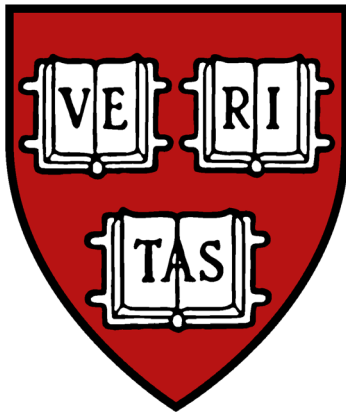




Harvard University Area Institutional Review Board
Member Handbook



HARVARD UNIVERSITY
Office of the Vice Provost for Research
Harvard University-Area Institutional Review Board

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Thank you for serving on the Harvard University Area Institutional Review Board

The Harvard University Area IRB aims to promote a culture of compliance and to establish across the University the highest expectations for performance and oversight of research involving human subjects. The Harvard University Area IRB is also committed to education of the Harvard research community and outreach to collaborating institutions.

The mission of the IRB is to assure that all participants are protected from any unnecessary risk when enrolled in a research study; that they can make an informed decision to participate, and when possible, that participant and/or society at large benefits from the knowledge gained from the research study. The goal of the IRB is to assist Investigators in developing appropriate research protocols in accordance with federal, and University policies, and within accepted ethical guidelines.

All Human Subjects Research conducted by Harvard University investigators, regardless of source of funding or location of the research, is guided by the ethical principles of respect for persons, beneficence, and justice, as set forth in the April 18, 1979 report of The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research entitled *Ethical Principles and Guidelines for the Protection of Human Subjects of Research*, also known as “The Belmont Report.”

IRB Membership and Meeting Information

Membership: The IRB is made up of members in the disciplines of research typically reviewed. In accordance with 45 CFR § 46.107, each IRB is comprised of at least five members, with at least one member who is *not* affiliated with Harvard University (either directly or through an immediate family member); at least one member whose “primary concern” is in a scientific area, and at least one member whose “primary concerns” are in a non-scientific area and who must be present at each meeting.

Meetings: Convened meetings of the IRB occurs the third Thursday of each month. The IRB may hold interim review sessions, called by the Chair at the request of any IRB member or Institutional Official, to consider matters regarding the rights and welfare of any participant, or participant population.

Responsibilities of IRB Members

Expectations of IRB Members: IRB members attend the monthly IRB meeting and prepare for these meetings by reading the materials sent to them a week in advance. IRB members must be knowledgeable about federal human research regulations and familiar with standards of professional conduct and practice. IRB members participate in study discussions, voicing any concerns they may have with the study under review, vote on protocols, and recuse themselves in the event that they have a conflict of interest (either financial, personal or professional) with the research under review.

IRB members are expected to maintain confidentiality about IRB deliberations and discussions, with the IRB chair and staff acting as the conduits of information to Investigators. IRB should disclose the content of deliberations or discussions only to University and school officials who have responsibility for IRB activities or related compliance obligations, or otherwise as required by law. The purpose of confidentiality in IRB deliberations and discussions is to encourage IRB members to offer their frank opinions to one another.

IRB Member Conflict of Interest: At the beginning of each IRB meeting, the Chair asks the IRB if any members have a conflict of interest (professional, financial, or personal) with the particular research study under review that might influence his/her evaluation and thus might jeopardize the rights and welfare of the research participants or the credibility of the IRB. IRB members and consultants also have a conflicting interest when their spouse, partner, or relative has a professional or financial conflict of interest. All IRB members with a potential conflict identify themselves and the nature of the conflict. IRB members with conflicts may provide additional information about the project; however they may not be present for the vote. Consultants and ad hoc members must disclose any potential conflicts. Any conflict revealed at the meeting is documented in the minutes and the IRB members who recuse themselves are not counted towards the quorum for that particular vote.

IRB Member Indemnification: IRB staff and members are agents of the University. Thus, they ordinarily will be indemnified by the University in the event of lawsuits against them based on their involvement with the IRB actions as IRB members, provided of course that they were acting within the scope of their duties and in good faith. Indemnification means that the University will defend a lawsuit (incurring all legal fees and other expenses) and pay any judgment or settlement.

How to Review an IRB Protocol

Per federal regulations, 45 CFR Part 46.111 (DHHS) and 21 CFR Part 56.111 (FDA), in order to approve research, the IRB must determine that all of the following requirements are satisfied:

- Risks to subjects are minimized:
 - by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and
 - whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.
- Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result.
 - In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research).
 - The IRB should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.
- Selection of subjects is equitable.
 - In making this assessment the IRB should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons.
- Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by 45CFR Part 46.116.
- Informed consent will be appropriately documented, in accordance with, and to the extent required by 45 CFR Part 46.117.
- When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.
- When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.
- When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects.

➤ **See HRP-314-WORKSHEET-Criteria for Approval**

Before the Full Committee Meeting:

- Read the assigned materials at least 2-3 days in advance of the meeting. The HUA IRB utilizes a primary reviewer system; therefore, if you are assigned as either the primary or secondary

reviewer it is your responsibility to thoroughly review the IRB application materials in ESTR in advance of the meeting.

- Get all questions answered before the meeting. IRB Members are not expected to be the absolute experts about the protocols they are assigned to review. Talk with others as needed.

Feel free to contact the:

- IRB Chair
- Co- reviewer
- Informal Consultant* (e.g., colleague w/ expertise)
- HUA IRB Staff

Furthermore, do not hesitate to contact the Lead Researcher if you have questions. Collegial interaction between researchers and IRB members facilitates the IRB review process and research compliance as well as fosters respect for human subjects protection.

- Contact the IRB Chair and Administrator if you have serious concerns about the protocol.
- Write comments and recommendations on the Reviewer's checklist and be prepared to present them to the Committee.
- Be organized (bring packet materials to the meeting).

** Informal verbal consultation is encouraged. However, IRB members must uphold the Members Standards by maintaining all committee proceedings and documents that contain personal, confidential and proprietary information in strict confidence. Such information may not be used for any purpose other than the IRB review and may not be disclosed to anyone outside of the IRB.*

The process of reviewing an IRB protocol:

1. Read the consent document first. The consent document should be in lay language and therefore, should provide a good introduction to the research.
 - First read the consent form for general information about the study;
 - Can you clearly describe the study after reading the Consent Form?
 - For studies involving medical treatments, can you distinguish standard-of-care from research procedures?
 - Then read it again for readability (6th—8th grade level);
 - Did it seem easy, or did you have to re-read it for understanding?
 - Can a junior-high school student explain the study after reading the consent form?
2. Read the protocol. Although the language may differ; the narrative and the consent form should be consistent in the description of the purpose of the study, the procedures, the study timeframe, the possible risks and potential benefits, compensation and costs, confidentiality of data, etc.

Consider the following questions:

- Background and Purpose of the Study
 - Are the specific aims, hypotheses, and research questions clearly identified?
 - Is there sufficient preliminary data to justify the research?
 - If the study is a drug, biologic, or device trial, are the safety and efficacy data sufficient to warrant the proposed phase of testing?

- Background and Expertise of Study Team
 - Is there sufficient expertise on the research team to conduct the study given the procedures and the study population(s)?
 - Are the researchers' experience, specific roles and responsibilities clearly defined?
- Does anyone on the research team have a financial conflict of interest?
 - If so, has the fCOI been managed? What does the fCOI Management Plan indicate?
- **See HRP-055 - SOP - HUA - Financial Conflicts of Interests**
- Research Methodology/Study Procedures
 - Are the scientific design and research procedures adequately described and justified?
 - Is the design appropriate to answer the research question? (Scientific merit should be considered in the context of whether individuals should be exposed to unnecessary risk).
 - Does the description differentiate between standard-of-care procedures and research procedures, if applicable?
- **See HRP-320-WORKSHEET-Scientific or Scholarly Review**
- Subjects (participants, charts, records and/or specimens)
 - Is the proposed subject population appropriate given the research question?
 - Are the inclusion and exclusion criteria explained and appropriate?
 - Is the inclusion or exclusion of women, minorities, and minors justified?
 - Does the proposed population include vulnerable participants (e.g., minors, prisoners, cognitively impaired, Harvard University students/staff)? If yes, consider special protections (e.g., parental permission, minor assent, surrogate consent, minimize undue influence or coercion to ensure voluntariness).
 - Does the researcher include a projected sample size and appropriate justification? Is the projected sample sufficient to answer the research question, yet small enough to limit number of individuals placed at risk?
- Recruitment/Informed Consent Process
 - Are the recruitment procedures clearly described?
 - Are the location and timing of the recruitment procedures appropriate considering the proposed populations?
 - Are the recruitment procedures appropriate (ensure that they do not violate an individual's right to privacy)?
 - Is the informed consent process sufficiently described?
 - If requesting a waiver of informed consent (does not require researcher to obtain informed consent) or a waiver of documentation of informed consent (does not require a signed consent form, however still requires an informed consent discussion), does the researcher provide adequate justification?

- If recruiting minors, does the researcher address parental permission and minor assent procedures?
- If recruiting elderly subjects or potentially cognitively/emotionally impaired groups, does the researcher explain how competency will be determined and who will make the determination?
- Is the researcher requesting to obtain surrogate consent? Does the researcher adequately justify use of a surrogate? Does the researcher have a specific plan that will be employed to acquire and document surrogate consent? Is the plan appropriate?
- If recruiting minority groups or non-English speakers, does the researcher acknowledge that s/he will obtain informed consent or assent using a consent/assent form translated into the appropriate language?

➤ **See HRP-315-WORKSHEET-Advertisement**

- Anticipated Risks/Risk Management
 - Are the potential risks sufficiently identified, evaluated (probability and severity) and described?
 - Are the risks minimized to the lowest level possible?
 - After reviewing potential direct benefits to the participant and societal benefits, are the risks appropriate in relation to the anticipated benefits?
 - If research includes vulnerable populations (e.g., minors, pregnant women, prisoners) determine which regulatory category of risk the research falls within and whether all the criteria within the category or Subpart are addressed?
- Potential Benefits
 - Are the potential benefits (to participant and society) sufficiently identified, evaluated and described?
- Adverse Event Reporting/Management, if applicable according to risk of study
 - Is there a data safety monitoring plan or board/committee in place?
 - Does the protocol specify criteria for stopping (for a subject or for the project)?
- Compensation
 - Is the amount and type of compensation reasonable (does not appear to unduly influence one to participate)?
 - Does the researcher explain that compensation will be prorated and provides a schedule of payment?

➤ **See HRP-316-WORKSHEET-Payments**

- Privacy and Confidentiality of Research Data
 - Are there appropriate procedures in place to protect the participant's privacy? How are participants being recruited? In what setting is the research being conducted?
 - Does the researcher explain who will have access to the data?



Human Research Protection Program Plan



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SCOPE

Throughout this document “Institution” refers to Harvard University Area.

PURPOSE

This Institution is committed to protecting the rights and welfare of subjects in Human Research. 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.

This Institution’s Human Research Protection Program is a comprehensive system to ensure the protection of the rights and welfare of subjects in 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.

DEFINITIONS

AGENT

An individual who is an employee is considered an agent of this Institution for purposes of engagement in Human Research when that individual is on-duty in any capacity as an employee of this Institution.

In accordance with the September 22, 2003 vote of the President and Fellows of Harvard College, the jurisdiction of the CUHS extends to 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. Research under the auspices of the University-Area institutions includes research conducted by or under the direction of any employee or agent of the University-Area institutions (including students) in connection with their institutional responsibilities, conducted by or under the direction of any employee or agent of the University-Area institutions using any of their property or facilities or involving the use of these institutions’ non-public information to identify or contact human subjects for research purposes.

An individual who is not an employee is considered an agent of this Institution for purposes of engagement in Human Research when that individual has been specifically authorized to conduct Human Research on behalf of this Institution.

Legal counsel has the ultimate authority to determine whether someone is acting as an agent of this Institution.

CLINICAL TRIAL

A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes.

ENGAGED IN HUMAN RESEARCH

In general, this Institution is considered engaged in Human Research when this Institution’s employees or agents for the purposes of the Human Research obtain: (1) data about the subjects of the research through intervention or interaction with them; (2) identifiable private information about or identifiable biospecimens from the subjects of the research; or (3) the informed consent of human subjects for the research. This Institution follows OHRP guidance on “Engagement of Institutions in Research”¹ to apply this definition and exceptions to this definition.

¹ <http://www.hhs.gov/ohrp/policy/engage08.html>



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HUMAN RESEARCH:

Any activity that either:

- Is “Research” as defined by DHHS and involves “Human Subjects” as defined by DHHS (“DHHS Human Research”); or
- Is “Research” as defined by FDA and involves “Human Subjects” as defined by FDA (“FDA Human Research”).

HUMAN SUBJECT AS DEFINED BY DHHS

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. For the purpose of this definition:

- **Intervention** means both physical procedures by which information or biospecimens are gathered (for example, venipuncture) and manipulations of the subject or the subject’s environment that are performed for research purposes.
- **Interaction** means communication or interpersonal contact between investigator and subject.
- **Private Information** means information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and that the individual can reasonably expect will not be made public (for example, a medical record).
- **Identifiable Private Information** means private information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information.
- **Identifiable Biospecimen** means a biospecimen for which the identity of the subject is or may readily be ascertained by the investigator or associated with the biospecimen.

HUMAN SUBJECT AS DEFINED BY FDA

An individual who is or becomes a subject in research, either as a recipient of the test article or as a control. A subject may be either a healthy human or a patient. A human subject includes an individual on whose specimen (identified or unidentified) a medical device is used.

When medical device research involves in vitro diagnostics and unidentified tissue specimens, the FDA defines the unidentified tissue specimens as human participants.

INVESTIGATOR

The person responsible for the conduct of the Human Research at one or more sites. If the Human Research is conducted by a team of individuals at a trial site, the investigator is the responsible leader of the team and may be called the principal investigator.

RESEARCH AS DEFINED BY DHHS

A systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.²

² For research conducted within the Bureau of Prisons: Implementation of Bureau programmatic or operational initiatives made through pilot projects is not considered to be research.



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The following activities are not considered Research as Defined by DHHS:

- Scholarly and journalistic activities (e.g., oral history, journalism, biography, literary criticism, legal research, and historical scholarship), including the collection and use of information, that focus directly on the specific individuals about whom the information is collected.
- Public health surveillance activities conducted by a public health authority, limited to those necessary to allow a public health authority to identify, monitor, assess, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance.
 - Including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority.
 - Including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products.
 - Including those associated with providing timely situational awareness and priority setting during the course of an event or crisis that threatens public health (including natural or man-made disasters).
- Collection and analysis of information, biospecimens, or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes.
- Authorized operational activities (as determined by the relevant federal agency) in support of intelligence, homeland security, defense, or other national security missions.
- Secondary research involving non-identifiable newborn screening blood spots.

RESEARCH AS DEFINED BY FDA

Any experiment that involves a test article and one or more human subjects, and that meets any one of the following:

- Must meet the requirements for prior submission to the Food and Drug Administration under section 505(i) of the Federal Food, Drug, and Cosmetic Act meaning any use of a drug other than the use of an approved drug in the course of medical practice, OR
- Must meet the requirements for prior submission to the Food and Drug Administration under section 520(g) of the Federal Food, Drug, and Cosmetic Act meaning any activity that evaluates the safety or effectiveness of a device; AND
- Any activity the results of which are intended to be later submitted to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit.

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.

ETHICAL REQUIREMENTS

In the oversight of all Human Research, this Institution (including its investigators, research staff, students involved with the conduct of Human Research, the Institution's institutional review boards (IRBs), IRB members and chairs, IRB staff, the Institutional Official/Organizational Official (IO/OO), and employees) follows the ethical principles outlined in the April 18, 1979 report of The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research titled "Ethical Principles and Guidelines for the Protection of Human Subjects of Research," also known as "The Belmont Report":

- Respect for Persons



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- Beneficence
- Justice

LEGAL REQUIREMENTS

This Institution commits to apply its ethical standards to all Human Research regardless of funding.

All Human Research must undergo review by one of the Institutionally designated IRBs. Activities that do not meet the definition of Human Research do not require review and approval by one of the Institution's IRBs and do not need to be submitted to one of the Institution's IRBs unless there is a question regarding whether the activity is Human Research.

When this Institution is engaged in DHHS Human Research that is conducted, funded, or otherwise subject to regulations by a federal department or agency who is a signatory of the Common Rule, the Institution commits to apply the regulations of that agency relevant to the protection of Human Subjects.

When this Institution is engaged in FDA Human Research, this Institution commits to apply the FDA regulations relevant to the protection of Human Subjects.

Any questions about whether an activity meets the regulatory definitions of Human Research should be referred to the IRB Office who will provide a determination.

OTHER REQUIREMENTS

When reviewing research that involves community-based research, the IRB obtains consultation, receives education, or includes IRB members with expertise in community-based participatory research.

All policies and procedures are applied identically to all research regardless of whether the research is conducted domestically or in another country, including:

- Confirming the qualifications of investigators for conducting the research
- Conducting initial review, continuing review, and review of modifications to previously approved research
- Post-approval monitoring
- Handling of complaints, non-compliance, and unanticipated problems involving risks to subjects or others
- Consent process and other language issues
- Ensuring all necessary approvals are met
- Coordination and communication with local IRBs
- The oversight of human subjects research and protection of research participants is strongest and most successful when performed in an open culture and framework that values and embodies diversity, equity, and inclusion. To support investigators to involve community members in the research process, including the design and implementation of research and the dissemination of results, when appropriate, when there may be challenges recruiting due to community attitudes toward investigators or stigma about the research topic, to identify relevant community members, to obtain expertise in hard-to-reach populations, and to assist in the periodic evaluation of racial or ethnic demographic characteristics of subjects enrolled in research to evaluate whether participation in research reflects the demographics of the community, when appropriate, the following resources are available:
 - The Harvard University Community Engagement Program which offers consultations and trainings for community impact, strategic science seminars, community engagement studios, community coalition for equity in research, pilot grants, and a policy atlas. Contact the program [here](#).



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- The Harvard University Office for Equity, Diversity, Inclusion, and Belonging offers a variety of resources that range from university-wide offices and School/Unit-based departments to role specific organizations and resource groups. Resources may be found [here](#).
- For clinical trials, this Institution commits to apply the “International Conference on Harmonisation – Good Clinical Practice E6” (ICH-GCP) when required by industry-sponsored studies.
- This Institution prohibits payments to professionals in exchange for referrals of potential subjects (“finder’s fees”) and payments designed to accelerate recruitment that were tied to the rate or timing of enrollment (“bonus payments.”)
- When Human Research is conducted or funded by the Department of Justice (DOJ), this Institution commits to apply 28 CFR §22. When Human Research is conducted with the federal Bureau of Prisons (DOJ), the Institution commits to comply with 28 CFR §512.
- When Human Research is conducted or funded by the Department of Defense (DOD), this Institution commits to apply the Department of Defense (DOD) Directive 3216.02, which includes the requirement to apply 45 CFR §46 Subparts B, C, and D³. This Institution will comply with the terms of the DFARS clause or comparable language used in the agreement with the Department of Defense (DOD) Component supporting the research involving human subjects.
- When Human Research is conducted or funded by the Department of Education (ED), this Institution commits to applying 34 CFR §97 Subpart D (equivalent to 45 CFR §46 Subpart D), 34 CFR §98.3, 34 CFR §98.4, 34 CFR §356.3, and 34 CFR §99.
- When Human Research is conducted or funded by the Department of Energy (DOE), this Institution commits to applying the Department of Energy (DOE) O 443.1C which includes the requirements to apply 10 CFR §745 and Subparts B, C, and D of 45 CFR §46, as applicable, and additional DOE requirements outlined in HRP-318 - WORKSHEET - Additional Federal Agency Criteria.
 - DOE requirements apply to all research conducted with DOE funding, at DOE institutions (regardless of funding source), or by DOE or DOE contractor personnel (regardless of funding source or location conducted), whether done domestically or in an international environment, including classified and proprietary research.
 - When research involves contractors, DOE “Contractor Requirements Document” describing contractor responsibilities for protecting human research participants must be included in contracts.
- When Human Research is conducted or funded by, or when the results of research are intended to be submitted to or held for inspection by the Environmental Protection Agency (EPA), this Institution commits to applying 40 CFR §26, which includes the requirement to apply 45 CFR §46 Subparts B and D.
- When Human Research is subject to the European Economic Area (EEA) General Data Protection Regulations (GDPR), this Institution coordinates with legal counsel to ensure that the research

³ Quick applicability table for DHHS Subparts:

	DHHS	DOD	ED	EPA
Subpart B	X	X		X
Subpart C	X	X		
Subpart D	X	X	X	X



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activities conform to broader institutional policies related to GDPR, where applicable, as well as legal counsel's interpretation of study-specific GDPR requirements.

SPONSORED HUMAN RESEARCH

For both sponsored and non-sponsored Human Research this Institution abides by its ethical principles, regulatory requirements and its policies and procedures.

SCOPE OF HUMAN RESEARCH PROTECTION PROGRAM

The categories of Human Research overseen include:

- Research conducted or funded by the Department of Defense (DOD)
 - DOD research involving Experimental Subjects
 - DOD classified research
 - Research on DOD personnel
 - DOD research involving chemical or biological agents under an exception
- Research conducted or funded by the Department of Justice (DOJ)
- Research conducted or funded by the Department of Education (ED)
- Research conducted or funded by the Department of Energy (DOE)
 - Department of Energy (DOE) human terrain mapping research
- Research conducted, funded, or subject to oversight by the Environmental Protection Agency (EPA)
- Federally funded research
- Research involving fetuses.
- Research involving *in vitro* fertilization.
- FDA-regulated research.
- *Research involving drugs that require an IND*.*
- Research involving devices that require an abbreviated IDE.
- *Research involving devices that require an IDE issued by FDA*.*
- Investigator held abbreviated IDE.
- *Investigator held IND or IDE*.*
- Research involving pregnant women as subjects.
- Research involving non-viable neonates.
- Research involving neonates of uncertain viability.
- Research that plans to or is likely to involve prisoners as subjects.
- Research involving children as subjects.
- Research involving children, pregnant women, fetuses, or neonates that is not otherwise approvable without approval of an agency secretary or director.
- Research using the short form of consent documentation.
- International research

* The HUA IRB will enter into a reliance agreement with an appropriate IRB for review of these studies.



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The categories of Human Research not overseen include:

- Research conducted or funded by the Veteran Administration (VA)
- Research involving a waiver of consent for planned emergency research.
- Emergency use of a test article in a life-threatening situation.
- Activities involving humanitarian use devices.
- Classified Research (Classified research is secret research to which access is restricted by law to a particular hierarchical class of people. A security clearance is required to review classified research.)

HUMAN RESEARCH PROTECTION PROGRAM POLICIES AND PROCEDURES

Policies and procedures for the Human Research Protection Program are available in the ESTR Library on the following Web site: irb.harvard.edu

HUMAN RESEARCH PROTECTION PROGRAM COMPONENTS

INSTITUTIONAL OFFICIAL/ORGANIZATIONAL OFFICIAL

The University Chief Research Compliance Officer is designated as the Institutional Official/Organizational Official (IO/OO) for the University Area IRB.

The IO/OO has the authority to take the following actions or delegate these authorities to a designee:

- Create the Human Research Protection Program budget.
- Allocate resources within the Human Research Protection Program budget.
- Appoint and remove IRB members and IRB chairs.
- Hire and fire research review staff.
- Determine what IRBs the Institution will rely upon.
- Approve and rescind authorization agreements for IRBs.
- Place limitations or conditions on an investigator's or research staff's privilege to conduct Human Research.
- Create policies and procedures related to the Human Research Protection Program that are binding on the Institution.
- Suspend or terminate research approved by one of the Institution's IRBs.
- Disapprove research approved by one of the Institution's IRBs.
- Establish a contingency plan for transferring oversight of one or more studies to another institution or IRB in the event the IRB is unable to continue oversight of the studies in an emergency/disaster scenario (e.g., natural disasters, man-made disasters, infectious disease pandemics, etc.).

The IO/OO has the responsibility to:

- Oversee the review and conduct of Human Research under the jurisdiction of the Human Research Protection Program.
- Periodically review this plan to assess whether it is providing the desired results and recommend amendments as needed.
- Establish policies and procedures designed to increase the likelihood that Human Research will be conducted in accordance with ethical and legal requirement.



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- Institute regular, effective, educational and training programs for all individuals involved with the Human Research Protection Program.
- Ensure that the research review process is independent and free of coercion or undue influence, and ensure that officials of the Institution cannot approve research that has not been approved by one of the IRBs designated by the Institution.
- Ensure that the IRB Chair(s) and members have direct access to the IO/OO for appeal if they experience undue influence or if they have concerns about the function of the IRB.
- Implement a process to receive and act on complaints and allegations regarding the Human Research Protection Program.
- Follow-up on findings of serious or continuing non-compliance of IRB staff and IRB members.
- Implement an auditing program to monitor compliance and improve compliance in identified problem areas.
- Investigate and remediate identified systemic problem areas, and where necessary removal of individuals from involvement in the Human Research protection program.
- Ensure that the Human Research Protection Program has sufficient resources, including IRBs appropriate for the volume and types of Human Research to be reviewed, so that reviews are accomplished in a thorough and timely manner.
- Review and sign federal assurances (FWA) and addenda.
- Fulfill educational requirements mandated by OHRP.

ADMINISTRATION

With respect to a variety of administrative functions, Harvard treats the University Area institutions as one unit. The University Area is comprised of the John F. Kennedy School of Government, Harvard Graduate School of Education, Harvard Law School, Harvard Divinity School, Harvard Graduate School of Design, Radcliffe Institute for Advanced Study, Harvard School of Engineering and Applied Sciences, and the Harvard Business School. The largest among the University Area institutions is the Faculty of Arts and Sciences (FAS), which is responsible for Harvard College and the Graduate School of Arts and Sciences, as well as the Harvard Extension and Summer School programs.

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.

Individuals who are responsible for business development are prohibited from carrying out day-to-day operations of the review process.



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IRB/THE COMMITTEE ON THE USE OF HUMAN SUBJECTS

The Harvard University Area IRB (also known as The Committee on the Use of Human Subjects) designated by the IO/OO to be the IRB relied upon by the Human Research Protection Program and the scope of review of this IRB is listed in the IRB rosters available from the IRB Office. IRB members and IRB staff have the responsibility to follow Human Research Protection Program policies and procedures that apply to IRB members and staff.

RELYING ON AN EXTERNAL IRB

This Institution may rely upon IRBs of another Institution provided one of the following is true:

- The IRBs are part of an AAHRPP accredited Institution;
- The IRBs are not part of an AAHRPP accredited institution or organization, but where reasonable steps have been taken to ensure that subjects are adequately protected. For example, for research that is no greater than Minimal Risk, there may be an assurance that the IRBs will adhere to applicable ethical standards and regulations. For research that is greater than Minimal Risk, the institutions may agree on more extensive oversight.
- The IRBs are part of an established reliance network (e.g. Smart IRB) that has established contractual and SOP-level procedures to clarify the roles and responsibilities associated with IRB reliance and to establish mechanisms to ensure quality and consistency in the review process among institutions.
- The sIRB has been pre-determined by study sponsor or grant or established by prior arrangement.
- This Institution's investigator is a collaborator on Human Research that is primarily conducted at another institution or organization and the investigator's role does not include interaction or intervention with subjects.
- The Institution is engaged in the Human Research solely because it is receiving federal funds. (Employees and agents of the institution do not interact or intervene with subjects, gather or possess private identifiable information about subjects, nor obtain the consent of subjects.)

Reliance on an external IRB requires an [Authorization Agreement](#) and an active Institutional Profile, as well as a local review for compliance with local policies of the Institution. When Human Research carried out at this institution or by its agents is reviewed by an IRB at another institution or organization, this HRPP will follow established policies and procedures that specify which studies are eligible for reliance, how reliance is determined, and will provide information to researchers about reliance criteria and the process for seeking IRB reliance.

The IRBs relied upon by this Institution have the authority to:

- Approve, require modifications to secure approval, and disapprove all Human Research overseen and conducted by the Institution. All Human Research must be approved by one of the IRBs designated by the IO/OO. Officials of this Institution may not approve Human Research that has not been approved by one of the Institution's IRBs.
- Suspend or terminate approval of Human Research not being conducted in accordance with an IRBs' requirements or that has been associated with unexpected serious harm to subjects.
- Observe, or have a third party observe, the consent process and the conduct of the Human Research.
- Determine whether an activity is Human Research.
- Evaluate financial interests of investigators and research staff and have the final authority to decide whether the financial interest and management plan, if any, allow the Human Research to be approved.
- Serve as the Privacy Board, as applicable, to fulfill the requirements of the HIPAA Privacy Rule for use or disclosure of protected health information for research purposes.



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This institution will comply with the determinations of the reviewing IRB, follow reporting and conflict of interest disclosure requirements as specified in the authorization agreement, conduct monitoring, identify an appropriate contact person, ensure researchers have appropriate qualifications and provide local context information (and any updates) to the reviewing IRB.

SERVING AS THE IRB OF RECORD

When this institution provides IRB review for other institutions, this HRPP will follow established policies and procedures to ensure that the composition of the IRB is appropriate to review the research and will comply with applicable laws of the relying site. This includes ensuring the IRB is appropriately constituted, members are appropriately qualified, members will not participate in the review of research in which they have a conflict of interest; and that the IRB separates business functions from ethical review.

The IRB will review the research in accordance with established policies and procedures to determine that research is ethically justifiable, according to all applicable laws, including initial review, continuing review, review of modifications to previously approved research and unanticipated problems involving risks to subjects or others. The IRB will also have the ability to suspend or terminate IRB approval; as well as have the final authority to decide whether researcher or research staff conflict of interest and its management, if any, allows the research to be approved and request audits of research reviewed.

The IRB will notify the researcher (and organization) of its decisions, make relevant IRB policies and records available to the relying institution or organization and specify an IRB contact for communication.

Please refer to WORKSHEET - HUA - sIRB Considerations (HRP-833).

INVESTIGATORS AND RESEARCH STAFF

Investigators and research staff have the responsibility to:

- Follow the Human Research Protection Program requirements described in the INVESTIGATOR MANUAL (HRP-103).
- Comply with all determinations and additional requirements of the IRB, the IRB chair, and the IO/OO.
- Develop and implement emergency/disaster response procedures for their research depending on location and the nature of the research.

LEGAL COUNSEL

Legal Counsel has the responsibility to:

- Provide advice upon request to the IO/OO, IRB, and other individuals involved with the Human Research Protection Program.
- Determine whether someone is acting as an agent of the Institution.
- 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.
- Determine whether any Human Research involving personal data about individuals located in (but not necessarily citizens of) European Union member states, Norway, Iceland, Liechtenstein, and Switzerland conforms with EEA General Data Protection Regulations (GDPR).

OFFICERS/DEANS

Officers and Deans have the responsibility to:

- Oversee the review and conduct of Human Research in their department or school.



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- Forward complaints and allegations regarding the Human Research Protection Program to the IO/OO.
- Ensure that each Human Research study conducted in their department or school has adequate resources.

OFFICE FOR SPONSORED PROGRAMS (OSP)

The Office for Sponsored Programs (OSP) has the responsibility to review contracts and funding agreements for compliance with Human Research Protection Program policies and procedures.

EDUCATION AND TRAINING

This plan is made available to the human research community via the IRB website. To maintain awareness of HRPP policies and procedures, new information, revised materials and opportunities for continuing education are communicated to the research community by way of various communication channels targeted to appropriate audiences.

IRB members, IRB staff, and others involved in the review of Human Research, including the IO/OO, must complete initial and continuing training utilizing the Collaborative Institutional Training Initiative (CITI) human subjects online training program, or equivalent. Training is valid for a three-year period, after which time refresher training must be completed.

Investigators and research staff must complete the initial and continuing training described in the INVESTIGATOR MANUAL (HRP-103).

HRPP staff will coordinate with organizational officials in the development and implementation of training materials related to emergency preparedness and response plans specific to human research conducted at the organization. The HRPP emergency preparedness plan will be made available to the human research community via the IRB website. The organization is responsible for notifying research teams when the organization's emergency response plan is activated.

EMERGENCY PREPAREDNESS

The organization routinely assesses potential emergency scenarios and threats to the institution to improve its emergency preparedness and response plan. The HRPP Director, or their designee, collaborates with organizational leadership to develop, implement, and assess, emergency preparedness procedures for the HRPP.

Depending on the nature of the event, the HRPP Director will collaborate with institutional leadership to determine the types of research that might continue and the types that the organization may need to temporarily postpone. The organization proactively identifies external IRBs on which it can rely on temporarily during an emergency.

The IRB staff will work with IT resources and/or electronic system vendors to ensure continuity of operations in the event that electronic systems are inaccessible or not operational for extended periods of time during an emergency/disaster. The HRPP Director will collaborate with the vendor of the IRB's electronic system to ensure that records are maintained on a secure server that is accessible in the event of an emergency.

The organization will implement alternative review procedures, including leveraging online and virtual platforms, to ensure that IRB meetings can continue in scenarios where the IRB cannot meet in person. In instances where the convened IRB is unable to meet and IRB approval for a study may lapse, the IRB Chair can determine whether subjects can continue to participate in research activities if it is in the best interest of already enrolled subjects.

QUESTIONS AND ADDITIONAL INFORMATION FOR THE IRB

The IRB Office wants your questions, information, and feedback.



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Contact and location information for the IRB Office is:

Harvard University
Committee on the Use of Human Subjects
The Richard A. and Susan F. Smith Campus Center, Suite 645
1350 Massachusetts Ave
Cambridge, MA 02138
(617) 496-2847
cuhs@harvard.edu

REPORTING AND MANAGEMENT OF CONCERNS

Questions, concerns, complaints, allegations of undue influence, allegations or findings of non-compliance, or input regarding the Human Research Protection Program may be reported orally or in writing. Employees are permitted to report concerns on an anonymous basis. Concerns may be reported to the IRB Chair, IRB Office, IO/OO, Legal Counsel, Deans, or Department Chairs.

The IRB has the responsibility to investigate allegations and findings of non-compliance and take corrective actions as needed. The IO/OO has the responsibility to investigate all other reports and take corrective actions as needed.

Employees who report in good faith possible compliance issues should not be subjected to retaliation or harassment as a result of the reporting. Concerns about possible retaliation should be immediately reported to the IO/OO or designee.

To make such reports, contact the IO/OO:

Ara Tahmassian, Ph.D.
University Chief Research Compliance Officer and Institutional Official/Organizational Official
Office of the Vice Provost for Research
The Richard A. and Susan F. Smith Campus Center, Room 679
1350 Massachusetts Avenue
Cambridge, MA 02138
617-384-9451
ara_tahmassian@harvard.edu

MONITORING AND AUDITING

In order to monitor and ensure compliance, internal or external auditors who have expertise in federal and state statutes, regulations and Institutional requirements will conduct periodic audits. Audits will focus on areas of concern that have been identified by any entity, i.e., federal, state or institutional. Random audits may also be conducted.

DISCIPLINARY ACTIONS

The IO/OO may place limitations or conditions on an investigator's or research staff's privilege to conduct Human Research whenever in the opinion of the IO/OO such actions are required to maintain the Human Research Protection Program.

APPROVAL AND REVISIONS TO THE PLAN

This Human Research Protection Program Plan is to be approved by the Chief Executive Officer. This plan is intended to be flexible and readily adaptable to changes in regulatory requirements. The IO/OO has the responsibility to review this plan to assess whether it is providing the desired results. At the request of the IO/OO the Chief Executive Officer has the authority to amend this plan as deemed necessary.



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Approved:

A blue ink signature of Ara Tahmassian, written in a cursive style.

Ara Tahmassian, Ph.D.

Harvard University Chief Research Compliance Officer and Institutional Official/Organizational Official

January 2, 2024

THE BELMONT REPORT

Office of the Secretary

Ethical Principles and Guidelines for the Protection of Human Subjects of Research

The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research

April 18, 1979

AGENCY: Department of Health, Education, and Welfare.

ACTION: Notice of Report for Public Comment.

SUMMARY: On July 12, 1974, the National Research Act (Pub. L. 93-348) was signed into law, there-by creating the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. One of the charges to the Commission was to identify the basic ethical principles that should underlie the conduct of biomedical and behavioral research involving human subjects and to develop guidelines which should be followed to assure that such research is conducted in accordance with those principles. In carrying out the above, the Commission was directed to consider: **(i)** the boundaries between biomedical and behavioral research and the accepted and routine practice of medicine, **(ii)** the role of assessment of risk-benefit criteria in the determination of the appropriateness of research involving human subjects, **(iii)** appropriate guidelines for the selection of human subjects for participation in such research and **(iv)** the nature and definition of informed consent in various research settings.

The Belmont Report attempts to summarize the basic ethical principles identified by the Commission in the course of its deliberations. It is the outgrowth of an intensive four-day period of discussions that were held in February 1976 at the Smithsonian Institution's Belmont Conference Center supplemented by the monthly deliberations of the Commission that were held over a period of nearly four years. It is a statement of basic ethical principles and guidelines that should assist in resolving the ethical problems that surround the conduct of research with human subjects. By publishing the Report in the Federal Register, and providing reprints upon request, the Secretary intends that it may be made readily available to scientists, members of Institutional Review Boards, and Federal employees. The two-volume Appendix, containing the lengthy reports of experts and specialists who assisted the Commission in fulfilling this part of its charge, is available as DHEW Publication No. (OS) 78-0013 and No. (OS) 78-0014, for sale by the Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402.

Unlike most other reports of the Commission, the Belmont Report does not make specific recommendations for administrative action by the Secretary of Health, Education, and Welfare. Rather, the Commission recommended that the Belmont Report be adopted in its entirety, as a statement of the Department's policy. The Department requests public comment on this recommendation.

National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research

Members of the Commission

Kenneth John Ryan, M.D., Chairman, Chief of Staff, Boston Hospital for Women.

Joseph V. Brady, Ph.D., Professor of Behavioral Biology, Johns Hopkins University.

Robert E. Cooke, M.D., President, Medical College of Pennsylvania.

Dorothy I. Height, President, National Council of Negro Women, Inc.

Albert R. Jonsen, Ph.D., Associate Professor of Bioethics, University of California at San Francisco.

Patricia King, J.D., Associate Professor of Law, Georgetown University Law Center.

Karen Lebacqz, Ph.D., Associate Professor of Christian Ethics, Pacific School of Religion.

**** David W. Louisell, J.D., Professor of Law, University of California at Berkeley.*

Donald W. Seldin, M.D., Professor and Chairman, Department of Internal Medicine, University of Texas at Dallas.

**** Eliot Stellar, Ph.D., Provost of the University and Professor of Physiological Psychology, University of Pennsylvania.*

**** Robert H. Turtle, LL.B., Attorney, VomBaur, Coburn, Simmons & Turtle, Washington, D.C.*

**** Deceased.*

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Ethical Principles & Guidelines for Research Involving Human Subjects

Scientific research has produced substantial social benefits. It has also posed some troubling ethical questions. Public attention was drawn to these questions by reported abuses of human subjects in biomedical experiments, especially during the Second World War. During the Nuremberg War Crime Trials, the Nuremberg code was drafted as a set of standards for judging physicians and scientists who had conducted biomedical experiments on concentration camp prisoners. This code became the prototype of many later codes [1] intended to assure that research involving human subjects would be carried out in an ethical manner.

The codes consist of rules, some general, others specific, that guide the investigators or the reviewers of research in their work. Such rules often are inadequate to cover complex situations; at times they come into conflict, and they are frequently difficult to interpret or apply. Broader ethical principles will provide a basis on which specific rules may be formulated, criticized and interpreted.

Three principles, or general prescriptive judgments, that are relevant to research involving human subjects are identified in this statement. Other principles may also be relevant. These three are comprehensive, however, and are stated at a level of generalization that should assist scientists, subjects, reviewers and interested citizens to understand the ethical issues inherent in research involving human subjects. These principles cannot always be applied so as to resolve beyond dispute particular ethical problems. The objective is to provide an analytical framework that will guide the resolution of ethical problems arising from research involving human subjects.

This statement consists of a distinction between research and practice, a discussion of the three basic ethical principles, and remarks about the application of these principles.

Part A: Boundaries Between Practice & Research

A. Boundaries Between Practice and Research

It is important to distinguish between biomedical and behavioral research, on the one hand, and the practice of accepted therapy on the other, in order to know what activities ought to undergo review for the protection of human subjects of research. The distinction between research and practice is blurred partly because both often occur together (as in research designed to evaluate a therapy) and partly because notable departures from standard practice are often called "experimental" when the terms "experimental" and "research" are not carefully defined.

For the most part, the term "practice" refers to interventions that are designed solely to enhance the well-being of an individual patient or client and that have a reasonable expectation of success. The purpose of medical or behavioral practice is to provide diagnosis, preventive treatment or therapy to particular individuals [2]. By contrast, the term "research" designates an activity designed to test an hypothesis, permit conclusions to be drawn, and thereby to develop or contribute to generalizable knowledge (expressed, for example, in theories, principles, and statements of relationships). Research is usually described in a formal protocol that sets forth an objective and a set of procedures designed to reach that objective.

When a clinician departs in a significant way from standard or accepted practice, the innovation does not, in and of itself, constitute research. The fact that a procedure is "experimental," in the sense of new, untested or different, does not automatically place it in the category of research. Radically new procedures of this

description should, however, be made the object of formal research at an early stage in order to determine whether they are safe and effective. Thus, it is the responsibility of medical practice committees, for example, to insist that a major innovation be incorporated into a formal research project [3].

Research and practice may be carried on together when research is designed to evaluate the safety and efficacy of a therapy. This need not cause any confusion regarding whether or not the activity requires review; the general rule is that if there is any element of research in an activity, that activity should undergo review for the protection of human subjects.

Part B: Basic Ethical Principles

B. Basic Ethical Principles

The expression "basic ethical principles" refers to those general judgments that serve as a basic justification for the many particular ethical prescriptions and evaluations of human actions. Three basic principles, among those generally accepted in our cultural tradition, are particularly relevant to the ethics of research involving human subjects: the principles of respect for persons, beneficence and justice.

1. Respect for Persons. — Respect for persons incorporates at least two ethical convictions: first, that individuals should be treated as autonomous agents, and second, that persons with diminished autonomy are entitled to protection. The principle of respect for persons thus divides into two separate moral requirements: the requirement to acknowledge autonomy and the requirement to protect those with diminished autonomy.

An autonomous person is an individual capable of deliberation about personal goals and of acting under the direction of such deliberation. To respect autonomy is to give weight to autonomous persons' considered opinions and choices while refraining from obstructing their actions unless they are clearly detrimental to others. To show lack of respect for an autonomous agent is to repudiate that person's considered judgments, to deny an individual the freedom to act on those considered judgments, or to withhold information necessary to make a considered judgment, when there are no compelling reasons to do so.

However, not every human being is capable of self-determination. The capacity for self-determination matures during an individual's life, and some individuals lose this capacity wholly or in part because of illness, mental disability, or circumstances that severely restrict liberty. Respect for the immature and the incapacitated may require protecting them as they mature or while they are incapacitated.

Some persons are in need of extensive protection, even to the point of excluding them from activities which may harm them; other persons require little protection beyond making sure they undertake activities freely and with awareness of possible adverse consequence. The extent of protection afforded should depend upon the risk of harm and the likelihood of benefit. The judgment that any individual lacks autonomy should be periodically reevaluated and will vary in different situations.

In most cases of research involving human subjects, respect for persons demands that subjects enter into the research voluntarily and with adequate information. In some situations, however, application of the principle is not obvious. The involvement of prisoners as subjects of research provides an instructive example. On the one hand, it would seem that the principle of respect for persons requires that prisoners not be deprived of the opportunity to volunteer for research. On the other hand, under prison conditions they may be subtly coerced or unduly influenced to engage in research activities for which they would not otherwise volunteer. Respect for persons would then dictate that prisoners be protected. Whether to allow

prisoners to "volunteer" or to "protect" them presents a dilemma. Respecting persons, in most hard cases, is often a matter of balancing competing claims urged by the principle of respect itself.

2. Beneficence. — Persons are treated in an ethical manner not only by respecting their decisions and protecting them from harm, but also by making efforts to secure their well-being. Such treatment falls under the principle of beneficence. The term "beneficence" is often understood to cover acts of kindness or charity that go beyond strict obligation. In this document, beneficence is understood in a stronger sense, as an obligation. Two general rules have been formulated as complementary expressions of beneficent actions in this sense: **(1)** do not harm and **(2)** maximize possible benefits and minimize possible harms.

The Hippocratic maxim "do no harm" has long been a fundamental principle of medical ethics. Claude Bernard extended it to the realm of research, saying that one should not injure one person regardless of the benefits that might come to others. However, even avoiding harm requires learning what is harmful; and, in the process of obtaining this information, persons may be exposed to risk of harm. Further, the Hippocratic Oath requires physicians to benefit their patients "according to their best judgment." Learning what will in fact benefit may require exposing persons to risk. The problem posed by these imperatives is to decide when it is justifiable to seek certain benefits despite the risks involved, and when the benefits should be foregone because of the risks.

The obligations of beneficence affect both individual investigators and society at large, because they extend both to particular research projects and to the entire enterprise of research. In the case of particular projects, investigators and members of their institutions are obliged to give forethought to the maximization of benefits and the reduction of risk that might occur from the research investigation. In the case of scientific research in general, members of the larger society are obliged to recognize the longer term benefits and risks that may result from the improvement of knowledge and from the development of novel medical, psychotherapeutic, and social procedures.

The principle of beneficence often occupies a well-defined justifying role in many areas of research involving human subjects. An example is found in research involving children. Effective ways of treating childhood diseases and fostering healthy development are benefits that serve to justify research involving children -- even when individual research subjects are not direct beneficiaries. Research also makes it possible to avoid the harm that may result from the application of previously accepted routine practices that on closer investigation turn out to be dangerous. But the role of the principle of beneficence is not always so unambiguous. A difficult ethical problem remains, for example, about research that presents more than minimal risk without immediate prospect of direct benefit to the children involved. Some have argued that such research is inadmissible, while others have pointed out that this limit would rule out much research promising great benefit to children in the future. Here again, as with all hard cases, the different claims covered by the principle of beneficence may come into conflict and force difficult choices.

3. 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." An injustice occurs when some benefit to which a person is entitled is denied without good reason or when some burden is imposed unduly. Another way of conceiving the principle of justice is that equals ought to be treated equally. However, this statement requires explication. Who is equal and who is unequal? What considerations justify departure from equal distribution? Almost all commentators allow that distinctions based on experience, age, deprivation, competence, merit and position do sometimes constitute criteria justifying differential treatment for certain purposes. It is necessary, then, to explain in what respects people should be treated equally. There are several widely accepted formulations of just ways to distribute burdens and benefits. Each formulation mentions some relevant property on the basis of which burdens and benefits should be distributed. These formulations are **(1)** to each person an equal share, **(2)** to each person according to individual need, **(3)** to each person according to individual effort, **(4)** to each person according to societal contribution, and **(5)** to each person according to merit.

Questions of justice have long been associated with social practices such as punishment, taxation and political representation. Until recently these questions have not generally been associated with scientific research. However, they are foreshadowed even in the earliest reflections on the ethics of research involving human subjects. For example, during the 19th and early 20th centuries the burdens of serving as research subjects fell largely upon poor ward patients, while the benefits of improved medical care flowed primarily to private patients. Subsequently, the exploitation of unwilling prisoners as research subjects in Nazi concentration camps was condemned as a particularly flagrant injustice. In this country, in the 1940's, the Tuskegee syphilis study used disadvantaged, rural black men to study the untreated course of a disease that is by no means confined to that population. These subjects were deprived of demonstrably effective treatment in order not to interrupt the project, long after such treatment became generally available.

Against this historical background, it can be seen how conceptions of justice are relevant to research involving human subjects. For example, the selection of research subjects needs to be scrutinized in order to determine whether some classes (e.g., welfare patients, particular racial and ethnic minorities, or persons confined to institutions) are being systematically selected simply because of their easy availability, their compromised position, or their manipulability, rather than for reasons directly related to the problem being studied. Finally, whenever research supported by public funds leads to the development of therapeutic devices and procedures, justice demands both that these not provide advantages only to those who can afford them and that such research should not unduly involve persons from groups unlikely to be among the beneficiaries of subsequent applications of the research.

Part C: Applications

C. Applications

Applications of the general principles to the conduct of research leads to consideration of the following requirements: informed consent, risk/benefit assessment, and the selection of subjects of research.

1. Informed Consent. — Respect for persons requires that subjects, to the degree that they are capable, be given the opportunity to choose what shall or shall not happen to them. This opportunity is provided when adequate standards for informed consent are satisfied.

While the importance of informed consent is unquestioned, controversy prevails over the nature and possibility of an informed consent. Nonetheless, there is widespread agreement that the consent process can be analyzed as containing three elements: information, comprehension and voluntariness.

Information. Most codes of research establish specific items for disclosure intended to assure that subjects are given sufficient information. These items generally include: the research procedure, their purposes, risks and anticipated benefits, alternative procedures (where therapy is involved), and a statement offering the subject the opportunity to ask questions and to withdraw at any time from the research. Additional items have been proposed, including how subjects are selected, the person responsible for the research, etc.

However, a simple listing of items does not answer the question of what the standard should be for judging how much and what sort of information should be provided. One standard frequently invoked in medical practice, namely the information commonly provided by practitioners in the field or in the locale, is inadequate since research takes place precisely when a common understanding does not exist. Another standard, currently popular in malpractice law, requires the practitioner to reveal the information that reasonable persons would wish to know in order to make a decision regarding their care. This, too, seems insufficient since the research subject, being in essence a volunteer, may wish to know considerably more about risks gratuitously undertaken than do patients who deliver themselves into the hand of a clinician for

needed care. It may be that a standard of "the reasonable volunteer" should be proposed: the extent and nature of information should be such that persons, knowing that the procedure is neither necessary for their care nor perhaps fully understood, can decide whether they wish to participate in the furthering of knowledge. Even when some direct benefit to them is anticipated, the subjects should understand clearly the range of risk and the voluntary nature of participation.

A special problem of consent arises where informing subjects of some pertinent aspect of the research is likely to impair the validity of the research. In many cases, it is sufficient to indicate to subjects that they are being invited to participate in research of which some features will not be revealed until the research is concluded. In all cases of research involving incomplete disclosure, such research is justified only if it is clear that **(1)** incomplete disclosure is truly necessary to accomplish the goals of the research, **(2)** there are no undisclosed risks to subjects that are more than minimal, and **(3)** there is an adequate plan for debriefing subjects, when appropriate, and for dissemination of research results to them. Information about risks should never be withheld for the purpose of eliciting the cooperation of subjects, and truthful answers should always be given to direct questions about the research. Care should be taken to distinguish cases in which disclosure would destroy or invalidate the research from cases in which disclosure would simply inconvenience the investigator.

Comprehension. The manner and context in which information is conveyed is as important as the information itself. For example, presenting information in a disorganized and rapid fashion, allowing too little time for consideration or curtailing opportunities for questioning, all may adversely affect a subject's ability to make an informed choice.

Because the subject's ability to understand is a function of intelligence, rationality, maturity and language, it is necessary to adapt the presentation of the information to the subject's capacities. Investigators are responsible for ascertaining that the subject has comprehended the information. While there is always an obligation to ascertain that the information about risk to subjects is complete and adequately comprehended, when the risks are more serious, that obligation increases. On occasion, it may be suitable to give some oral or written tests of comprehension.

Special provision may need to be made when comprehension is severely limited -- for example, by conditions of immaturity or mental disability. Each class of subjects that one might consider as incompetent (e.g., infants and young children, mentally disable patients, the terminally ill and the comatose) should be considered on its own terms. Even for these persons, however, respect requires giving them the opportunity to choose to the extent they are able, whether or not to participate in research. The objections of these subjects to involvement should be honored, unless the research entails providing them a therapy unavailable elsewhere. Respect for persons also requires seeking the permission of other parties in order to protect the subjects from harm. Such persons are thus respected both by acknowledging their own wishes and by the use of third parties to protect them from harm.

The third parties chosen should be those who are most likely to understand the incompetent subject's situation and to act in that person's best interest. The person authorized to act on behalf of the subject should be given an opportunity to observe the research as it proceeds in order to be able to withdraw the subject from the research, if such action appears in the subject's best interest.

Voluntariness. An agreement to participate in research constitutes a valid consent only if voluntarily given. This element of informed consent requires conditions free of coercion and undue influence. Coercion occurs when an overt threat of harm is intentionally presented by one person to another in order to obtain compliance. Undue influence, by contrast, occurs through an offer of an excessive, unwarranted, inappropriate or improper reward or other overture in order to obtain compliance. Also, inducements that would ordinarily be acceptable may become undue influences if the subject is especially vulnerable.

Unjustifiable pressures usually occur when persons in positions of authority or commanding influence -- especially where possible sanctions are involved -- urge a course of action for a subject. A continuum of

such influencing factors exists, however, and it is impossible to state precisely where justifiable persuasion ends and undue influence begins. But undue influence would include actions such as manipulating a person's choice through the controlling influence of a close relative and threatening to withdraw health services to which an individual would otherwise be entitled.

2. Assessment of Risks and Benefits. — The assessment of risks and benefits requires a careful array of relevant data, including, in some cases, alternative ways of obtaining the benefits sought in the research. Thus, the assessment presents both an opportunity and a responsibility to gather systematic and comprehensive information about proposed research. For the investigator, it is a means to examine whether the proposed research is properly designed. For a review committee, it is a method for determining whether the risks that will be presented to subjects are justified. For prospective subjects, the assessment will assist the determination whether or not to participate.

The Nature and Scope of Risks and Benefits. The requirement that research be justified on the basis of a favorable risk/benefit assessment bears a close relation to the principle of beneficence, just as the moral requirement that informed consent be obtained is derived primarily from the principle of respect for persons. The term "risk" refers to a possibility that harm may occur. However, when expressions such as "small risk" or "high risk" are used, they usually refer (often ambiguously) both to the chance (probability) of experiencing a harm and the severity (magnitude) of the envisioned harm.

The term "benefit" is used in the research context to refer to something of positive value related to health or welfare. Unlike, "risk," "benefit" is not a term that expresses probabilities. Risk is properly contrasted to probability of benefits, and benefits are properly contrasted with harms rather than risks of harm. Accordingly, so-called risk/benefit assessments are concerned with the probabilities and magnitudes of possible harm and anticipated benefits. Many kinds of possible harms and benefits need to be taken into account. There are, for example, risks of psychological harm, physical harm, legal harm, social harm and economic harm and the corresponding benefits. While the most likely types of harms to research subjects are those of psychological or physical pain or injury, other possible kinds should not be overlooked.

Risks and benefits of research may affect the individual subjects, the families of the individual subjects, and society at large (or special groups of subjects in society). Previous codes and Federal regulations have required that risks to subjects be outweighed by the sum of both the anticipated benefit to the subject, if any, and the anticipated benefit to society in the form of knowledge to be gained from the research. In balancing these different elements, the risks and benefits affecting the immediate research subject will normally carry special weight. On the other hand, interests other than those of the subject may on some occasions be sufficient by themselves to justify the risks involved in the research, so long as the subjects' rights have been protected. Beneficence thus requires that we protect against risk of harm to subjects and also that we be concerned about the loss of the substantial benefits that might be gained from research.

The Systematic Assessment of Risks and Benefits. It is commonly said that benefits and risks must be "balanced" and shown to be "in a favorable ratio." The metaphorical character of these terms draws attention to the difficulty of making precise judgments. Only on rare occasions will quantitative techniques be available for the scrutiny of research protocols. However, the idea of systematic, nonarbitrary analysis of risks and benefits should be emulated insofar as possible. This ideal requires those making decisions about the justifiability of research to be thorough in the accumulation and assessment of information about all aspects of the research, and to consider alternatives systematically. This procedure renders the assessment of research more rigorous and precise, while making communication between review board members and investigators less subject to misinterpretation, misinformation and conflicting judgments. Thus, there should first be a determination of the validity of the presuppositions of the research; then the nature, probability and magnitude of risk should be distinguished with as much clarity as possible. The method of ascertaining risks should be explicit, especially where there is no alternative to the use of such vague categories as small or slight risk. It should also be determined whether an investigator's estimates of the probability of harm or benefits are reasonable, as judged by known facts or other available studies.

Finally, assessment of the justifiability of research should reflect at least the following considerations: **(i)** Brutal or inhumane treatment of human subjects is never morally justified. **(ii)** Risks should be reduced to those necessary to achieve the research objective. It should be determined whether it is in fact necessary to use human subjects at all. Risk can perhaps never be entirely eliminated, but it can often be reduced by careful attention to alternative procedures. **(iii)** When research involves significant risk of serious impairment, review committees should be extraordinarily insistent on the justification of the risk (looking usually to the likelihood of benefit to the subject -- or, in some rare cases, to the manifest voluntariness of the participation). **(iv)** When vulnerable populations are involved in research, the appropriateness of involving them should itself be demonstrated. A number of variables go into such judgments, including the nature and degree of risk, the condition of the particular population involved, and the nature and level of the anticipated benefits. **(v)** Relevant risks and benefits must be thoroughly arrayed in documents and procedures used in the informed consent process.

3. Selection of Subjects. — Just as the principle of respect for persons finds expression in the requirements for consent, and the principle of beneficence in risk/benefit assessment, the principle of justice gives rise to moral requirements that there be fair procedures and outcomes in the selection of research subjects.

Justice is relevant to the selection of subjects of research at two levels: the social and the individual. Individual justice in the selection of subjects would require that researchers exhibit fairness: thus, they should not offer potentially beneficial research only to some patients who are in their favor or select only "undesirable" persons for risky research. Social justice requires that distinction be drawn between classes of subjects that ought, and ought not, to participate in any particular kind of research, based on the ability of members of that class to bear burdens and on the appropriateness of placing further burdens on already burdened persons. Thus, it can be considered a matter of social justice that there is an order of preference in the selection of classes of subjects (e.g., adults before children) and that some classes of potential subjects (e.g., the institutionalized mentally infirm or prisoners) may be involved as research subjects, if at all, only on certain conditions.

Injustice may appear in the selection of subjects, even if individual subjects are selected fairly by investigators and treated fairly in the course of research. Thus injustice arises from social, racial, sexual and cultural biases institutionalized in society. Thus, even if individual researchers are treating their research subjects fairly, and even if IRBs are taking care to assure that subjects are selected fairly within a particular institution, unjust social patterns may nevertheless appear in the overall distribution of the burdens and benefits of research. Although individual institutions or investigators may not be able to resolve a problem that is pervasive in their social setting, they can consider distributive justice in selecting research subjects.

Some populations, especially institutionalized ones, are already burdened in many ways by their infirmities and environments. When research is proposed that involves risks and does not include a therapeutic component, other less burdened classes of persons should be called upon first to accept these risks of research, except where the research is directly related to the specific conditions of the class involved. Also, even though public funds for research may often flow in the same directions as public funds for health care, it seems unfair that populations dependent on public health care constitute a pool of preferred research subjects if more advantaged populations are likely to be the recipients of the benefits.

One special instance of injustice results from the involvement of vulnerable subjects. Certain groups, such as racial minorities, the economically disadvantaged, the very sick, and the institutionalized may continually be sought as research subjects, owing to their ready availability in settings where research is conducted. Given their dependent status and their frequently compromised capacity for free consent, they should be protected against the danger of being involved in research solely for administrative convenience, or because they are easy to manipulate as a result of their illness or socioeconomic condition.

[1] Since 1945, various codes for the proper and responsible conduct of human experimentation in medical research have been adopted by different organizations. The best known of these codes are the Nuremberg Code of 1947, the Helsinki Declaration of 1964 (revised in 1975), and the 1971 Guidelines (codified into Federal Regulations in 1974) issued by the U.S. Department of Health, Education, and Welfare. Codes for the conduct of social and behavioral research have also been adopted, the best known being that of the American Psychological Association, published in 1973.

[2] Although practice usually involves interventions designed solely to enhance the well-being of a particular individual, interventions are sometimes applied to one individual for the enhancement of the well-being of another (e.g., blood donation, skin grafts, organ transplants) or an intervention may have the dual purpose of enhancing the well-being of a particular individual, and, at the same time, providing some benefit to others (e.g., vaccination, which protects both the person who is vaccinated and society generally). The fact that some forms of practice have elements other than immediate benefit to the individual receiving an intervention, however, should not confuse the general distinction between research and practice. Even when a procedure applied in practice may benefit some other person, it remains an intervention designed to enhance the well-being of a particular individual or groups of individuals; thus, it is practice and need not be reviewed as research.

[3] Because the problems related to social experimentation may differ substantially from those of biomedical and behavioral research, the Commission specifically declines to make any policy determination regarding such research at this time. Rather, the Commission believes that the problem ought to be addressed by one of its successor bodies.



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1 PURPOSE

- 1.1 This policy establishes the definitions followed by the human research protection program. This is a non-exhaustive list and regulatory agencies should be referenced for complete definitions where applicable.

2 REVISIONS FROM PREVIOUS VERSION

- 2.1 See [HRPP Toolkit Tracking Spreadsheet](#)

3 POLICY

- 3.1 Adverse Event (AE): An AE in research can be any unfavorable or unintended event, including abnormal laboratory findings, symptom or disease, or death associated with the research or the use of a medical investigational test article. An AE in research may occur even in the absence of any error or protocol deviation and does not necessarily have to be caused by any identifiable aspect of the research.
- 3.2 Allegation of Non-Compliance: An unproved assertion of Non-Compliance.
- 3.3 Ancillary Review: Ancillary reviews allow individuals, departments, offices, and other additional reviewers to give feedback, approval, and/or provide documentation on the submission in parallel with the IRB review. During IRB review, staff of the IRB office will manually select the reviewer or reviewing organization/department each time a review is needed or required. IRB staff can add ancillary reviewers to a study, modification, or continuing review.
- 3.4 Assurance of Compliance (Human Subjects) or Federalwide Assurance: A legally binding written document that commits an institution to complying with the Federal Policy (Common Rule) and other applicable Federal and VA standards for the protection of human subjects.
- 3.5 Authorization Agreement: Also called a Reliance Agreement, is the agreement that documents respective authorities, roles, responsibilities, and communication between an institution/organization providing the ethical review and a participating institution relying on the ethical review.
- 3.6 Certification: The official notification by the institution to the supporting Federal department or agency component that a research project or activity involving human subjects has been reviewed and approved by an IRB in accordance with an approved assurance.
- 3.7 Clinical Trial: A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes.
- 3.8 Collaborative Study: A study in which two or more institutions coordinate, with each institution completing a portion of the research activities outlined in a specific protocol.
- 3.9 Conflicting Interest: An individual involved in research review is considered to have a conflicting interest when the individual or the individual's spouse, domestic partner, children, and/or dependents have any of the following interests in the sponsor, product or service being tested, or competitor of the sponsor held by the individual or the individual's immediate family:
 - 3.9.1 Involvement in the design, conduct, or reporting of the research.
 - 3.9.2 Ownership interest, stock options, or other ownership interest of any value exclusive of interests in publicly-traded, diversified mutual funds.
 - 3.9.3 Compensation of any amount in the past year or of any amount expected in the next year, excluding compensation for costs directly related to conducting research.
 - 3.9.4 Proprietary interest including, but not limited to, a patent, trademark, copyright or licensing agreement.
 - 3.9.5 Board or executive relationship, regardless of compensation.
 - 3.9.6 Reimbursed or sponsored travel by an entity other than a federal, state, or local government agency, higher education institution or affiliated research institute, academic teaching hospital, or medical center.
 - 3.9.7 Any other reason for which the individual believes that he or she cannot be independent.



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- 3.9.8 Refer to the [Harvard University Policy on Individual Financial Conflicts of Interest for Persons Holding Faculty and Teaching Appointments](#) for the de minimus threshold.
- 3.10 Continuing Non-Compliance: A pattern of Non-Compliance that suggests the likelihood that, without intervention, instances of Non-Compliance will recur, a repeated unwillingness to comply, or a persistent lack of knowledge of how to comply.
- 3.11 Controverted Issue: Controverted issues are those that cause controversy and dispute among the IRB membership during a convened meeting.
- 3.12 Designated Reviewer: The IRB chair or an Experienced IRB Member designated by the IRB chair to conduct Non-Committee Reviews. For the purpose of non-committee reviews, IRB staff who meet the definition of an Experienced IRB Member conduct the review.
- 3.13 ESTR: The Electronic Submission, Tracking, and Reporting system that automates the IRB submission and review process for the Harvard IRBs.
- 3.14 Experienced IRB Member: An IRB member is considered experienced if the IRB chair considers the IRB member to have sufficient experience in and knowledge of conducting IRB reviews.
- 3.15 Experimental Subject: For Department of Defense (DOD) research, research involving an “experimental subject” is an activity, for research purposes, where there is an intervention or interaction with a living individual for the primary purpose of obtaining data regarding the effect of the intervention or interaction. Research involving “experimental subjects” is a subset of research involving human participants.
- 3.16 Expiration Date: The first date that the protocol is no longer approved. The date after the end date of the approval period.
- 3.17 Finding of Non-Compliance: Non-Compliance in fact.
- 3.18 Harvard Master Agreement: When a Cede Request only involves a component of Harvard (Harvard University Area and Harvard Longwood Campus), the Harvard Master Agreement is used. The Harvard Master Agreement is a standing document between the Harvard IRBs that acts like a permanent reliance agreement: it outlines the conditions for reliance, the responsibilities for each researcher, as well as the general terms and conditions of the reliance.
- 3.19 Harvard University Area (HUA): Harvard University Area is comprised of the Cambridge and Allston campuses and includes the Faculty of Arts and Sciences, as well as the following schools: John F. Kennedy School of Government, Harvard Graduate School of Education, Harvard Law School, Harvard Divinity School, Harvard Graduate School of Design, Radcliffe Institute for Advanced Study, Harvard School of Engineering and Applied Sciences, and the Harvard Business School.
- 3.20 Harvard University Area (HUA) Advisory Committee: The Harvard Office of the Vice Provost of Research (OVPR) appointed a University-Area Advisory Committee to provide the OVPR with advice and input in the operational aspects of the human research protection program. This Committee fulfills a distinct role from that of the IRB, which is charged with the regulatory oversight of the program and policy development. The primary mission of Advisory Committee is to ensure the University Area human subject’s protection program effectively and efficiently provides services to the investigators and thus maximizes research potential. Meetings are held quarterly and include the review of key metrics, IRB composition and School/Department representation, and outreach and other initiatives that occur during a given timeframe.
- 3.21 Harvard University Area IRB (HUA IRB): The Harvard University-Area IRB, the Committee on the Use of Human Subjects (CUHS), is the IRB for the Cambridge and Allston campuses.
- 3.22 HRPP Toolkit Tracking Spreadsheet: A spreadsheet maintained locally that documents all revisions that are made to HRPP Toolkit documents (SOP’s, worksheets, checklists).
- 3.23 HUA Administrative Manual: An internal HUA IRB office document that outlines administrative procedures related to the IRB office operations.
- 3.24 Human Research: Any activity that either:¹

¹ The terms “Human Subject Research,” “Research Involving Human Subjects,” “Clinical Research,” “Clinical Investigation,” “Clinical Study” and similar phrases are considered to be synonyms for the term Human Research.

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- 3.24.1 Is Research as Defined by DHHS and involves Human Subjects as Defined by DHHS; or
- 3.24.2 Is Research as Defined by FDA and involves Human Subjects as Defined by FDA.
- 3.25 Human Subject as Defined by DHHS: 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. For the purpose of this definition:
- 3.25.1 Intervention: Physical procedures by which information or biospecimens are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.
- 3.25.2 Interaction: Communication or interpersonal contact between investigator and subject.
- 3.25.3 Private Information: Information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and that the individual can reasonably expect will not be made public (for example, a medical record).
- 3.25.4 Identifiable Private Information: Private Information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information.
- 3.25.5 Identifiable Biospecimen: A biospecimen for which the identity or the subject is or may be readily ascertained by the investigator or associated with the biospecimen.
- 3.26 Human Subject as Defined by FDA: An individual who is or becomes a subject in research, either as a recipient of the test article or as a control. A subject may be either a healthy human or a patient. A human subject includes an individual on whose specimen a medical device is used. When medical device research involves in vitro diagnostics and unidentified tissue specimens, the FDA defines the unidentified tissue specimens as human participants.
- 3.27 Immediate Family: Spouse, domestic partner; and dependent children.
- 3.28 Individual Investigator: An institution holding an OHRP-approved FWA may extend the applicability of its FWA to cover two types of collaborating individual investigators: collaborating independent investigators and collaborating institutional investigators. A collaborating independent investigator is: 1) not otherwise an employee or agent of the assured institution; 2) conducting collaborative research activities outside the facilities of the assured institution; and 3) not acting as an employee of any institution with respect to his or her involvement in the research being conducted by the assured institution. A collaborating institutional investigator is: 1) not otherwise an employee or agent of the assured institution; 2) conducting collaborative research activities outside the facilities of the assured institution; 3) acting as an employee or agent of an institution that does not hold an OHRP-approved FWA with respect to his or her involvement in the research being conducted by the assured institution; and employed by, or acting as an agent of, an institution that does not hold an OHRP-approved FWA and does not routinely conduct human subjects research.
- 3.29 Individual Investigator Agreement: A permissible mechanism under which an institution holding an Office for Human Research Protections (OHRP)-approved Federalwide Assurance (FWA) may extend – for one or more research protocols – the applicability of its FWA to cover two types of individual investigators: collaborating independent investigators and collaborating institutional investigators employed by a non-assured institution.
- 3.30 Institutional Official / Organizational Official (IO/OO):
- 3.30.1 Institutional Official (IO): Term utilized by DHHS.
- 3.30.1.1 The Institutional Official (IO) is the individual who is legally authorized to act for the institution and, on behalf of the institution, obligates the institution to the Terms of the Assurance. The IO is responsible for ensuring that the Human Research Protection Program (HRPP) functions effectively and that the institution provides the resources and support necessary to comply with all requirements applicable to research involving human subjects. The IO



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represents the institution named in the Federalwide Assurance (FWA)². The IO is the University Chief Research Compliance Officer.

3.30.2 Organizational Official (OO): Term utilized by AAHRPP.

3.30.2.1 An identified, knowledgeable leader of the HRPP who is responsible for the program and has the authority to implement the program. This individual may rely on others for the interpretation of laws, regulations, codes, and guidance and the day-to-day operations of the HRPP and should have a basic understanding of the relevant laws, codes, regulations and guidance that govern research involving human participants, the responsibilities of an organizational official, and the responsibilities of the IRB or EC and researchers and research staff in protecting research participants. This individual should be directly involved in the allocation of resources to the HRPP. In some circumstances, more than one individual serves in this capacity³. At Harvard University Area, the OO is the University Chief Research Compliance Officer.

3.31 Institutional Profile: A record of information an institution keeps about another collaborating institution/organization for one or more Collaborative Studies or Multi-Site Studies.

3.32 Investigation: A searching inquiry for facts; detailed or careful examination.

3.33 Legally Authorized Representative (LAR): An individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research.

3.33.1 If there is no applicable law addressing this issue, then this individual is recognized by institutional policy as acceptable for providing consent in the non-research context on behalf of the prospective subject to the subject's participation in the procedure(s) involved in the research.

3.33.2 See "SOP - HUA -: LARs, Children, and Guardians (HRP-013)" for who may serve as a Legally Authorized Representative at this institution.

3.34 Minimal Risk: 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.⁴

3.34.1 For research involving prisoners Minimal Risk is the probability and magnitude of physical or psychological harm normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons.

3.34.2 When following Department of Defense regulations, the definition of minimal risk in 32 CFR 219 does not include the inherent occupational risks that certain participants face in their everyday life, such as those:

3.34.2.1 Encountered by Service members, law enforcement, or first responders while on duty.

3.34.2.2 Resulting from or associated with high-risk behaviors or pursuits.

3.34.2.3 Experienced by individuals whose medical conditions involve frequent tests or constant pain.

² <https://www.hhs.gov/ohrp/sachrp-committee/recommendations/2008-september-18-letter-attachment/index.html>

³ AAHRPP Evaluation Instrument (2018-10-15); <http://www.aahrpp.org/apply/web-document-library/domain-i-organization>

⁴ The phrase "ordinarily encountered in daily life or during the performance of routine physical or physiological examinations or tests" should not be interpreted to include the inherent risks certain categories of subjects face in their everyday life. For example, the risks imposed in research involving human subjects focused on a special population should not be evaluated against the inherent risks encountered in their environment (e.g., emergency responder, pilot, soldier in a combat zone) or having a medical condition (e.g., frequent medical tests or constant pain).

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- 3.35 Multi-Site Study: A study in which two or more institutions coordinate, with each institution completing all research activities outlined in a specific protocol.
- 3.36 Non-Committee Review: Any of the following:
- 3.36.1 Determination of whether an activity is Human Research.
 - 3.36.2 Determination of whether Human Research is exempt from regulation.
 - 3.36.3 Reviews of non-exempt research using the expedited procedure.
 - 3.36.4 Determinations of which subjects can continue in expired research.
- 3.37 Non-Compliance: Failure to follow the regulations, or the requirements or determinations of the IRB.
- 3.37.1 In the case of research funded or conducted by the Department of Defense (DOD), Non-Compliance includes failure of a person, group, or institution to act in accordance with Department of Defense (DOD) instruction 3216.02, its references, or applicable requirements
- 3.38 Participating Site: An institution that participates in a Single IRB (sIRB) Study.
- 3.39 Prisoner: Any individual involuntarily confined or detained in a penal institution. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing.
- 3.39.1 For Department of Defense (DOD) research the term includes military personnel in either civilian or military custody.
- 3.40 Protocol Exception: a one-time, intentional action or process that departs from the approved protocol. Protocol Exceptions are generally for a single subject (e.g., the subject does not meet eligibility criteria or is allergic to one of the medications provided as supportive care). IRB approval of the Protocol Exception is required prior to implementation by the study team.
- 3.41 Related to the Research: A financial interest is Related to the Research when the interest is in:
- 3.41.1 A sponsor of the research;
 - 3.41.2 A competitor of the sponsor of the research;
 - 3.41.3 A product or service being tested; or
 - 3.41.4 A competitor of the product or service being tested.
- 3.42 Research as Defined by DHHS: A systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.
- 3.42.1 The following activities are not considered Research as Defined by DHHS:
 - 3.42.1.1 Scholarly and journalistic activities (e.g., oral history, journalism, biography, literary criticism, legal research, and historical scholarship), including the collection and use of information, that focus directly on the specific individuals about whom the information is collected.
 - 3.42.1.2 Public health surveillance activities conducted by a public health authority, limited to those necessary to allow a public health authority to identify, monitor, assess, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance.
 - 3.42.1.2.1 Including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority.
 - 3.42.1.2.2 Including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products.
 - 3.42.1.2.3 Including those associated with providing timely situational awareness and priority setting during the course of an event or crisis that threatens public health (including natural or man-made disasters).



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- 3.42.1.3 Collection and analysis of information, biospecimens, or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes.
- 3.42.1.4 Authorized operational activities (as determined by the relevant federal agency) in support of intelligence, homeland security, defense, or other national security missions.
- 3.42.1.5 Secondary research involving non-identifiable newborn screening blood spots.
- 3.43 Research as Defined by FDA: Any experiment that involves a test article and one or more Human Subjects, and that meets any one of the following:
 - 3.43.1 Must meet the requirements for prior submission to the Food and Drug Administration under section 505(i) of the Federal Food, Drug, and Cosmetic Act meaning any use of a drug other than the use of an approved drug in the course of medical practice;
 - 3.43.2 Must meet the requirements for prior submission to the Food and Drug Administration under section 520(g) of the Federal Food, Drug, and Cosmetic Act meaning any activity that evaluates the safety or effectiveness of a device; OR
 - 3.43.3 Any activity the results of which are intended to be later submitted to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit.
- 3.44 Restricted: Applies to investigators who are delinquent in meeting IRB requirements.
- 3.45 Serious Adverse Event (SAE): An untoward occurrence, whether or not considered related to a subject's participation in Human Research, that results in death, a life-threatening experience, inpatient hospitalization, prolongation of hospitalization, persistent or significant disability or incapacity, congenital anomaly or birth defect, or that requires medical, surgical, behavioral, social or other intervention to prevent such an outcome.
- 3.46 Serious Non-Compliance: Non-Compliance such that the failure to comply could adversely affect the rights, safety, or welfare of a human subject; place a human subject at increased risk of harm; cause harm to a human subject; affect a human subject's willingness to participate in research; or damage or compromise the scientific integrity of research data.
 - 3.46.1 For Department of Defense (DOD) research Serious Non-Compliance includes failure of a person, group, or institution to act in accordance with Department of Defense (DOD) Instruction 3216.02 and its references such that the failure could adversely affect the rights, safety, or welfare of a human subject; place a human subject at increased risk of harm; cause harm to a human subject; affect a human subject's willingness to participate in research; or damage or compromise the scientific integrity of research data.
- 3.47 Single IRB (sIRB) Study: A study in which two or more institutions (Participating Sites, or pSites) coordinate to complete the research activities, but all institutions rely on a single institution's/organization's IRB for ethical review. The reviewing IRB may or may not be affiliated with any of the Participating Sites.
- 3.48 SMARTIRB: An online reliance system to request, track, and document reliance agreements between institutions.
- 3.49 Suspension of IRB Approval: An action of the IRB, IRB designee, Institutional Official/Organizational Official, or designee of the Institutional Official/Organizational Official to temporarily or permanently withdraw IRB approval of some or all research procedures short of a Termination of IRB Approval. Suspended studies remain open and are subject to continuing review.
- 3.50 Termination of IRB Approval: An action of the IRB, IRB designee, Institutional Official/Organizational Official, or designee of the Institutional Official/Organizational Official to permanently withdraw IRB approval of all research procedures. Terminated studies are permanently closed and no longer require continuing review.



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- 3.51 Unanticipated Problem Involving Risks to Subjects or Others: Any information that is (1) unanticipated, (2) related to the research, and (3) indicates that subjects or others are at increased risk of harm.⁵
- 3.51.1 For Department of Defense (DOD) research the term Unanticipated Problem Involving Risks to Subjects or Others includes any incident, experience, or outcome that meets ALL three of the following conditions:
- 3.51.1.1 Is unexpected (in terms of nature, severity, or frequency) given the procedures described in the research protocol documents (e.g., the IRB-approved research protocol and informed consent document) and the characteristics of the human subject population being studied.
- 3.51.1.2 Is related or possibly related to participation in the research (in this Instruction, possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research).
- 3.51.1.3 Suggests that the research places Human Subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized, even if no harm has actually occurred.

4 RESPONSIBILITIES

- 4.1 Individuals writing policies and procedures are to indicate terms defined in this policy with a double underline.
- 4.2 Individuals using policies and procedures are to consult this policy for the definitions of double underlined terms.

5 PROCEDURE

- 5.1 None

6 MATERIALS

- 6.1 SOP: LARs, Children, and Guardians (HRP-013)

7 REFERENCES

- 7.1 45 CFR §46.102.
- 7.2 21 CFR §50.3, 21 CFR §56.102, 21 CFR §312.3, 21 CFR §812.2(a), 21 CFR §812.3(p)
- 7.3 Harvard University Policy on Individual Financial Conflicts of Interest for Persons Holding Faculty and Teaching Appointments - http://files.vpr.harvard.edu/files/vpr-documents/files/harvard_university_fcoi_policy.pdf / http://files.vpr.harvard.edu/files/vpr-documents/files/hu_guidance_on_phs_rule_implementation_0.pdf
- 7.4 AAHRPP elements I.1.A, I.1.E, I.5.D, I.6.B, I.7.C, I-9, II.1.D, II.2.A, II.2.B, II.2.G, II.2.H, II.2.E-II.2.E.2, II.2.F-II.2.F.3, II.2.I, II.3.A, II.4.A, III.1.B, III.2.D

⁵ See OHRP guidance “Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events: OHRP Guidance (2007)” at <https://www.hhs.gov/ohrp/regulations-and-policy/guidance/reviewing-unanticipated-problems/index.html>



SOP: IRB Meeting Conduct				
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1 PURPOSE

- 1.1 This procedure establishes the process to conduct convened meetings.
- 1.2 The process begins when the IRB members gather for a convened meeting.
- 1.3 The process ends when the meeting is adjourned.

2 REVISIONS FROM PREVIOUS VERSION

- 2.1 See [HRPP Toolkit Tracking Spreadsheet](#)

3 POLICY

- 3.1 The IRB reviews research in accordance with the applicable regulatory criteria for approval.
- 3.2 The IRB chair votes as a regular member.
- 3.3 Meetings are conducted in person or via teleconference.
- 3.4 IRB attendance is captured by documenting in the IRB meeting minutes the IRB members and alternates in attendance, replacement of a voting member by an alternate, attendance of IRB members who participate through teleconference, and IRB members who are recused due to a conflicting interest.
- 3.5 If quorum is lost during a meeting, the IRB cannot take votes until the quorum is restored, even if more than half of the members are still present.
- 3.6 Substantive changes or requirements, requests for more information for IRB consideration, and other issues related to the criteria for approval require review and approval by the convened IRB.
- 3.7 Minor or prescriptive changes or requirements (modifications required to secure approval) may be reviewed for approval by the IRB chair or a [Designated Reviewer](#).
- 3.8 The worksheets and checklists described in "WORKSHEET - HUA - Review Materials (HRP-301)" and listed below in "Section 6: MATERIALS" are provided to IRB members in advance of meetings per "SOP - HUA - IRB Meeting Preparation (HRP-040)" to conduct meetings and meet regulatory requirements.

4 RESPONSIBILITIES

- 4.1 The IRB chair carries out these procedures, unless otherwise noted.
- 4.2 Primary reviewers lead IRB members through consideration of the regulatory criteria for approval.

5 PROCEDURE

- 5.1 Call the meeting to order.
- 5.2 Ask IRB members whether anyone has a [Conflicting Interest](#) in any item on the agenda and note the responses.
- 5.3 Ask IRB members if there are any questions about the previous IRB meeting minutes document that was made available to the IRB prior to the meeting. Have the IRB members acknowledge the IRB meeting minutes.
- 5.4 Ask IRB members if there are any questions about the report of completed [Non-Committee Reviews](#) that was made available to the IRB prior to the meeting. Have the IRB members acknowledge the completed [Non-Committee Reviews](#).



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- 5.5 For each agenda item:
- 5.5.1 Table the item when notified by IRB staff that requirements for review of a specific item as defined in “WORKSHEET: Quorum and Expertise (HRP-305)” are not met.¹
 - 5.5.2 If there are IRB members with a Conflicting Interest, invite the IRB to ask questions of those members and then ask those members to leave for discussion and voting or if present by teleconference, be placed on hold or disconnect for discussion and voting.
 - 5.5.3 If there is a consultant present, ask the consultant to present his or her review to the IRB.
 - 5.5.4 If a consultant provided written information to the IRB, ask the primary reviewer to present that information to the IRB.
 - 5.5.5 Ask the scientific or scholarly reviewer or primary reviewer to present the scientific or scholarly review to the IRB following SOP – HUA – Scientific or Scholarly Review (HRP-046).
 - 5.5.6 Ask the primary reviewer to lead the IRB through a discussion of the criteria in the “WORKSHEET: Criteria for Approval (HRP-314)” to have the convened IRB determine which regulatory criteria are met (or continue to be met), which are not met (or no longer met), and which would be met if the investigator modified the protocol as requested by the IRB.
 - 5.5.6.1 See [HUA IRB Member Handbook](#) for more information.
 - 5.5.7 Ask whether the secondary reviewer, if assigned, has any additional comments followed by other members of the convened IRB.
 - 5.5.8 Ask the IRB staff assigned as coordinator for the item under review to provide a summary of all applicable checklists (see item 6, below).
 - 5.5.9 Restate the IRB’s consensus regarding any protocol specific findings justifying a determination when required by a checklist and not previously determined and documented.
 - 5.5.10 Request a motion from the primary reviewer for one of the following actions:
 - 5.5.10.1 Approve (with a specific continuing review interval for initial or continuing review when applicable): Made when all criteria for approval are met. Include in motions for initial and continuing review the period of approval and the level of risk.
 - 5.5.10.2 Modifications Required to Secure Approval (with a specific continuing review interval for initial or continuing review when applicable): Made when IRB members require specific modifications such that an IRB staff member can determine whether an investigator has made the required changes without judging whether a change meets the regulatory criteria for approval. When making this motion, the assigned primary reviewer restates the modifications required by the IRB members and the IRB members’ reasons for those changes
 - 5.5.10.3 Defer: Made when the research does not qualify for Approval or Modifications Required to Secure Approval and the IRB has recommendations that might make the protocol approvable. When making this motion, the assigned primary reviewer describes the IRB members’

¹ If the Board is not ready to vote – be it a lack of information, a sensitive topic people need more time to process or deliberate, or other urgent matters came up – a member may make a motion to “table” the item. The motion needs a second. It is NOT debatable/open to discussion. And then it needs a majority to carry the motion. The important point to remember; however, is that it must be re-addressed at the next official meeting, or when appropriate.

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- reasons for the decision and describes recommendation to make the research approvable.
- 5.5.10.4 Disapprove: Made when the research does not qualify for Approval or Modifications Required to Secure Approval and the IRB has no recommendations that might make the protocol approvable. When making this motion, the assigned primary reviewer describes the IRB members' reasons for the decision.
 - 5.5.10.5 Suspension or Termination of IRB Approval: Made when current approved research does not qualify for Approval or Modifications Required to Secure Approval. When making this motion, have the primary reviewer use the "WORKSHEET: Review of Information Items (HRP-321)" to lead the convened IRB through a discussion of what actions are needed, if any, to protect subjects. The assigned primary reviewer describes the IRB members' reasons for the decision.
 - 5.5.11 Request a second on the motion from any IRB member in attendance to confirm the previous stated motion.
 - 5.5.12 Review any modifications required to secure approval to ensure that the IRB staff has recorded them.
 - 5.5.12.1 Ensure that the required modifications include all final contingencies on "CHECKLIST: Pre-Review (HRP-401)."
 - 5.5.12.2 Ensure that the required modifications include all final contingencies in the Pre-Review activity.
 - 5.5.12.3 For a pending financial interest review indicate that a determination that the financial interest is not a Conflicting Interest or has been eliminated and can be verified by the IRB staff in coordination with the School's Conflict of Interest Officer. If there is a management plan put in place by the School's Conflict of Interest Officer relating, it must return to the convened IRB for review.
 - 5.6 For each agenda item that is new information (Unanticipated Problem Involving Risks to Subjects or Others, Serious Non-Compliance, Continuing Non-Compliance, Suspension of IRB Approval, or Terminations of IRB Approval):
 - 5.6.1 Have the primary reviewer use the "WORKSHEET: Review of Information Items (HRP-321)" to lead the convened IRB through a discussion of what actions are needed, if any, to protect subjects.
 - 5.6.2 Restate the IRB's consensus regarding any actions that need to be taken to protect subjects.
 - 5.6.3 Make a motion for the IRB's determination(s) regarding the action items (e.g. the motion is for the Principal Investigator to provide the IRB additional information regarding the status of currently enrolled subjects).
 - 5.6.4 Open the floor for additional discussion.
 - 5.7 Call for a vote.
 - 5.7.1 Only IRB members may vote.
 - 5.7.2 If a member and an alternate are both present, only one may vote.
 - 5.7.3 Consultants may not vote.
 - 5.7.4 For a motion to be approved, it needs the approval of more than half of the members present at the meeting. (If there are 10 or 11 members present at the meeting, 6 votes are required for approval, which is greater than 5 and 5.5, respectively.)
 - 5.8 Re-invite IRB members with a Conflicting Interest back into the meeting.
 - 5.9 Provide any written information provided by a member or consultant to the IRB staff.



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5.10 Adjourn the meeting when notified by IRB staff that quorum has been lost or when there is no further business.

6 MATERIALS

- 6.1 SOP - HUA - IRB Meeting Preparation (HRP-040)
- 6.2 SOP – HUA – Scientific or Scholarly Review (HRP-046)
- 6.3 WORKSHEET - HUA - Review Materials (HRP-301)
- 6.4 WORKSHEET - Quorum and Expertise (HRP-305)
- 6.5 WORKSHEET - Pre-Review (HRP-308)
- 6.6 WORKSHEET - Criteria for Approval (HRP-314)
- 6.7 WORKSHEET - Advertisements (HRP-315)
- 6.8 WORKSHEET - Payments (HRP-316)
- 6.9 WORKSHEET - Short Form of Consent Documentation (HRP-317)
- 6.10 WORKSHEET - Additional Federal Agency Criteria (HRP-318)
- 6.11 WORKSHEET - Scientific or Scholarly Review (HRP-320)
- 6.12 WORKSHEET - Review of Information Items (HRP-321)
- 6.13 CHECKLIST - Pre-Review (HRP-401)
- 6.14 CHECKLIST - Waiver or Alteration of Consent Process (HRP-410)
- 6.15 CHECKLIST - Waiver of Written Documentation of Consent (HRP-411)
- 6.16 CHECKLIST - Pregnant Women (HRP-412)
- 6.17 CHECKLIST - Non-Viable Neonates (HRP-413)
- 6.18 CHECKLIST - Neonates of Uncertain Viability (HRP-414)
- 6.19 CHECKLIST - Prisoners (HRP-415)
- 6.20 CHECKLIST - Children (HRP-416)
- 6.21 CHECKLIST - Cognitively Impaired Adults (HRP-417)
- 6.22 CHECKLIST - Non-significant Risk Device (HRP-418)
- 6.23 CHECKLIST - Information Security Level Determination (HRP-442)
- 6.24 CHECKLIST - Use of Human Fetal Tissue in Research (HRP-445)
- 6.25 HUA IRB Member Handbook, https://projects.iq.harvard.edu/files/irb-members-page/files/irb_member_handbook.pdf

7 REFERENCES

- 7.1 21 CFR §50.20, §50.25, §50.27, §56.109, §56.111
- 7.2 45 CFR §46.109, §46.116, §46.117
- 7.3 AAHRPP elements I.1.F, I.5.A, I.5.D, I.6.B, I.7.A, I-9, II.1.B, II.1.D, II.1.E, II.2.D, II.2.G, II.2.E-II.2.E.2, II.2.F-II.2.F.3



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Human Research Protection Program

WORKSHEET: Review Materials - <i>Harvard University Area IRB</i>		
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The purpose of this worksheet is to provide support for IRB staff who prepare review materials for convened IRB meetings or prepare materials for Non-Committee Review. This worksheet lists the information that each IRB member/Designated Reviewer, scientific/scholarly reviewer, or consultant needs to review and the worksheets or checklist to be used. For individuals who have electronic (computer) access to or provided all information, this document describes the subset of materials the IRB member is expected to access and review. For individuals who are provided a subset of the information, this document describes the subset of materials the IRB staff are to provide to each individual.¹

1 GENERAL INFORMATION FOR ALL IRB MEMBERS FOR CONVENED MEETINGS

- ☐ List of protocols approved using the expedited procedure
- ☐ Information for Other Business items
- ☐ Educational Materials

¹ This document satisfies AAHRPP elements I.1.F, I.5.D, I-9, II.1.B, II.2.D, II.2.G, II.2.E-II.2.E.2, II.2.F-II.2.F.3

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2 FOR EACH PROTOCOL UNDERGOING INITIAL REVIEW		
Documents for All IRB Members and Alternate IRB Members	Additional Items for the Scientific/Scholarly Reviewer	Items for Consultants and individuals without reviewer access to the submission
Include when the protocol involves these items: ☐ WORKSHEET: Advertisements (HRP-315) ☐ WORKSHEET: Payments (HRP-316) ☐ WORKSHEET: Criteria for Approval (HRP-314) ☐ WORKSHEET: Short Form of Consent Documentation (HRP-317) ☐ WORKSHEET: Additional Federal Agency Criteria (HRP-318) ☐ WORKSHEET: Certificate of Confidentiality (HRP-333) ☐ CHECKLIST: Waiver or Alteration of Consent Process (HRP-410) ☐ CHECKLIST: Waiver of Written Documentation of Consent (HRP-411) ☐ CHECKLIST: Pregnant Women (HRP-412) ☐ CHECKLIST: Non-Viable Neonates (HRP-413) ☐ CHECKLIST: Neonates of Uncertain Viability (HRP-414) ☐ CHECKLIST: Prisoners (HRP-415) ☐ CHECKLIST: Children (HRP-416) ☐ CHECKLIST: Cognitively Impaired Adults (HRP-417) ☐ CHECKLIST: Non-Significant Risk Device (FDA) (HRP-418)	Include: ☐ WORKSHEET: Scientific or Scholarly Review (HRP-320) Include when they exist: ☐ Scientific evaluation	Include: ☐ Cover letter to consultants Include as appropriate materials provided to any other reviewer.

WORKSHEET: Review Materials - <i>Harvard University Area IRB</i>		
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3 FOR EACH PROTOCOL UNDERGOING CONTINUING REVIEW	
Documents for All IRB Members and Alternate IRB Members	Documents for Consultants and individuals without reviewer access to the submission
Include when the protocol involves these items: ☐ WORKSHEET: Advertisements (HRP-315) ☐ WORKSHEET: Payments (HRP-316) ☐ WORKSHEET: Criteria for Approval (HRP-314) ☐ WORKSHEET: Short Form of Consent Documentation (HRP-317) ☐ WORKSHEET: Additional Federal Agency Criteria (HRP-318) ☐ WORKSHEET: Certificate of Confidentiality (HRP-333) ☐ CHECKLIST: Waiver or Alteration of Consent Process (HRP-410) ☐ CHECKLIST: Waiver of Written Documentation of Consent (HRP-411) ☐ CHECKLIST: Pregnant Women (HRP-412) ☐ CHECKLIST: Non-Viable Neonates (HRP-413) ☐ CHECKLIST: Neonates of Uncertain Viability (HRP-414) ☐ CHECKLIST: Prisoners (HRP-415) ☐ CHECKLIST: Children (HRP-416) ☐ CHECKLIST: Cognitively Impaired Adults (HRP-417) ☐ CHECKLIST: Non-Significant Risk Device (FDA) (HRP-418)	Include: ☐ Cover letter to consultants Include as appropriate materials provided to any other reviewer.

WORKSHEET: Review Materials - <i>Harvard University Area IRB</i>		
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4 FOR EACH PROTOCOL UNDERGOING REVIEW OF MODIFICATIONS		
Documents for All IRB Members and Alternate IRB Members	Additional Documents for the Scientific/Scholarly Reviewer	Documents for Consultants and individuals without reviewer access to the submission
Include: ☐ WORKSHEET: Criteria for Approval (HRP-314) Add when modification involves these items: ☐ WORKSHEET: Advertisements (HRP-315) ☐ WORKSHEET: Payments (HRP-316) ☐ WORKSHEET: Short Form of Consent Documentation (HRP-317) ☐ WORKSHEET: Additional Federal Agency Criteria (HRP-318) ☐ WORKSHEET: Certificate of Confidentiality (HRP-333) ☐ CHECKLIST: Waiver or Alteration of Consent Process (HRP-410) ☐ CHECKLIST: Waiver of Written Documentation of Consent (HRP-411) ☐ CHECKLIST: Pregnant Women (HRP-412) ☐ CHECKLIST: Non-Viable Neonates (HRP-413) ☐ CHECKLIST: Neonates of Uncertain Viability (HRP-414) ☐ CHECKLIST: Prisoners (HRP-415) ☐ CHECKLIST: Children (HRP-416) ☐ CHECKLIST: Cognitively Impaired Adults (HRP-417) ☐ CHECKLIST: Non-Significant Risk Device (FDA) (HRP-418)	Include: ☐ WORKSHEET: Scientific or Scholarly Review (HRP-320) (if the amendments are substantive)	Include: ☐ Cover letter to consultants Include as appropriate materials provided to any other reviewer.



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5 FOR EACH PROBLEM (UNANTICIPATED PROBLEM INVOLVING RISKS TO SUBJECTS OR OTHERS, OR SERIOUS OR CONTINUING NON-COMPLIANCE)	
Documents for All IRB Members, Alternate IRB Members, Primary Reviewer, Prisoner Representative, and Scientific/Scholarly Reviewer	Documents for Consultants and individuals without reviewer access to the submission
Include: ☐ WORKSHEET: Review of Information Items (HRP-321) ☐ WORKSHEET: Criteria for Approval (HRP-314) Add when the problem involves a protocol and the new information affects these items: ☐ WORKSHEET: Advertisements (HRP-315) ☐ WORKSHEET: Payments (HRP-316) ☐ WORKSHEET: Short Form of Consent Documentation (HRP-317) ☐ WORKSHEET: Additional Federal Agency Criteria (HRP-318) ☐ WORKSHEET: Certificate of Confidentiality (HRP-333) ☐ CHECKLIST: Waiver or Alteration of Consent Process (HRP-410) ☐ CHECKLIST: Waiver of Written Documentation of Consent (HRP-411) ☐ CHECKLIST: Pregnant Women (HRP-412) ☐ CHECKLIST: Non-Viable Neonates (HRP-413) ☐ CHECKLIST: Neonates of Uncertain Viability (HRP-414) ☐ CHECKLIST: Prisoners (HRP-415) ☐ CHECKLIST: Children (HRP-416) ☐ CHECKLIST: Cognitively Impaired Adults (HRP-417) ☐ CHECKLIST: Non-Significant Risk Device (FDA) (HRP-418)	Include: ☐ Cover letter to consultants Include as appropriate materials provided to any other reviewer.

**WORKSHEET: Criteria for Approval**

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The purpose of this worksheet is to provide support for IRB members reviewing research. This worksheet is to be used, it does not need to be completed or retained. (LAR = subject's Legally Authorized Representative)¹

1 General Considerations (Check if "Yes" or "N/A". All must be checked)

- ☐ The convened IRB (or Designated Reviewer) has, or has obtained through consultation, adequate expertise.
- ☐ For initial review the principal investigator is not Restricted. (N/A if not initial review) N/A: ☐
- ☐ Materials are complete.

2 Criteria for Approval of Research: (Check if "Yes" or N/A. All must be checked) (Applies to initial, continuing, modifications)

- ☐ Risks to subjects are minimized by using procedures that are consistent with sound research design and that do not unnecessarily expose subjects to risk.
- ☐ Risks to subjects are minimized by using procedures already being performed on the subjects for diagnostic or treatment purposes. (N/A if none) N/A: ☐
- ☐ Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result.ⁱ
- ☐ Selection of subjects is equitable.ⁱⁱ (Consider the purpose and setting of the research, involvement of vulnerable subjects, selection criteria, and recruitment, enrollment, and payment procedures.)
- ☐ The research plan makes adequate provision for monitoring collected data to ensure the safety of subjects. (N/A if Minimal Risk) N/A: ☐ ⁱⁱⁱ
- ☐ There are adequate provisions to protect the privacy of subjects.^{iv}
- ☐ There are adequate provisions to maintain the confidentiality of data.^v
- ☐ Additional safeguards have been included in the study to protect the rights and welfare of subjects vulnerable to coercion or undue influence.^{vi} (N/A if no vulnerable subjects) N/A: ☐
- ☐ The informed consent process meets one of these sections or checklists
☐ Section 5: Consent Process ☐ Waiver or alteration of consent process (HRP-410) ☐ Permanently closed to enrollment
- ☐ The informed consent documentation meets one of these sections, worksheets, or checklists
☐ Section 6: Long Form ☐ Waiver of documentation (HRP-411) ☐ Permanently closed to enrollment
☐ Short Form (HRP-317) ☐ Waiver or alteration of consent process (HRP-410)
- ☐ Additional applicable criteria^{vii} are met (N/A if none) N/A: ☐

3 Additional Considerations (Check all that apply.)

- ☐ The research involves no more than Minimal Risk to subjects.
- ☐ The research requires Continuing review. (Note that for FDA or DOJ overseen research or research subject to Pre-2018 Requirements, there is no option not to require Continuing review.)
The research does not require Continuing review if one of the following apply:
☐ The research is eligible for expedited review. (See HRP-313-WORKSHEET: Expedited Review)
☐ The research has progressed to the point that it involves only one or both of the following, which are part of the IRB-approved study: (A) Data analysis, including analysis of identifiable private information or identifiable biospecimens, or (B) Accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care.
- ☐ Review should take place more often than annually.^{viii} If so, specify period.
- ☐ Verification is needed from sources other than the investigator that no material changes have occurred since prior review.^{ix} (N/A if initial) N/A: ☐
- ☐ New information needs to be provided to subjects because it may affect their willingness to continue participation. (N/A if initial) N/A: ☐

4 Primary Reviewer Criteria for Initial review (Check if "Yes" or "N/A". All must be checked; May be determined by a primary reviewer)

- ☐ The research has the resources necessary to protect subjects. (Time to conduct and complete the research; adequate facilities, subject pool, and medical/psychosocial resources; qualified investigators and research staff; appropriate qualifications for international research.)
- ☐ The plan for communication among sites is adequate to protect subjects. (N/A if not a Multi-Site Study where PI is the lead or not initial) N/A: ☐
- ☐ There are no inconsistencies between the DHHS grant and protocol. (N/A if research subject to 2018 Requirements or if there is no DHHS grant.) N/A: ☐

Complete remaining items when applicable**5 Consent Process** (Check if "Yes". All must be checked)

- ☐ The investigator will obtain the legally effective informed consent of the subject or LAR.
- ☐ The circumstances of consent provide the prospective subject or LAR sufficient opportunity to consider whether or not to participate.
- ☐ The circumstances of consent minimize the possibility of coercion or undue influence.
- ☐ Information to be given to the subject or LAR will be in language understandable^x to the subject or LAR.

¹ This document satisfies AAHRPP elements I.1.E, I.1.F, I.7.C, I-9, II.1.E, II.2.E-II.2.E.2, II.2.F-II.2.F.3, II.2.I, II.3.A, II.3.B, II.3.C-II.3.C.1, II.3.D, II.3.E, II.3.F, II.3.G, II.4.A, II.4.B, III.1.F

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- ☐ The prospective subject or the LAR must be provided with the information that a reasonable person would want to have in order to make an informed decision about whether to participate, and an opportunity to discuss that information. **(N/A if research is subject to Pre-2018 Requirements) N/A:** ☐
- ☐ Informed consent must begin with a concise and focused presentation of the key information that is most likely to assist a prospective subject or LAR in understanding the reasons why one might or might not want to participate in the research. This part of the informed consent must be organized and presented in a way that facilitates comprehension. **(N/A if research is subject to Pre-2018 Requirements) N/A:** ☐
- ☐ Informed consent as a whole must present information in sufficient detail relating to the research, and must be organized and presented in a way that does not merely provide lists of isolated facts, but rather facilitates the prospective subject's or LAR's understanding of the reasons why one might or might not want to participate. **(N/A if research is subject to Pre-2018 Requirements) N/A:** ☐
- ☐ There is no exculpatory language^{xi} through which the subject or LAR is made to waive or appear to waive the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution or its agents from liability from negligence.
- ☐ Consent will disclose the elements in **Section 7: Elements of Consent Disclosure**

6 Long Form of Consent Documentation (Check if "Yes" or "N/A". All must be checked) **(N/A if long form not implemented N/A:** ☐**)**

- ☐ The written consent document is accurate, complete, and consistent with the protocol.
- ☐ The written consent document embodies the elements in **Section 7: Elements of Consent Disclosure** (N/A if alteration is in place) **N/A** ☐
- ☐ The investigator will give either the subject or LAR adequate opportunity to read the consent document before it is signed.
- ☐ The subject or LAR will sign and date the consent document. (N/A if no signature line) **N/A** ☐
- ☐ The person obtaining consent will sign and date the consent document. **N/A** ☐
- ☐ A copy of the signed and dated consent document will be given to the person signing the document.
- ☐ If there is a LAR or parent signature line, the IRB has approved inclusion of adults unable to consent or children. (N/A if no signature line) **N/A** ☐
- ☐ When a subject or LAR is unable to read: An impartial witness will be present during the entire consent discussion and the consent document notes that the witness attests that the information in the consent document and any other information provided was accurately explained to, and apparently understood by, the subject or LAR, and that consent was freely given. **(N/A if all subjects are able to read) N/A:** ☐

7 Elements of Consent Disclosure^{xii} (Check if "Yes" or "N/A". All must be checked)**Required:** (*Can be omitted if there are none.)

- ☐ The study involves research.
- ☐ The purposes of the research.
- ☐ The expected duration of the subject's participation.
- ☐ The procedures to be followed.
- ☐ Identification of any procedures, which are experimental.*
- ☐ Any reasonably foreseeable risks or discomforts to the subject.*
- ☐ Any benefits to the subject or to others, which may reasonably be expected from the research.*^{xiii}
- ☐ Appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject.*
- ☐ The extent, if any, to which confidentiality of records identifying the subject will be maintained.*
- ☐ How to contact the research team for questions, concerns, or complaints about the research.
- ☐ How to contact someone independent of the research team for questions, concerns, or complaints about the research; questions about the subjects' rights; to obtain information; or to offer input.
- ☐ Whom to contact in the event of a research-related injury to the subject.
- ☐ Participation is voluntary.
- ☐ Refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled.
- ☐ The subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

Required for Clinical Trials that Follow ICH-GCP

- ☐ The approval of the IRB.
- ☐ The probability for random assignment to each treatment.
- ☐ The subject's responsibilities.
- ☐ When applicable, the reasonably foreseeable risks or inconveniences to an embryo, fetus, or nursing infant.
- ☐ The important potential benefits and risks of the alternative procedures or courses of treatment that may be available to the subject.
- ☐ When there is no intended clinical benefit to the subject, a statement to this effect.
- ☐ The monitors, auditors, IRB, and regulatory authorities will be granted direct access to the subject's original medical records for verification of clinical trial procedures and data, without violating the confidentiality of the subject, to the extent permitted by applicable laws and regulations and that, by signing the consent document, the subject or LAR is authorizing such access.
- ☐ If the results of the trial are published, the subject's identity will remain confidential.

Required for FDA-Regulated Research^{xiv}

- ☐ The possibility that the Food and Drug Administration may inspect the records and should not state or imply that FDA needs permission from the subject for access to the records^{xv}.
- ☐ The data collected on the subject to the point of withdrawal remains part of the study database and may not be removed.
- ☐ The investigator should ask a subject who is withdrawing whether the subject wishes to provide further data collection from routine medical care.
- ☐ For controlled drug/device trials (except Phase I drug trials) and pediatric device surveillance trials: "A description of this clinical trial will be available on <http://www.ClinicalTrials.gov>, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time."

Additional: (Include when appropriate.)

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| <p>☐ One of the following statements about any research that involves the collection of <u>identifiable private information</u> or <u>identifiable biospecimens</u>:</p> <p>☐ A statement that identifiers might be removed from the <u>identifiable private information</u> or <u>identifiable biospecimens</u> and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from the subject or the <u>LAR</u>, if this might be a possibility; or</p> <p>☐ A statement that the subject's information or biospecimens collected as part of the research, even if identifiers are removed, will not be used or distributed for future research studies.</p> <p>(N/A if research is subject to Pre-2018 Requirements) N/A: ☐</p> <p>Required for More than Minimal Risk Research</p> <p>☐ Whether any compensation is available if injury occurs and, if so, what it consists of, or where further information may be obtained.</p> <p>☐ Whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained.</p> | <p>☐ The particular treatment or procedure may involve risks to the subject, which are currently unforeseeable.</p> <p>☐ If the subject is or becomes pregnant, the particular treatment or procedure may involve risks to the embryo or fetus, which are currently unforeseeable.</p> <p>☐ Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent.</p> <p>☐ Any additional costs to the subject that may result from participation in the research.</p> <p>☐ The consequences of a subject's decision to withdraw from the research.</p> <p>☐ Procedures for orderly termination of participation by the subject.</p> <p>☐ Significant new findings developed during the course of the research, which may relate to the subject's willingness to continue participation will be provided to the subject.</p> <p>☐ Approximate number of subjects involved in the study.</p> <p>☐ Amount and schedule of all payments.</p> <p>☐ A statement that the subject's biospecimens (even if identifiers are removed) may be used for commercial profit and whether the subject will or will not share in this commercial profit. (N/A if research is subject to Pre-2018 Requirements)</p> <p>☐ A statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions. (N/A if research is subject to Pre-2018 Requirements)</p> <p>☐ For research involving biospecimens, whether the research will (if known) or might include whole genome sequencing (<i>i.e.</i>, sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen). (N/A if research is subject to Pre-2018 Requirements)</p> <p>☐ Any additional information which should be given to subjects when in the IRB's judgement the information would meaningfully add to the protection of the rights and welfare of subjects.^{xvi}</p> <p>☐ When the study involves genetic testing, a statement that outlines the protections afforded to the subject under the Genetic Information Nondiscrimination Act (GINA).</p> |
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8 Additional Considerations for Electronic Consent^{xvii}

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|--------------------------|---|
| ☐ | Electronic consent document includes all elements in Section 7-Elements of Consent Disclosure (N/A if alteration is in place) N/A: ☐ |
| ☐ | The date of the electronic signature will be captured (N/A if waiver of documentation of consent is requested and justified) N/A: ☐ |
| ☐ | Questions or methods to gauge subject comprehension of key study elements are clearly defined in the informed consent procedures. |
| ☐ | Electronic consent process includes age appropriate materials to facilitate comprehension. |
| ☐ | Electronic consent process is suitable to the study population or procedures are outlined to accommodate subject's needs. |
| ☐ | Electronic consent document/process allows subjects to proceed forward or backward or pause for review later. |
| ☐ | Measures are present to ensure that subjects have access to all of the consent related materials, including hyperlinks or other external documents. |
| ☐ | Plans are adequate to maintain external hyperlinks or documents and subject access to these documents throughout the lifespan of the study until completion are detailed in the informed consent procedures. |
| ☐ | The informed consent process outlines in detail how any included documents will be utilized. |
| ☐ | Measures are present to ensure that the identity of the signer and the integrity of the data can be verified when consent is not witnessed by the study team. |
| ☐ | For FDA-Regulated <u>Clinical Trials</u> including children as research subjects, if the parent or guardian initially documents the child's assent, procedures are in place to verify the child's identity and assent when the child initially presents to the investigator.
(N/A if the research is not an FDA-Regulated Clinical Trial) N/A: ☐ |

ⁱ In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). The IRB should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.

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- ii In making this assessment the IRB should take into account the purposes of the research and the setting in which the research will be conducted. The IRB should be particularly cognizant of the special problems of research that involves a category of subjects who are vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons.
- iii When the IRB determines that data and safety monitoring is appropriate, the IRB will evaluate the adequacy of those plans by considering such issues as reporting mechanisms, the frequency of the monitoring, the entity that will conduct the monitoring, the specific data to be monitored, procedures for analysis and interpretation of the data, actions to be taken upon specific events or end points, and procedures for communication from the data monitor to the IRB and sites. (AAHRPP Tip Sheet #6, section 5)
- iv The IRB will consider it appropriate to include adequate provisions to protect the privacy of subjects when there is a reasonable expectation that prospective research subjects will want to control how, and with whom, they interact and communicate, particularly on issues that may be "sensitive" or "private." The IRB will determine whether there are adequate provisions to protect the privacy of subjects by considering subjects' potential comfort with the procedures being performed, comfort with the research setting, and comfort with the information being sought. (AAHRPP Tip Sheet #5 section 2b-c)
- v The Secretary of HHS will, after consultation with the Office of Management and Budget's privacy office and other Federal departments and agencies that have adopted this policy, issue guidance to assist IRBs in assessing what provisions are adequate to protect the privacy of subjects and to maintain the confidentiality of data. In the interim, the IRB will consider it appropriate to make adequate provisions to maintain confidentiality of data any time confidentiality is promised by the investigator, or when there are legal/ethical requirements to maintain data confidentiality. The IRB will determine whether there are adequate provisions to maintain the confidentiality of that data based on a review of the procedures that are in place to meet those promises or legal/ethical requirements (e.g. What information is included in the data, how it is stored, how long it will be stored, who will have access to it, and who will be responsible for receiving/transmitting it.) (AAHRPP Tip Sheet #4 section 2b-c)
- vi When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects.
- vii Advertisements (HRP-315); Payments (HRP-316); Additional Federal Agency Criteria (HRP-318); Pregnant Women (HRP-412); Non-Viable Neonates (HRP-413); Neonates of Uncertain Viability (HRP-414); Prisoners (HRP-415); Children (HRP-416); Cognitively Impaired Adults (HRP-417); Non-Significant Risk Device (HRP-418)
- viii Consider nature and level of risks; degree of uncertainty regarding the risks; subject vulnerability; investigator experience; IRB's experience with investigator or sponsor; projected rate of enrollment; and whether study involves novel procedures.
- ix Implement when the veracity of the information provided is questioned.
- x "Understandable" means the information presented to prospective subject is in a language and at a level the subjects can comprehend (including an explanation of scientific and medical terms) FDA's Informed Consent Guidance for IRBs, Clinical Investigators, and Sponsors (August 2023) <https://www.fda.gov/media/88915/download>
- xi FDA considers exculpatory language to be language that has the general effect of freeing or appearing to free an individual or an entity from malpractice, negligence, blame, fault, or guilt FDA's Informed Consent Guidance for IRBs, Clinical Investigators, and Sponsors (August 2023) <https://www.fda.gov/media/88915/download>
- xii For additional guidance for FDA-regulated research on the elements of consent (including examples and recommendations on language), please see FDA's Informed Consent Guidance for IRBs, Clinical Investigators, and Sponsors (August 2023) <https://www.fda.gov/media/88915/download>
- xiii If payments, including reimbursement for research-related expenses incurred by subjects due to participation, are provided, the consent process should not identify them as benefits FDA's Informed Consent Guidance for IRBs, Clinical Investigators, and Sponsors (August 2023) <https://www.fda.gov/media/88915/download>
- xiv The FDA generally recommends against including statements such as "FDA has given permission for the clinical investigation to proceed" or "FDA has approved the clinical investigation" in the informed consent process, because such statements may suggest to subjects that the investigation has FDA's endorsement. FDA's Informed Consent Guidance for IRBs, Clinical Investigators, and Sponsors (August 2023) <https://www.fda.gov/media/88915/download>
- xv FDA's Informed Consent Guidance for IRBs, Clinical Investigators, and Sponsors (August 2023) <https://www.fda.gov/media/88915/download>
- xvi 21 CFR 56.109 (b): (b) An IRB shall require that information given to subjects as part of informed consent is in accordance with 50.25. The IRB may require that information, in addition to that specifically mentioned in 50.25, be given to the subjects when in the IRB's judgment the information would meaningfully add to the protection of the rights and welfare of subjects.
- xvii [Use of Electronic Informed Consent: Questions and Answers | HHS.gov](#). According to this guidance, electronic informed consent refers to the use of electronic systems and processes that may employ multiple electronic media, including text, graphics, audio, video, podcasts, passive and interactive Web sites, biological recognition devices, and card readers, to convey information related to the study and to obtain and document informed consent.