

Agency Guidance Snapshot: Frequently Asked Questions: Limited Institutional Review Board Review and Related Exemptions (*Draft Guidance*)

The Yale Human Research Protection Program (HRPP) has launched the “*Agency Guidance Snapshot*” series. The purpose of the Agency Guidance Snapshots is to highlight recent agency guidance from the Food and Drug Administration (FDA), Office for Human Research Protections (OHRP)¹, and other federal agencies that specifically impacts Yale University and affiliate stakeholders who conduct or oversee *human subjects research*.

Please Note: Yale University does not expect any immediate changes to policies due to this guidance; however, this guidance will be taken into consideration as policies and procedures are reviewed and revised in the future. Yale University may have additional requirements related to the topics covered in this guidance. For more information, please refer to the following Yale University Human Research Protection Program (HRPP) documents located on the HRPP website ([Policies, Procedures, Guidance, and Related Documents](#)) and in the Yale HRPP IRES-IRB Library ([IRES IRB LOGIN](#)): 1) [Yale HRPP Policy and Standard Operating Procedure Manual](#); 2) [Yale HRPP Investigator Manual](#); 3) [Yale IRB Members and Chairs Manual](#); and 4) [HRPP Supplemental Guidance Manual](#). Please also refer to [University Policies & Procedures](#) and policies published by the various Yale University schools and departments.

Title of Document:	Frequently Asked Questions: Limited Institutional Review Board Review and Related Exemptions (<i>Draft Guidance</i>)
Federal Agency:	OHRP
Document Release Date:	June 2023
Stakeholders Impacted:	Investigators <input checked="" type="checkbox"/> Sponsors <input checked="" type="checkbox"/> Sponsor/Investigators <input checked="" type="checkbox"/> IRB/HRPP Staff, Chairs, & Members <input checked="" type="checkbox"/> Research Administrators/Institutional Officials <input checked="" type="checkbox"/> Funding Agencies <input checked="" type="checkbox"/> General Public <input checked="" type="checkbox"/> Other <input type="checkbox"/>
Hyperlink to Document:	https://www.hhs.gov/ohrp/regulations-and-policy/requests-for-comments/draft-guidance-frequently-asked-questions-limited-institutional-review-board-review-related-exemptions/index.html

Overview of Guidance Document:

The guidance discusses the concept of limited IRB review and provides information about how limited review may be conducted. As there are many regulatory provisions that are interconnected with limited IRB

¹ This guidance, when finalized, will represent 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.

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review, OHRP recommends reviewing this guidance document in conjunction with a copy of the [regulatory text of the 2018 Requirements](#).

This document also discusses IRB and investigator responsibilities when reviewing and conducting exempt research that requires limited IRB review as a condition of exemption. Note that limited IRB review is a provision that is only included in the 2018 Requirements. If a research study is covered by the pre-2018 Requirements, then limited IRB review is not a consideration.

The target audience for this document includes IRBs, investigators, research administrators and other relevant institutional officials, and funding agencies that may be responsible for review or oversight of human subjects research conducted or supported by HHS, and the general public.

Background on Limited IRB Review

The 2018 Requirements attempt to better align the level of IRB review required for a given research activity with its risk profile, while retaining appropriate protections for human subjects. For research in which the primary risks relate to **privacy** and **confidentiality**, the 2018 Requirements create a new type of IRB review, called “**limited IRB review**.” Research that qualifies for an exemption requiring limited IRB review under the 2018 Requirements generally would have required IRB review either through the expedited review procedure or by a convened IRB under the pre-2018 Requirements. **The purpose of limited IRB review is to reduce the administrative burden imposed by IRB review while also helping to ensure human subjects are appropriately protected.**

This new form of IRB review is required for research that falls within one or more of four exemption categories:

- 45 CFR 46.104(d)(2)(iii)
- 45 CFR 46.104(d)(3)(i)(C)
- 45 CFR 46.104(d)(7)
- 45 CFR 46.104(d)(8)

To meet these exemptions, an IRB, through either a convened meeting or an expedited procedure, must review specific, more limited aspects of a proposed research study as opposed to considering all of the criteria for IRB approval of research found at 45 CFR 46.111.

Key points for Researchers, IRB/HRPP Staff, Chairs, & Members:

When do the Exemptions Require Limited IRB Review and What Determinations Must an IRB Make?

Four exemption categories in the 2018 Requirements call for an IRB to make certain determinations through limited IRB review as a criterion of the exemption:

- **45 CFR 46.104(d)(2)** –The exemption for research that only includes interactions involving educational tests, survey procedures, interview procedures, or observation of public behavior.
 - This exemption has three subparts (criteria) (i, ii, iii) and applies if the conditions of at least one of the criteria is met.
 - For detailed information on criteria i and ii, please review Section III (Part A) of the [full guidance document](#).
 - The third criterion 45 CFR 46.104(d)(2)(iii) requires an IRB to conduct a limited review to make the determinations required by 45 CFR 46.111(a)(7);

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that is, to determine that when appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data. Limited IRB review in this case is required because, unlike the other two criterion, the information obtained is recorded by the investigator in such a manner that the identity of the human subjects can be readily ascertained, directly or through identifiers linked to the subjects, and disclosure of the human subjects' responses outside the research might reasonably place them at risk of a variety of types of harms. Note that this criterion may not be applied to research subject to subpart D (Additional Protections for Children Involved as Subjects in Research) (45 CFR 46.104(b)(3)).

- **45 CFR 46.104(d)(3)(i)** - The exemption for benign behavioral interventions in conjunction with the collection of information from adult subjects if the subject prospectively agrees to the intervention and information collection.
 - This exemption has three subparts (criteria) (A, B, C) and applies if the conditions of at least one of the criteria is met.
 - For detailed information on criteria A and B, please review Section III (Part B) of the [full guidance document](#).
 - The third criterion 45 CFR 46.104(d)(3)(i)(C) requires an IRB to conduct a limited review to make the determinations required by 45 CFR 46.111(a)(7); that is, to determine that when appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data. Limited IRB review in this case is required because, unlike the other two criterion, the information obtained is recorded by the investigator in such a manner that the identity of the human subjects can be readily ascertained, directly or through identifiers linked to the subjects, and disclosure of the human subjects' responses outside the research might reasonably place them at risk of a variety of types of harms.
- **45 CFR 46.104(d)(7)** - The exemption for storage or maintenance of identifiable biospecimens or identifiable private information for secondary research for which broad consent is required.
 - Please note, Yale did not adopt the broad consent provisions and does not grant exemption determinations under category 45 CFR 46.104(d)(7). However, for detailed information on limited review for this exemption category, please review Section III (Part C) of the [full guidance document](#).
- **45 CFR 46.104(d)(8)** - The exemption for secondary research involving the use of identifiable private information or identifiable biospecimens for which broad consent is required.
 - Please note, Yale did not adopt the broad consent provisions and does not grant exemption determinations under category 45 CFR 46.104(d)(8). However, for detailed information on limited review for this exemption category, please review section III (Part D) of the [full guidance document](#).

The OHRP guidance document includes the following additional Q&As related to **limited IRB review and related exemptions**, which may be beneficial for our research community to understand. Detailed answers to the questions below can be found in the [full guidance document](#):

- **IV.** Who may conduct limited IRB review and how may it be conducted?

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- **V.** What aspects of the 2018 Requirements apply when limited IRB review is conducted?
- **VI.** Which provisions of the 2018 Requirements need not be followed when limited IRB review is conducted?
- **VII.** What happens when an investigator contemplates making changes to an exempt research activity that requires limited IRB review as a condition of exemption? When must an IRB conduct a new limited review before such changes can be implemented?
- **VIII.** Can limited review be conducted using an expedited procedure?
- **IX.** How may an IRB obtain sufficient expertise to review provisions for protecting privacy and confidentiality?
- **X.** What should an IRB consider when reviewing provisions protecting privacy and confidentiality when a study eligible to be exempt under 45 CFR 46.104(d)(7) involves a change to storage or maintenance of the information or biospecimens made for research purposes?
- **XI.** What should an IRB consider when reviewing whether a specific secondary study is within the scope of a broad consent?

For more related information, please see the following links to additional resources:

- [HHS Website - Office for Human Research Protections](#)
- [SACHRP Recommendations on OHRP Draft Guidance “Frequently Asked Questions: Limited Institutional Review Board Review and Related Exemptions”](#)
- [CITI Program - HHS Issues Draft Guidance on Limited IRB Review and Related Exemptions](#)

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