



Human Research Protection Program Plan

September 2023

Throughout this document “University” refers to Case Western Reserve University.

Table of Contents

Purpose.....	4
Definitions.....	4
Mission.....	7
Scope.....	7
Ethical Principles and Regulatory Mandates	7
Legal Requirements.....	7
Institutional Oversight of Federalwide Assurance	8
Responsibilities of the IRB under the Federalwide Assurance	9
Policy Oversight Committee	10
Institutional Review Board Advisory Committee (IAC).....	10
Other Requirements.....	10
Sponsored Human Research.....	12
Scope of Human Research Protection Program	12
Human Research Protection Program Policies and Procedures	12
Human Research Protection Program Components	12
Institutional Official	12
Plan to Evaluate Resources Needed for the HRPP	13
Organizational Official	14
The Organizational Officials have the responsibility to:	14
Institutional Review Board (IRB)	15
Responsibilities of the IRB	16
CWRU Investigators and Study Staff.....	18
Legal Counsel.....	19
Dean/Department Chairs	19
Office of Research Administration	20
Education and Training	20
Questions and Additional Information for the IRB	20
Reporting and Management of Concerns.....	20
For Research Participants.....	21
IRB working with CWRU’s Conflict of Interests Committee.....	21

Relying on another IRB.....22
 Ensuring AAHRPP Standards when Relying on another IRB.....22
 Reliance Request Process22
Monitoring and Auditing.....23
Disciplinary Actions23
Approval and Revisions to the Plan24

Purpose

The promotion of scholarship and the discovery of new knowledge through research are among the major functions of Case Western Reserve University (CWRU) as an institution of higher learning. If this research is to be meaningful and beneficial to humanity, involvement of human subjects as study participants is necessary. It is imperative that investigators in all disciplines protect the rights, welfare and privacy of human research subjects.

University policy and federal regulations mandate compliance with all applicable requirements. Moreover, faculty investigators also have a moral obligation to humankind. The interests of society and the rights of individual subjects must be protected as investigators carry out the mandate to advance knowledge. Research may entail risks to human subjects. Therefore, investigators are obligated to weigh those risks in light of potential benefits to the subject and/or to society.

The CWRU HRPP Policies are outlined in the Human Research section of the Faculty Handbook.

Definitions

Agent: An individual who is faculty member, employee, or student is considered an agent of this Organization for purposes of engagement in Human Research when that individual is on-duty in any capacity as an employee of this Organization

- An individual who is not a faculty member, employee, or student is considered an agent of this Organization for purposes of engagement in Human Research when that individual has been specifically authorized to conduct Human Research on behalf of this Organization.
- An organizational official has the ultimate authority to determine whether someone is acting as an agent of this Organization.

Clinical Trial: A biomedical research study of human subjects designed to answer specific questions about therapeutic interventions (drugs, treatments, devices, or new ways of using known drugs, treatments, or devices). Clinical trials are used to determine whether new therapeutic interventions are safe and effective.

NIH Definition of a 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 those interventions on health-related biomedical or behavioral outcomes.

Engaged in Human Research: In general, this Organization is considered engaged in Human Research when this Organization's faculty members, employees or students 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 the subjects of the research; -OR-
3. Informed consent of human subjects for the research. This Organization follows OHRP guidance on “Engagement of Institutions in Research”¹ to apply this definition and exceptions to this definition.

Human Subjects Research: The CWRU IRB has the sole authority to determine whether an activity meets the definition of “Human Subjects Research”. When activities are conducted that might represent “Human Subjects Research”, the activities must be submitted to the IRB for a determination. An Investigator may request a determination that an activity is “Not Human Subjects Research,” but the final determination will be made by the IRB. The IRB will make a determination whether an activity is “Human Subject Research” by considering whether the activity either:

1. Meets the regulatory definitions of “research” that involves “human subjects,” or
2. Meets the regulatory definition of “clinical investigation”.

Human Subject as Defined by DHHS: A living individual about whom an investigator (whether professional or student) conducting research obtains:

1. Data through Intervention or Interaction with the individual, or
2. Information that is both Private Information and Identifiable Information.

For the purpose of this definition:

- **Intervention:** Includes both physical procedures by which data are gathered (e.g., fMRI, attaching leads, etc.) and manipulations of the subjects’ environment that are performed for research purposes.
- **Interaction:** Includes communication or interpersonal contact between an Investigator or his/her research staff and the research participant.
- **Private information:** includes 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 which the individual can reasonably expect will not be made public (for example, an educational record).
- **Individually identifiable:** means that the identity of the subject is or may readily be ascertained by the investigator or associated with the information.

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.

Institutional Review Board as Defined by DHHS

A specially constituted review body established or designated by an entity to protect the rights and welfare of human subjects in biomedical or behavioral research.

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

Principal Investigator: The person responsible for the conduct of a human research study at one or more sites, whether on- or off-campus. If the human research study is conducted by a team of individuals, the principal investigator (PI) is the responsible leader of the team. A principal investigator can assign a PI Proxy or multiple Proxies to perform responsibilities on behalf his/her behalf in communicating with the CWRU IRB for the research protocol submissions. The principal investigator is held accountable for ensuring that the team complies with all rules and regulations and engages with human subjects properly and ethically.

Co-Investigator: An individual involved with the principal investigator in the scientific development or execution of a project. A co-investigator typically devotes a specified percentage of time to the project.

Key Personnel: Other individuals who contribute to the scientific development or execution of a research project in a substantive way.

Research as Defined by DHHS: A systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.² Therefore, any systematic investigation designed to generate results for the purpose of publication (e.g., dissertation, thesis, journal, book, or technical report) or public presentation (e.g., speech, poster, panel, and symposium) is considered to be research.

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
- 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-
- 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.

Minimal Risk Defined by DHHS: “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.

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.

Mission

The mission of CWRU's Human Research Protection Program (HRPP) is to protect the rights and welfare of human research subjects by ensuring that the oversight of human research is appropriate and in accordance with institutional, federal, state and local requirements, as well as the ethical principles promulgated by the Belmont Report.²

Scope

The CWRU HRPP covers all human research conducted by any student, employee, trainee, or faculty member (whether paid or unpaid) of CWRU ("CWRU investigator"). It includes any human research conducted at cooperating institutions pursuant to a grant, contract, cooperative agreement, or other award to CWRU. Cooperating institutions include University Hospitals of Cleveland (UHC), MetroHealth System (MHS), Veterans Affairs Northeast Ohio Healthcare System (VANEOHS) and the Cleveland Clinic Foundation (CCF). Reliance agreements in place allow CWRU to defer to the IRBs at these institutions for local protocol review. Hereafter, these institutions shall be referred to as "member institutions" under the CWRU HRPP.

Ethical Principles and Regulatory Mandates

Human research conducted under the auspices of the CWRU HRPP must be carried out in an ethical manner and in accordance with the principles promulgated by the Belmont Report: respect for persons, beneficence, and justice. In addition, investigators must comply with all applicable federal, state and local requirements related to the protection of human subjects, including Department of Health and Human Services (DHHS) regulations (i.e., 45 CFR 46) and all relevant requirements of other regulatory and funding agencies. CWRU maintains a Federalwide Assurance (FWA) with DHHS.

Research must not begin until investigators have received review and approval or verification of exemption by one of the Institutional Review Boards (IRBs) listed on the CWRU FWA. CWRU applies its ethical standards to all human research regardless of funding.

All human research, except as explicitly exempted in 45 CFR 46.101(b), must undergo review by an appropriate designated IRB(s). Activities that do not meet the definition of human research (e.g., most classroom activities, quality improvement activities, non-scholarly program evaluation, and certain health surveillance activities) do not require review and approval by one of the IRBs within the CWRU HRPP. When CWRU is engaged in human research that is conducted, funded, or otherwise subject to regulations by a federal department or agency, it will apply the regulations of that agency relevant to the protection of human subjects.

Legal Requirements

This Organization commits to apply its ethical standards to all Human Research regardless

of funding. All Human Research must undergo review by the CWRU IRB.

Activities that do not meet the definition of Human Research do not require review and approval by the CWRU IRB and does not need to be submitted to the IRB unless there is a question regarding whether the activity is Human Research.

When this Organization 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 Organization commits to apply the regulations of that agency relevant to the protection of Human Subjects.

When this Organization is engaged in FDA Human Research, this Organization 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 Administration Office who will provide a determination.

Institutional Oversight of Federalwide Assurance

CWRU maintains a Federalwide Assurance (FWA) with DHHS. A complete copy of the current CWRU FWA is maintained by the Executive Director for the Human Research Protection Program (HRPP) within the Office of Research Administration and information regarding its updated approval and expiration dates are available on the CWRU IRB website.

The CWRU Senior Vice President for Research has ultimate responsibility for the institutional commitment made in the institution's FWA and is the Signatory Official for the HRPP. The Senior Vice President for Research is appointed and reports to the President of CWRU. They have been authorized to act for CWRU and assume, on behalf of the President and the CWRU Board of Trustees, the obligations of its FWA and of the Federal regulations. Accordingly, the CWRU Senior Vice President for Research, in consultation with the Executive Director for CWRU HRPP, is authorized to assure that CWRU complies with the terms of the FWA and are ultimately responsible for the review and conduct of human subjects' research conducted or supported by CWRU. They also serve as the central authority for the CWRU HRPP.

Additionally, the Senior Vice President for Research possesses knowledge about the requirements of Federal regulations, applicable state law, the institution's Assurance, and institutional policies and procedures for the protection of human subjects. The Senior Vice President for Research, in consultation with the Executive Director for the HRPP, has full responsibility for leading the strategic planning, operational management, quality improvement, and development of all research conducted at, administered by or affiliated with CWRU.

The CWRU FWA is based on the following principles in order to safeguard the rights and welfare of human participants in research and other research activities.

- Any student, employee, trainee, or faculty member (whether paid or unpaid) of CWRU ("CWRU investigator") are subject to the Assurance of this policy. This includes any

research for which an Assurance or another formal agreement (e.g., IRB Authorization Agreement) identifies the CWRU IRB as the IRB of record.

- CWRU agrees to uphold the ethical principles of the Belmont Report to all proposed research involving human participants. The ethical principles set forth in the Belmont Report are:
 1. **Respect for Persons:** Recognition of the personal dignity and autonomy of individuals and special protection for those persons with diminished autonomy.
 2. **Beneficence:** Obligation to protect persons from harm by maximizing anticipated benefits and minimizing possible risk of harm.
 3. **Justice:** Fairness in the distribution of research benefits and burdens
- CWRU further agrees to apply additional regulations such as the U.S. Food and Drug Administration Human Subject Regulations ([21 CFR 50, 56, 312 and 812](#)), DHHS regulations ([45 CFR 46](#)), and the Health Insurance Portability and Accountability Act of 1996 (HIPAA), when applicable, to research involving human participants.
- This Assurance applies to research conducted within the jurisdiction with which CWRU resides (both local jurisdiction, state jurisdiction and US jurisdiction) as well as to research outside of the jurisdiction of CWRU (international human subject research in which CWRU faculty/staff/personnel are “engaged”)

Responsibilities of the IRB under the Federalwide Assurance

All information provided under the CWRU Assurance must be updated at least every 60 months, even if no changes have occurred, in order to maintain an active Assurance approved by the Office for Human Research Protections (OHRP). Amendments to the Assurance must be reported promptly to OHRP. This includes the addition or deletion of a legally recognized entity related to CWRU.

The CWRU IRB will maintain an Investigator Manual and SOPs reflecting the current practices of the IRB in conducting reviews and approvals under its Assurance. These will be maintained and kept current by the UHCMC IRB and will be reviewed at least every 36 months.

On an annual basis, the Senior Vice President for Research, in consultation with the Associate Vice President for Research, Executive Director for the HRPP, Institutional Review Board; and the IRB Chair; along with any other reviewers, as deemed necessary, will evaluate whether the number of IRBs is appropriate to the volume and types of human research being reviewed, so that reviews are accomplished in a thorough and timely manner.

In addition, the IRB administrative personnel and budget will be reviewed on an annual basis by the Senior Vice President for Research, Associate Vice President for Research, and Executive Director for the HRPP. Modifications in space, facilities, and staff will be made as necessary to accommodate the volume and types of research reviewed.

Policy Oversight Committee

Leadership of the CWRU HRPP will review and approve policies and SOPs as the Policy Oversight Committee. The Committee is constituted with the Associate Vice President for Research, Executive Director for the HRPP, and as applicable IRB administrators.

Institutional Review Board Advisory Committee (IAC)

CWRU and its affiliated hospitals comprise the largest human subject research center in Cleveland, Ohio. The CWRU Human Research Protection Program (HRPP) covers all human research conducted by any student, employee, or faculty member of Case Western Reserve University (CWRU), University Hospitals of Cleveland (UHC) and MetroHealth System (MHS) as part of his or her job responsibilities with that organization, or any human research conducted by an independent contractor of these organizations as part of the organization's contract. In addition, for any human research in which CWRU acts as the grantee, employees of the Veterans Affairs Northeast Ohio Healthcare System (VANEOLS) and the Cleveland Clinic Foundation (CCF) are also responsible for complying with the CWRU HRPP. The integration of the above-mentioned institutions allows for enhanced oversight of human participant research between the financially separate institutions since resources are shared, including IRB review, education of researchers and compliance monitoring.

The core mission of the Institutional Review Board Advisory Committee is to ensure that the oversight of research involving human participants is appropriate and in accordance with institutional policies, federal regulations, and state and local laws, as well as The Belmont Report. The secondary mission of the IAC is to share resources and best practices among member institutions to facilitate multi-institutional research.

Other Requirements

When reviewing research that involves community-based research, the IRB obtains consultation or training.

Written policies and procedures are applied 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
- In certain situations, equivalent protections may be applied. For example, chart reviews under the pre-2018 Common Rule that are not federally funded or FDA

regulated may have been assigned a three year approval period. Any equivalent protections will be described in writing.

CWRU 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.”)

The CWRU HRPP complies with the guidelines established under Good Clinical Practices (GCP) and the International Conference on Harmonization (ICH) to the extent required by the U.S. Food and Drug Administration. However, for industry-sponsored studies with contract requirements for institutional adherence to ICH GCP guidance (E6), the CWRU IRB will comply with all of the GCP statements outlined in ICH-GCP guidance (E6).

When Human Research is conducted or funded by the Department of Defense (DOD), CWRU 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 Organization 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 Justice, CWERU commits to apply the additional regulations for Department of Justice (DOJ) Research conducted in the Federal Bureau of Prisons, which includes 45 CFR §46 Subparts B, C, and D3. Additionally any researcher who is a non-employee of the Bureau of Prisoners must sign a statement in which the investigator agrees to adhere to the requirements of 28 CFR §512.

When Human Research is conducted or funded by the Department of Education, CWRU commits to apply the additional regulations for Department of Education (DOE), which includes 45 CFR §46 Subparts B, C, and D3. Each school at which the research is conducted must provide an assurance that they comply with the Family Educational Rights and Privacy Act (FERPA) and the Protection of Pupil Rights Amendment (PPRA). Other specific requirements of the Department of Education (ED) Research can be found in the “Additional Requirements for Department of Education (ED) Research” section in the IRB’s “WORKSHEET: Additional Federal Criteria (HRP-318).”

³ Quick applicability table for DHHS Subparts:

	DHHS	DOD
Subpart B	X	X
Subpart C	X	X
Subpart D	X	X

Please Note: While references to Department of Energy (DOE), Environmental Protection Agency (EPA) and the Veterans Administration (VA) may appear in CWRU IRB SOPs, Policies, Checklists and Worksheets, this University does not currently follow those regulations. References remain because UH, which also utilizes this system and shares the documents, does follow those regulations.

Sponsored Human Research

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

Scope of Human Research Protection Program

The Case Western Reserve University Institutional Review Board reviews social science, behavioral, and educational, and low-risk biomedical research for CWRU faculty, staff, and students.

Any questions about whether a research activity is considered biomedical or otherwise subject to FDA regulations should be referred to the Research Compliance Officer or a Compliance Manager from the CWRU IRB who will provide assistance.

*Per Central VA policy, the Veterans Affairs Northeast Ohio Healthcare System (VANEOHS) IRB cannot be the IRB of record for CWRU research. Therefore, unless the CWRU PI has a VA appointment and is conducting research under their VA appointment, the CWRU IRB, one of its affiliated hospital IRB, or a commercial IRB (Advarra) is required to be the IRB of record for CWRU for biomedical research conducted at the VANEOHS. The CWRU Research Compliance Officer facilitates this process.

Human Research Protection Program Policies and Procedures

Policies and procedures for the Human Research Protection Program are available on the following Website: <https://case.edu/research/faculty-staff/compliance/cwru-human-research-protection-program/institutional-review-board>

Human Research Protection Program Components

If individuals designated as the Institutional Official, Associate Vice President for Research, or IRB Chairperson engage in research, it is the responsibility of those individuals to ensure that they recuse themselves from all determinations or decisions related to their research.

Furthermore, individuals under the direct supervision of investigators must recuse themselves from the review of such research. Investigators holding the aforementioned roles remain subject to all CWRU IRB and Institutional policies and procedures.

Institutional Official

CWRU's Senior Vice President for Research is designated as the Institutional Official (IO) for the CWRU HRPP. In addition to oversight of the HRPP, the Institutional Official

ensures that CWRU evaluates Conflict of Interests in research and conducts education on the responsible conduct of research.

The Institutional Official has the authority to take the following actions or delegate these authorities to a designee:

- Allocate university resources within the HRPP budget
- Appoint and remove CWRU IRB members and IRB chairs
- Approve and rescind authorization agreements for CWRU IRB
- Suspend or terminate research approved by the CWRU IRB
- Disapprove research approved by the CWRU IRB

The Senior Vice President for Research meets bi-monthly with his Leadership Committee which is composed of the Associate Vice President for Research, Assistant Vice President for Sponsored Projects, Director for School of Medicine Grants and Contracts Office, Assistant Vice President for Research Integrity, Executive Director for Technology Management, Executive Director for HRPP, Executive Director of the Data Use Agreements and Contracts Office, Director of the Strategic Partnerships and Research Collaborative (SPARC), Executive Director of Regulatory Committees, University Chief Compliance and Privacy Officer, Executive Director for Director, Institutional Animal Care and Use Committee, Director for Animal Resource Center, and Executive Director, Institute for Smart, Secure and Connected Systems (ISSACS). These meetings include activities such as monitoring the effectiveness of existing compliance programs, developing new or revised policies as changes in requirements occur, strategic planning to enhance research at CWRU and disseminating updated compliance information to the research community.

The Senior Vice President for Research, who is the Institutional Official, meets monthly with the Executive Director for HRPP to discuss compliance matters, new matters that arise, discussion of new initiatives and way to improve the quality, efficiency, and effectiveness of the HRPP.

Plan to Evaluate Resources Needed for the HRPP

The IO is responsible for ensuring that the CWRU HRPP and IRB(s) have the resources and support necessary to comply with all organizational policies, laws, and regulations that govern research involving human subjects. As part of the annual CWRU budget process, the IO conducts / documents a review of HRPP and IRB function, requirements, and resources and makes adjustments as needed. Such resources include, but are not limited to:

- Sufficient IRBs – number, composition, leadership and frequency of meetings;
- Staffing commensurate with the size and complexity of the research program;
- Appropriate office space, equipment, materials, and technology;
- Resources for the production, maintenance, and secure storage of HRPP and IRB records;
- Resources for quality improvement, auditing and other compliance activities and investigation of non-compliance;
- Access to legal counsel, conflict of interest and scientific/scholarly

- consultation;
- Support for community outreach and education; an
- Supporting educational opportunities related to human research protection for IRB members, relevant administrative staff, and all members of the research team.

The IO is also responsible for:

- Fostering, supporting and maintaining an organizational culture that supports the ethical conduct of all research involving human subjects and the adherence to regulations and organizational policies;
- Ensuring that the IRB functions independently by, among other mechanisms, being directly accessible to the IRB Chair(s) and members if they experience undue influence or if they have concerns about the function of the IRB;
- Oversight of the Institutional Review Board (IRB);
- Oversight over the conduct of research conducted by all CWRU investigators; and
- Oversight of the development and implementation of an educational plan for IRB members, staff and investigators.

In the performance of these duties, the IO has the authority to delegate such activities as may be necessary in order to effectively administer the program. However, the IO is ultimately responsible and is expected to be knowledgeable about all Human Research protections responsibilities at the University.

Organizational Official

The Associate Vice President for Research and Executive Director for the Human Research Protection Program are designated as the Organizational Officials. The Organizational Officials are responsible for oversight of, among other things, policies, procedures, and business decisions related to how research and sponsored project administration are overseen and monitored. The Organizational Officials have the authority to take the following actions or delegate these authorities to a designee:

- Create the HRPP budget.
- Make IRB staff personnel decisions.
- Determine upon which IRBs the university will rely
- Place limitations or conditions on an investigator's or research staff's privileges to conduct human research.
- Develop policies and procedures related to the HRPP that are binding on the university.

The Organizational Officials have the responsibility to:

- Oversee the review and conduct of human research under the jurisdiction of the HRPP
- 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 all applicable ethical and legal requirements.

- Institute regular, effective, educational and training programs for all individuals involved with the HRPP
- Ensure that the research review process is independent and free of undue influence and ensure that officials of the organization cannot approve research that has not been approved by one of the IRBs designated by the organization.
- Implement a process to receive and act on complaints and allegations regarding the HRPP.
- Implement an auditing program to monitor compliance and improve compliance in identified problem areas.
- Investigate and remediate identified systemic problem areas and, where necessary, remove individuals from involvement in the HRPP.
- Ensure that the HRPP 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.
- Fulfill federally-mandated educational requirements.
- Hire and fire research review staff
- Determine what IRBs CWRU will rely upon
- Place limitations or conditions on the investigators or research staff's privilege to conduct human research
- Create policies and procedures related to the HRPP that are binding to the university
- Ensure that the IRB Chair(s) and members have direct access to the IO for appeal if they experience undue influence or if they have concerns about the function of the IRB
- 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 HRPP
- Ensure that the HRPP 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
- Fulfill federally mandated educational requirement

The Associate Vice President for Research meets bi-monthly with the administrators in the Office of Research Administration to discuss effectiveness of existing compliance programs, expansion of research activities, implementation of new initiatives and enhance communication between the multiple divisions of the department.

The Associate Vice President for Research meets bi-monthly with the Executive Director for the Human Research Protection Program to discuss updates and compliance matters of the CWRU HRPP. Additionally, as applicable, reviews of the audits and surveys are discussed to continue improvement of the quality, efficiency and effectiveness of the HRPP.

Institutional Review Board (IRB)

The IRB operates under the rules set forth under DHHS FWA00004428 for Protection of Human Subjects and Code of Federal Regulations (45CFR46) as well as FDA

regulations for the performance of reach activities that involve human subjects (21 CFR 50 and 56) as required.

Reliance on an IRB that is not at a cooperating institution requires an Institutional Authorization Agreement for IRB review (IAA) executed by the Institutional or an Organizational Official.

The CWRU IRB, as well as any IRBs relied upon by CWRU, has the authority to, for the studies they are monitoring:

- Determine whether an activity is human research
- Ensure equitable selection of subjects (Belmont Report – Justice)
- Maintain an equitable balance between potential benefits of the research to the subjects and/or society and the risks assumed by the subject (Belmont Report – Beneficence)
- Protect human subjects from undue risk and deprivation of human rights and dignity
- Ensure that participation by subjects is voluntary, as indicated by a voluntary and fully informed consent
- Determine that the research design and study methods of a protocol are appropriate to the objectives of the research and the field of study
- Determine whether additional protections are warranted for studies involving vulnerable subject populations
- Assist the investigator by providing peer review and institutional approval
- Ensure compliance of protocols with the regulations of the FDA, DHHS, and other funding agencies when appropriate
- Approve, require modifications to secure approval, and disapprove human research.
- Disapprove studies of no scientific merit (Belmont Report – Respect of Persons)
- Suspend or terminate approval of human research not being conducted in accordance with an IRB's requirements or that has been associated with unexpected serious harm to subjects
- Observe, or have a third party observe, the consent process
- 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
(http://www.case.edu/president/facsen/frames/handbook/conflicts_of_interest.htm)

Responsibilities of the IRB

The CWRU IRB has been designated by the Institutional Official to be the IRB relied upon by the CWRU HRPP. The scope of review of the IRB is listed in the IRB roster, which is available from the HRPP Office.

CWRU may rely upon IRBs of another organization provided that the IRBs are part of an AAHRPP accredited organization or after a review of the external IRB policies and procedures to confirm they are compatible with the Federal regulations. Reliance on an external IRB not

listed on CWRU's FWA requires an Institutional Authorization Agreement (IAA) or Reliance Review Agreement (RRA) for IRB review and local review for compliance with local policies of the university. The IAA is executed by the Institutional Official and the RRA is executed by the Institutional Official or Executive Director for the HRPP and a local review for compliance with local policies of the university.

The IRBs relied upon by CWRU have the authority to, for the studies they are monitoring:

- Approve, require modifications to secure approval, and disapprove all Human Research overseen and conducted by the Organization. All Human Research must be approved by one of the IRBs designated by the Institutional Official or Executive Director for the HRPP. Officials of this Organization may not approve Human Research that has not been approved by the CWRU IRB.
- Suspend or terminate approval of human research not being conducted in accordance with an IRB's requirements or that has been associated with unexpected serious harm to subjects
- Observe, or have a third party observe, the consent process.
- Determine whether an activity is human research
- Determine whether additional protections are warranted for studies involving vulnerable subject populations.
- 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.

http://www.case.edu/president/facsen/frames/handbook/conflicts_of_interest.ht

IRB members and IRB staff have the responsibility to follow HRPP policies and procedures, including disclosure of outside financial interests and recusal from review of protocols with which the member or staff may have a conflict.

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

CWRU IRB Review of Policies, Standard Operating Procedures and Processes/Guidance Documents

There are three types of policies, procedures, and processes that the CWRU IRB and IRB Office oversee.

1. University Policy on Human Research Protections (HRPs),
2. CWRU IRB Standard Operating Procedures (SOPs) and
3. Process/Guidance Documents
 - HRPP Plan
 - IRB Member Manual
 - CWRU IRB Investigator Manual

The process begins when the Research Compliance Officer (RCO), Institutional Official (IO), Organizational Official (OO) or designee determines that the University Policy on HRPPs, or a Procedure or Process document needs to be created or modified.

The University Policy on Human Research Protections (HRPPs) is the overarching policy of the CWRU Human Research Protection Program, which can be found in the Faculty Handbook on pages 74-81 and on the CWRU IRB website under the Local Policies and Federal Regulations tab.

These procedures are followed to update the University Policy on HRPPs:

1. The author updates the University Policy with tracked changes.
2. The updated document is shared with the RCO, OO or designee for review.
3. The updated document is submitted to the CWRU IRB members for their review and acknowledgment of it at a full board meeting.
4. The CWRU IRB acknowledged document is sent to the Faculty Senate Research Committee for their review.
5. The document is sent to the Faculty Senate for their review and approval of it.
6. Then the document is sent to the Board of Trustees (BOT) for their review and approval.
7. Once all these steps are completed, the Faculty Handbook is updated with the new version of the document and the corresponding date it was approved by the BOT.

***CWRU IRB Standard Operating Procedures (SOPs)** are the overall procedures of the CWRU IRB that include the functions of the SpartaIRB electronic protocol system and can be found in the SpartaIRB under the IRB/Library/SOPs tabs.

***CWRU's Processes/Guidance Documents** which include the HRPP Plan, IRB Member Manual and Investigator Manual are documents that provide additional information for IRB members and the IRB Office and researchers to follow or better understand the Federal Regulations for Human Research, local policies, or HRPP procedures. These documents can be found on the CWRU IRB website under the Local Policies and Federal Regulations tab.

* These procedures are followed to update the CWRU IRB SOPs and Processes/Guidance Documents:

1. The author creates or updates the SOP or Processes/Guidance Document.
2. The new or updated document is shared with the RCO, OO or designee for review.
3. Then the new or updated document is submitted to the CWRU IRB members for their review and acknowledgment of it at a full board meeting.

CWRU Investigators and Study Staff

CWRU faculty members, employees and students from any school or administrative unit within the University may submit a research protocol to the CWRU IRB. CWRU has the following schools: Weatherhead School of Management, School of Law, the Jack, Joseph and Morton Mandel School of Applied Social Sciences (MSASS), the College of Arts and Sciences, the

School of Dental Medicine, the Frances Payne Bolton School of Nursing, the School of Medicine and the School of Engineering. Individuals working in any central administrative units at the university may also submit a social, behavioral, educational or low-risk biomedical protocol submission to the CWRU IRB.

Investigators and research staff have the responsibility to:

- Follow the HRPP requirements described in the *Investigator Manual* (HRP-103)
- Understand 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 in the CWRU FWA
- Follow IRB policies and procedures
- Comply with institutional, federal, state and local requirements, as well as the ethical principles promulgated by the Belmont Report
- Comply with all determinations and additional requirements of the IRB, the IRB chairperson, and the Institutional Official
- Report allegations of undue influence regarding the oversight of the HRPP or concerns about the HRPP to the Organizational Official.
- Report allegations or findings of non-compliance with the requirements of the HRPP to the IRB.

Legal Counsel

The IRB considers and adheres to all applicable state and local laws in the jurisdictions where the research is taking place. The HRPP and IRB rely on CWRU's Office of General Counsel for the interpretation and application of Ohio law and the laws of any other jurisdiction where research is conducted as they apply to research involving human participants. The IRB will also ensure that informed consent forms are consistent with applicable state and local laws.

- Legal counsel has the responsibility to:
- Provide advice upon request to the Institutional Official, IRB, and other individuals involved with the HRPP
- Determine whether someone is acting as an agent of the university
- 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

Dean/Department Chairs

Deans and Department Chairs have the responsibility to:

- Assure scientific review is completed on IRB submissions to the CWRU IRB
- Oversee the review and conduct of human research in their department or school.
- Forward complaints and allegations regarding the HRPP to the Executive Director for the HRPP
- Ensure that each human research study conducted in their department or school has adequate resources.

Office of Research Administration

The Office of Research Administration's Sponsored Projects Office and the School of Medicine Grants and Contracts Office, with delegated authority, have the responsibility to review contracts and funding agreements for compliance with HRPP policies and procedures.

The Executive Director for HRPP and the Associate Vice President for Sponsored Projects and Director for SOM Grants and Contracts Office meet on an ad-hoc basis to discuss and develop new or updated policies or procedures as changes in requirements occur and disseminate updated compliance information to the research community.

Education and Training

IRB members, IRB staff, and others involved in the review of Human Research must complete a initial CITI Basic Course to be enrolled in the CREC Program and continued training on the protection of human subjects.

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

Questions and Additional Information for the IRB

The HRPP Office wants your questions, information and feedback:

Contact and location for the HRPP Administration Office is:

Kim Volarcik
Executive Director, HRPP
Office of Research Administration
10900 Euclid Avenue
Cleveland, OH 44106-7230
Email: kav6@case.edu
(216) 368-0134

Reporting and Management of Concerns

Questions, concerns, complaints, allegations of undue influence, allegations or findings of non-compliance, or input regarding the HRPP may be reported orally or in writing. Employees are permitted to report concerns on an anonymous basis. Concerns may be reported to the IRB Office, the IRB Chair, the Executive Director for the HRPP, Office of General Counsel, Integrity Hotline, Internal Audit Department, Deans, or Department Chairs.

The IRB has the responsibility to investigate allegations and findings of non-compliance related to conduct of research for studies under its jurisdiction and take corrective actions as needed. The Institutional Official has the responsibility to investigate all other reports and take corrective actions as needed.

Employees who report in good faith possible compliance issues shall not be subjected to retaliation or harassment as a result of the reporting. Concerns about possible retaliation should be immediately reported to the Executive Director for the HRPP.

To make such reports, contact:

Kim Volarcik
Executive Director for HRPP
Office of Research Administration
10900 Euclid Avenue
Cleveland, OH 44106-7230
Email: kav6@case.edu
(216) 368-0134

For Research Participants

If the researchers cannot be reached, or if research participants would like to talk to someone other than the researcher(s) about; concerns regarding the study; research participant's rights; research-related injury; or other human subject issues, they should:

- Call the CWRU HRPP Office at 216-368-0134
- Email the CWRU IRB at cwru-irb@case.edu
- Write to:

Executive Director for HRPP
Office of Research Administration
Case Western Reserve University
10900 Euclid Avenue
Sears Library Bldg.- Room 663
Cleveland, Ohio, 44106-7230

These communications will be answered by IRB administration staff, who will work to resolve issues with the study team. The calls will be tracked, summarized, and reported to the IO or designee annually.

IRB working with CWRU's Conflict of Interests Committee

The IRB collaborates with the Conflict of Interests Committee to ensure the COI of researchers and research staff are identified and managed before the IRB completes its review of any research protocol submission. If the COI committee has not completed its review, the IRB will defer the research protocol submission review or prohibit participation by the researcher with a potential COI until the COI Committee review process is completed and the results are made available to the IRB. The IRB has final authority to determine whether the research, the COI and the COI management plan (CMP), if any, allow the research to be approved. With regard to the CMP issued by the COI Committee, the IRB shall either affirm or request changes to strengthen it. The IRB can require additional measures to manage a COI so that the research may be

approved. However, the IRB cannot weaken a CMP approved by the COI Committee. In the event the conflict cannot be effectively managed, the full board of the IRB may disapprove the research.

Relying on another IRB

Case Western Reserve University does not limit the type of studies eligible for review by an external IRB by type of study or other attribute, but does consider the level of risk, the type of research, research funding, and the required resources for the study when evaluating a proposal to rely on an external IRB. When a CWRU Investigator would like to rely on an external IRB, the investigator is encouraged to contact the CWRU HRPP Office to discuss the circumstances around the preference and to obtain approval to rely on an external IRB, see below for the Reliance Request Process.

CWRU will conduct additional reviews as needed, such as biosafety, radiation safety, recombinant DNA, human stem cell research, and conflict of interests. The CWRU HRPP Office will work with the external IRB to establish if the research falls under additional regulatory requirements, such as Department of Justice or the Department of Education. The Investigator continues to be part of the reliance process and is informed of their responsibilities and any additional institutional requirements.

The IRB Authorization Agreement between CWRU and the external IRB, which will be the IRB of record for the designated study or program, will outline the responsibilities of each entity with regard to any issues found in the associated reviews as well as noncompliance, education, and reporting mechanisms.

Ensuring AAHRPP Standards when Relying on another IRB

When Case Western Reserve University relies on an external IRB that is not AAHRPP accredited additional review steps are taken. The Research Compliance Officer (RCO), Associate Director, IRB or designated HRPP personnel will review the external institution's IRB Policies and Procedures to ensure they meet the relevant accreditation standards.

The CWRU IRB will also review the external IRBs policies and procedures to evaluate appropriate harmony with the federal, state and local regulations as well as CWRU's HRPP framework.

The IRB Authorization Agreement between CWRU and the external IRB that is not AAHRPP accredited will reflect additional requirements as needed to ensure that the standards of the CWRU HRPP program are maintained.

Reliance Request Process

1. The CWRU Investigator should contact the RCO to identify his/her (funded or unfunded) research study and the collaborating relationship with the outside entity.
2. The RCO reviews the type of research and the context in which it will happen and makes the final decision about whether CWRU can rely on the external IRB for the research

study.

3. Once the RCO gives permission for CWRU to rely on the external IRB, the CWRU investigator completes a *Relying on an External Site Protocol* through the CWRU SpartaIRB system. The review of this request will entail a departmental scientific review, a conflict of interests review, and a review of each CWRU study member to ensure their Human Research education training is updated, which requires that their CREC Certificates are active.
4. The RCO works closely with the external IRB to execute an IRB Authorization or Reliance Review Agreement with all involved entities. This may be done through the SmartIRB process or with an independent IRB Authorization Agreement.
5. The RCO communicates the results of the following reviews with the external IRB, as appropriate:
 - Department Scientific review
 - Conflict of Interests Disclosure
 - Local requirements
 - Local research context issues relevant to the IRB's determinations (prior to IRB review)

The CWRU IRB office serves as the liaison between the external IRB and the COI Committee. If CWRU researchers and CWRU research staff disclose a conflict of interests, they are required to follow the CWRU COI Policy. The CWRU COI Committee will work with the individual accordingly to manage the conflict as appropriate. If a management plan is needed, the external IRB will be notified by the CWRU IRB Office.

Unanticipated problems, participant complaints, protocol deviations, and other events that occur at a CWRU site will be reported to the external IRB in a timeframe consistent with the executed IRB Reliance Agreement and their local policies as applicable.

Researchers and research staff can contact the CWRU Research Compliance Officer to obtain answers to questions, express concerns, and convey suggestions when working with an external IRB.

Monitoring and Auditing

In order to monitor and ensure compliance, internal or external auditors who have expertise in federal and state statutes, regulations and organizational 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 IRB and the Institutional Official may terminate or suspend IRB approval. In addition, the IRB and/or the Institutional Official may place limitations or conditions on an investigator's or research staff's privilege to conduct human research whenever, in the opinion of the IRB and/or the Institutional Official, such actions are required to maintain the integrity of the HRPP.

Approval and Revisions to the Plan

This plan is intended to be flexible and readily adaptable to changes in regulatory requirements. The Institutional Official has the responsibility to review this plan to assess whether it is providing the desired results. At the request of the Institutional Official the Executive Director for the HRPP has the authority to amend this plan as deemed necessary.