How Do I Review Thee? Let Me Count the Ways: The Types and Manners of IRB Review

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

July 25, 2023

OASH | Office for Human Research Protections

Disclaimer

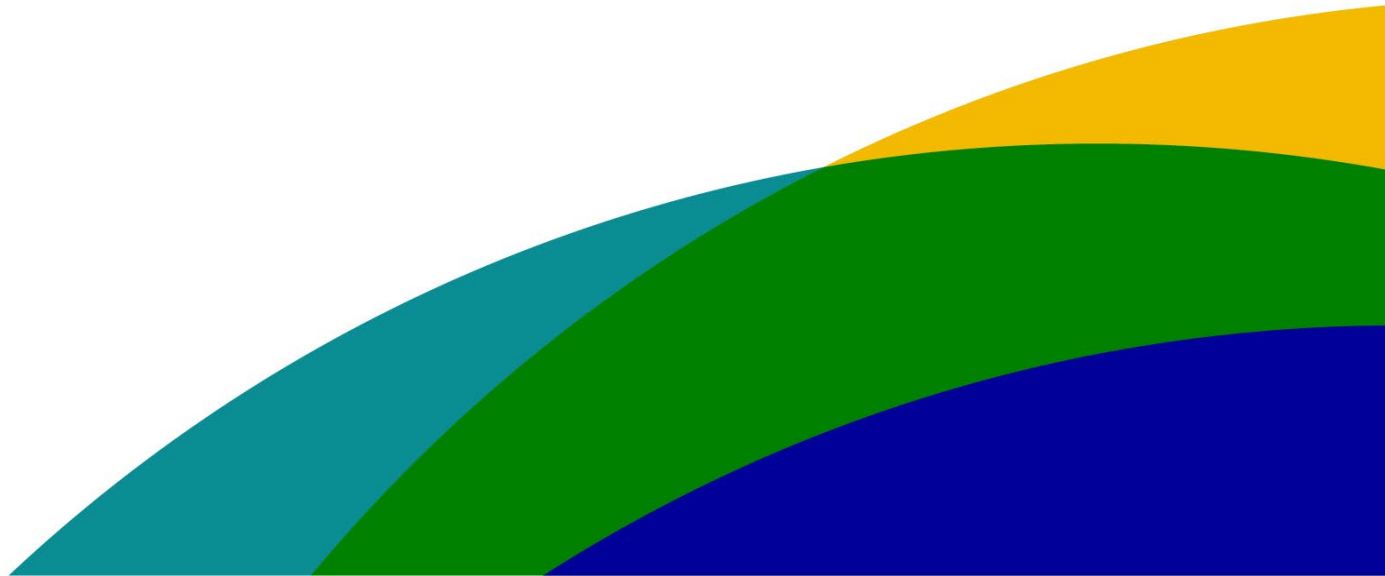
The opinions expressed are those of the presenter and do not necessarily reflect the policy of the U.S. Department of Health and Human Services.

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

- Explain expedited and convened IRB review
- Describe review of some common study lifecycle actions
- Discuss limited IRB review

Expedited and Convened IRB Review



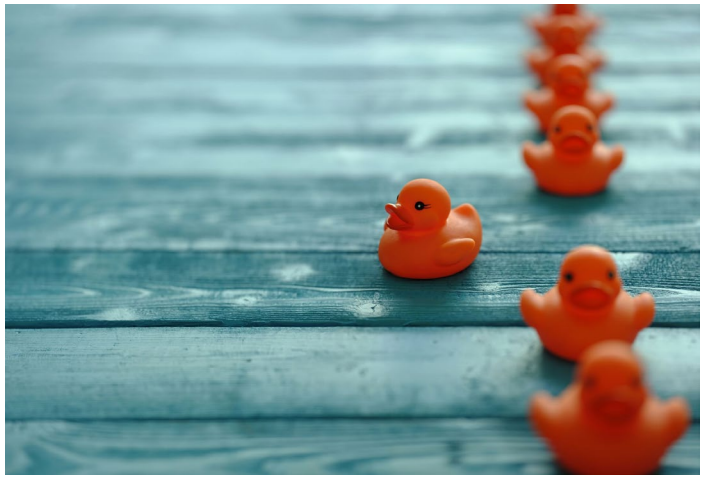
OASH | Office for Human Research Protections

Requirements for Review of Nonexempt Research

- The Common Rule applies to nonexempt human subjects research that is conducted or supported by a Common Rule agency
- The regulations establish the requirements for IRB review of research but provide institutions the ability to decide how they will be implemented
- Institutions must have written procedures for:
  - Initial reviews
  - Continuing reviews
  - Amendments
  - Reportable events such as:
    - Unanticipated problems
    - Serious or continuing noncompliance
    - Suspension or termination of IRB approval

Two Mechanisms for Review

- Expedited Review
  - Performed by one IRB member, the IRB Chair or an experienced member designated by the Chair
  - At any time convenient for the member; operational flexible
- Convened Review
  - Conducted by a group of IRB members;
  - At a convened meeting; operationally less flexible
- For both mechanisms of review, the reviewers must review and approve research according to the criteria at 46.111



When Can Expedited Review be Used?

- For review of nonexempt humans subjects research when:
  - The research presents no more than minimal risk to the participants; AND
  - The research fits within one of the 9 expedited review categories
- For minor changes to already approved nonexempt research
- For limited IRB review

Under the revised Common Rule, continuing review is not required for research eligible for expedited review but the IRB can decide otherwise. This decision must then be documented

What is Minimal Risk?

The **probability and magnitude** of harm or discomfort anticipated in the research are **not greater in and of themselves than those ordinarily encountered** in daily life or during the performance of routine physical or psychological examinations or tests.

- Consider the likelihood (probability) and severity (magnitude) of the harm or discomfort; and
- How this compares to the harms or discomforts of:
  - Daily life
  - Routine physical examinations or tests
  - Routine psychological examinations or tests

Expedited Review Categories

The 9 expedited review categories are found in the 1998 Expedited Activities

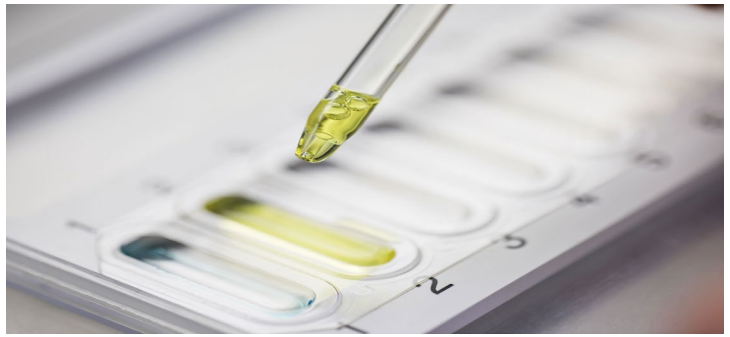
1. Studies of drugs and medical devices when an IND or IDE is not required
2. Collection of blood samples
3. Prospective collection of biological specimens for research purposes by noninvasive means
4. Collection of data through noninvasive procedures
5. Research involving materials that have been collected, or will be collected solely for nonresearch purposes
6. Collection of data from voice, video, digital, or image recordings made for research purposes
7. Research on behavior employing survey, interview, oral history, focus group
8. Continuing review for previously reviewed research through convened meeting
9. Continuing review for minimal risk research not fitting an expedited category

Expedited Review - Types of Decisions

- A reviewer may:
  - Approve “as is”
  - Approve with changes
  - Refer to the full board
    - ONLY the full board may disapprove!
- Each IRB must establish procedures for keeping all members of the IRB informed of approved decisions made through expedited review

Expedited Categories: Spotlight on 5 & 7

- Category 5: Research involving materials (data, documents, records, or specimens) that have been collected [*for research or non-research purposes*] or will be collected solely for non-research purpose

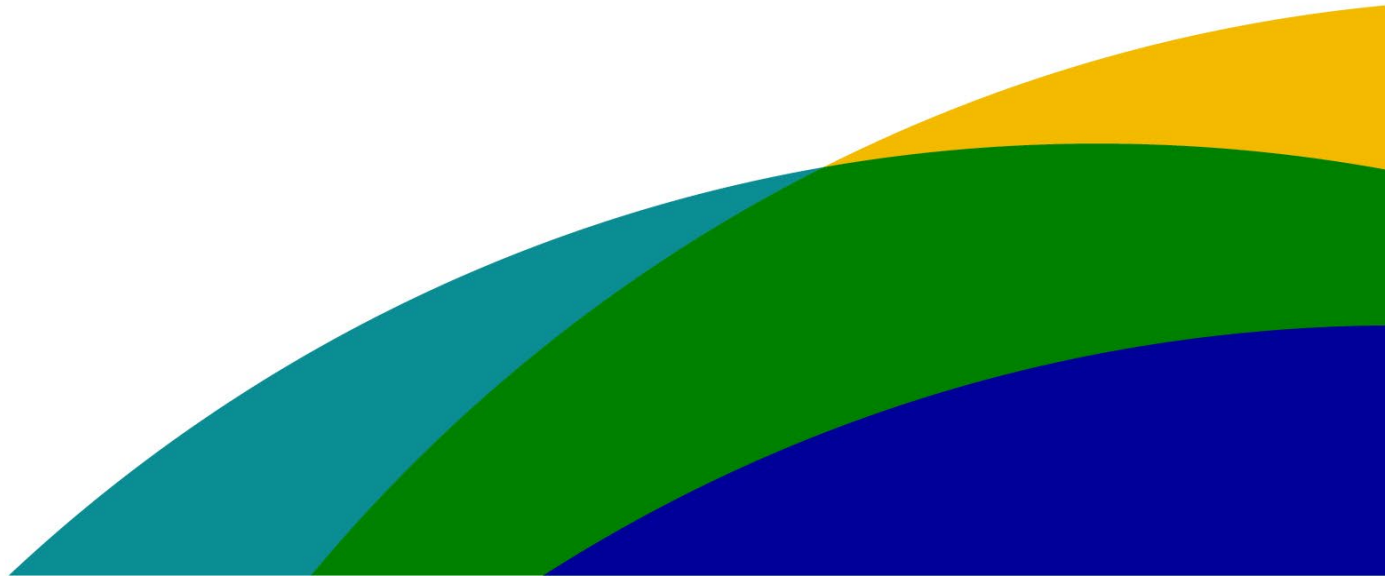


- Category 7: Research on individual or group characteristics or behavior; or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies

The Convened IRB Meeting

- Any nonexempt research that does not qualify for expedited review must proceed through a review at the convened meeting (full board)
- A group of diverse, knowledgeable IRB members meet to review study activities to see if regulatory requirements are met and vote
- There must be quorum present
  - This is a majority of the primary voting members and the nonscientist
- All actions reviewed and the outcomes should be documented
- Institution should have a policy for:
  - How research is reviewed (primary/secondary reviewer)
  - How documents are submitted and distributed
  - Managing alternates and conflicts of interest

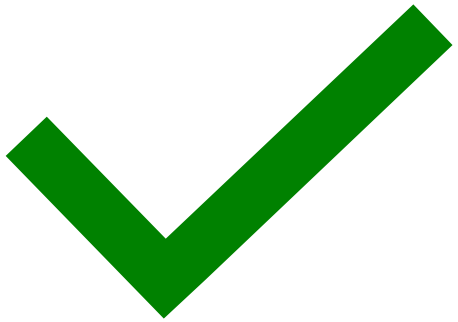
Review of Common Study Lifecycle Actions



OASH | Office for Human Research Protections

Initial Review of Nonexempt Research

- Before nonexempt human subjects research can commence, it must be reviewed and approved by an IRB, of particular note:
  - The IRB makes sure that all of the requirements of 46.111 are satisfied
  - The IRB must make sure that the informed consent requirements of 46.116 are met (or appropriately waived/ altered) and documented accordingly (46.117)
  - Decisions must be communicated to investigators and appropriate officials
- **These criteria apply whether it's a convened or expedited review!**



Continuing Review

- Studies that require review by the convened board must have a continuing review performed at least once a year
  - Expiration dates are calculated using the approval date (by board or reviewer)
- The IRB may begin with the presumption that all of the preliminary approval criteria have been met and focus on whether any new information provided would alter the IRB's prior determinations
- When conducting continuing review and evaluating whether research continues to satisfy the criteria for IRB approval of research, IRBs should pay particular attention to the following four aspects of the research:
  - Risk assessment and monitoring;
  - Adequacy of the process for obtaining informed consent;
  - Investigator and institutional issues; and
  - Research progress

When Expedited Review Can Be Used for Continuing Review

- For continuing review of research previously approved by the convened IRB:
  - 8 (a) Enrollment is closed, all research interventions are complete, and only long-term follow-up remains
  - 8 (b) There have yet to be any enrollees and no new risks have been identified
  - 8 (c) The only research activities are data analysis
  - 9 Research not under an IND or IDE, does not fit into an expedited category but the IRB has determined is not greater than minimal risk, and no new risks have been identified

Case #1 – Continuing Review

A vaccine study is approved at a convened meeting as greater than minimal risk. The IRB may be able to use an expedited review mechanism for continuing review of this study when (select all that apply):

- ❑ Continuing review can always be expedited
- ☑ No new risks have been identified and no one has enrolled
- ☑ If all participant involvement is complete and the study team is only writing manuscripts
- ❑ The study cannot be expedited and must be reviewed by the full board at a convened meeting

What Happens When Changes Need to be Made to Approved Research?

- When investigators submit changes to research, the IRB must have policies in place for the following:
  - Determining what might be minor changes (allowing for expedited review)
  - Providing what changes necessitate revising informed consent
  - Communicating decisions
- Changes may not be implemented without IRB approval (except for participant safety)
  - Processes must be established for promptly notifying the IRB of these changes that occurred to eliminate apparent immediate hazards to participants

Limited IRB Review

What is Limited IRB Review?

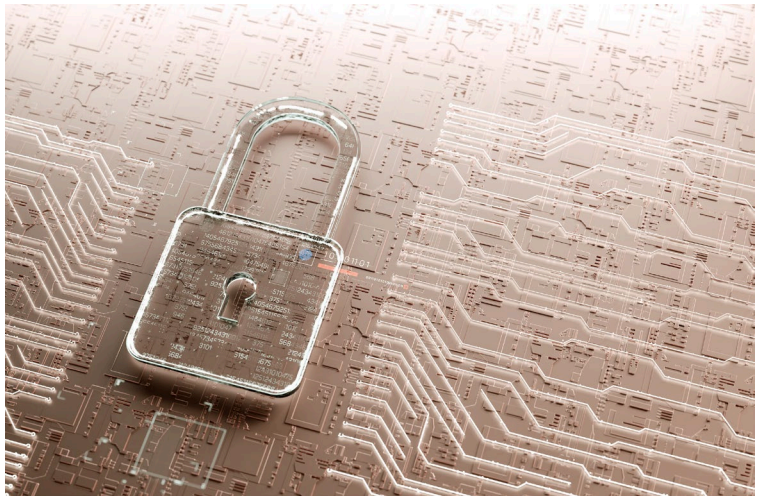
- Limited IRB is a specialized, narrow in scope, review
- This is NOT a complete review of all of the 46.111 criteria for IRB approval of research
- When is it used?
  - Exemption 2: Educational tests, surveys, interviews, or observation of public behavior 46.104(d)(2)(iii)
  - Exemption 3: Benign behavioral interventions 46.104(d)(3)(c)
  - Exemptions 7 & 8: Broad Consent

What is Limited IRB Review? (CONT.)

- Limited IRB review is **NOT** used to review nonexempt human subjects research
- Hence, exempt research requiring limited IRB review does **NOT** require:
  - Continuing review
  - Posting of consent forms
  - Reporting unanticipated problems or serious or ongoing noncompliance

Limited IRB Review for Exempt Categories 2 & 3

- For exemptions 2 & 3: When the information is recorded by the investigator that the identity of the human subjects can readily be ascertained
- The IRB reviewer confirms “there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.” 46.111(a)(7)



Limited IRB Review for Exempt Category 7

- Exemption 7 requires broad consent and is for the storage or maintenance of identifiable private information or identifiable biospecimens for secondary research
- Requirements:
  - Limited IRB review of the broad consent process and form
  - Limited IRB review of privacy and confidentiality considerations if there are changes to the storage and maintenance

Limited IRB Review for Exempt Category 8

- Category 8 requires broad consent and is for secondary research using identifiable private information or identifiable biospecimens
- Requirements
  - Limited IRB review of whether the research falls under the broad consent
  - Limited IRB review of the privacy and confidentiality safeguards
  - The investigator does not include returning individual research results to subjects as part of the study plan except when required by law
  - Documentation or waiver of documentation of consent provisions has occurred

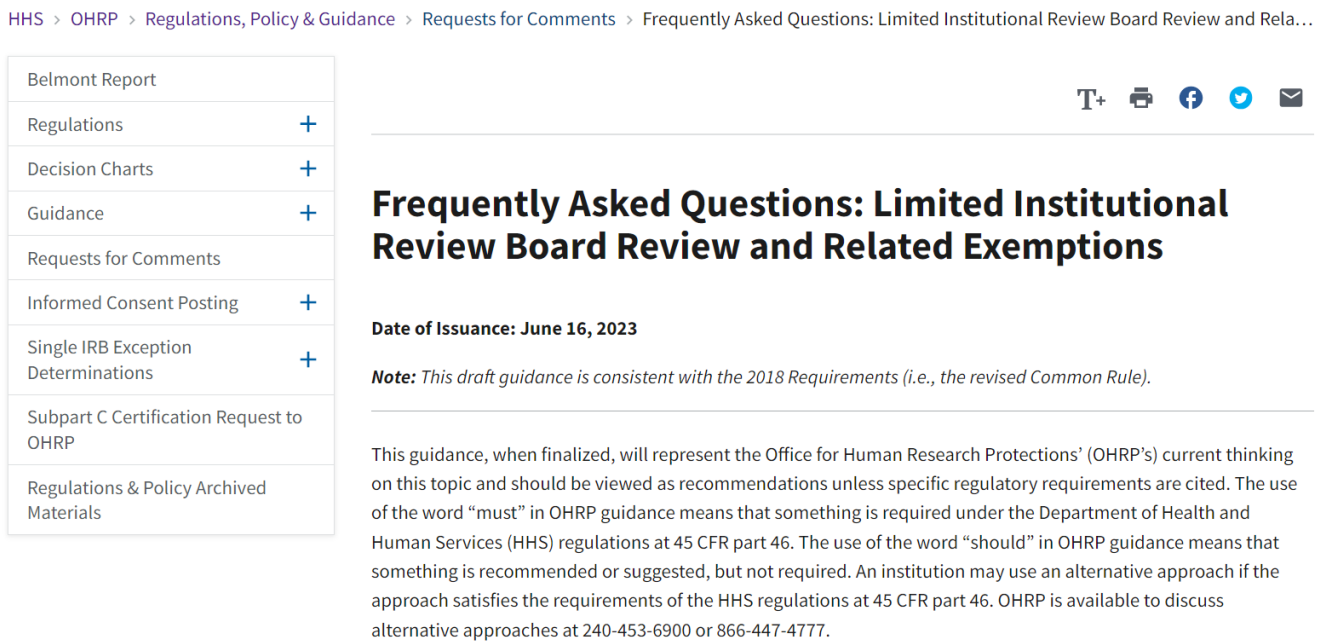
Case #2 – Exempt Determinations

Steve is an IRB administrator at County Hospital. While Steve is not an IRB member, the Chair of the IRB has appointed him to make exempt determinations. This means that Steve can (select the best answer):

- ❑ Cannot make exempt determinations, only IRB members can
- ☑ Make exempt determinations but not conduct limited IRB review
- ❑ Make exempt determinations and conduct limited IRB review
- ❑ Make exempt determinations, conduct limited IRB review, and expedited review for minimal risk research

Check Out Our Draft Limited IRB Guidance

- OHRP published draft guidance about limited IRB review on June 16, 2023 and there is a 60-day public comment period through August 15



HHS › OHRP › Regulations, Policy & Guidance › Requests for Comments › Frequently Asked Questions: Limited Institutional Review Board Review and Rela…

- Belmont Report
- Regulations +
- Decision Charts +
- Guidance +
- Requests for Comments
- Informed Consent Posting +
- Single IRB Exception Determinations +
- Subpart C Certification Request to OHRP
- Regulations & Policy Archived Materials

Frequently Asked Questions: Limited Institutional Review Board Review and Related Exemptions

Date of Issuance: June 16, 2023

Note: *This draft guidance is consistent with the 2018 Requirements (i.e., the revised Common Rule).*

This guidance, when finalized, will represent the Office for Human Research Protections' (OHRP's) current thinking on this topic and should be viewed as recommendations unless specific regulatory requirements are cited. The use of the word "must" in OHRP guidance means that something is required under the Department of Health and Human Services (HHS) regulations at 45 CFR part 46. The use of the word "should" in OHRP guidance means that something is recommended or suggested, but not required. An institution may use an alternative approach if the approach satisfies the requirements of the HHS regulations at 45 CFR part 46. OHRP is available to discuss alternative approaches at 240-453-6900 or 866-447-4777.

Case #3 – Expedited Review

Ella is a member of the County Hospital IRB. The Chair designates her to conduct expedited reviews. Ella can do which of the following? (select the best answer):

- ❑ Make exempt determinations
- ❑ Make exempt determinations and conduct limited IRB review
- ☑ Make exempt determinations, conduct limited IRB review, and expedited review
- ❑ Approve, refer to the board, and disapprove research

Closing Thoughts

- For both expedited and full board review of nonexempt human subjects research, the IRB reviewer must review and approve research following the 46.111 criteria
- For an expedited review of nonexempt research, check it is both minimal risk AND fits into one or more of the expedited categories
  - Expedited categories
- Changes to research can affect the risk classification and the manner in which a study is reviewed
- The regulations serve as a floor for protecting participants. Institutions will have additional requirements for how the regulations are implemented and may provide additional safeguards beyond the regulations

Resources

- Institutional Review Board Written Procedures: Guidance for Institutions and IRBs
- Continuing Review Guidance
- Reportable Event Guidance
- Draft Limited IRB Review Guidance
- Mini-tutorial on IRB Membership
- Mini-tutorial on Quorum & Voting