

Performing Expedited Review of Research Involving Human Participants

SOP 113.2
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Purpose and Scope

This Standard Operating Procedure (SOP) documents the procedures for conducting expedited review of research requiring or conducted under the approval of the University of Hawaii (UH) Institutional Review Board (IRB).

This SOP applies to applications submitted to a UH IRB for:

1. initial review of research,
2. continuing review of research,
3. review of requests for minor modifications in IRB-approved research
4. review of research for which limited IRB review is a condition of exemption.

This SOP only governs research involving human subjects and is applicable to HSP personnel and IRB members who conduct expedited review of such research.

Introduction

What is Expedited Review?

During Initial or Continuing Review

Expedited review is review of research by an Institutional Review Board (IRB) Chair or IRB member using an expedited review procedure. The expedited review procedure is a complete and thorough IRB review, just not at a convened IRB meeting. The expedited reviewer:

- May only approve or require modifications in (to secure approval) the research.
- May not disapprove research.

Research that involves one or more of the following categories and is evaluated to be no more than minimal risk may be reviewed by the IRB through the expedited review procedure authorized by 45 CFR 46.110 and 21 CFR 56.110. A study is presumed to be minimal risk and thus eligible for expedited review if the study only involves categories described in this document, unless the reviewer determines and it is documented why the study involves more than minimal risk (§___.115(a)(8)).

The criteria for IRB approval of research as stipulated in 45 CFR 46.111 and 21 CFR 56.111, including but not limited to requirements for informed consent and documentation of informed consent, as applicable, apply when expedited review procedures are used by the IRB.

Under an expedited review procedure, the review may be carried out by the IRB Chairperson or by one or more experienced reviewers designated by the chairperson from among members of the IRB.

Evaluating if Proposed Activities are No More than Minimal Risk

Most research falling within one or more of the categories below will, ordinarily, present no more than minimal risk to subjects and will be eligible for review through the expedited review procedure. However, the IRB reviewer is required to evaluate all proposed research and consider whether the proposed research is more than minimal risk.

In evaluating if the proposed research presents no more than minimal risk, an IRB reviewer should consider the nature of the study procedures, the implications of study findings for the subject (e.g., the results of genetic testing of blood samples), other study characteristics, and steps taken to minimize risk. The IRB reviewer should also consider the characteristics of the subject population, including but not limited to age, health conditions, social or economic circumstances and experience in relation to the anticipated harms and discomforts.

The expedited review procedure may not be used, for example, when identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, insurability, reputation, educational advancement, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal. In evaluating the risks, the IRB reviewer should consider only those risks that may result from the research (as distinguished from the risks of therapies subjects would receive even if not participating in the research).

Under the Final Rule, a study is presumed to be minimal risk if it meets one of the categories of the HHS Secretary's list (below). If the expedited reviewer determines that the study involves more than minimal risk, the reviewer can override that presumption, but the review has to document his/her rationale.

Applicability

- A. Categories one (1) through fourteen (14) apply to initial IRB review of research that has been determined to be no more than minimal risk.
- B. Category fifteen (15) applies to continuing review of research previously approved by the convened IRB that does not otherwise qualify for expedited review.
- C. The categories in this document apply regardless of the age of subjects, except as noted.
- D. Research eligible for expedited review under §__110(b)(1)(i) must fit within one or more of the categories below.
- E. Examples are intended to suggest the types of research activities and procedures that pose no more than minimal risk and may be approved using expedited procedures. However, the applicability of the category is not limited to the specific examples provided.
- F. The expedited review procedure may not be used for classified research involving human subjects.

- G. Unless an IRB determines otherwise, continuing review of research is not required for research eligible for and approved by expedited review in accordance with §__.109(f)(1)(i).

Research Categories

1. Research involving the use of drugs and medical devices only when condition (a) or (b) is met.
 - a. Research involving use of “over-the-counter” drugs, when used within their approved indications and dosages, and exempt from the IND requirements of 21 CFR 312.
 - b. Research involving use of medical devices exempt from the IDE requirements of 21 CFR 812.¹
2. The collection of blood specimens for research purposes using techniques consistent with routine clinical practice to minimize pain and risk of infection and within the following limits:
 - a. from adults whose health will not be adversely affected by the blood draws who weigh at least 50 kg, the amounts collected should not exceed 550 ml in an 8-week period; or
 - b. from children ² and other adults whose health will not be adversely affected by the blood draws, the amounts collected should not exceed the lesser of 150 ml or 3 ml per kg in an 8-week period. Examples: Finger stick, heel stick, ear stick, venipuncture, collection of blood from an indwelling peripheral venous catheter (not including a PICC line) placed for research purposes, or collection of blood from an indwelling catheter already in place for clinical purposes.
3. Prospective collection of biological specimens, excluding blood, for research purposes by noninvasive means and not requiring sedation for research purposes.

Examples:

 - a. tissues and fluids that the body produces continuously or sheds as a normal process (including hair, nails), which are collected in a non-disfiguring manner;
 - b. deciduous teeth at time of exfoliation;
 - c. excreta and external secretions (including sweat, urine, stool);
 - d. uncannulated saliva;
 - e. placenta removed at delivery;
 - f. amniotic fluid obtained at the time of rupture of the membrane prior to or during labor;
 - g. supra - and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques;
 - h. mucosal and skin cells collected by buccal scraping or mouth washings;
 - i. sputum collected after saline mist nebulization
4. Prospective collection of biological specimens, excluding blood, for research purposes by minimally invasive means and not requiring sedation for research purposes.

Examples:

¹ In research involving the use of investigational devices that require a non-significant risk (NSR) determination, the determination should be made by the convened IRB. Continuing review of research where the FDA or the IRB has determined that a device is NSR may be eligible for continuing review under category 10(c).

² Children are defined in the HHS [45 CFR 46.402(a)] and FDA [21 CFR 50.3(o)] regulations as "persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted."

- a. tissues from non-facial, non-genital skin punch biopsy with allowable local anesthesia and limited to 2mm in diameter and not requiring sutures;
 - b. Specimens collected by swab (nasal, oral, urethral, vaginal, rectal);
 - c. teeth if routine patient care indicates a need for extraction.
5. Collection of additional information or biological specimens, excluding blood, for research purposes during procedures already being performed for clinical purposes, provided the additional collection does not introduce more than a minimal increase in risk, pain or discomfort over that imposed by the underlying procedure. When extension of general anesthesia is required, it must meet the criteria for minimal risk.³

Examples:

- a. collection of additional bodily fluids and tissues (e.g., peritoneal fluid, bone marrow or cerebrospinal fluid);
 - b. tissue collected from pap smears;
 - c. collection of additional clinical information (e.g., vital signs, electroencephalography or echocardiography).
6. Collection of information for research purposes through noninvasive procedures and interventions routinely employed in clinical practice and not requiring general anesthesia or sedation.

Examples:

- a. physical sensors that are applied either to the surface of the body or used at a distance;
 - b. testing sensory acuity;
 - c. magnetic resonance imaging without use of contrast agent and using magnet and sequence parameters within accepted clinical use guidelines;
 - d. electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, Doppler blood flow, and transthoracic echocardiography;
 - e. measures of cognitive functioning;
 - f. exposure to ionizing radiation with a total effective dose not exceeding 0.1 mSv (the amount typically associated with a single chest x-ray) provided appropriate shielding techniques are employed.⁴
7. Collection of information for research purposes through activities performed by persons in daily life in individuals and groups whose health will not be adversely affected by the activities.

Examples:

- a. moderate exercise, muscular strength testing, body composition assessment, and flexibility testing;

³ Extension of anesthesia time may be considered minimal risk when: the extension of anesthesia time is limited to no more than 15 minutes; the appropriate level of anesthesia has been achieved and the patient is determined to be clinically stable by an anesthesiologist uninvolved in the research protocol; the method/mode of anesthesia to be used is determined not by the research protocol but is in accordance with current standard clinical practice; the same anesthetic agents are utilized for the extension of time required for research; the same clinical care team responsible for administering and monitoring the anesthesia remain with the subject during the research procedure, and; the same level and frequency of monitoring will be maintained throughout the research procedures.

⁴ The U.S. Nuclear Regulatory Commission's allowable annual exposure to individual members of the public is 0.1 rem (1 mSv) per year. 10CFR20.1031(a)(1) <https://www.nrc.gov/reading-rm/doc-collections/cfr/part020/part020-1301.html>

- b. measures of symptoms, mobility, range of motion, quality of life and activities of daily living in patient and non-patient populations by clinical or other trained personnel (e.g., nurses, physicians, social workers, physical and occupational therapists);
 - c. manipulations of diet and lifestyle;
 - d. measuring height, weight, circumference;
 - e. assessment of reading levels.
- 8. Activities at statistical and data coordinating centers or biospecimen repositories that are not responsible for the primary oversight of the primary data collection activities and are not involved in the primary collection of information or specimens, which may be ongoing at other sites.
- 9. Collection of information from voice, video, digital, or image recordings made for research purposes that are not exempt under §__.104(d).
- 10. Research that only includes interaction involving
 - a. educational tests (cognitive, diagnostic, aptitude, achievement);
 - b. survey procedures, interview procedures, or observation of public behavior (including visual and auditory recording) not eligible for exemption under §__.104(d)(2) either because there are risks to subjects other than informational risks, or because the informational risks are not addressed as specified under §__104(d)(2)(i) through (iii);
 - c. other data collection procedures (e.g., written or computer-assisted interactions or assessments) where the subject provides self-reports for the purposes of the research and/or may choose what data to provide;
 - d. non-invasive physical or behavioral tasks or manipulation of the subject's environment; and
 - e. observations of individual group behavior where the subject is a voluntary participant in the behavior and is aware that data are being collected.
- 11. Benign behavioral interventions that are not eligible for exemption under §__.104(d)(3) because they
 - a. involve children as subjects;
 - b. involve individuals with impaired decision-making capacity;
 - c. are conducted without the prospective agreement of the subject, including interventions involving deception;
 - d. are not brief in duration, or;
 - e. are not limited to verbal or written responses by the subject, data entry by the subject, or observation of the subject.
- 12. Creation and maintenance of subject databases to which subjects have provided prospective informed consent or informed consent has been waived by an IRB and does not qualify for exemption under §__.104(d)(7).
Examples:
 - a. collection of identifiable information for the purpose of establishing subject pools;
 - b. disease-specific patient registries;
 - c. screening protocols including interviews, questionnaires and minimally invasive physical assessments, when performed for research purposes, that could not be expedited under one of the categories listed above.
- 13. Secondary research uses of identifiable private information or identifiable biospecimens that are not exempt under §__.104(d)(4) because

- a. the identifiable private information or identifiable biospecimens are not publicly available;
 - b. information, which may include information about biospecimens, is recorded by the investigator in such a manner that the identity of human subjects can be readily ascertained directly or through identifiers linked to the subjects, or the investigator intends to contact the subjects or will re-identify subjects;
 - c. research use of identifiable health information not regulated under 45 CFR parts 160 and 164, subparts A and E.
14. Research involving the use of identifiable private information or identifiable biospecimens for secondary research use that is not exempt under § 104(d)(8) because the investigator includes returning individual research results to subjects as part of the study plan.

Continuing Review of Previously Approved Research

15. Research previously approved by the convened IRB and not otherwise eligible for expedited review under categories (1) through (13) above, where one of the following conditions apply:
- a. the research remains active only for long-term follow-up of subjects;⁵ or
 - b. no subjects have been enrolled at sites under the purview of the reviewing IRB and no additional risks have been identified; or
 - c. the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk (including, when applicable, a non-significant risk (NSR) determination was initially made by a convened IRB for research involving investigational medical devices), and no additional risks have been identified. In such cases, the exemption from further continuing review at § 109(f)(1)(i) does not apply.

Elimination of Continuing Review

When the research involves no more than minimal risk, the regulations no longer specify that continuing review must occur. Continuing review is no longer required for:

- a. Research initially approved under expedited review.
- b. Ongoing research approved by a convened IRB (when only certain specified activities are all that remain for the study).
- c. Research reviewed in accordance with limited IRB review.

If an IRB chooses to conduct continuing review even when it is not required by the regulation (as described in 46.109(f)(1)), the rationale for doing so must be documented 46.115(a)(3). Expedited review procedures may still be used for optional continuing review. Optional administrative review does not need to occur within any specified period of time, and institutions have the option to decide that re-review after initial approval is not required at all.

⁵ No continuing review is required for research that has progressed to the point that it involves only one or both of the following, which are part of the IRB-approved study: (A) Data analysis, including analysis of identifiable private information or identifiable biospecimens, or (B) Accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care. (45 CFR 46.109(f)(1)(iii))

Minor Modifications

Under 45 C.F.R. § 46.110(b)(2), the IRB may also use the expedited review procedures to review minor changes to previously-approved research during current approved period. To qualify as a minor modification, the proposed change must not materially:

- a. alter the assessment of risks and potential benefits of the study;
- b. increase the level of risk to the physical, emotional, or psychological well-being of participants, including loss of confidentiality; or
- c. change the specific aims or design of the study.

Examples of minor modifications include:

- a. Substituting assessment procedures or tools with alternate assessment procedures or tools when the changes do not increase the level of risk to participants;
- b. Adding new study tools, e.g., questionnaires or recruitment notices, that do not increase the level of risk to participants;
- c. Revising a consent form to make:
- d. Editorial or administrative changes, e.g., changes in an address or telephone number;
- e. Minor changes in compensation or estimated time of participation; or
- f. Improvements in the accuracy or clarity of information provided to participants, provided that the changes do not alter the content or intent of the information.
- g. Making administrative or editorial changes to other study documents or modifying the documents to improve formatting or clarity, provided the changes do not alter the content or intent of the information;
- h. Increasing or decreasing enrollment supported by a reasonable justification;
- i. Narrowing the range of inclusion criteria;
- j. Broadening the range of exclusion criteria;
- k. Decreasing the number or volume of biological samples, provided the changes do not affect the nature of the information to be collected;
- l. Adding or deleting qualified investigators;
- m. Adding or deleting study sites; and
- n. Other minor modifications determined by the Program that meet federal requirements.

Modifications (minor) eligible for expedited review must meet all of the following criteria, based on the judgment of the IRB reviewer:

1. Any increase in risk is less than minimal risk.
2. All additional activities or procedures would have been eligible for expedited review had they been included in the initial protocol or proposal review.
3. Either the research is minimal risk or the proposed changes do not alter the study design.

If the modification changes the review type appropriate for the research, HSP personnel will move the protocol or proposal to the appropriate review type status. The IRB reviewer makes the final determination of whether changes to the research are “major” or “minor.”

Limited IRB Review

Limited IRB review is a new concept added by the Final Rule and is relevant to certain new exemptions (Categories 2, 3, 7, and 8). In a limited IRB review, an IRB must conduct a review and make certain determinations as a condition of exemption. For example, that “there are adequate provisions to

protect the privacy of subjects and to maintain the confidentiality of data” (46.111(a)(7)). Limited review for Categories 2, 3, and 8 invokes criteria at 46.111(a)(7), however, limited review for Category 7 invokes criteria at 46.111(a)(8).

The expedited review procedure may be used to conduct limited IRB review. The fact that expedited review may be used for categories of review eligible for exemption is a departure from the pre-2018 regulations that required no IRB determinations or involvement regarding how exemption decisions are made.

Waiver or Alteration of HIPAA Privacy Rule Authorization

The IRB may use an expedited review procedure to review a waiver of authorization required by the HIPAA privacy rule.⁶ The HIPAA Privacy Rule allows an IRB to use expedited review procedures as permitted by the Common Rule to review and approve requests for waiver of authorizations. An expedited review process permits covered entities to accept documentation of waiver of authorization when only one or more members of the IRB or Privacy Board have conducted the review.

In order to waive or alter a HIPAA authorization, the PI must provide sufficient information on which the IRB can determine that it meets the following three (3) findings specified by the Privacy Rule (45 C.F.R. § 164.512(i)(2)(ii)):

1. The use or disclosure of PHI involves no more than minimal risk to the privacy of individuals based on;
 - a. An adequate plan to protect the identifiers from improper use and disclosure;
 - b. An adequate plan to destroy the identifiers at the earliest opportunity consistent with conduct of the research, unless there is a health or research justification for retaining the identifiers, or such retention is otherwise required by law; and
 - c. Adequate written assurances that the protected health information will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research project, or for other research for which the use or disclosure of protected health information would be permitted by the Privacy Rule;
2. The research could not be practically conducted without the waiver or alteration; and
3. The research could not be practically conducted without access to and use of the protected health information.

Procedures

Responsible Parties

1. **Who Determines Whether a Study May Be Under Expedited Review?** The Human Studies Program (the Program) personnel, the IRB chair (the Chair), or the IRB at a convened meeting.
 - a. The investigator may request an expedited review; but, the IRB will make the final determination based on a review of the written application and applicable federal regulations.

⁶ “How Does the Rule Help Institutional Review Boards (IRB) Handle the Additional Responsibilities Imposed by the HIPAA Privacy Rule?” DHHS (March 14, 2006), <https://www.hhs.gov/hipaa/for-professionals/faq/307/how-does-the-rule-help-institutional-review-boards-handle-additional-responsibilities/index.html>

- b. The IRB or the Program personnel will not determine the type of review, e.g., expedited or convened-IRB review if the written application is not complete.
2. **Who May Be an Expedited Reviewer?** Only the Chair or an experienced IRB member designated by the Chair may review research under an expedited review procedure.

Application Review and Determination

1. **Submitting an Application for Review.** There is no separate application for expedited review. The same application form is used for expedited review and convened-IRB review. Which application form to use depends on whether the study is applying for initial review, continuing review, or modification requests. The investigator must submit a complete application, along with all required attachments. When submitting the application, the investigator may request expedited review.
2. **Prescreening by the Program.** The Program personnel will screen all applications for initial or continuing review and modification requests and determine whether they qualify for expedited review. If qualified, the appropriate category will be identified and documented.
3. **Assigning to Reviewers.** The Program personnel will assign applications to expedited reviewers who have the appropriate expertise and do not have a conflict of interest with the study.
4. **Distributing Review Materials.** The Expedited Reviewer will receive the application, research protocol or proposal, consent forms, study instruments, and all other documents necessary to perform a comprehensive and meaningful review of the study. The review materials distributed to the expedited reviewer during initial or continuing review are the same as those distributed to IRB members when an application is under a convened-IRB review.
 - a. Application materials / study documents are accessible to the assigned reviewer electronically via the secure application system.
 - b. **Additional Information.** If, during the process of expedited review, the reviewer requires additional information or documents from the Investigator, the reviewer will communicate this request to the Program personnel who will contact the investigator for the information.
 - i. However, the reviewer may choose to contact the Investigator directly during the review process for more information or clarification.
5. **Verifying.** Reviewers should verify that the assigned studies qualify for expedited review and under which categories, if applicable, the studies are qualified.
 - a. An expedited reviewer may determine the application should be reviewed by the convened IRB even if it qualifies for expedited review.
6. **Reviewing.** The reviewer will review the application to verify that it meets the approval criteria using the reviewer's worksheet for initial review, continuing review, or modification requests and communicate any conditions and the reasons for them to the Program personnel who will communicate this information to the Investigator.

7. **If Not Approved Under Expedited Review.** If the expedited reviewer determines a study should not be approved, the reviewer will notify the Program personnel, who will place the study on the agenda of the next convened IRB meeting for a final determination.
8. **Notifying the Investigator.** The Program personnel will prepare and transmit written correspondence to the investigator, communicating the IRB's or the reviewer's determinations.
9. **Notifying the IRB.** After the expedited reviewer completes the review, the Program personnel will include the approved studies in a list and present the list for review by the convened IRB at the next IRB meeting.
 - a. All IRB members will receive the list before the IRB meeting.
 - b. If the IRB accepts the list during the IRB meeting, the Program personnel will append the list to the minutes.⁷
 - c. If the convened IRB requests a study for substantive clarifications or modifications that are directly related to the criteria for approval by an IRB, the study will be turned over to the convened IRB and may not be approved by expedited procedures.

Decisions by Reviewers

Types of Actions

1. **Disapproval Not Allowed.** An expedited reviewer acts with the full authority of the convened IRB except that the reviewer may not disapprove research. Research may be disapproved only after a convened-IRB review. It can be returned to the investigator if incomplete, or referred to the Convened IRB if the reviewer does not approve the research.
2. **Allowable Types of Actions.** An expedited reviewer may adopt one of the following actions:
 - (a) approval if all criteria for IRB approval are met,
 - (b) approval with stipulations (equivalent to "approval with conditions" as termed by federal regulations),
 - (c) deferral to the convened IRB for actions such as additional discussion or disapproval.

Approval Date

1. If the study is approved, the approval date is the date when the study is approved by the expedited reviewer.
2. If the study is approved with stipulations, the approval date is when the reviewer or a person designated by the reviewer determines the stipulations are met.

Documentation of review decisions

The Program personnel will document in writing the specific expedited review categories and the expedited reviewer's decisions. The Documentation may also be evidenced by a completed reviewer worksheet or in "Comments" in the online application.

⁷ 45 C.F.R. § 46.110(c) (2012).

Materials

- APP 04 New Research Protocol/ Proposal for Initial Approval – Non-Exempt Research
- APP 05 Modification Request Form
- APP 07 Continuing Review
- WKSH 303 Non-Exempt Reviewer Worksheet
- WKSH 311 Reviewer Worksheet for Continuing Review, Modification or Study Closure
- WKSH 313 Expedited Review Categories
- TMP 412 Initial Review – Approval Letter - Expedited Review
- TMP 418 Modification – Approval Letter – Expedited Review
- TMP 423 Continuing Review – Approval Letter – Expedited Review

References

- The IRB has and follows written policies and procedures to conduct reviews by the convened IRB (**AAHRPP Element II.2.D.**)
 - Element II.2.D.1. – Initial review
- The IRB has and follows written policies and procedures to conduct reviews by the expedited procedure (**AAHRPP Element II.2.E.**).
 - Element II.2.E.1. – Initial review
 - Element II.2.E.2. – Continuing review
 - Element II.2.E.3. – Review of proposed modifications to previously approved research

U.S. Department of Health and Human Services (HHS). 2017. “Federal Policy for the Protection of Human Subjects.” Federal Register 82(12):7149-274.