The ORARC Quality Improvement Program (QIP) Can Help!

- **QIP Services**
  - QIP Consultation
  - IRB/ESTR Submission Assistance
  - Study Management Tools (e.g., logs and Regulatory Binder)
  - Investigator/Study Staff Training

- **QIP Service Request Form**

- **QIP Education Sessions**
  - November: Internal Study Monitoring and What You Should Know. Common Human Research Audit Findings and Information on Reportable New Information (November 9th, 10 -11 AM EST)

  - Registration for all sessions now available via the [Harvard Training Portal](#).

- **Contact QIP with any little (or big) question at all!**
Submitting to the IRB: What every HLC investigator should know

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Agenda

• The IRB’s Function
• Is your Project Human Subjects Research
• What to Submit
• Types of IRB Review
• PI Responsibilities
• Plan Ahead!
• IRB Approved, now what?
• Tips
• Questions?

Reference: Glossary of Key Regulatory Definitions (last slide)
IRB’s Primary Function

• To Ensure:
  • Participant Protection:
    • Rights and Welfare
    • Safety
    • Privacy and Confidentiality
  • Compliance with IRB-approved protocol, Institutional policies, and federal regulations

* The Harvard Longwood Campus (HLC) IRBs serve Harvard Medical School, Harvard School of Dental Medicine, and Harvard T.H. Chan School of Public Health
Is Your Project Human Subjects Research?

Research:

A **systematic investigation** including research development, testing and evaluation, designed to develop or contribute to **generalizable** knowledge.

Human Subjects:

A **living** individual **about whom** an investigator (whether professional or student) conducting research:

1. Obtains information or biospecimens through **intervention or interaction** with the individual, and uses, studies, or analyzes the information or biospecimens; or

2. Obtains, uses, studies, analyzes, or generates **identifiable private information** or **identifiable biospecimens**.

QIP Tip: “De-identified” data **Cannot contain participant codes/IDs if there is a link to identifiable information in existence**
I am ONLY working with data, what do I need to know?

When working with data, the IRB will expect the following specifics described in your IRB application:

1. Identify what research activities are taking place at Harvard, including data storage, management, and/or analysis.
2. Explain who is providing the data (e.g. a colleague, repository, CMS, public website)
3. Describe the data provider's involvement in the research (e.g. solely provides a secondary dataset with no further involvement, is a collaborator on this project)
4. Know the level of identifiability of your data (HLC definitions here).
5. Adhere to any data provider requirements for data access (e.g. data use agreements).

What is a Data Use Agreement (DUA)? Do I need one?

- A DUA is a contract between organizations governing the transfer and use of data that is typically confidential, proprietary, or otherwise considered sensitive (e.g. medical records). The organization providing the data will tell the recipient receiving the data what their requirements are.

- For more information (including executing DUAs) contact the relevant office at your HLC School:
  - HMS/HSDM: SPAContracts@hms.harvard.edu
  - HSPH: dua@hsph.harvard.edu
  - DUAs go through “Agreements” portal in ESTR
To Submit or Not to Submit? That is the question.

Investigators can use the IRB Decision Tool to determine:

• if their activities are research,
• if their research involves human subjects, and/or
• if they need to submit an IRB application.

• The final page of the tool summarizes the responses input by the user (which can be retained for their records) and a set of instructions on next steps, if there are any (e.g. how to submit an IRB application within the IRB e-submission system).

http://bit.ly/2LBTcYx

(HarvardKey required for log-in)
## The Five Types of IRB Determinations

<table>
<thead>
<tr>
<th>Human Subjects Research</th>
<th>Not Human Subjects Research</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1. Not Research</strong> - Activities do not meet the regulatory definition of “research” (e.g. program evaluation, quality improvement, journalistic activities, literature review, analysis of policies, facts about a process, facility data, historical scholarship)</td>
<td></td>
</tr>
<tr>
<td><strong>2. Not Human Subjects Research</strong> - Activities do not meet the regulatory definition of research involving “human subjects”</td>
<td></td>
</tr>
</tbody>
</table>

| Human Subjects Research | | Human Subjects Research |
|-------------------------|-----------------------------|
| **3. Exempt** - Research activities involving human subjects that fall into one of the six Exemption categories (defined in 45 CFR 46.101). |
| **4. Expedited** - Research activities involving human subjects that involve no more than minimal risk. Expedited categories are defined in 45 CFR 46.110 [HHS] and 21 CFR 56.110 [FDA]. |
| **5. Convened IRB** - Research involving human subjects that does not qualify for Exempt or Expedited review, typically involving greater than minimal risk to subjects. Review occurs at monthly meeting; submission deadlines approx. 30 days prior to meeting. |

*1-3 any HLC affiliate can serve as PI; 4-5 only HLC Faculty can serve as PI*
Let’s pause here for questions before moving on.
Principal Investigator Responsibilities

• Do not start Human Research activities obtaining all required institutional approvals

• Submit to the IRB in a timely manner:
  • Proposed modifications to the previously-approved Human Research.
  • A continuing review application (to avoid a lapse in approval).
  • A continuing review application when the Human Research is closed.

• Maintain adequate and accurate records and make these records available to the IRB or QA/QI Program for review.

• Personally conduct or supervise the Human Research.

• Etc. see Appendix C and D of the ORARC Investigator Manual
Plan Ahead!

• Submit as soon as possible.
  • You cannot begin research with human subjects or identifiable data before obtaining HLC and Local IRB determination, even if you’ve booked your flight!
  • Discuss with Local Collaborators
• Allow sufficient time for review(s)
  • Review times dependent on completeness of submission
Plan Ahead Continued: Turn Around Times

<table>
<thead>
<tr>
<th>Type of Determination or Review</th>
<th>Average review turnaround times</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not Human Subjects Research Determination</td>
<td>1 week</td>
</tr>
<tr>
<td>Exemption Determination</td>
<td>1 week</td>
</tr>
<tr>
<td>Expedited</td>
<td>2-3 weeks</td>
</tr>
<tr>
<td>Convened IRB Review</td>
<td>1 month</td>
</tr>
</tbody>
</table>
Your study has been IRB approved. Now what?

• Carefully read your approval letter
  • Your approval letter may require additional items prior to study start up

• Review QIP’s study management tools
  • QIP has created templates, such as enrollment logs and informed consent/assent check lists, that can be implemented to maintain study compliance

• Create a regulatory binder to organize regulatory documentation
  • Binders can either be paper or electronic
  • Templates for both (paper and electronic) can be found on our website

• Need to make a change after approval? Submit a modification in ESTR.
  • Modifications must be submitted and approved prior to implementing the requested change

• Once your study is complete, submit a Continuing Review in ESTR to close your record.
Tips

• Once you submit your application sit tight and let the reviewers do their jobs
  • If the status of your submission hasn’t been changed to “assigned” within 48 hours feel free to check in.

• Contact QIP for Submission Assistance

• Make sure to have the PI hit “submit” in ESTR

• Find Mentors to help you along the way!

• Use resources available to you
Questions?

Quality Improvement Program Staff

• Lisa Gabel, lgabel@hsph.harvard.edu
• Amy Harchelroad, aharchelroad@hsph.harvard.edu
• Alyssa Speier, aspeier@hsph.harvard.edu

Department Assigned Review Specialist:

• https://www.hsph.harvard.edu/regulatory-affairs-and-research-compliance/department-assignments/

ORARC Resources

• ORARC Website: https://www.hsph.harvard.edu/regulatory-affairs-and-research-compliance/
• IRB Getting Started: https://www.hsph.harvard.edu/regulatory-affairs-and-research-compliance/getting-started-2/
• Investigator Manual: https://www.hsph.harvard.edu/regulatory-affairs-and-research-compliance/investigator-manual/
• ESTR Support and Training: https://estrsupport.fss.harvard.edu/study-submission-guide
• IRB Submission Decision Tool: http://bit.ly/2LBTcYx

Non-ORARC Resources

• Community Based Research/Community Advisory Board (CAB) Resource, Community Coalition for Equity in Research: https://catalyst.harvard.edu/community-engagement/community-coalition/
# Harvard Longwood Campus IRB Review Requirements

(assuming an HLC School is involved in the project)

<table>
<thead>
<tr>
<th>Research Type</th>
<th>Activities Involved/ Examples (not exhaustive)</th>
<th>Is IRB Review Required?</th>
<th>Can I make my own determination?</th>
<th>What IRB application do I fill out?</th>
<th>I’m collaborating with individuals external to Harvard, is a reliance agreement appropriate?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not Research &amp; Not Human Subjects Research</td>
<td>• Activities that do not meet the regulatory definition of research (e.g. Program evaluation, quality improvement, journalism, literature review, analysis of policies, facility data) • Activities that do not meet the regulatory definition of research involving “human subjects” (e.g. Utilizing de-identified data/specimens; Studies of the deceased)</td>
<td>No. NR/ NHSR do not require IRB review/approval. Determinations are provided as a courtesy to investigators who require documentation.</td>
<td>Yes, researchers can self-determine using the following HLC IRB resources: • Investigator Manual guidance regarding when an IRB application is required • Worksheet: Human Research Determination • IRB Decision Tool • Getting Started FAQ website</td>
<td>Create an ESTR application; complete and upload the Not Human Subjects Research Request Determination Form</td>
<td>Reliance ineligible for such activities. External collaborators should check in with their home institution/IRB to follow necessary requirements, if any.</td>
</tr>
<tr>
<td>Exempt Human Subjects Research</td>
<td>Research activities within one of the Exempt categories listed in §46.104 (e.g. Survey, focus group, interview with adults; Secondary analysis of medical records)</td>
<td>Yes. Researchers must submit an application in ESTR for IRB review (irb.harvard.edu)</td>
<td>No, only the IRB has the authority to approve human subjects research.</td>
<td>Create an ESTR application; complete and upload the HLC Research Protocol Template</td>
<td>Reliance ineligible for such activities. External collaborators should check in with their home institution/IRB to follow necessary requirements, if any.</td>
</tr>
<tr>
<td>Expedited Human Subjects Research</td>
<td>Research activities within one of the Expedited categories listed in §46.110 (e.g. Research with children, pregnant women, or prisoners; Prospective/identifiable specimen collection; Body measurements; Data collection using smartphone, app, or wearable)</td>
<td>Yes. Researchers must submit an application in ESTR for IRB review (irb.harvard.edu)</td>
<td>No, only the IRB has the authority to approve human subjects research.</td>
<td>Create an ESTR application; complete and upload the HLC Research Protocol Template</td>
<td>Reliance eligible. Contact HLC Reliance Specialist Julie Chamberlin to discuss HLC reliance process.</td>
</tr>
<tr>
<td>Human Subjects Research Requiring Review by Convened IRB</td>
<td>Research activities not listed above; Research activities that pose greater than minimal risk to participants (e.g. Investigational studies on drugs, devices, biologics; Randomized clinical trials; Interventions; Research on alternatives to standard of care; Some vulnerable population research (e.g. undocumented persons))</td>
<td>Yes. Researchers must submit an application in ESTR for IRB review (irb.harvard.edu)</td>
<td>No, only the IRB has the authority to approve human subjects research.</td>
<td>Create an ESTR application; complete and upload the HLC Research Protocol Template</td>
<td>Reliance eligible. Contact HLC Reliance Specialist Julie Chamberlin to discuss HLC reliance process.</td>
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Glossary of Key Regulatory Definitions

- **Research** - a systematic investigation designed to develop or contribute to generalizable knowledge
- **Human subject** - a living individual about whom an investigator conducting research obtains:
  - Data through intervention or interaction with the individual, or
  - Identifiable private information
- **Intervention** - both physical procedures by which data are gathered (e.g. blood draw) and manipulations of the subject/subject's environment performed for research purposes
- **Interaction** - communication/contact between investigator and subject
- **Private information** - information about behavior that occurs in a context in which an individual can reasonably expect that no observation/recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (e.g. a medical record)
- **Minimal risk** - the probability and magnitude of harm/discomfort anticipated in the research are not greater than those ordinarily encountered in daily life or during the performance of routine physical/psychological exams or tests
<table>
<thead>
<tr>
<th>What the IRB Says</th>
<th>What the IRB Means</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anonymous</strong></td>
<td>Participant data and/or specimens obtained and stored without the collection of any identification that may link to a specific individual. Use of data/specimens that do not include any elements that could be used to identify an individual deductively.</td>
<td><em>Primary Collection:</em> A researcher surveys first-year students. They will not solicit, nor record, any identifiers, direct or indirect, as part of this research. <em>Secondary Use:</em> Population-level information (e.g., samples come from “patients with diabetes” or data includes aggregate procedure/ICD-10 codes collected on a statewide level).</td>
</tr>
<tr>
<td><strong>De-identified</strong></td>
<td>Participant data and/or specimens that may have been acquired from identified participants, but all identifiers or codes have been removed and destroyed. Use of data/specimens that have either been 1) completely stripped of identifiers and the provider has no residual information that could identify an individual or 2) an expert applies statistical/scientific principles to determine re-identification is very small.</td>
<td><em>Primary Collection:</em> A researcher collects email address on the final page of an online survey from participants who wish to be enrolled in a raffle. Those email address are kept separately from the research data and are deleted once the raffle is complete. <em>Secondary Use:</em> A researcher receives a data set that includes, along with other data, participant name, study ID, address, and medical record number. Upon receipt of the data set, they strip the data set of all of the above.</td>
</tr>
<tr>
<td><strong>Coded</strong></td>
<td>Participant data and/or specimens are labeled with a unique code (e.g., a number), rather than a person’s name or other direct identifier. The researcher has access to the coding system/crosswalk, which links individual participants to their unique code, either directly or given to them from the data/specimen provider. According to <a href="https://cdn1.sph.harvard.edu/wp-content/uploads/sites/2352/2022/05/HRP-103-HLC-Investigator-Manual.pdf#page=71">federal guidance</a>, coded data/specimens are considered identifiable when an investigator has access to the coding system/crosswalk.</td>
<td><em>Primary Collection:</em> A researcher collects data and assigns a 6-digit ID number to each participant. The researcher maintains a coding system that captures participant ID and name. <em>Secondary Use:</em> A researcher receives two datasets on parent-child dyads. The dyads are labeled with a code and the researcher receives the coding system to retain identifiable data linkages between dyads.</td>
</tr>
<tr>
<td><strong>Identifiable</strong></td>
<td>Participant data and/or specimens are directly identified with participant name or other personal identifier (e.g., phone number, SSN, address, email address, etc.)</td>
<td><em>Primary Collection:</em> A researcher surveys first-year students. They collect participant name, address, and telephone number on the survey. <em>Secondary Use:</em> A researcher receives blood samples from a biorepository in tubes labeled with individuals’ names and DOB.</td>
</tr>
</tbody>
</table>