Lesson 4

INDEPENDENT REVIEW OF RESEARCH

OASH Office for Human Research Protections

INDEPENDENT REVIEW OF RESEARCH

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

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.

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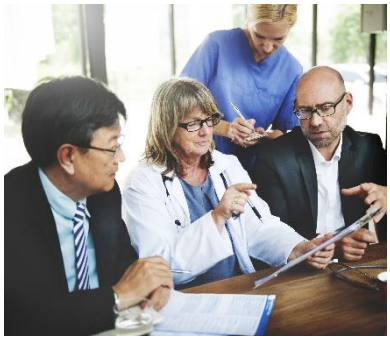
Part 1: HRPP or IRB Office

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 applications. The professionals in this office help to make sure that the research complies with applicable regulations, relevant ethical standards, and any legal and institutional requirements.

In Lesson 2, we 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.

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.**

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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.

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.

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.
- 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.

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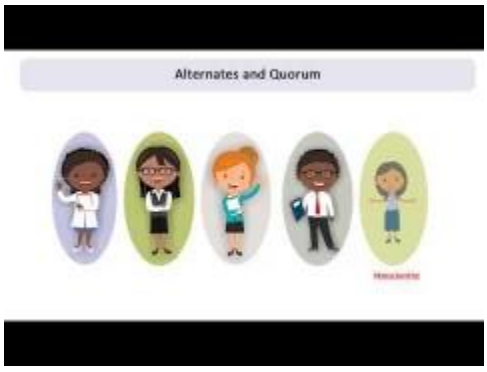
We will explain these elements of the process in more detail.

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 nonscientist. 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.

Please review OHRP's mini-tutorial Quorum and Voting for details.

Quorum and Voting in IRB Meetings



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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, she may pass it on to the full board for consideration.

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.

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. Offers include a program examining the concept of equitable selection of subjects in research and one on how to minimize risks in research.

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Video – Balancing Society's Mandates: I.R.B. Review Criteria

Watch the video from the late Dr. Edmund Pellegrino of the Kennedy Institute of Ethics explaining the IRB review process and criteria.

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.

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.

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.

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.

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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.

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.