True or false?

Answer: A. True

Question 4 of 6

A common reason for delays in approval of research is protocol submissions that are missing required information. True or false?

Answer: A. True

Question 5 of 6

Which actions can a reviewer conducting an expedited review of research take about a research protocol? (Select all that apply)

Answers: A. Approve the research, C. Request changes to the research, D. Request changes to the informed consent form

Question 6 of 6

Which of the following statements is true?

Answer: B. Expedited review can be done by one designated IRB member

Quiz 4 Answers: Criteria for IRB Review and Approval

Return to Quiz 4

Question 1 of 2

Expedited reviews can be "expedited" because the review criteria are fewer and less stringent. True or false?

Answer: B. False

Question 2 of 2

The Common Rule requires the IRB to review research using which of the following criteria? (Select all that apply)

Answers: A. Risks to subjects are minimized, D. Selection of subjects is equitable, E. Additional protections for vulnerable populations

Quiz 5 Answers: Initial and Continuing IRB Reviews

Return to Quiz 5

Question 1 of 4

Recruitment of human participants can begin prior to IRB approval. True or false?

Answer: B. False

Question 2 of 4

After an IRB administrator confirmed to the investigator that her protocol submission package was complete, the investigator began consenting people to participate in her NIH-funded study. This is:

Answer: D. Inconsistent with the regulations because consenting people to participate is considered a human subjects research activity and may not begin prior to IRB approval

Question 3 of 4

IRBs are not allowed to request changes to research and consent documents. True or false?

Answer: B. False

Question 4 of 4

For research that was approved under an expedited category, which of the following statements is true?

Answer: D. Continuing review is not required under the revised Common Rule, unless the IRB determines otherwise

Quiz 6 Answer: Protocol Amendments

Return to Quiz 6

Question 1 of 1

During the onset of the COVID-19 pandemic, an investigator conducting a series of in-person interviews at the hospital quickly switched to online interviews to avoid unnecessary exposure to the novel coronavirus. The investigator also added a supplemental research survey. They will notify the IRB of these changes in the near future. Which is true about the two changes to the protocol:

Answer: B. The switch to online interviews could be implemented without prior IRB approval to eliminate apparent immediate hazards to subjects, but the new survey requires prior IRB approval

Quiz 7 Answer: Reporting to IRBs

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Question 1 of 1

Which of the following statements about what investigators should do is true? (Select the best answer)

Answer: B. Obtain IRB approval before making changes to approved research, unless there are immediate hazards to subjects