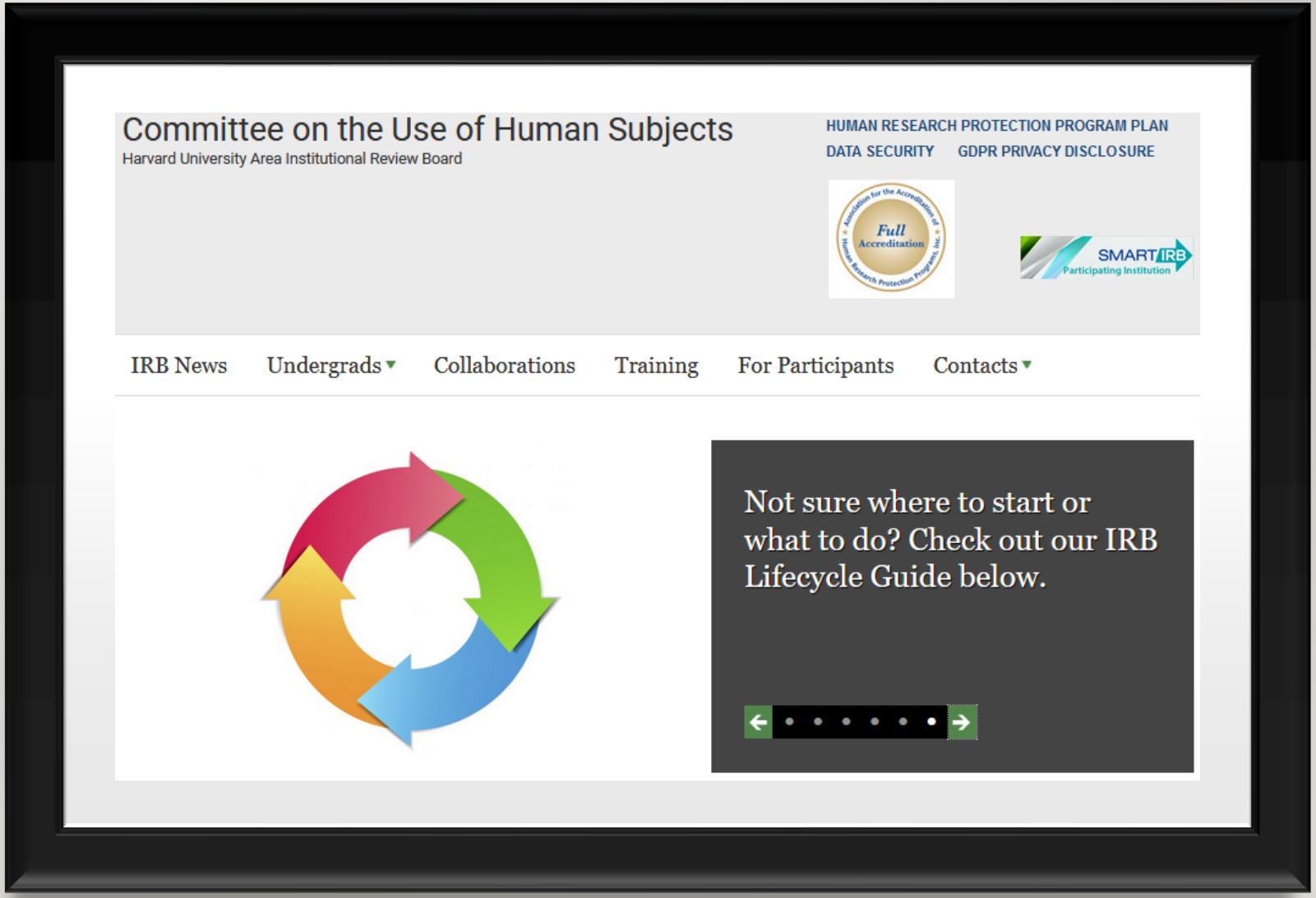
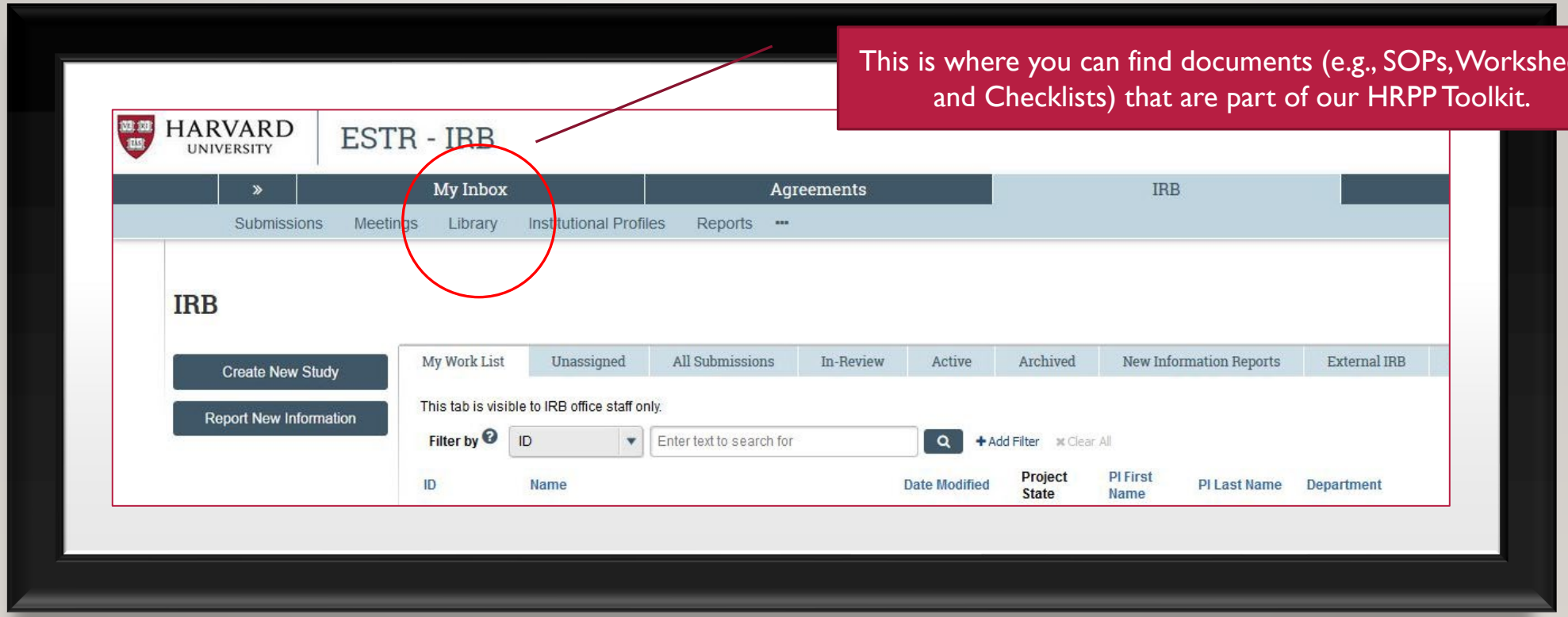
HUA HUMAN RESEARCH PROTECTION PROGRAM

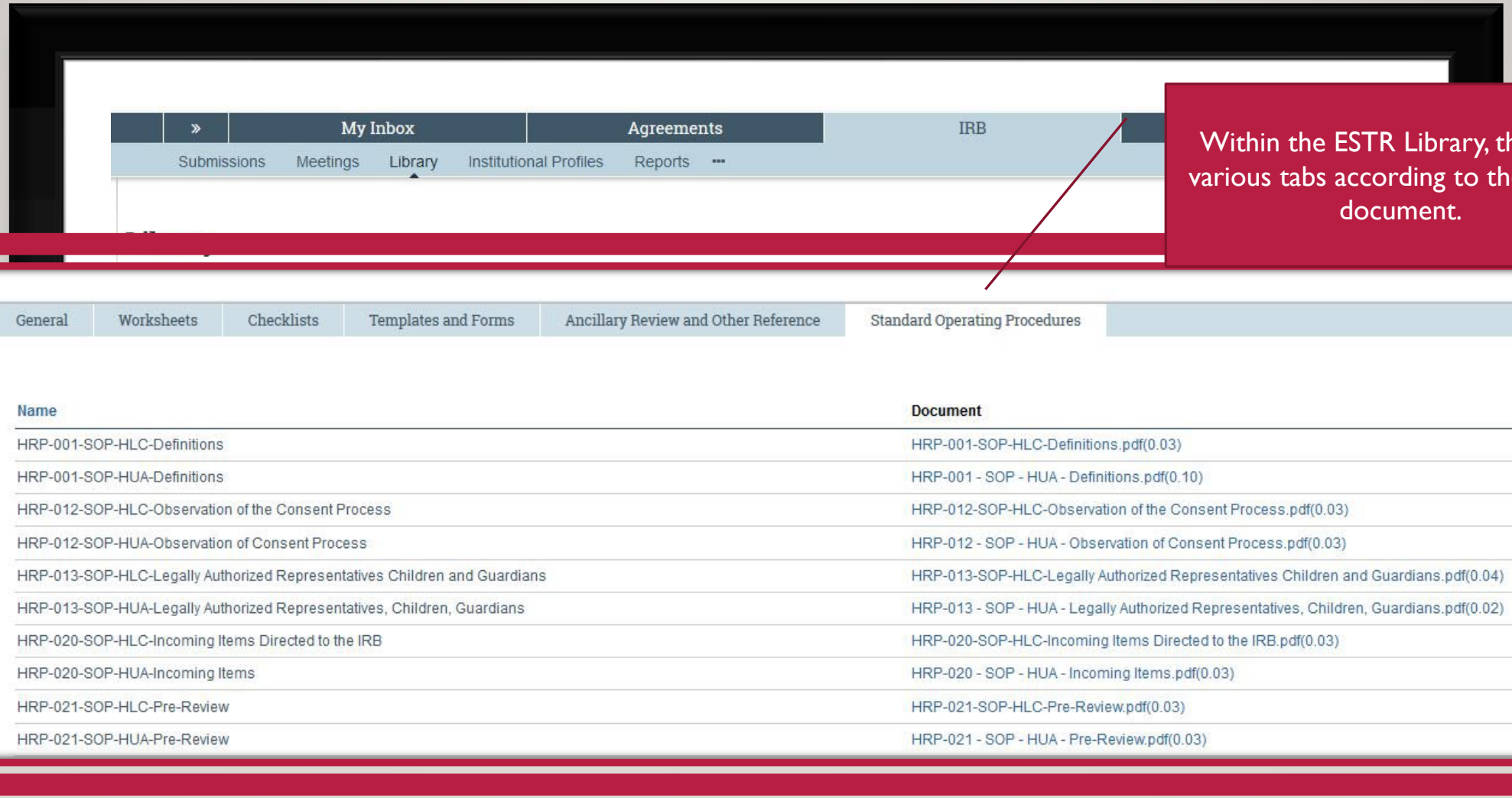
RESOURCES

CUHS WEBSITE (CUHS.HARVARD.EDU)





ESTR WEBSITE (IRB.HARVARD.EDU)


»
My Inbox
Agreements
IRB
Submissions
Meetings
Library
Institutional Profiles
Reports
Within the ESTR Library, there are various tabs according to the type of document.
General
Worksheets
Checklists
Templates and Forms
Ancillary Review and Other Reference
Standard Operating Procedures
Name
Document
HRP-001-SOP-HLC-Definitions
HRP-001-SOP-HLC-Definitions.pdf(0.03)
HRP-001-SOP-HUA-Definitions
HRP-001 - SOP - HUA - Definitions.pdf(0.10)
HRP-012-SOP-HLC-Observation of the Consent Process
HRP-012-SOP-HLC-Observation of the Consent Process.pdf(0.03)
HRP-012-SOP-HUA-Observation of Consent Process
HRP-012 - SOP - HUA - Observation of Consent Process.pdf(0.03)
HRP-013-SOP-HLC-Legally Authorized Representatives Children and Guardians
HRP-013-SOP-HLC-Legally Authorized Representatives Children and Guardians.pdf(0.04)
HRP-013-SOP-HUA-Legally Authorized Representatives, Children, Guardians
HRP-013 - SOP - HUA - Legally Authorized Representatives, Children, Guardians.pdf(0.02)
HRP-020-SOP-HLC-Incoming Items Directed to the IRB
HRP-020-SOP-HLC-Incoming Items Directed to the IRB.pdf(0.03)
HRP-020-SOP-HUA-Incoming Items
HRP-020 - SOP - HUA - Incoming Items.pdf(0.03)
HRP-021-SOP-HLC-Pre-Review
HRP-021-SOP-HLC-Pre-Review.pdf(0.03)
HRP-021-SOP-HUA-Pre-Review
HRP-021 - SOP - HUA - Pre-Review.pdf(0.03)

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.

HUMAN RESEARCH PROTECTION PROGRAM (HRPP) PLAN

HRPP MISSION

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

KEY PLAYERS IN HRPP PLAN

ALL MEMBERS OF THE INSTITUTION

- INSTITUTIONAL OFFICIAL (IO)/ ORGANIZATIONAL OFFICIAL (OO)
- HUA IRB/CUHS
- INVESTIGATORS AND RESEARCH STAFF
- OFFICE OF GENERAL COUNSEL (OGC)
- OFFICE FOR SPONSORED PROGRAMS (OSP)
- OFFICERS/DEANS

ALL MEMBERS OF THE INSTITUTION

- All individuals within the Institution have the responsibility to:
  - Be aware of the **definition of Human Research**.
  - **Consult the IRB** when there is uncertainty about whether an activity is Human Research.
  - Not conduct Human Research or allow Human Research to be conducted without **review and approval** by an IRB designated by the IO/OO.
  - **Report** allegations of undue influence regarding the oversight of the Human Research Protection Program or concerns about the Human Research Protection Program to the IO/OO.
  - **Report** allegations or finding of non-compliance with the requirements of the Human Research Protection Program to the IRB.

INSTITUTIONAL OFFICIAL/ORGANIZATIONAL OFFICIAL

AUTHORITY OVER

- IRB budget
- IRB membership and staffing
- Reliance agreements
- PI restrictions
- Suspend, terminate, disapprove research

NOTE: May delegate these authorities (generally to IRB Director)

OVERALL RESPONSIBILITY FOR

- IRB reviews conducted by HRPP
- HRPP policies/procedures
- HRPP training initiatives
- Independence of IRB from Institution
- Report of complaints/concerns about research, as well as from IRB Chairs and Members
- Signatory of the Federalwide Assurance (FWA)

See **HRP-101** HUA Human Research Protection Program Plan for more information on the IO/OO

WHAT IS AN IRB?

- An **I**nstitutional **R**eview **B**oard is responsible for reviewing all research that involves human subjects
- Enforce the Federal Regulations for the Protection of Human Subjects and other state and local regulations as they apply
- IRBs have the authority to approve, disapprove, suspend, and terminate research involving human subjects

INSTITUTIONAL REVIEW BOARD (IRB)

- Panel of individuals from various backgrounds:
  - Regulatory experts, scientists, faculty
  - Diverse in race, gender, cultural background, etc.
  - At least one:
    - Prisoner representative
    - Non-affiliated community member
- Harvard University-Area IRB/ Committee on the Use of Human Subjects (**CUHS**)
- Meets once per month

HARVARD UNIVERSITY AREA ("INSTITUTION")

- Faculty of Arts and Sciences
- John F. Kennedy School of Government
- Harvard Graduate School of Education
- Harvard Law School
- Harvard Divinity School
- Harvard Graduate School of Design
- Harvard University Health Services
- Radcliffe Institute for Advanced Study
- Harvard School of Engineering and Applied Sciences
- Harvard Business School

PRINCIPAL INVESTIGATOR RESPONSIBILITIES

- Follow the Human Research Protection Program requirements described in **HRP-103** Investigator Manual
- Comply with all determinations and additional requirements of the IRB, IRB chair, and IO/OO

PRINCIPAL INVESTIGATOR RESPONSIBILITIES

Secure IRB approval prior to implementation

Conduct study according to IRB approved protocol

Submit Continuing Review, Modifications to IRB as required

Ensure adequate facilitates, equipment on site

Ensure study staff are qualified

Report new information

STUDY STAFF RESPONSIBILITIES

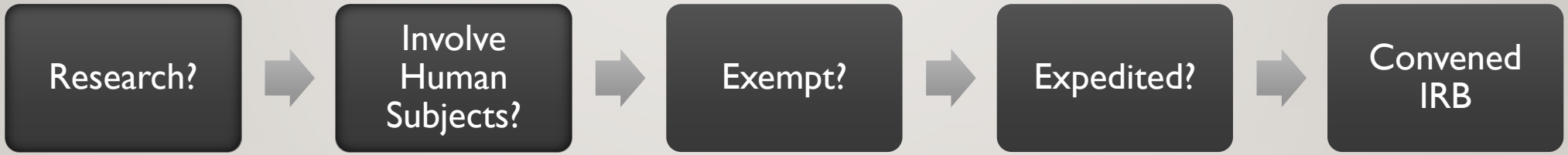
HUMAN SUBJECTS TRAINING

CONDUCT STUDY ACCORDING TO IRB APPROVED PROTOCOL

REPORT ANY DISCREPANCIES/ISSUES/SUBJECT COMPLAINTS TO SUPERVISOR/PI AND THE IRB

NOTE: **CITI** training is the most used human subjects training. Training last **3 years**.
More information on training options may be found at: https://cuhs.harvard.edu/required-ethics-training

DOES MY PROJECT REQUIRE IRB REVIEW? 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

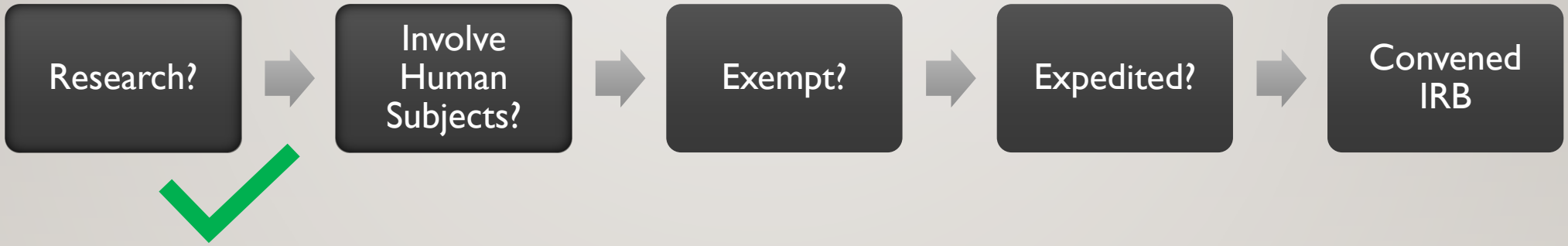
  and/or

- 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:

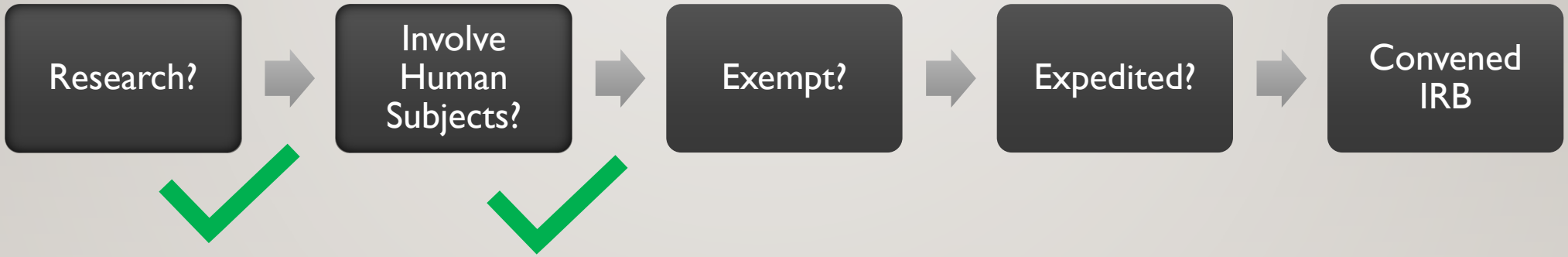
Uses information from intervention or interaction with the individual

OR

Uses private, identifiable information

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

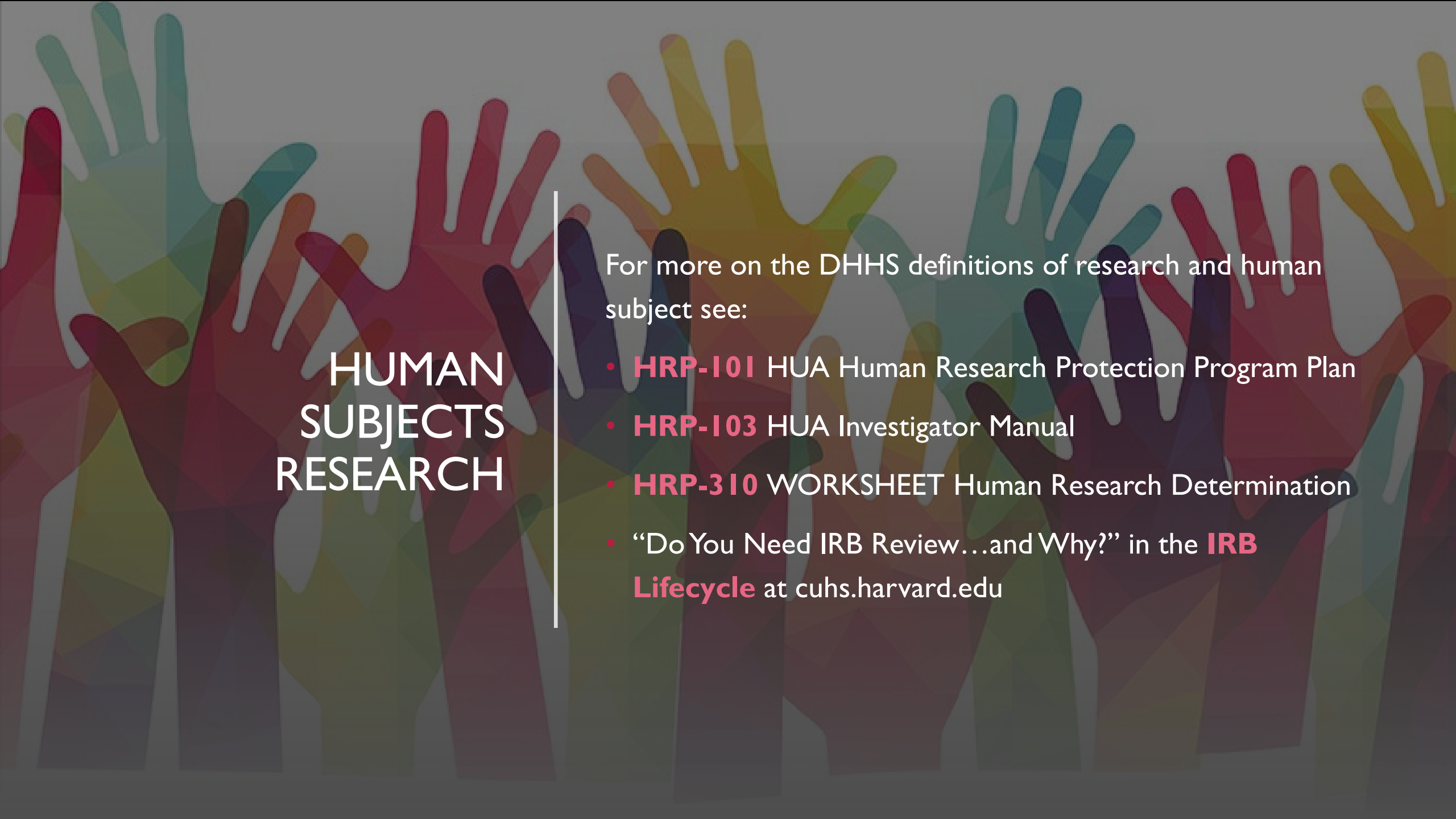
Review approx. 5% of studies

- *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*



HUMAN SUBJECTS RESEARCH

For more on the DHHS definitions of research and human subject see:

- **HRP-101** HUA Human Research Protection Program Plan
- **HRP-103** HUA Investigator Manual
- **HRP-310** WORKSHEET Human Research Determination
- "Do You Need IRB Review…and Why?" in the **IRB Lifecycle** at cuhs.harvard.edu

REPORTING AND MANAGEMENT OF CONCERNS

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**

+RISKS

+HARMS

WHEN
UPIRTSO?

NON-COMPLIANCE

AUDIT

WHEN UPIRTSO?

STUDY MONITOR

PROTOCOL NONADHERENCE

WHEN UPIRTSO?

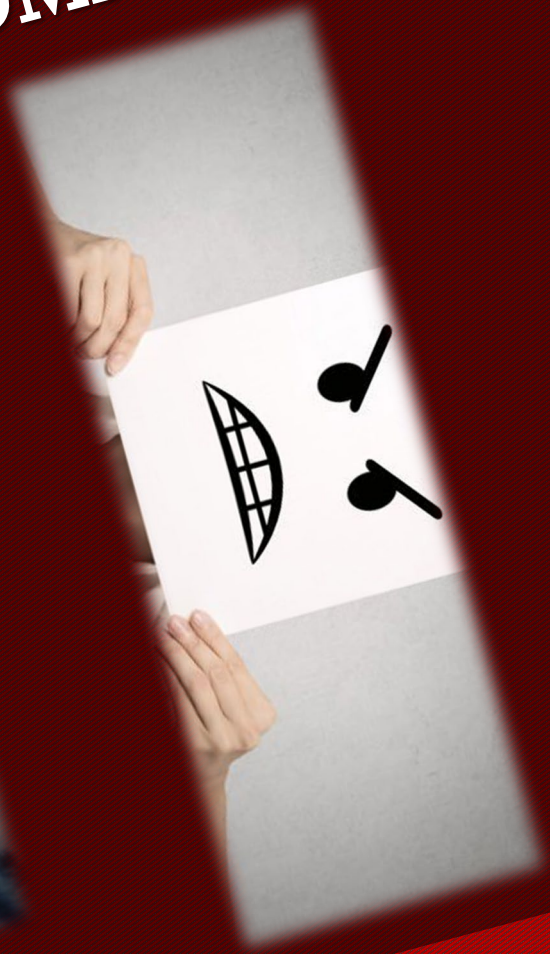
BREACH

ELIMINATE HAZARD

WHEN UPIRTSO?

INCARCERATION

COMPLAINT



WHEN UPIRTSO?

WHEN UPIRTSO?

SUSPENSION/ TERMINATION

ADVERSE DEVICE

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)

IRB DETERMINES

- Not noncompliance or an unanticipated problem
- Minor noncompliance: Noncompliance that is neither serious nor continuing
- An unanticipated problem involving risks to subjects or others
- Serious or continuing non-compliance with the regulations or the requirements or determinations of the IRB
- Necessitates suspension or termination of IRB approval

IRB DETERMINES

Potential Corrective Actions

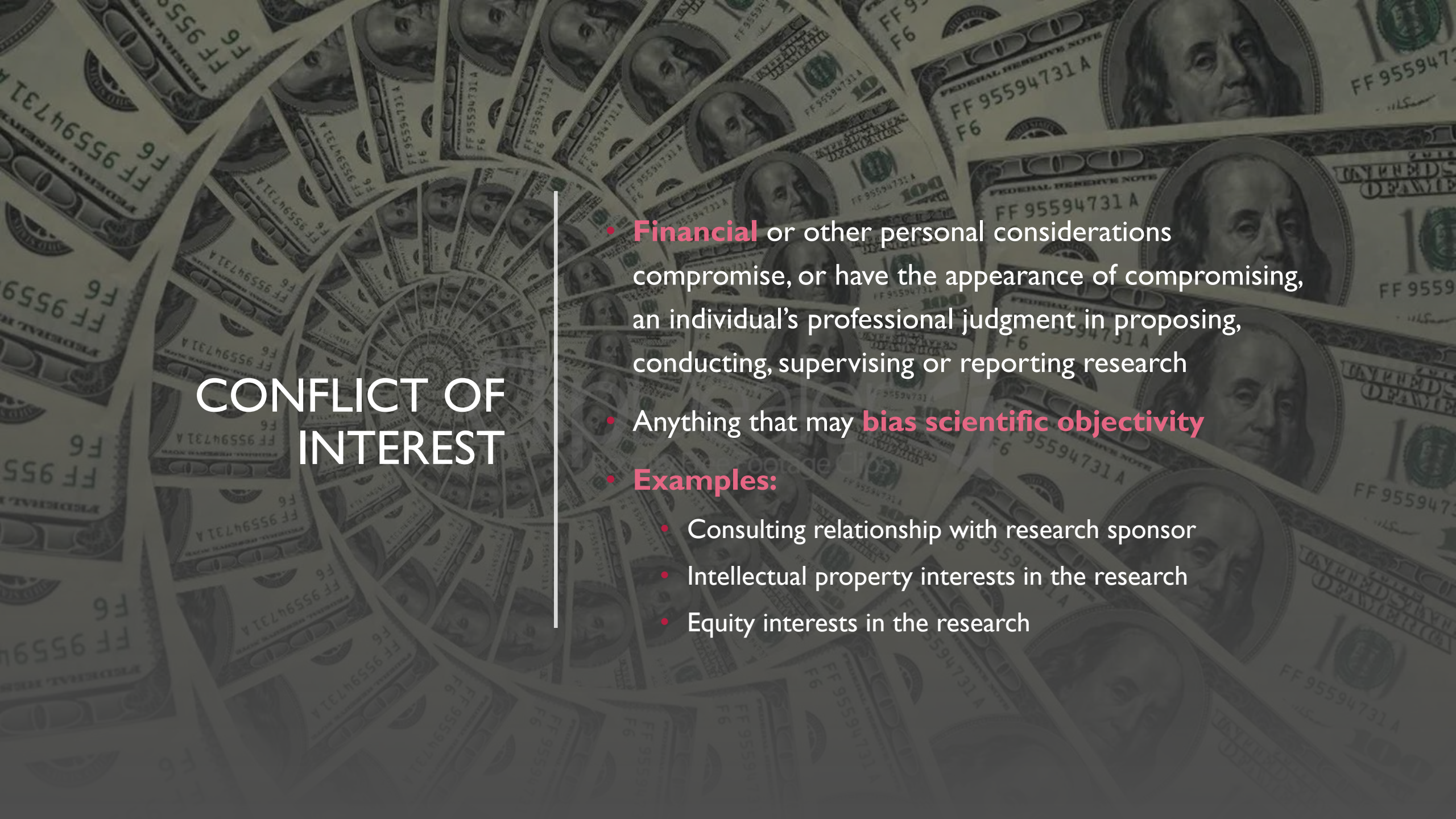
- Modify protocol or consent process
- Give additional info to participants
- Observation by IRB and/or monitor
- Request PI receive training
- Notify other relevant parties
- Transfer, suspend, or terminate study

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

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

FINANCIAL CONFLICT OF INTEREST

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-450** CHECKLIST fCOI Determination
- **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

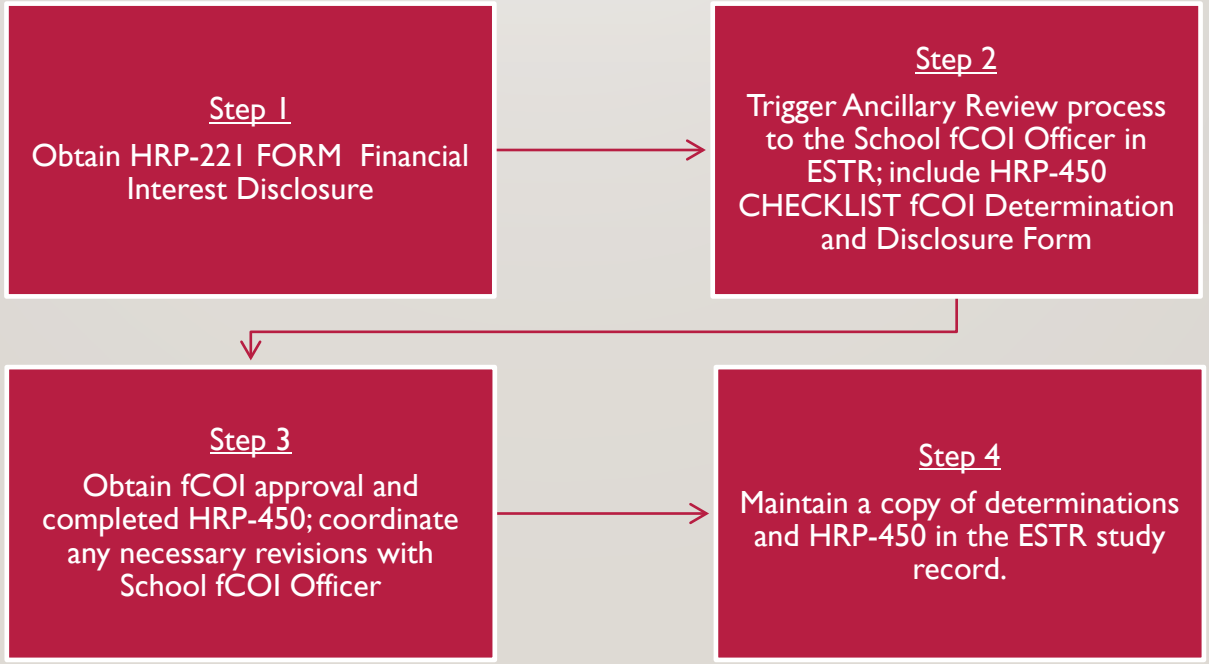
Harvard fCOI

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



BONUS: HRPP KEY PLAYERS

OGC RESPONSIBILITIES

- Provide **advice** upon request
- Determine whether someone is acting as an **agent**
- Determine who meets the definition of "**legally authorized representative**" and "**children**" when Human Research is conducted in jurisdictions not covered by policies and procedures
- **Resolve conflicts** among applicable laws
- Institutional adherence to EEA General Data Protection Regulations (**GDPR**)

OSP RESPONSIBILITIES

OSP has the responsibility to **review contracts** and **funding agreements** for compliance with Human Research Protection Program policies and procedures

OFFICERS/DEANS

Oversee	Forward	Ensure
Oversee the review and conduct studies in their department or school	Forward complaints and allegations to IRB or IO/OO	Ensure studies conducted in their department or school has adequate resources

BONUS:
CRITERIA FOR APPROVAL

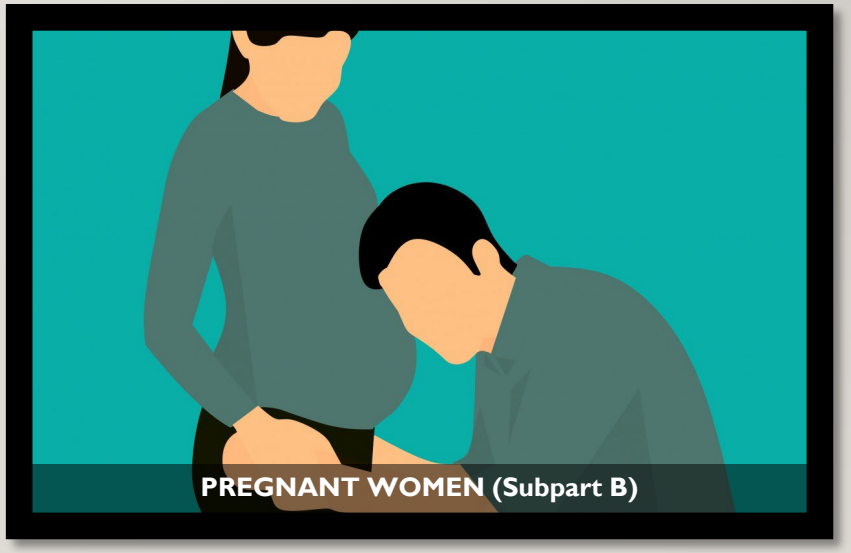
CRITERIA FOR APPROVAL

- 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

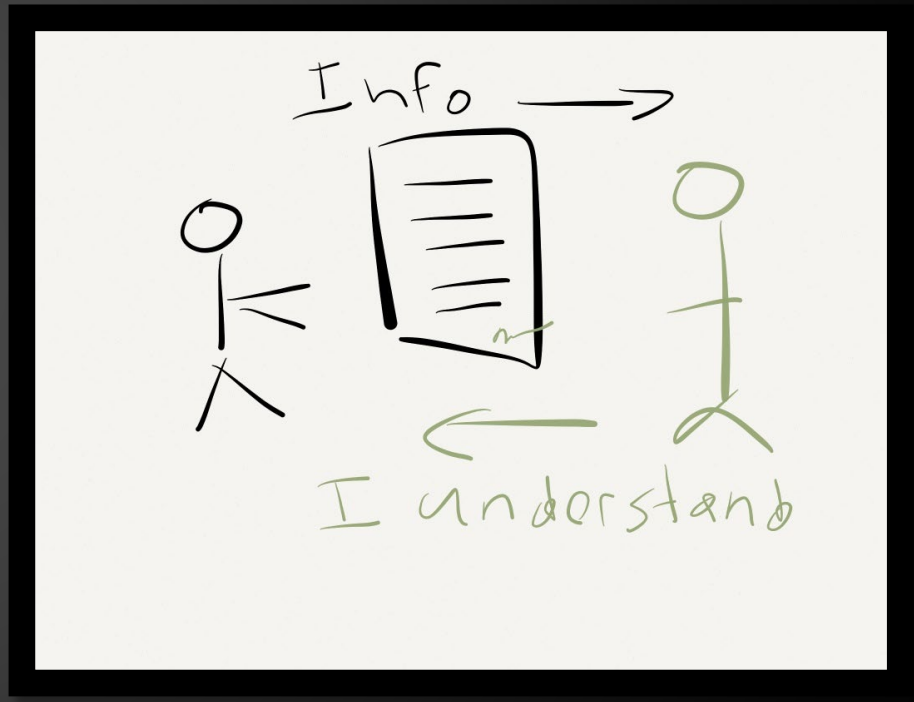


POTENTIALLY VULNERABLE POPULATIONS

- 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

- Informed consent – a process
- Participants must understand
  - purpose
  - procedures
  - risks and benefits
- Agreement to participate must be voluntary
  - Free of coercion or undue influence
- Consent process begins with recruitment

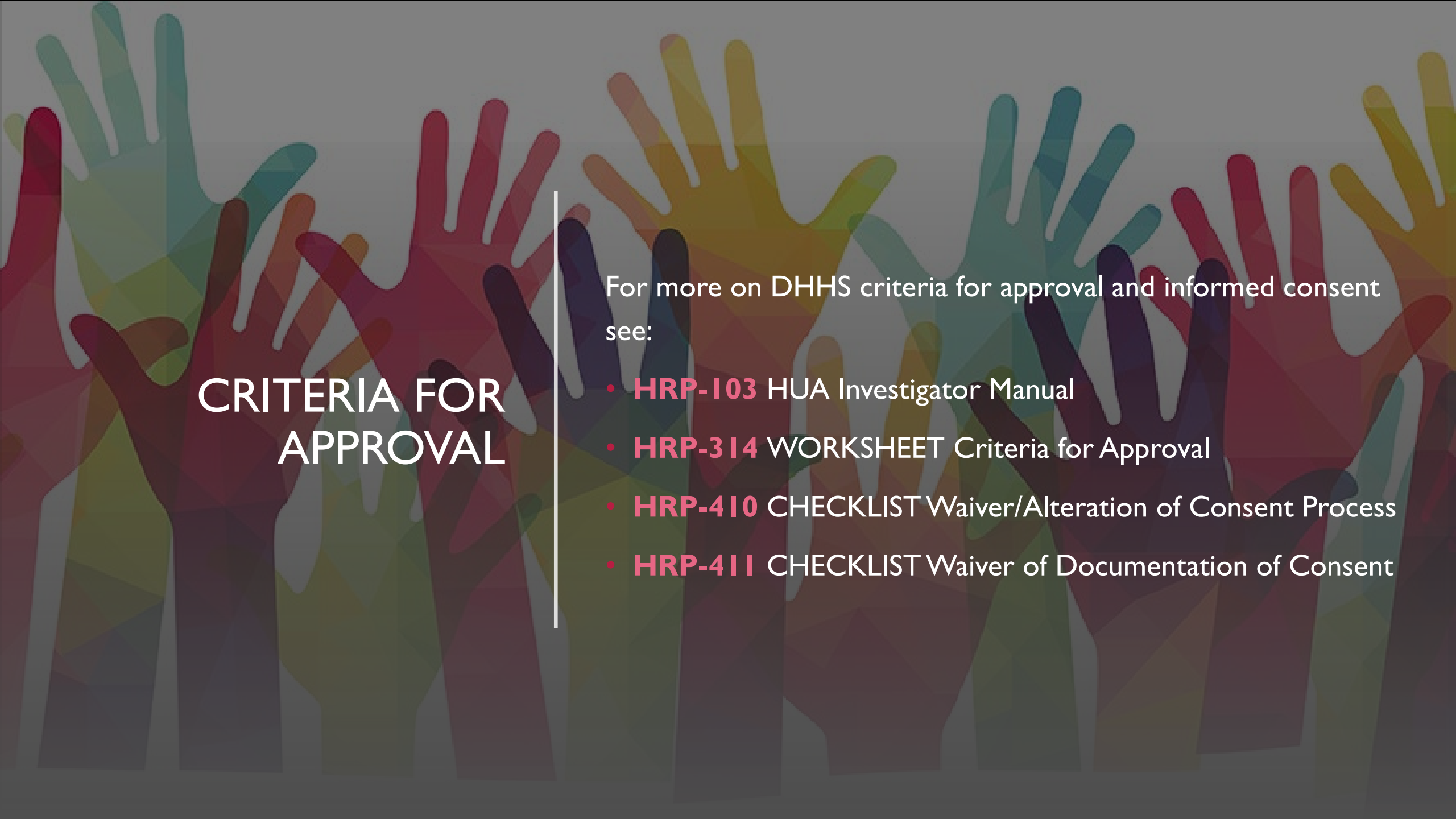
INFORMED CONSENT: ELEMENTS OF CONSENT

- 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



CRITERIA FOR APPROVAL

For more on DHHS criteria for approval and informed consent see:

- **HRP-103** HUA Investigator Manual
- **HRP-314** WORKSHEET Criteria for Approval
- **HRP-410** CHECKLIST Waiver/Alteration of Consent Process
- **HRP-411** CHECKLIST Waiver of Documentation of Consent

BONUS: ADDITIONAL CONSIDERATIONS

ADDITIONAL REGULATORY CONSIDERATIONS

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 POLICY 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

PROVOSTIAL REVIEW

- For research studies that may pose management challenges and/or reputational risk
- Separate and distinct from IRB review
- Most often **Expedited review and take place in a foreign country** or studies that may cause a reputational risk to the university

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