Human Research Protection Program Plan

April 2023

[1] http://www.hhs.gov/ohrp/policy/engage08.html

[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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Scope

Throughout this document, "University" refers to Case Western Reserve University.

Purpose

The University is committed to protecting the rights and welfare of participants in Human Research. The purpose of this plan is to describe this University's plan to comply with ethical and legal requirements for the conduct and oversight of Human Research.

The University's Human Research Protection Program (HRPP) is a comprehensive system to ensure the protection of the rights, welfare and privacy of participants in Human Research. The HRPP is based on all individuals in this University along with the key individuals and committees fulfilling their roles and responsibilities described in this plan.

Definitions

Many important terms and concepts related to the HRPP are defined in "SOP: Definitions (HRP-001). The below information outlines key terms used in the conduct of Human Research.

Agent:

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

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

Clinical Trial:

A research study of human participants 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 participants 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.

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Engaged in Human Research:
In general, this University is considered engaged in Human Research when this University's faculty members, employees or students for the purposes of the Human Research obtain:

1. Data about the participants of the research through intervention or interaction with them;
2. Identifiable private information about the participants of the research; -OR-
3. Informed consent of human participants for the research. This University follows OHRP guidance
4. on "Engagement of Institutions in Research"[1] to apply this definition and exceptions to this definition.

Human Research:

The CWRU IRB has the sole authority to determine whether an activity meets the definition of "Human Research".

- When activities are conducted that might represent "Human 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 Research" by considering whether the activity either:
    1. Meets the regulatory definitions of "research" that involves "human participants," or
    2. Meets the regulatory definition of "clinical investigation".

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

- Data through Intervention or Interaction with the individual, or
- 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

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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 participant is or may readily be ascertained by the investigator or associated with the information.

Human Participant as Defined by FDA:
An individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A participant may be either a healthy human or a patient. A human participant 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 participants in biomedical or behavioral research.

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 participants 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.

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Research as Defined by FDA:

Any experiment that involves a test article and one or more human participants, 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."

Mission

The mission of this HRPP plan is to assure that appropriate steps are taken to protect the rights and welfare of participants involved in Human Research that is overseen by this University.

This protection of research participants at this University is a shared responsibility, with the University, researchers, IRB committees, research partners and affiliates, and the HRPP working

together toward this common goal by ensuring the following standards are met:

- The rights and welfare of human research participants are adequately protected.
- Is conducted with the highest level of expertise and integrity.
- Such research is guided by the ethical principles of respect for persons, beneficence, and justice as set forth in the Belmont Report.
- Oversight of human research is appropriate and in accordance with institutional, federal, state and local requirements.

Ethical Principles

In the oversight of all Human Research, this University (its investigators, research staff, students involved with the conduct of Human Research, the Institution's institutional review board (IRB), IRB

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members and chairs, IRB staff, the Institutional Official, Organizational Officials and employees) follows the ethical principles outlined in the Belmont Report:

- **Respect for Persons**: Recognition of the personal dignity and autonomy of individuals and special protection for those persons with diminished autonomy.
- **Beneficence**: Obligation to protect persons from harm by maximizing anticipated benefits and minimizing possible risk of harm.
- **Justice**: Fairness in the distribution of research benefits and burdens

Scope of CWRU Human Research Protection Program

The CWRU HRPP oversees all Human Research at Case Western Reserve University that falls under behavioral, social, educational, and low-risk biomedical research for CWRU faculty (CWRU Principal Investigator), employees and students. It includes any human research conducted at cooperating institutions employee (CWRU faculty member), trainee or student pursuant to a grant, contract, cooperative agreement, or other award to CWRU. Cooperating institutions include: the Cleveland Clinic, MetroHealth System, University Hospitals, and Veterans Affairs Northeast Ohio Healthcare System. Institutional Review Board Authorization Agreements are in place to 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.

Conduct of Biomedical Research

When CWRU investigators wish to engage in biomedical human research, including all human research subject to FDA regulations (tests of drugs, devices, and biologics, and other biomedical interventions), they must seek review and approval from the IRB at the affiliated clinical site where the study will take place. The CWRU affiliated hospital IRBs that have agreements with CWRU to review biomedical research are:

- University Hospitals of Cleveland
- MetroHealth System
- The Cleveland Clinic Foundation
- *Veterans Affairs Northeast Ohio Healthcare System

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

*Per Central VA policy, the VANEOHS IRB cannot be the IRB of record for CWRU research. Therefore, unless the CWRU PI has a VA appointment and the funding of the study does not flow through CWRU, another CWRU affiliated hospital IRB or external third-party IRB will need to be the IRB of record for CWRU for biomedical research conducted at the LSCVAMC. The Executive Director for the HRPP facilitates this process.

Multi-site or Collaborative Research Oversight

When multi-site or collaborative research is conducted, the CWRU IRB may use joint review,

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reliance upon the review of another qualified IRB, or similar arrangements aimed at avoiding duplication of effort. Each organization is responsible for safeguarding the rights and welfare of human participants and for complying with applicable federal regulations at that site.

Legal and Regulatory Requirements

This University commits to apply its ethical standards to all Human Research regardless of funding. All Human 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 Federalwide Assurance (FWA).

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 the CWRU IRB and do not need to be submitted to the IRB unless there is a question regarding whether the activity is Human Research.

Any questions about whether an activity meets the regulatory definitions of Human Research should be referred to the IRB Office (cwru-irb@case.edu), who will provide a determination. The IRBs use "*WORKSHEET: Human Research (HRP-310)*" to guide the determination of whether an activity is Human Research.

When this University 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 University commits to apply the regulations of that agency relevant to the protection of human participants. The HRPP uses "*WORKSHEET: Engagement (HRP-311*)" to guide the determination of whether this University is engaged in DHHS Human Research.

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

Sponsored Human Research

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

Other Requirements

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

Written policies and procedures are applied to all research regardless of whether the research is

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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 participants 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.

The University's IRB committees also serve as the Privacy Board for Human Research in which the Privacy Rule (45 CFR Parts 160 and 164) of the Health Insurance Portability and Accountability Act of 1996 apply.

The University follows Ohio state laws that affect Human Research. These laws and requirements are listed in "Ohio Laws Affecting Human Research."-OHIO REVISED CODE: https://codes.ohio.gov/ohio-revised-code. Any questions related to these laws will be discussed with CWRU Office of General Counsel.

For clinical trials, the University 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 HRPP will comply with all of the GCP statements outlined in ICH-GCP guidance (E6). CWRU INVESTIGATOR MANUAL HRP-103

The University prohibits payments to professionals in exchange for referrals of potential participants ("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 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 D[3]. This University 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 participants.

When Human Research is conducted or funded by the Department of Education (ED), this University

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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 Justice (DOJ), this University commits to apply 28 CFR §22. When Human Research is conducted with the federal Bureau of Prisons (DOJ), the University commits to comply with 28 CFR §512.

When Human Research is subject to the European Union General Data Protection Regulations (GDPR), this Institution coordinates with legal counsel or the Data Use and Contracts Office to ensure that the research activities conform to broader institutional policies related to GDPR, where applicable, as well as legal counsel's interpretation of study-specific GDPR requirements.

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 Institution does not currently follow those regulations. References remain because UH, which also utilizes this system and shares the documents, does follow those regulations.

Institutional Review Board Advisory Committee (IAC)

The CWRU's HRPP Office has established an Institutional Review Board Advisory Committee (IAC) composed of IRB Chairs and IRB administrators from the Cleveland Clinic, CWRU, MetroHealth System, University Hospitals, and Veterans Affairs Northeast Ohio Healthcare System. It is primarily a coordinating and communicative body that does not exercise any oversight activities with respect to individual IRB activities. The IAC has established educational and auditing programs related to human participants' protections and responsible conduct of research.

The core mission of the IAC 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.

The CWRU HRPP Office and members of the IAC identify information that may affect the members' HRPP, including laws, regulations, policies, procedures, and emerging ethical and scientific issues. The IAC will also determine whether the required Continuing Research Education Credit (CREC)

[3] Quick applicability table for DHHS Subparts:

	DHHS	DOD	ED
Subpart B	X	X	
Subpart C	X	X	
Subpart	X	X	X

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Program should be revised based on any new information. Investigators are encouraged to monitor the IRB, CREC and HRPP Web sites for new postings.

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 IRB administrators (as applicable).

Human Research Protection Program Policies & Procedures

When policies and procedures are added, removed, or revised affected individuals will be informed through at least one of the following methods: monthly newsletters, emails, web-site postings, meetings, training/education sessions, or mentoring.

National Emergency, Natural Disaster, or Pandemic Policies & Procedures

The HRPP is committed to implementing policies and procedures that will ensure the safety and welfare of research participants during a national emergency, natural disaster or pandemic, which includes (e.g., extreme weather events, natural disasters, man-made disasters, infectious disease pandemics, etc.). Ensuring the safety, welfare and protection of research participants is essential. The HRPP will ensure that ethical principles and related regulatory requirements continue to be followed despite potential pressure to speed or shortcut usual research, research review or processes. The HRPP is aware that, in the absence of an applicable Secretarial or FDA waiver or agency guidance that may be issued, all regulatory requirements continue to apply.

In the event of a national emergency, natural disaster, or pandemic, the HRPP has the authority to immediately modify existing HRPP policies and procedures to the extent allowed by federal or state law and regulations governing human research to allow for timely response efforts. Modifications to policies and procedures may include the following:

- Requirement for researchers to pause some or all research activities.
- These types of mandates to pause research, whether imposed by the organization, or by funding agencies, are not the same as IRB-initiated suspensions and terminations.
- As such, they do not require the IRB report to the FDA or OHRP under 21 CFR 56.113 and 45 CFR 56.108(4)(ii).
- The CWRU IRB Chairperson and Co-Chairpersons will review national emergency, natural disaster or pandemic related protocols under the jurisdiction of the CWRU IRB.
- Collaborate with institutional officials regarding the deployment of resources, acceptability of the proposed research in terms of institutional commitments, as well as the overall merit through prior review of proposed research activities.
- Conduct ongoing review or cede IRB review, to maintain research that is ethically appropriate, maximizes the safety of study participants and research teams, scientifically valid and compliant with the regulations.

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- Adjust IRB submission requirements or processes for pandemic-related research protocols.
- Reprioritize IRB submissions and reviews.
- Implement requirements and measures to increase social distancing, or other actions to protect the health and well-being of research participants and everyone involved in research. This plan is created in conjunction with the:
- Executive Director for the HRPP will collaborate with Office of the President Chief of Staff and Assistant Vice President, University Health and Counseling Services to enable the *Checklist for In-person Human Research Activities* and implement the required sign-off on the document. The CWRU IRB has the final review of this form as it relates the corresponding research protocol.
- Adjust auditing and monitoring procedures conducted by the Quality Improvement Review Program or other institutional monitoring entities to protect the health and
- well-being of researchers and research participants.
- Collaboration with the CWRU Renew and Reemerge Committee (the IO and OO (Executive Director for the HRPP) are members of the University Committee, which is empowered to make the policies, procedures and framework to protect and provide for the University's faculty, employees, students, visitors and Human Research participants.

Emergency Preparedness

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

The University created, emerged and continues to keep the Renew and Reemerge Committee, which is comprised of leadership from all schools and units of the University. This committee is charged with keeping the University prepared and geared to appropriately respond to emergencies to keep all faculty, employees, students, visitors (including Human Research participants) apprised and protected.

Oversight for the Human Research Protection

If individuals designated as the Institutional Official, Associate Vice President for Research, Executive Director for HRPP or IRB Chair 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.

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Institutional Official

The President of CWRU has appointed the Senior Vice President for Research 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

Organizational Officials

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 upon
- 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

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- 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
- Ensure that the IRB Chair, Vice-Chairs 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

HRPP staff

Members of the HRPP staff are responsible for supporting the work of the University's IRBs and for completing work for other HRPP functions. HRPP staff are required to follow policies and procedures as stated in the HRPP Toolkit documents.

IRB members

IRB members have the responsibility to follow the review requirements described in the IRB MEMBER MANUAL (HRP-100).

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.

Dean/Department Chairs

Deans and Department Chairs have the responsibility to:

- Assure departmental 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.

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.

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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 and IRB policies and procedures 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 by the Institutional Official or CWRU's FWA
- 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 chair, and the Institutional Official
- Comply with emergency/disaster response procedures for their research based upon institutional or federal guidance, location and nature of the research.
- Report allegations or findings of non-compliance with the requirements of the HRPP to the IRB.

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

All members of the University

All individuals within the University 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 Institutional Official
- Report allegations of undue influence regarding the oversight of the HRPP or concerns about the HRPP to the Institutional Official or a Deputy Institutional Official.
- Report allegations or finding of non-compliance with the requirements of the HRPP to the IRB.

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

Components of the Human Research Protection Program

Case Western Reserve University Institutional Review Board

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

[1] http://www.hhs.gov/ohrp/policy/engage08.html

[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.

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 research activities that involve human participants (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) or Reliance Review Agreement 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:

- Approve, require modifications to secure approval, and disapprove all Human Research overseen and conducted by the University. 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 Institution 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 participants
- 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 participant 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)

External IRBs- ***Reliance Review Agreement Program***
CWRU may rely upon IRBs of another organization not listed on CWRU's FWA provided that the criteria for reliance in have been met. The HRPP reserves the right to update those criteria as review needs (of being the relying site) or changes to regulatory requirements.

Reliance on an external IRB requires an IRB reliance agreement and a local review for compliance with local policies of the University.

The University requests that external IRB committees serve as the Privacy Board for Human Research in which the Privacy Rule (45 CFR Parts 160 and 164) of the Health Insurance Portability and Accountability Act of 1996 apply. When the external IRB will not serve as the Privacy Board, the CWRU IRB will do so.

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Quality Improvement Program (QIP)

The HRPP Quality Improvement Program (QIP) is a component of the HRPP that evaluates regulatory compliance of investigators and improves investigator performance through systematic and independent examination of Human Research activities and documents. QIP efforts are guided by a risk-based strategy. The Quality Improvement Review Program also evaluates IRB performance as required by the Association for the Accreditation of Human Research Programs (AAHRPP) and includes methods to assess the quality, effectiveness, and efficiency of the HRPP.

The Quality Improvement Review Program has the responsibility to:

- Conduct quality assurance assessments of investigator compliance
- Conduct direct observation of the informed consent process
- Conduct assessments to verify PI compliance with IRB-directed corrective actions.
- Conduct quality assurance assessments of IRB performance
- Report IRB Serious or Continuing Non-Compliance, and Suspensions and Terminations determinations, to department leadership, institutional officials, and regulatory agencies
- Develop and implement reporting metrics related to IRB performance; and reporting activities and results of Quality Assurance Program work
- Receive and follow-up on complaints, concerns, and questions from the research participants or study team members

Continuing Research Education Credit (CREC) Office

IRB members, IRB staff, and others involved in the review of human research must complete an initial Collaborative Institutional Training Initiative (CITI) Basic Course to be enrolled in the Continuing Research Education Credit (CREC) Program and continued training on the protection of human participants.

Education and Training is described in the *INVESTIGATOR MANUAL* (HRP-103).

Conflict of Interests Office

The Conflict of Interest Office (COI): https://case.edu/research/faculty-staff/compliance/conflict-interests-committee-coi administers the University's Policies on conflict of interest with the aim of preserving the integrity of the University and its members and maintaining compliance with applicable federal regulations, while respecting academic freedom and encouraging outside scholarly and entrepreneurial activities. The faculty member as the Principal Investigator, Co-investigators and study staff are required to complete and submit a COI disclosure form to have on file before the IRB protocol can be designated as exempt or approved for non-exempt protocol submissions.

Office of Sponsored Projects and School of Medicine Grants & Contracts

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.

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Contracts & Data Use Agreements Office

The Office of Research Administration's (ORA) Contracts and Data Use Agreements Office: https://case.edu/research/about/meet-our-staff/contracts-duas is responsible for the review and negotiation of data use agreements (DUAs). This office assists with the preparation and execution of these documents. Every DUA is required to be signed by an authorized signatory for the University; this can only be done by the ORA.

Technology Transfer Office

The Technology Transfer Office (TTO): https://case.edu/research/faculty-staff/technology-transfer/material-transfer-data-use-agreements works to get the revolutionary technologies that result from University research into the hands of the public.

The CWRU Technology Transfer Office is responsible for the review and negotiation of material transfer agreements (MTAs). Every MTA is required to be signed by an authorized signatory for the university; this can only be done by the TTO.

University Compliance Program

The University Chief Compliance and Privacy Officer (https://case.edu/compliance/) is responsible for ensuring that individually identifiable health information is handled appropriately across the entire University.

Since the primary function of CWRU is not to provide healthcare, CWRU is permitted to designate itself as a "hybrid entity," which allows it to apply the Privacy Rule only to those parts of CWRU that, if standing alone, would be a Covered Entity. As a hybrid entity, CWRU must designate its "healthcare components," which includes departments that provide support for healthcare components.

Healthcare components at CWRU are:

- CWRU School of Dental Medicine
- CWRU School of Dental Medicine Faculty Practice
- CWRU Student Self-Insured Health Plan and Optional Dependent Medical Plan
- CWRU Employee Health Plan
- CWRU Postdoctoral Benefits Program
- Prion Disease Pathology Surveillance Center
- Frances Payne Bolton (FPB) School of Nursing Clinical Practice

Office of General Counsel

Legal counsel has the responsibility to:

- Provide advice upon request to the Institutional Official, IRB, and other individuals involved with the HRPP

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- 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

Additional Provisions for the HRPP

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.

Questions and Additional Information for the IRB

The HRPP Office wants your questions, information and feedback.

Contact and location for the HRPP 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

[1] http://www.hhs.gov/ohrp/policy/engage08.html

[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.

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 participant 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.

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.

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