The mission of this Institution’s Human Research protection program plan is to protect the rights and welfare of subjects involved in Human Research that is overseen by this Institution.
HRPP SCOPE

All research (whether funded or not, and regardless of funding source) involving human subjects conducted by investigators under the auspices of the University-Area Institutions.

- See HRP-101 HUA Human Research Protection Program Plan for specific categories of research overseen and not overseen
ETHICAL REQUIREMENTS

• Outlined in 1979 “Ethical Principles and Guidelines for the Protection of Human Subjects of Research,” also known as “The Belmont Report”

• Institutional baseline for all researchers, IRBs, and associated staff
THE BELMONT REPORT

• Respect for Persons
  • 1) Individuals should be treated as autonomous agents,
  • 2) Persons with diminished autonomy are entitled to protection.

• Beneficence
  ▪ 1) Protecting the individual subjects against risk of harm
  ▪ 2) Consideration of not only the benefits for the individual, but also the societal benefits that might be gained for research

• Justice
  • Who ought to receive the benefits of research and bear its burdens? This is a question of justice, in the sense of "fairness in distribution" or "what is deserved."
LEGAL REQUIREMENTS

- Ensure all Human Research undergoes review by designated IRB
- Apply Common Rule (45 CFR 46)
- Apply additional regulations of relevant federal funding agency
  - See HRP-318 WORKSHEET Additional Federal Agency Criteria
  - See HRP-103 Investigator Manual
- Apply FDA regulations when applicable
THE COMMON RULE
DOES MY PROJECT REQUIRE IRB REVIEW?
WHAT REQUIRES IRB REVIEW? / WHAT IS RESEARCH?

SYSTEMATIC INVESTIGATION

GENERALIZABLE KNOWLEDGE
WHAT REQUIRES IRB REVIEW?

A systematic investigation involves:

- Methodical procedure and plan
- Theoretically grounded
- Well-defined research question
- Informed by empirical findings
WHAT REQUIRES IRB REVIEW?

- Results applicable to population beyond data collection site or specific subjects studied

  and/or

- Results intended to be used to develop, test, or support theories, principles, and statements of relationships, or to inform policy beyond the study
NOT (REGULATED) RESEARCH

Additionally

• Case studies
• Journalism/documentary activities
• Oral history
• Standard public health surveillance or prevention activities
• Criminal justice investigations
• National intelligence/security missions
• Secondary use of non-identifiable newborn screening blood spots
DOES MY PROJECT REQUIRE IRB REVIEW?
HUMAN SUBJECTS RESEARCH

**Human Subject**

A living individual about whom an investigator:

- Uses information from intervention or interaction with the individual
- Uses private, identifiable information

OR
NOT HUMAN SUBJECTS RESEARCH

- Secondary analysis of publicly available data sets
- Secondary analysis of de-identified data sets stripped of all identifiable information
LEVELS OF REVIEW

WHO REVIEWS WHAT

CONVENED IRB/FULL BOARD
Review approx. 5% of studies
• Greater than Minimal Risk
• Unknown Risk
• Does not fit into Expedited or Exempt regulatory category

STAFF MEMBERS (WHO ARE ALTERNATE IRB MEMBERS)
Review approx. 95% of studies
• Expedited Approvals
• Exempt Determinations
• Not Engaged Determinations
• Not Human Subjects Research Determinations
• Not Research Determinations
**WHAT’S THE DIFFERENCE?**

<table>
<thead>
<tr>
<th>Research Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not Human Subjects Research Determination</td>
<td>Research does not fit the regulatory definition for research with human subjects. The determination can be made by the investigator or through review by IRB staff. See <a href="#">HRP-310 WORKSHEET Human Research Determination</a>.</td>
</tr>
<tr>
<td>Exempt Determination</td>
<td>The project is human subjects research and fits one of the 8 Exempt categories in the regulations. The determination of Exemption is made by the IRB staff. See <a href="#">HRP-312 WORKSHEET Exemption</a>.</td>
</tr>
<tr>
<td>Expedited Approval</td>
<td>The project is human subjects research that is minimal risk and fits one of the 9 Expedited categories in the regulations. For most categories, the determination is made by IRB staff on behalf of the HUA IRB, acting in their capacity as Alternate IRB members. See <a href="#">HRP-313 WORKSHEET Expedited Review</a>.</td>
</tr>
<tr>
<td>Convened IRB/Full Board Review</td>
<td>Research that may be more than minimal risk, does not fit in one of the regulatory categories, or for any reason the IRB staff believe it must be reviewed by the Convened IRB.</td>
</tr>
</tbody>
</table>

For more information, explore the stages of [IRB Lifecycle](#) at cuhs.harvard.edu
CONVENED IRB AND CRITERIA FOR APPROVAL
BEFORE THE MEETING

1. ASSESS
2. READ
3. ASK
IRB MEMBER HANDBOOK TIP

1. **Read the consent document first:** The consent document should be in **lay language** and therefore should provide a good introduction to the research.
   - Can you clearly describe the study after reading the Consent Form?
   - Then read it again for readability (6th—8th grade level)

2. **Read the protocol:** Although the language may differ, the narrative and the consent form should be **consistent** in the description of the purpose, procedures, timeframe, risks and benefits, compensation and costs, confidentiality of data, etc.
FULL BOARD REVIEW ACTIONS

- Approved
- Modifications Required to Secure Approval
- Deferred
- Tabled
- Disapproved
FULL BOARD REVIEW ACTIONS

**Modifications Required to Secure Approval**
- Meets Criteria for Approval
  - (HRP-314 WORKSHEET)

**Deferral**
- May meet Criteria for Approval
  - (HRP-314 WORKSHEET)

**Disapproval**
- Does not meet Criteria for Approval
  - (HRP-314 WORKSHEET)
  - *Violation of Belmont Report*

For more information see **HRP-103 HUA Investigator Manual** and “Before You Begin to Prepare Your IRB Application” in the **IRB Lifecycle** at cuhs.harvard.edu
CRITERIA FOR APPROVAL

- Risks to subjects are minimized
- Risks are reasonable in relation to benefits
- Selection of subjects is equitable
- Adequate provisions for monitoring data, ensuring its confidentiality and the safety of subjects
- Adequate provisions for privacy
- Safeguards for any vulnerable populations
**MINIMAL RISK** means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.
RISK DOES NOT ONLY MEAN PHYSICAL RISK
PROTECTED POPULATIONS

PRISONERS (Subpart C)

CHILDREN (Subpart D)

PREGNANT WOMEN (Subpart B)
In addition to protected populations:
- Economically disadvantaged
- Cognitively impaired
- Low literacy
- LGBTQ+
- Racial/ethnic minorities
- Students/employees of investigator
- Undocumented status, refugees
CRITERIA FOR APPROVAL

- Informed consent is obtained
  - Information
  - Comprehension
  - Voluntary agreement
- Informed consent is documented
INFORMED CONSENT: ELEMENTS OF CONSENT

- The study involves research
- Purpose and procedures, including duration
- Risks/ discomforts and benefits
- Confidentiality provisions
- Participation is voluntary
- No penalty or loss of benefits if do not participate or withdraw
- Future use of participant data
- Contact information

See HRP-314 WORKSHEET Criteria for Approval for additional DHHS elements as well as FDA and clinical trial requirements
INFORMED CONSENT

- Informed consent requirements may be altered or waived
- Most commonly for...
  - *Deception*: active misinformation
  - *Incomplete disclosure*: withholding specific details
- May omit purpose and/or procedures or waive fully
  - IF required of the research design *(practicability)*
  - IF rights and welfare are otherwise protected
  - IF no more than minimal risk
FULL BOARD REVIEW ACTIONS

**Modifications Required to Secure Approval**
- Identify prescriptive actions
- No risk or regulatory considerations remain outstanding

**Deferral**
- Ask open-ended questions
- Seek info on risk, regulatory considerations
- Provide suggestions

**Disapproval**
- Explain violation of Belmont Report
- Provide suggestions…to a point
- Opportunity for appeal

For more information see HRP-103 HUA Investigator Manual and “Before You Begin to Prepare Your IRB Application” in the IRB Lifecycle at cuhs.harvard.edu
ADDITIONAL CONSIDERATIONS
INTERNATIONAL RESEARCH

• Additional institutional review
• Additional ethical reviews/permissions may be needed
• Local context
HRP-027
CERTIFICATE OF CONFIDENTIALITY

AUTOMATICALLY ISSUED

REQUESTED
AUTOMATICALLY ISSUED

• **NIH CoC Policy** applies to research:
  • Funded or supported by NIH,
  • Using identifiable, sensitive information, and
  • Active after December 13, 2016

• CoC automatically granted in **terms** of award

• PI and IRB confirm that Policy applies

• Protocol and **consent** must reflect awarded CoC
  • Includes ongoing studies commenced before Policy
• Non-NIH funded studies

**PI requested:**
• Needs to notify IRB of status of request
• Protocol/consent need to reflect CoC

**IRB requested:**
• IRB determines CoC needed to protect privacy and confidentiality
• Protocol/consent need to reflect CoC
HEALTH INSURANCE PORTABILITY AND ACCOUNTABILITY ACT (HIPAA)

• Establishes national standards for protection of health information (PHI)
• Applies to covered entities (e.g., providers with electronic records)
• Harvard University Health Services and Harvard School of Dental Medicine are covered entities

FAMILY EDUCATIONAL RIGHTS AND PRIVACY ACT (FERPA)

• Research with identifiable student education records
• Access requires written parent permission (for minors) or from the adult student unless exceptions met
• No defined role for IRB; advises as needed

For more information see HRP-103 HUA Investigator Manual, HRP-330 WORKSHEET HIPAA Authorization, and HRP-331 WORKSHEET FERPA Compliance
ADDITIONAL CONSIDERATIONS

HARVARD RESEARCH DATA SECURITY POLICY (HRDSP)

The IRB’s responsibility is to **assign a level of sensitivity** (Non-Sensitive or Sensitive) based data collected/used in the research and described in the IRB application.

FDA REGULATIONS

**_DEVICES** and **DRUGS**

Clinical investigation means any experiment that involves a **test article** and one or more **human subjects**, and that either must meet the requirements for prior submission to the FDA or the results of which are intended to be later submitted to, or held for inspection by, the FDA as part of an application for a research or marketing permit.

For more information see [HRP-309 WORKSHEET HUA Harvard Policies](#), [HRP-335 WORKSHEET Provost Review](#), and [HRP-336 WORKSHEET Harvard Research Data Security Level Decision Aid](#).
RESOURCES
CUHS WEBSITE
(CUHS.HARVARD.EDU)

Not sure where to start or what to do? Check out our new IRB Lifecycle Guide located on our homepage banner.
ESTR WEBSITE (IRB.HARVARD.EDU)
ESSENTIAL READING

HUMAN RESEARCH PROTECTION PROGRAM PLAN

• HRP-101 (ESTR Library → General)

• The purpose of this plan is to describe this Institution’s plan to comply with ethical and legal requirements for the conduct and oversight of Human Research.

• The Human Research Protection Program is based on all individuals in this Institution along with key individuals and committees fulfilling their roles and responsibilities described in this plan.

INVESTIGATOR MANUAL

• HRP-103 (ESTR Library → General)

• The Investigator Manual is designed to guide investigators and study staff through policies and procedures related to the conduct of Human Research that are specific to the Harvard University Area (HUA) IRB office.

• General information regarding Human Research protections, as well as relevant federal regulations and guidance, has been incorporated throughout the manual where applicable.
BONUS: REPORTING AND MANAGEMENT OF CONCERNS
Questions, concerns, complaints, allegations of undue influence, allegations or findings of non-compliance, or input regarding the HRPP may be reported orally or in writing.

The IRB has the responsibility to investigate allegations and findings of non-compliance and take corrective actions.

The IO/OO has the responsibility to investigate all other reports and take corrective actions.

**UPIRTSO**: Unanticipated Problem Involving Risks to Subjects or Others

Report within **5 days**
REPORTING AND MANAGEMENT OF CONCERNS

• Contact the IRB office with questions (cuhs@harvard.edu)

• Submit Report of New Information (RNI) in ESTR

• Contact the IO/OO

Ara Tahmassian, Ph.D.
(ara_tahmassian@harvard.edu)
REPORTING AND MANAGEMENT OF CONCERNS

For more on reporting see:

• HRP-101 HUA Human Research Protection Program Plan
• HRP-103 HUA Investigator Manual
• HRP-321 WORKSHEET Review of Information Items
• “Researcher Responsibilities After Review” in the IRB Lifecycle at cuhs.harvard.edu
BONUS: CONFLICT OF INTEREST
CONFLICT OF INTEREST

- **Financial** or other personal considerations compromise, or have the appearance of compromising, an individual's professional judgment in proposing, conducting, supervising or reporting research
- Anything that may **bias scientific objectivity**
- **Examples:**
  - Consulting relationship with research sponsor
  - Intellectual property interests in the research
  - Equity interests in the research
The IRB requires that all individuals involved in the design, conduct, or reporting of the research report financial interests related to the research. See:

- **HRP-221** FORM Financial Interest Disclosure
- **HRP-309** WORKSHEET HUA Harvard Policies
Each School’s policy is outlined in a School Implementation Plan

Individuals have institutional responsibility and are subject to this procedure when they have fCOI

Violations can lead to:
- Loss or restriction of privileges to conduct Human Research
- Other employment actions

Related records to be retained for at least 3 years from completion of Human Research
IRB PROCEDURES

Step 1
Obtain HRP-221 FORM
Financial Interest Disclosure

Step 2
Trigger Ancillary Review process to the School fCOI Officer in ESTR

Step 3
Obtain fCOI approval and written management plan; coordinate any necessary revisions with School fCOI Officer

Step 4
Maintain a copy of determinations and management plans in the ESTR study record.