



Human Research Protection Program / Institutional Review Board
Standard Operating Procedure
Pre-2018 Common Rule

**For Studies Initially Approved on
or Before January 20, 2019**

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1 IRB Reliance Arrangements in Multi-Site Research

MaineHealth investigators involved in multi-site research are encouraged to discuss with collaborators the possibility of shared IRB review, i.e., having one IRB review on behalf of all sites.

If the research is part of a multicenter grant awarded from NIH, single IRB (sIRB) review is required under most circumstances (<https://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-094.html>). The reader is referred to Section 9 for details specific to compliance with the NIH sIRB policy.

Investigators should contact ORC early in the multi-site grant/contract process to discuss possible sIRB options as discussed in 8.2 (MaineHealth Serving as the Reviewing IRB) and 8.3 (MaineHealth Ceding Review to an External IRB) below.

1.1 Reliance Agreements

Reliance agreements must be in place for all ceded IRB review arrangements. ORC ensures that these agreements are negotiated to reflect study-specific, respective responsibilities of the reviewing IRB and the relying Institutions. The Reliance Agreement:

- Documents the respective authorities, roles, responsibilities, and communication between an organization providing the ethical review and a participating organization relying on a reviewing IRB.
- Describes the responsibilities of all parties and how communication between parties will occur, for example, notifications of the outcome of regulatory review and management of federally-mandated reports such as reports of unanticipated problems, serious or continuing noncompliance, and suspensions or terminations of IRB approval.
- When IRB certification requirements apply (e.g., for NIH Genomic Data Sharing etc.), the agreement or written procedures will indicate who is responsible for meeting the certification requirements.
- Specifies contact information and personnel for both the sIRB and relying institution(s).
- Addresses whether the replying organization applies its FWA to some or all research, and ensure that the IRB review is consistent with requirements in the relying organization's FWA.
- Addresses which organization is responsible for obtaining any additional approvals from DHHS when the research involves Subpart B, C, or D determinations, or any applicable federal agency or department (e.g., DOD, etc.).

The institution that is awarded the funding for the research is responsible for maintaining all agreements and for ensuring that adequate and appropriate communication channels between the sIRB and participating sites are in place. Participating sites are responsible for maintaining copies of the site agreement in accordance with the terms of their FWA.

1.2 MaineHealth Serving as the Reviewing IRB

1.2.1 Factors Considered by ORC to have MaineHealth provide IRB Services

ORC Staff evaluate the following factors, and others as appropriate, when considering a request for an MaineHealth IRB to serve as the IRB of record for a particular study or studies:

1. The terms of the external site(s) FWA;
2. The accreditation status of the external site(s)
3. Prior experience with the site(s) and investigators;
4. The compliance history of the site(s) and investigators (e.g., outcomes of prior audits or inspections, corrective actions);
5. The research activities to be conducted at the external site(s);
6. The willingness of the external site(s) to accept MaineHealth's reliance terms and procedures; and/or
7. The ability of the site(s) to collaboratively provide meaningful oversight of the proposed research, taking into account factors such as:
 - a. The risks and procedures of the research;
 - b. The resources available at each site and ability to accommodate or collaborate with each other in observing the consent process, performing compliance reviews, investigations of potential noncompliance, and similar matters;
 - c. The expertise and experience of the MaineHealth IRB with the proposed research, subject population, and applicable regulations;
 - d. The ability of the MaineHealth IRB to comply with the relevant local context considerations of the external site(s), as provided by that site(s); and/or
 - e. The willingness or ability of the external site(s) to provide information and respond to questions regarding investigator qualifications, conflicts of interest, organizational requirements, local context, and other matters that may inform the IRB review.

The ORC staff member will present relevant factors for consideration by the Director of ORC (in consultation with the IO, as applicable) who will make the final decision regarding whether or not the MaineHealth IRB will serve as the reviewing IRB. The PI will be notified of the decision.

1.2.2 Responsibilities when MaineHealth is the Reviewing IRB

1.2.2.1 Responsibilities of the MaineHealth IRB

- Policies and procedures in the conduct of review for all sites (MaineHealth and external) will mirror those outlined throughout these SOPs, as set forth in Domain II of the AAHRPP accreditation standards. Possible exceptions are noted in 8.4 below. Additionally, the following MaineHealth IRB responsibilities are to be applicable for all sites:
 - Have the final authority to decide whether MaineHealth or external researcher or research staffs' COI and its management, if any, allows the research to be approved
 - Have the authority to request or conduct an audit of research being reviewed.

- Make relevant IRB policies readily available to relying external sites, including their HRPP staff, researchers, and research staff, and ensure that changes to those policies are communicated as well.
- Ensure that a MaineHealth ORC contact person along with contact information is specified for researchers and research staff to obtain answers to questions, express concerns, and convey suggestions regarding the MaineHealth IRB.
- Adding sites to an already approved IRB study will be considered a modification, and will be conducted by the expedited or full board process. In order for the review to be conducted via the expedited process criteria, such a modification is usually considered a “minor change to previously approved research’. Factors that will indicate that a full review is required may include, e.g., involvement of investigators with FCOI, FDA 483 issues that have not been resolved adequately, or any other site-specific issues that are deemed questionable. Additional site amendments (regardless of type of review) do not change the expiration date of the IRB approval for the ‘main’ protocol.

1.2.2.2 Responsibilities of the MaineHealth Principal Investigator

- Submission of a plan for review to the IRB to ensure that the PI’s at collaborating sites have access to current information regarding study status and current protocols, consent documents, etc. regarding the study. (Alternatively, the IRB can review the plan provided by the MaineHealth PI to ensure open communication with the collaborating site(s)).
- Coordinate with ORC to ensure submission to the IRB information pertaining to the particular characteristics of each site’s local research context to be considered either (a) through knowledge of its local research context by the IRB, (b) through consultants, or (c) through review by appropriate designated institutional officials at external site(s). Additionally, the submission will also include details for the IRB’s evaluation regarding the management plan for information that is relevant to the protection of participants (e.g., unanticipated problems involving risks to participants or others, Interim results, protocol modifications). When the MaineHealth researcher is the lead researcher of a multi-site study, this information will also be made known to the IRB of record (e.g., Independent IRB, etc.).

1.3 MaineHealth Ceding IRB Review to an External IRB

1.3.1 Standing Reliance Agreements

MaineHealth has standing agreements in place for the review of specific categories of research to engage the services of external IRBs including:

- WIRB
- NCI’s Adult CIRB for NCI research involving adult subjects
- NCI’s Pediatric CIRB for NCI research involving children
- Quorum
- Advarra

MaineHealth is a participating institution in the SMART IRB initiative as well, having signed an overarching agreement indicating willingness to cede to other institutions' IRBs, pending satisfactory evaluation of factors identified below.

Research that falls within the above parameters must be registered with MaineHealth prior to submission to the external IRB following the procedures outlined below. Post-approval requirements for investigators are also summarized below.

1.3.2 Factors Considered by ORC in the decision to allow MaineHealth to Cede to an External IRB

MaineHealth may choose to enter into an agreement to rely upon other external IRBs, most commonly when required as a condition of a grant or contract. An ORC staff member evaluates the following factors, and others as appropriate, when considering a request to rely upon an external IRB:

1. The accreditation status of the proposed IRB;
2. The compliance history of the IRB (e.g., outcomes of prior audits or inspections, corrective actions);
3. Prior experience with the IRB;
4. The federal IRB registration and organizational FWA, as applicable;
5. The expertise and experience of the proposed IRB (e.g., with reviewing the type of research, research procedures, and subject population(s));
6. The research activities to be conducted at MaineHealth;
7. The risks and complexities of the proposed research;
8. The proposed reliance terms and procedures, including acceptance of MaineHealth local context issues, as well as the procedures for collaborative management of matters such as conflicts of interest processes, investigator training, noncompliance, unanticipated problems, and federal reports;
9. The plan for review and allowance of the incorporation of site-specific consent language; and
10. The plan for incorporation of other relevant local requirements or context information in the review process.

The ORC Staff member will present relevant factors for consideration to the ORC Director or designee (in consultation with the IO as applicable) who will make the final decision regarding whether or not to cede to the requested External IRB. The PI will be notified of the decision.

1.3.3 MaineHealth, External IRB, and MaineHealth Investigator Responsibilities When MaineHealth Cedes Review

1.3.3.1 The External IRB has the same authority as the MaineHealth IRB and all determinations and requirements of the external IRBs are equally binding. See section 8.4 for possible exceptions to external IRB vs. MaineHealth responsibilities.

1.3.3.2 MaineHealth remains responsible for the conduct of the research in which it engages. Research reviewed by external IRBs remains subject to review, approval, oversight, and monitoring by MaineHealth (in cooperation with the reviewing IRB when appropriate) and must adhere to all

applicable policies, procedures, and requirements of MaineHealth's HRPP. As with MaineHealth IRB-reviewed research, officials of MaineHealth may not approve research that is subject to a reliance agreement if it has not been approved by the reviewing IRB. See section 8.4 for possible exceptions to external IRB vs. MaineHealth responsibilities. ORC is responsible for notifying the reviewing IRB when MaineHealth policies that may impact IRB review are updated.

1.3.3.3 Responsibilities of the MaineHealth Investigator When Using an External IRB

- **General Compliance Requirement:**
 - The MaineHealth Investigator must be familiar with, and comply with the external IRB's policies and procedures for initial and continuing review, record keeping, prompt reporting, and any additional requirements or procedures outlined in the IRB reliance agreement or companion materials (e.g., reliance SOPs). All information requested by the reviewing IRB must be provided in a timely manner. MaineHealth will support investigator compliance with the terms of reliance agreements by providing investigators with a Reliance Arrangement Form that provides information relevant to their responsibilities.
 - Expectations of PI compliance, as detailed in these SOPs, remain in place regardless of the reviewing IRB.
 - Even though the External IRB may be reviewing the study, it must not commence at MaineHealth until all HSR training, COI disclosure, and required ancillary reviews and certifications have been satisfied.

1.3.4 Institutional Registration Requirement:

Studies that will be reviewed by external IRBs must be registered with MaineHealth, via submission of the following documents in IRBNet:

- MaineHealth SmartForm Wizard
- ICH GCP Supplemental Form
- Current Protocol
- Local Subject Materials (assessment tools, questionnaires, data collection forms, survey instruments, interview questions, screening forms, etc.)
- Local Recruitment Materials (e.g. advertisements, letters, radio or t.v. scripts, broadcast messages, etc.)
- Local Telephone Scripts/Screeners (including those for receipt of calls in response to general advertisements)
- The Proposed or previously approved Consent/Parental Permission/Assent Form(s) in Word Format
- Documentation of Departmental Review (signed form or email)

- Internal Services Sign-off (as applicable)
- Letter(s) of permission from any non-MaineHealth sites; or when applicable documentation of IRB approval or exemption from external sites, if not otherwise documented (by reliance agreements, contracts etc.)
- Patient Reimbursement Information (if applicable)
- IF USING WIRB, WIRB smartform (at time of initial submission and renewal submissions)
- If MaineHealth is to be the privacy board for the study:
 - Submission Form: HIPAA Request for Waiver or Alteration of Authorization (if applicable)
 - Submission Form: HIPAA Certification Form - Deidentification (if applicable)
 - Submission Form: HIPAA Certification Form - Limited Data Set (if applicable)

ORC will review the information and verify that CITI training, COI review, and any other applicable approvals or requirements have been completed, and determine the need for relaying local context information to the external IRB in accordance with the reliance agreement. Where waivers or alterations of HIPAA authorization are requested, and the external IRB will not be responsible for review (e.g., studies reviewed by the NCI CIRB), the ORC Staff member will forward such requests to an MaineHealth IRB Chair or a designated expedited reviewer for review. ORC will notify the investigators by e-mail or via IRBNet once the proposed research has been cleared for submission to the external IRB. Once approved by the external IRB, investigators must submit in IRBNet a copy of the approval letter and any approved consent document(s). If the protocol was modified during the external IRB review process, the approved version of the protocol should be provided as well.

1.3.5 Post-IRB Approval Requirements:

- Unless the external IRB's reporting process provides for simultaneous notification to ORC, Investigators approved through external IRB review will report in IRBNet:
 1. Findings from DSMB meetings that have occurred (if drives a change to the study)
 2. Audit or inspection reports (including internal audits, if applicable)
 3. Local unanticipated problems, complaints, and any noncompliance that meet local reporting criteria (serious AND unanticipated AND possibly related to the research);
 4. Changes in PI or study personnel

In general, Investigators are reminded that all other Institutional reporting requirements remain applicable in addition to HRPP reporting requirements. The documentation provided to the external IRB for these events will suffice for submission to the ORC. Such submissions will be reviewed by ORC to ensure that the conduct of the study meets institutional requirements for compliance and continuation of the study.

1.4 Exceptions to IRB vs. Local Site Responsibilities

Certain areas of responsibility can be handled by either the reviewing IRB or the local site HRPP, provided they have been agreed to in the reliance agreement or outlined in a companion document. For example, alternative procedures may be used for any of the following:

1. Conducting and documenting scientific review
2. Management and documentation of ancillary reviews and institutional permissions for research;
3. Training requirements and verification of qualifications and credentials for external investigators and staff;
4. For-cause and not-for-cause compliance reviews;
5. Site-specific consent language;
6. HIPAA compliance;
7. Handling of matters concerning noncompliance, including which institution is responsible for deciding whether each allegation of non-compliance has a basis in fact, whether an incident of noncompliance constitutes serious or continuing noncompliance, and who will handle reporting to federal agencies;
8. Handling of unanticipated problems, and responsibility of reporting to federal agencies when required;
9. Review of grant and IRB protocol for congruence;
10. Review of investigator financial disclosures for COI (note: the reviewing IRB must provide final approval of any management plans generated to mitigate investigator FCOI);
11. Managing organizational conflict of interest relating to the research
12. Procedures for submission and review of interim reports and continuing review materials; and/or
13. The communication of IRB determinations and other information to external investigators and organizations.
14. In the case of the termination of a reliance agreement, identification of the party responsible for continued oversight of active studies until closure or a mutually agreed upon transfer of the study.