
Yale University Human Research Protection Program

920 PR.4 Use of External IRBs for Review and Oversight of Research Involving Human Subjects

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1.0 Purpose

The purpose of this procedure is to outline the process for using an external Institutional Review Board (IRB) for the review and oversight of research involving human subjects.

2.0 Scope

This procedure applies to Yale University investigators and staff who are involved in the conduct, oversight, or management of research involving human subjects.

3.0 Overview

In accordance with Yale *Policy 920: Research Partnerships with Institutions and Other Organizations External to Yale*, a Principal Investigator (PI) or designee may submit a study to an external IRB if prior approval is obtained from the Yale University Human Research Protection Program (HRPP) office. In addition, the Yale HRPP may submit a study to an external IRB even if a PI does not submit a request to use an external IRB. The types of studies that may qualify for external IRB review, the criteria and process for approval, and oversight responsibilities if review is ceded to an external IRB, are summarized below.

4.0 Studies that May Qualify for External IRB Review

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Subject to the considerations outlined in section 5.0 below, the types of studies that may be approved by the Yale HRPP for external IRB review are divided into three categories: Category A, Category B, and Category C.

4.1 **Category A** studies are defined as:

- 4.1.1 Multicenter, investigator-initiated research that requires the use of a central IRB (e.g., by NIH policy, etc.)
- 4.1.2 Phase III and Phase IV clinical trials that are multicenter, industry-funded, and industry-authored
- 4.1.3 Device studies that are multicenter, industry-funded, and industry-authored

4.2 **Category B** studies are defined as:

- 4.2.1 Phase I, Phase II, and Phase IIB studies that are multicenter, industry-funded, and industry-authored
- 4.2.2 Federally funded biomedical studies
- 4.2.3 Non-biomedical studies (e.g., social behavioral, etc.)

4.3 **Category C** studies are defined as:

- 4.3.1 Planned emergency research
- 4.3.2 Research on surgical techniques or procedures that do not involve investigational devices.
- 4.3.3 Device studies that are first in human
- 4.3.4 Research involving investigational radiologic procedures and/or investigational radiologic drugs
- 4.3.5 Research involving gene therapy, gene transfer, or embryonic stem cell therapies
- 4.3.6 Research involving prisoners
- 4.3.7 Phase I trials in healthy controls
- 4.3.8 Research on transplant techniques, procedures, or other interventions

4.4 A study may be approved for external IRB review only if ALL of the following criteria are met:

- 4.4.1 All required ancillary committee approvals are in place and documented in the request for external IRB review unless the ancillary committee must receive IRB approval prior to conducting its review or another exception is noted in the request;
- 4.4.2 No restrictions on the research are imposed by any of the ancillary committees that would prevent the study to be reviewed by an external IRB;
- 4.4.3 The PI receives the requisite permission(s) to serve as the PI for the study; and
- 4.4.4 The Principal Investigator (PI) meets the Yale University requirement to serve as a PI on a research protocol.
- 4.4.5 There is no legal or regulatory prohibition that prevents the research from being reviewed by an external IRB.

4.5 As described further below, a study may not be submitted to an external IRB without prior written approval by the Yale HRPP office.

5.0 Submission Process to Yale HRPP for Review, Verification, and Consideration for Approval

5.1 No study may be submitted to an external IRB without the prior approval of the Yale HRPP. When submitting a request for approval to use an external IRB, the PI or designee must submit the following to the Yale HRPP office:

- 5.1.1 IRB Submission Request;
- 5.1.2 Approval letters from all ancillary committees required to review the study (e.g. PRC, PPRC, MRRC-PRC, RSC, etc.) unless the ancillary committee must receive IRB approval prior to conducting its review or another exception is noted in the request; and

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- 5.1.3 All required study-related documents (e.g., protocol, consent forms, IB, recruitment materials, etc.).
- 5.2 The Yale HRPP must verify the following, including:
 - 5.2.1 Eligibility for external IRB review;
 - 5.2.2 Ancillary committee approvals;
 - 5.2.3 Initial submission documents that will be sent to the external IRB;
 - 5.2.4 PI and staff compliance with training and Conflict of Interest (COI) requirements;
 - 5.2.5 Whether the study was previously reviewed or is in the process of being reviewed by the Yale IRB or another IRB;
 - 5.2.6 For industry-sponsored trials, consistency between the terms of “In Case of Injury” language (and any other Yale University preferred and/or negotiated language) in the consent form and the contract with the sponsor;
 - 5.2.7 For federally funded studies, congruency between the grant proposal and protocol to be submitted to the IRB.
- 5.3 In addition to the criteria set forth in section 4.0 above, the Yale HRPP will consider the following when deciding whether to approve or deny a request for external IRB review and which external IRB to use, including:
 - 5.3.1 The number of studies that have been approved by the Yale HRPP to be sent to an external IRB;
 - 5.3.2 Yale University’s internal IRB capacity;
 - 5.3.3 The type and complexity of the study, including the category of research and criteria that must be met as outlined in section 4.0 above;
 - 5.3.4 The budget impact on the Yale HRPP;
 - 5.3.5 Whether the study must be sent to an external IRB because of a Conflict of Interest or other reason;
 - 5.3.6 Whether the use of an external IRB is required by contract or is specifically requested by the PI with sound rationale clearly stated;
 - 5.3.7 Whether the Yale HRPP has evaluated and approved the use of a particular external IRB; and
 - 5.3.8 Whether an agreement is in place between Yale University and the external IRB to conduct IRB review on behalf of Yale.
- 5.4 If a study was previously reviewed or is in the process of being reviewed by the Yale IRB or another external IRB, the Yale HRPP generally will deny a request to send the study to a specific external IRB, but will consider the rationale for why the study should be transferred to the external IRB for review.
- 5.5 No study may be submitted to an external IRB without the prior approval of the Yale HRPP.
 - 5.5.1 Category A studies require approval by the Yale HRPP Director or designee.
 - 5.5.2 Category B studies require approval by the Yale HRPP Director or designee in consultation with the Yale IRB Executive Chair or a Yale IRB Chair/Vice-Chair.
 - 5.5.3 Category C studies require approval by the Yale HRPP Director or designee and the Institutional Official or designee in consultation with the Yale IRB Executive Chair or a Yale IRB Chair/Vice-Chair. (Note: Category C studies *generally do not qualify* for external IRB review, but may be approved on a case by case basis provided that adequate measures are in place to provide oversight of all or specific aspects of the study as required.)
 - 5.5.4 If a PI, group of PIs, or the University is the holder of the IND or IDE for a study, the Yale HRPP Director or designee must ensure that an adequate plan is in place to ensure that the sponsor obligations for the study are met.

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- 5.6 Once the verification and approval are complete, the Yale HRPP office will notify the PI regarding whether the request is approved or denied. If approved, the PI may proceed with a submission to the external IRB as identified and approved by the Yale HRPP.
- 5.7 Even if a study is approved, the Yale HRPP office may revoke permission to use an external IRB for one or more studies at any time.

6.0 Yale HRPP Decision to Use an External IRB without a PI Request

- 6.1 The Yale HRPP may submit a study to an external IRB even if a PI does not submit a request to use an external IRB. See section 5.0 above regarding the considerations for deciding whether to submit a study to an external IRB for review and the verification and approval process.
- 6.2 The Yale HRPP office will notify the PI regarding the decision to use an external IRB and will work with the PI as necessary to submit the study to the external IRB identified by the Yale HRPP office.

7.0 Yale University Fees for IRB review

The Yale HRPP charges an administrative review fee in accordance with Yale *Policy 110, Institutional Review Board Review Fees*. These charges apply to industry-sponsored studies sent to an external IRB and typically do not apply to other types of studies unless otherwise specified in that policy.

8.0 Protocol Changes and Continuing Review

- 8.1 Any subsequent submissions (e.g. amendments, etc.) related to a study under the purview of the external IRB must be sent directly by the PI or designee to the external IRB in accordance with the applicable external IRB's policies.
- 8.2 The PI or designee must notify the Yale HRPP of the following changes or modifications:
 - 8.2.1 Yale HRPP must be notified regarding a change in the PI, sub-investigator, and/or designated staff (personnel amendments) for verification of compliance with Conflict of Interest disclosure and training requirements prior to the external IRB submission;
 - 8.2.2 Yale HRPP must be notified regarding proposed modifications to the protocol if the modification would require approval from any of the ancillary committees at Yale (e.g. addition of minors to the protocol, increase in the levels of radiation for research purposes only, etc.);
 - 8.2.3 Yale HRPP must be notified regarding any changes to the Yale University consent form template (boilerplate) language in order to determine if the change requires institutional and/or Yale IRB approval before the external IRB reviews it.
 - 8.2.4 Yale HRPP must be notified regarding any changes to the grant proposal or protocol that may require a congruency review before the external IRB can review it.
- 8.3 The Yale HRPP will notify the PI regarding whether the change or modification is approved or denied. If approved, the PI may proceed with the subsequent submission to the external IRB.

9.0 Administrative Review by the Yale HRPP

The Yale HRPP will periodically review the frequency and composition of protocols that are approved and those that are rejected for external IRB review and will report its findings to the relevant components of the University, including the Institutional Official.

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10.0 External IRB Auditing by the Yale HRPP

The Yale HRPP will perform periodic audits of each external IRB with studies under its oversight in order to ensure compliance with all applicable laws, regulations, guidance, University policies, and contractual requirements.

11.0 PI's Ongoing Reporting Responsibility to Yale University

Instances of reportable information must be submitted directly to the designated external IRB in accordance with the external IRB's reporting requirements. The Yale HRPP will be notified by the external IRB regarding its determination as described below.

12.0 Contracting

An agreement between Yale University and the external IRB will include a division of roles and responsibilities between the parties. Yale University's and the external IRB's obligations and oversight responsibilities with regard to studies under the purview of an external IRB are outlined in sections 13.0 through 16.0 below. An agreement between Yale University and the external IRB may not in any way limit the legal and regulatory obligations of Yale University or the external IRB in fulfilling their respective obligations.

13.0 External IRB Responsibilities and Oversight

- 13.1 The external IRB shall be Yale University's IRB of record and will perform IRB functions in compliance with applicable laws, regulations, guidance, contractual obligations, and Yale University policy for the life of the study subject to the right of Yale University to withdraw a study from ceded review. The responsibilities of the external IRB include:
 - 13.1.1 Promptly notifying the PI, Yale HRPP or designee, and the Yale Institutional Official or designee of any potential reportable events (e.g., suspension, termination, unanticipated problems involving risks to participants or others, or serious or continuing noncompliance, etc.) in connection with a study.
 - 13.1.2 Promptly notifying the PI, Yale HRPP or designee, and the Yale Institutional Official or designee of any of the following:
 - 13.1.2.1 Termination or suspension of a study;
 - 13.1.2.2 Adverse events that it considers serious, were not anticipated in the external IRB-approved protocol, and are found to be possibly related to the research occurring at Yale University or at other sites if Yale University is the managing center in a multicenter trial;
 - 13.1.2.3 Instances of serious or continuing noncompliance with the federal regulations or the requirements and the determinations of the external IRB, along with an assessment as to how such noncompliance impacted research subjects and what remedial actions it recommends;
 - 13.1.2.4 Monitoring reports and any other information that comes to the attention of the external IRB that adversely affects Yale University's compliance with applicable regulations;
 - 13.1.3 Promptly notifying the PI and Yale HRPP or designee of any decisions to approve, disapprove, or recommend modifications of research studies.
 - 13.1.4 Reviewing conflict of interest (COI) information provided by Yale University (e.g., HRPP office, PI, etc.) to the external IRB, and, pursuant to Yale University's COI policies and institutional preferences, evaluating COI in the context of the study under review including the imposition of additional COI requirements as necessary in order to manage, reduce, or

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- eliminate the COI. (In no event shall the external IRB disapprove Yale University COI requirements that are more restrictive than what the external IRB requires.)
- 13.1.5 When necessary and upon request from the Yale HRPP Director or designee, conducting an Institutional Conflict of Interest review for Yale University.
 - 13.1.6 Ensuring that Yale required language is incorporated into the consent forms in accordance with previously agreed upon template (boilerplate) language.
 - 13.1.7 Contacting the PI or study coordinator directly to obtain additional information or necessary documents required for initial and continuing review. (Yale HRPP will assist the external IRB in soliciting this information if the external IRB has difficulty obtaining such information through the normal procedures of contacting the PI or study coordinator.)
 - 13.1.8 Providing upon request any documents or information in its possession relative to a protocol or PI, including but not limited to, protocol submission history, response time by the PI, copies of documents sent by the PI to the external IRB, together with any and all related documents.
 - 13.1.9 Having procedures in place to ensure knowledge of local context issues.
 - 13.1.10 Allowing designated individuals from Yale University to attend external IRB meetings and/or hold meetings/teleconferences as necessary to address local context or other questions/issues related to a study.
 - 13.1.11 When necessary, ensuring that the external IRB approvals related to a study are not released unless all Yale University ancillary reviews are complete.
 - 13.1.12 Assessing noncompliance regarding any Corrective and Preventative Action (CAPA) that is developed by the PI related to a study as required. (Yale HRPP will assist the external IRB in soliciting this information if the external IRB has difficulty obtaining such information from the PI or study coordinator. In addition, the external IRB will recommend appropriate remedial actions if necessary to address the noncompliance.)
 - 13.1.13 Ongoing monitoring of the study.
 - 13.1.14 Maintaining records under the external IRB's purview in accordance with applicable laws and regulations.

14.0 Yale University Obligations and Oversight

- 14.1 Yale University maintains overall responsibility for conduct of the research regardless of which IRB reviews the study. That responsibility is shared among multiple entities within Yale University, including the PI, the PI's Department, the Yale HRPP, the Yale Institutional Official, and the compliance and monitoring groups within the Yale HRPP and the Yale Center for Clinical Investigation (YCCI). Other obligations and oversight responsibilities and the entities typically charged with ensuring compliance with these obligations include:
 - 14.1.1 Conducting ancillary committee reviews as applicable and informing the external IRB of the reviews that will affect the study (HRPP);
 - 14.1.2 Informing the external IRB of any local context issues as requested by the external IRB (PI; HRPP);
 - 14.1.3 Promptly reporting to the external IRB any serious or continuing noncompliance in connection with a study in accordance with the external IRB's reporting requirements (PI, PI's Department);
 - 14.1.4 Promptly reporting to the external IRB any unanticipated problems involving risks to participants or others in connection with a study in accordance with the external IRB's reporting requirements (PI, PI's Department);
 - 14.1.5 Promptly reporting other events or issues in accordance with the external IRB's reporting requirements (PI, PI's Department);
 - 14.1.6 Maintaining a system for receiving and addressing subject complaints about the study and providing this information to the external IRB (HRPP); and

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- 14.1.7 Providing appropriate oversight as required by the study including assisting the PI with developing Corrective and Preventative Action (CAPA) and ensuring compliance in accordance with the CAPA (monitoring and compliance units within YCCI and HRPP).

15.0 Reportable Events; and Communications with Federal Agencies, Oversight Authorities, and Funding Agencies

- 15.1 The external IRB, Yale HRPP or designee, and Yale Institutional Official will promptly notify one other of any communications received from a federal agency (FDA, OHRP, etc.), funding agency, or oversight authority in connection with a study.
- 15.2 Before a report or communication is sent to a federal agency, oversight authority, or funding agency, the external IRB, Yale HRPP or designee, and Yale Institutional Official or designee will cooperate regarding any investigations and communications.
- 15.3 The agreement between the external IRB and Yale University shall specify whether the external IRB and the Yale Institutional Official or designee will jointly report, whether the parties will report separately, or whether one party will make the report. In no event shall the agreement between Yale University and the external IRB prevent the external IRB or the Yale Institutional Official or designee from reporting directly to a federal agency, oversight authority, or funding agency in order to satisfy its own reporting obligations.
- 15.4 If the external IRB or Yale Institutional Official or designee directly reports, the party making the report will copy the other party on the communication.

16.0 Yale HRPP Record Keeping

- 16.1 Yale HRPP will maintain a record of the study in an electronic system maintained by the HRPP office.
- 16.2 Yale HRPP will retain a record of any authorized changes regarding staff, modifications to the consent form template (boilerplate) language, and any modifications that would require approval from any of the Yale ancillary committees or departments.
- 16.3 Per the agreement with each external IRB, the Yale HRPP office will ensure that it is provided access to the study records and reviews conducted by the external IRB upon request.

17.0 Related Information

- 17.1 Policy 110: Institutional Review Board Review Fees
- 17.2 Policy 920: Research Partnerships with Institutions and Other Organizations External to Yale
- 17.3 Policy 110: Institutional Review Board Review Fees
- 17.4 Required Yale Consent Form Language
- 17.5 External IRB Contact Information
- 17.6 Guidance for Investigators Regarding External IRB Submissions
- 17.7 Procedural Work Instruction for HRPP Staff Regarding External IRB Submissions

18.0 Revision History

Effective 04/03/2017.