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Purpose

This Standard Operating Procedure (SOP) is to document policies and procedures for Institutional Review Board (IRB) review of research conducted in more than one member of the HMO Research Network (HMORN). The HMORN member institutions are:

- Geisinger Health System
- Group Health Cooperative
- Harvard Pilgrim Health Care
- HealthPartners Research Foundation
- Henry Ford Health System – Health Alliance Plan
- Kaiser Permanente Colorado
- Kaiser Permanente Georgia
- Kaiser Permanente Hawaii
- Kaiser Permanente Northern California
- Kaiser Permanente Northwest
- Kaiser Permanente Southern California
- Lovelace Clinic Foundation
- Marshfield Clinic Research Foundation/Security Health Plan of Wisconsin
- Meyers Primary Care Institute/Fallon Community Health Plan, Fallon Foundation and the University of Massachusetts Medical School
- Scott and White Health System

The objectives of this SOP are to:

1. Reduce the burden on investigators from one HMORN member who propose to conduct research in multiple HMORN member institutions, and
2. Protect the authority of each HMORN member IRB to choose to review research being conducted in its institution or to cede review authority to another HMORN member IRB, consistent with federal regulation (DHHS 45 CFR 46), the HMORN member's policies and procedures, and its Federalwide Assurance (FWA).

3. For purposes of this SOP only, each Kaiser Permanente region that is a member of the HMORN shall be considered a separate institution.

Scope

This SOP is meant to cover data-only studies in epidemiology, health services, health economics, and related research areas.

Clinical trials are not within the scope of this SOP.

A clinical trial is a prospective biomedical or behavioral research study of human participants involving a licensed or investigational drug, device, biologic, or a behavioral intervention that is designed to answer specific questions about biomedical or behavioral interventions (e.g., treatments, devices, drugs, or new ways of using known drugs, treatments, or devices). Clinical trials are used to determine whether new biomedical or behavioral interventions are safe and effective.

Definitions

The following definitions (indicated by ✓ in Appendix A, Definitions) and descriptions of responsibilities are essential to understanding this SOP.

- Ceding IRB
- Lead IRB
- Lead Principal Investigator (PI)
- Non-lead Principal Investigator (PI)
- Reviewing IRB

Please see Appendix A for all pertinent definitions.

Responsibilities

1. **Lead IRB**
 - 1.1 The **Lead IRB** is the designated IRB to which other HMORN member IRBs may cede. The Lead IRB's responsibilities include:

- a. Communicating with the Lead PI;
- b. Accepting responsibility for review and oversight of the inter-institutional study on behalf of any HMORN IRB that has ceded review authority to the Lead IRB;¹ and
- c. Providing study initial approval documentation to ceding IRB(s).

2. Lead PI

2.1 A **Lead PI** is generally the PI who develops the protocol, or otherwise is designated as Lead PI for an inter-institutional study. The Lead PI's responsibilities include:

- a. Overseeing in its entirety the study being conducted in the HMORN;
- b. Recruiting collaborating PIs in each HMORN member institution (i.e., Non-lead PIs) in which the study will be conducted;
- c. Preparing the Inter-institutional Research Application Cover Sheet (Cover Sheet) and IRB application and coordinating their submission to the appropriate HMORN IRBs;
- d. Communicating with the Lead IRB;
- e. Having the primary role in communicating with each Non-lead PI, including forwarding all correspondence from the Lead IRB to each Non-lead PI; and
- f. In conjunction with the Non-lead PIs, communicating with reviewing IRBs to provide them study information.

3. Non-lead PI

¹ The management of adverse events (e.g., confidentiality breaches) that occur at a ceding institution will be handled by that institution. The ceding institution will keep the Lead IRB fully informed of the actions it takes. Likewise, dealing with allegations of research misconduct at a ceding institution will be the responsibility of that institution, and the ceding institution will keep the Lead IRB fully informed. The Lead IRB will also inform the ceding institution's IRB of any adverse events that come directly to its attention.

- 3.1 A **Non-lead PI** is the HMORN member-specific investigator for an inter-institutional study when research activities will be conducted in that member. Non-lead PI responsibilities include:
 - a. Performing and/or supervising all research activities relating to the study conducted in his/her institution;
 - b. Assuring that these activities are conducted in compliance with federal and state regulations, institutional policies, the FWA, and IRB determinations of his/her institution;
 - c. Assuring that all IRB requirements at his/her institution are met;
 - d. Obtaining all institutional approvals including leadership, research review committee, and facility department approvals, etc., as required by the institution;
 - e. Submitting the Cover Sheet, IRB application, and institution-specific materials to the institution's IRB and other institution-mandated committees;
 - f. Communicating with his/her institution's IRB, as appropriate; and
 - g. Communicating with the Lead PI, including forwarding any correspondence from his/her institution's IRB to the Lead PI.
4. **Reviewing IRB**
 - 4.1 A **Reviewing IRB** is any HMORN IRB, including the Lead IRB, which reviews the inter-institutional study (i.e., which has decided **not** to cede review authority to the Lead IRB), and, therefore, will concurrently review the study. Responsibilities include:
 - a. Reviewing, approving, and overseeing the study in accordance with applicable federal and state regulations, institutional policies, the its FWA;
 - b. Communicating with the Non-lead PI; and
 - c. Obtaining information from the Non-lead PI and the Lead PI, as appropriate.

5. Ceding IRB

- 5.1 A **Ceding IRB** is any HMORN IRB that decides to cede review authority and oversight of the inter-institutional study to the Lead IRB. Responsibilities include:
- a. Reviewing the inter-institutional research application and determining whether the IRB will retain or cede review authority; and
 - b. Communicating directly with the Lead IRB about the ceding decision, including initiation of the required IRB Authorization Agreement.
 - c. Communicating with the Non-lead PI, including the decision to cede.

Policies

1. Investigators are required to comply with reviewing IRBs' policies, procedures, decisions, and conditions, as applicable to the study.
2. HMORN PIs or representatives will not attempt to influence any HMORN IRB to cede or not to cede review authority to another HMORN IRB.
3. There will be a Lead PI for each proposed study.
4. A Non-lead PI must be named for each HMORN member institution participating in the study that is not the Lead institution.
5. The Lead and Non-lead PIs should submit the HMORN inter-institutional research application to all the participating HMORN IRBs for review in approximately the same timeframe.
 - 5.1 The HMORN inter-institutional research application consists of the Cover Sheet (Appendix B) plus the Lead IRB's application form, plus any institution-specific information requested by a Non-lead IRB.
 - 5.2 If the Lead PI has already received approval of the study from the Lead IRB, a copy of that IRB's determination letter should be

submitted with the inter-institutional research application to the IRB of each HMORN member to which the application is being submitted.

6. The Lead IRB is typically the IRB of the institution of the Lead PI.
 - 6.1 If the Lead PI is not affiliated with a particular institution (e.g., as in the case of some Kaiser Permanente investigators), the Lead IRB is typically the IRB of the institution contributing the greatest number of research records.
7. All HMORN IRBs reviewing inter-institutional research will accept the Cover Sheet (Appendix B) and the Lead IRB's institutional application form.
 - 7.1 An HMORN IRB may ask the Non-lead PI to include in the inter-institutional application institution-specific information, and/or to respond to institution-specific supplemental questions that are not included in the Lead IRB's application form.
8. Each Non-lead IRB must decide whether to cede authority to the Lead IRB for the study, as requested by the Lead PI, or to review the research that is being conducted in its institution.
 - 8.1 The decision to cede authority to another IRB may be made under an expedited review process, if the proposed study qualifies for expedited review according to federal regulatory criteria.
 - 8.2 When an HMORN IRB cedes authority to the Lead IRB, the Lead IRB may also make necessary HIPAA Privacy Rule determinations (i.e., approve authorization forms and waiver or alteration of authorization).
 - 8.3 Other institutional HIPAA Privacy Rule contract responsibilities (e.g., data use agreements, business associate agreements, disclosure accounting) are the responsibility of each HMORN member institution.
 - 8.4 When an HMORN IRB cedes authority to the Lead IRB, it is assuring the Lead IRB that investigators and study staff meet the ceding institution's initial and on-going educational and training requirements.

- 8.5 When an HMORN IRB cedes authority to the Lead IRB, it is assuring the Lead IRB that investigators and study staff meet the ceding institution's Conflict of Interest requirements.
9. When more than one HMORN IRB reviews inter-institutional research (i.e., one or more IRBs decide not to cede review to the Lead IRB), the Reviewing IRBs are required to take reasonable steps necessary to minimize differences in decisions about, and requirements for, conducting the research, including documents associated with the research.
10. The Lead IRB will provide to the IRB(s) that ceded review authority to the Lead IRB notification when the research is complete.
11. Each Reviewing IRB must comply with applicable federal and state regulations, its institutional policies and FWA, and its own IRB policies and procedures.
12. The Lead IRB may approve an inter-institutional study using an expedited review procedure, if the study meets federal regulatory criteria. When approving research using expedited review, the IRB must comply with applicable federal and state regulations, its institutional policies and FWA, and its own IRB policies and procedures.
13. Each HMORN member institution may establish a policy requiring institutional leadership or other approval prior to submission of the proposed study to the IRB.
14. After ceding IRB review to another institution's IRB, the ceding institution remains responsible for ensuring compliance with the Lead IRB's determinations and with the terms of its FWA.

Procedures

1. **Designation of Lead IRB and Non-lead PIs**
 - 1.1 The Lead PI will request that one HMORN member institution's IRB (generally, his or her own) be designated as the Lead IRB.
 - 1.1.1 The Lead PI will contact the Administrator or the Chair of the proposed Lead IRB to confirm his/her willingness to accept this role.

1.1.2 If the proposed Lead IRB declines the role, the Lead PI may request that another HMORN member IRB be the Lead IRB.

1.2 The Lead PI will appoint a collaborating individual from each HMORN member institution that will be involved in the proposed research. This individual will function as the Non-lead PI for that institution.

2. HMORN Inter-institutional Research Application

2.1 The Lead PI, in collaboration with all Non-lead PIs, will complete a HMORN Inter-institutional Research Application Cover Sheet (Appendix B), the Lead institution's IRB application form, and submit it to the all participating HMORN IRBs.

2.1.1 The Lead PI will indicate on the Inter-institutional Research Application Cover Sheet which institutions propose to participate in the research and the designation of the Lead IRB.

2.2 The Lead PI's advance notice to Non-lead IRBs that an inter-institutional research application is forthcoming may minimize subsequent delays.

2.3 The Lead IRB should be the first to receive the HMORN inter-institutional research application, or roughly at the same time as the other HMORN IRBs.

2.4 The Lead PI will send a copy of the Inter-institutional Research Application Cover Sheet and Lead IRB application to each Non-lead PI for his/her review and approval.

2.5 Each Non-lead PI will review and sign the Lead IRB application, which indicates his/her support for the research, and willingness to serve as PI for the Non-lead institution.

2.6 Each Non-lead PI will obtain other non-IRB institution-required approvals (e.g., research review committee) necessary to conduct the study at his/her institution.

2.7 The Non-lead PI will submit the Cover Sheet and signed HMORN Lead IRB application and related documents to his/her institution's

IRB and other research review committees, as required by his/her institution.

2.7.1 Non-lead PIs should contact their institution's IRB for submission instructions.

3. Initial Inter-institutional IRB Review

3.1 Each institution's IRB will review the Cover Sheet and HMORN Lead IRB application and determine whether to cede review authority to the designated Lead IRB or to review the research.

3.1.1 If review authority is ceded, the ceding IRB will document its decision as per its standard practice.

3.1.2 When IRBs cede review to the Lead IRB, Privacy Rule determinations may also be ceded.²

3.2 Each Non-lead IRB will notify the Lead IRB and its Non-lead PI in writing when it decides to cede review authority to the Lead IRB.

3.2.1 Each Non-lead IRB will notify its Non-lead PI in writing (e-mail) when it decides **not** to cede authority to the Lead IRB.

3.3 When there are differences in the initial review decisions made by the Reviewing IRBs, the Chairs of the reviewing IRBs, or their designees, will attempt to resolve the differences in a reasonable timeframe. Please see Section 5 below.

4. Concurrent Review by the Lead and Reviewing IRBs

4.1 The Lead PI will submit continuing review reports, study modifications, and adverse events reports to the Lead IRB.

4.2 At institutions where the Non-lead IRB **did not** cede to the Lead IRB, the Lead PI will assist each Non-lead PI to submit the items to the Reviewing IRB at his/her institution for review.

4.3 When there are differences in the decisions made by the Reviewing IRBs, the Chairs of the Reviewing IRBs, or their designees, will

² When a Lead IRB reviews Privacy Rule authorization forms to be used in another state, they should contact the IRB Administrator for the institution(s) for which the study is being reviewed to assure that specific state law authorization requirements are being met.

attempt to resolve the differences in a reasonable timeframe (e.g., one month after differences among Reviewing IRBs arise). Please see Section 5 below.

5. Reconciling Multiple IRBs' Different Decisions

- 5.1 When more than one IRB reviews the study and there are differences in the decisions made by the Reviewing IRBs, the Chairs of the Reviewing IRBs, or their designees, will attempt to resolve the differences in a reasonable timeframe.
- 5.1.1 The Lead PI should notify the Lead IRB that differences in review decisions need to be resolved.
- 5.1.2 The Chairs of the Reviewing IRBs, or their designees, will meet via conference call and attempt to resolve any differences in review decisions.
- 5.1.3 If the proposed research requires full Board review, the Chairs of the Reviewing IRBs, or their designees, will present the proposed resolution to their institutional IRBs for approval.
- 5.1.4 If the proposed research can be expedited, the Chairs of the Reviewing IRBs, or their designees, may decide to expedite the proposed resolution.

6. Ceding Review Authority to the Lead IRB after Initial Review

- 6.1 After initial review, a Reviewing IRB may still decide to cede review authority to the Lead IRB.
- 6.1.1 The Non-lead PI or Lead PI should contact the Lead IRB Administrator or Chair to confirm the Lead IRB's willingness to accept review authority.
- 6.1.2 The Non-lead PI or Lead PI may make this request at the time of continuing review, or at other times, if the Non-lead PI or Lead PI determines this is necessary.
- 6.2 If the Reviewing IRB **does not** agree to cede after considering the request, the Reviewing IRB will notify its Non-lead PI of its decision.

- 6.3 If the Reviewing IRB **does** agree to cede after considering the request, the Reviewing IRB will notify its Non-lead PI **and** the Lead IRB of its decision.
 - 6.3.1 The Non-lead PI or the Non-lead IRB administrator will notify the Lead PI of the Reviewing IRB’s decision to cede.
 - 6.3.2 The Lead PI will submit a protocol modification request to the Lead IRB specifying which HMORN institution has ceded and the name and contact information of the Non-lead PI, and the new research activities at the institutional level for which the Lead IRB will have oversight responsibility.
 - 6.3.3 If the Lead IRB approves the protocol modification including accepting review authority of the other IRB, the Lead IRB will communicate its decision to the Lead PI.
 - 6.3.4 The Non-lead and Lead IRB administrators will determine which records, if any, need to be transferred to the Lead IRB.

Document History

Version # (dated):	Version & implementation instructions distributed on:	Implement prior to:
1 [Approved by the HMORN Governing Board – June 12, 2008]	June 13, 2008	September 1, 2008

Document Approval

The designated Institutional Official reviewed and approved this SOP. Approval signatures and dates are on file with the HMORN Member Institution's IRB Administrator.

Appendices

Appendix A: Definitions

Appendix B: HMORN Inter-institutional Research Application Cover Sheet

Appendix C: Process Flowchart

Appendix A: Definitions

Alteration of Authorization: An IRB-approved modification of a procedure or form that enables research participants to authorize use or disclosure of their protected health information (PHI) for a particular study. Such alterations must be consistent with the HIPAA Privacy Rule and documented in the IRB records.

Authorization: A written agreement by an individual to permit use and/or disclosure of his/her PHI for a particular research project according to HIPAA Privacy Rule standards. This agreement is commonly incorporated as a separate section in the research consent form.

✓ **Ceding IRB:** The HMORN IRB that transfers review authority to the Lead IRB.

Federalwide Assurance (FWA): An agreement between a research institution and the Office for Human Research Protections (OHRP), stipulating terms by which the institution will protect the safety, welfare and rights of research participants in accordance with federal regulation (45 CFR 46).

Food and Drug Administration (FDA): The federal agency that regulates food, drugs and cosmetics, including the process by which investigational drugs, devices and biologics are evaluated and approved for marketing.

HMO Research Network (HMORN): An organization of HMO research programs whose mission is to use their collective scientific capabilities to integrate research and practice for the improvement of health and health care among diverse populations.

Institution: For the purpose of this SOP, any member of the HMO Research Network, including each of the Kaiser Permanente members of the HMORN individually.

Institutional Review Board (IRB): A formal compliance committee comprised of scientific and non-scientific members with authority and responsibility to protect the safety, welfare and rights of research participants and to determine if proposed research can be conducted under its jurisdiction and under what conditions. IRBs are responsible for monitoring research until it is complete.

Investigational Device Exemption (IDE): A designation issued by the FDA, giving a device manufacturer or other sponsor the authority to conduct an evaluation of a "significant risk" investigational medical device.

Investigational New Drug (IND): A designation issued by the FDA, giving a "sponsor" the authority to evaluate an investigational drug by administering the investigational drug to human research participants according to FDA regulations.

✓**Lead IRB:** The HMORN IRB to which authority for review and oversight has been delegated by another HMORN IRB.

✓**Lead Principal Investigator (PI):** The HMORN representative who initiates or otherwise assumes HMORN-wide leadership over the conduct of a study.

✓**Non-lead Principal Investigator (PI):** The HMORN representative responsible for the conduct of research in his/her institution.

Office for Human Research Protections (OHRP): A federal regulatory office within the Department of Health and Human Services responsible for compliance with 45 CFR 46. OHRP enters into Federalwide Assurances with research institutions.

Privacy Rule: A comprehensive federal regulation regarding health information that implements the privacy requirements contained in HIPAA. The Privacy Rule establishes the conditions under which PHI may be used and/or disclosed by Covered Entities (CEs).

Protected Health Information (PHI): Identifiable health information, including any demographic or other descriptive data that could link the identity of an individual to his/her health information. It includes information maintained in paper medical records and in electronic databases or disease registries. It also includes identifiable information communicated verbally.

✓**Reviewing IRB:** HMORN IRBs that include the Lead IRB and any other IRB participating in the research which decide not to cede review authority to the Lead IRB.

Waiver of Authorization: A waiver of the requirement for a written agreement by an individual, permitting the use and/or disclosure of PHI, as approved by the IRB.

hmo research network

Inter-institutional Research Application Cover Sheet

Complete/Formal Study Title (and sponsor protocol number, if applicable)

Proposed Lead IRB (HMORN Member)

Administrator Name

Phone

Administrator E-mail

Fax

Information about the Lead Principal Investigator – Submission of this Cover Sheet by the Principal Investigator listed below (“Lead PI”) will verify that the Lead PI accepts responsibility for the information in the research application and agrees to be responsible for the conduct of the study throughout all participating HMORN institutions in compliance with all applicable federal regulations.

Lead PI Name

Address/Facility

Department

Phone

Fax

E-mail

Information about the non-lead Principal Investigator(s) – Submission of this Cover Sheet by any Principal Investigator listed below (“non-lead PI”) will verify that the submitting non-lead PI accepts responsibility for the information in the research application as it pertains to the conduct of the study in his or her institution, and that the submitting non-lead PI agrees to conduct the study within his or her institution in compliance with all applicable federal regulations and institutional policies and procedures.

Non-lead PI Name

HMORN Member Institution Name

Address

Phone

Fax

E-mail

Non-lead PI Name

HMORN Member Institution Name

Address

Phone

Fax

E-mail

Non-lead PI Name

HMORN Member Institution Name

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Phone

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Non-lead PI Name

HMORN Member Institution Name

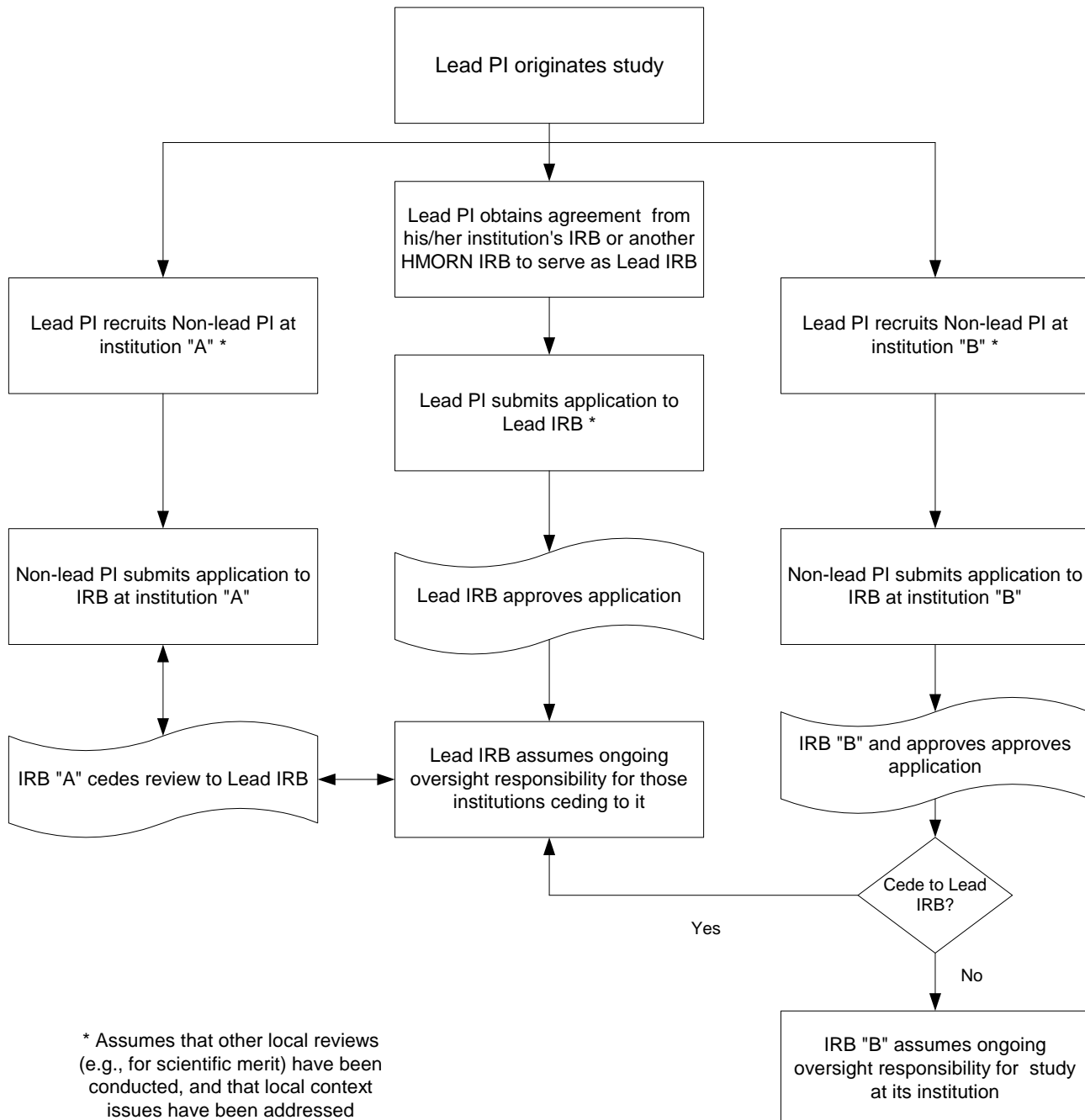
Address

Phone

Fax

E-mail

HMO RESEARCH NETWORK - OVERVIEW OF INTER-INSTITUTIONAL RESEARCH APPROVAL PROCESS



* Assumes that other local reviews (e.g., for scientific merit) have been conducted, and that local context issues have been addressed

PLEASE SEE NEXT PAGE

Lead IRB

- Reviews the proposed research submitted by the Lead PI
- Accepts responsibility for study oversight from a ceding IRB

Ceding IRB

- Reviews proposed research submitted by the Non-lead PI for its institution and cedes responsibility to the Lead IRB

Reviewing IRB

- Reviews proposed research submitted by the Non-lead PI for its institution and oversees the study in its institution
- Communicates primarily with the Non-lead PI, and communicates with Lead PI as required

Lead PI

- Originates the research protocol
- Oversees the study in its entirety in the HMORN
- Prepares the HMORN Inter-institutional Research Application Cover Sheet and the IRB application of the Lead IRB
- Recruits Non-lead PIs
- Submits the proposed research to the Lead IRB
- Assists the Non-lead PIs in preparing their research applications, as required
- Communicates with Reviewing IRBs as required

Non-lead PI

- Submits the proposed research to the Non-lead IRB
- Ensures that any institutional-specific application requirements are included in the inter-institutional research application