

University of Colorado Denver

**Human Research Protection Program
Policies & Procedures**

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1 Policy

The University of Colorado Denver (UCD) fosters a research environment that promotes the respect for the rights and welfare of individuals recruited for, or participating in, research conducted by or under the auspices of UCD. In the review and conduct of research, actions by UCD will be guided by the principles (i.e., respect for persons, beneficence, and justice) set forth in the ***Ethical Principles and Guidelines for the Protection of Human Subjects of Research*** (often referred to as the [Belmont Report](#)). The actions of UCD will also conform to all applicable federal, state, and local laws and regulations. In order to fulfill this policy, UCD has established a human research protections program (HRPP).

2 Mission

The mission of UCD is to protect the rights, the safety and well-being of research participants who choose to participate in biomedical or social-behavioral research at UCD. UCD is committed to having a model program that fosters a culture for protecting human research participants while affording researchers a supportive and service-oriented environment for conducting ethical research of the highest quality.

Protecting the rights and well-being of research participants who choose to participate in biomedical or social-behavioral research is a shared responsibility. UCD, the Colorado Multiple Institutional Review Board (COMIRB), the Human Studies Research Committee (HSRC), the IRB Offices, UCD schools, departments and investigators and the UCD affiliates conducting human research must allocate adequate resources and oversight to assure the protection of human research participants.

The mission of the UCD Human Research Protection Program (HRPP) is:

- To safeguard and promote the health and welfare of human research subjects by ensuring that their rights, safety and well-being are protected;
- To provide timely and high quality education, review, and monitoring of human research projects; and
- To facilitate excellence in human subjects research.

The HRPP is a multi-tiered program involving the Chancellor, the Vice Chancellor for Research, the Office of Regulatory Compliance and its divisions, research committees, investigators and research support staff. The HRPP includes mechanisms to:

- Establish a formal process to monitor, evaluate, and continually improve the protection of human research participants.
- Dedicate resources sufficient to do so.
- Exercise oversight of research protection.
- Educate investigators and study staff about their ethical responsibility to protect research participants.

- When appropriate, intervene in research and respond directly to concerns of research participants.

3 Definitions

Human Participants Research – means any activity that meets the definition of “research” and involves “human subjects” as defined by either the Common Rule or FDA regulations.

Human Subject. A human subject as defined by the Common Rule means 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) identifiable private information (45 CFR 46.102(f)).

- Intervention as defined by the Common Rule means both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject’s environment that are performed for research purposes. [45 CFR 46.102(f)]
- Interaction as defined by the Common Rule means communication or interpersonal contact between investigator and subject. [45 CFR 46.102(f)]
- Private information as defined by the Common Rule means information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). [45 CFR 46.102(f)]
- Identifiable information as defined by the Common rule means information that is individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information).

For research covered by Food and Drug Administration (FDA) regulations (21 CFR 50 and 56), human subject means an individual who is or becomes a participant in a clinical investigation (as defined below), either as a recipient of the test article or as a control. A subject may be in normal health or may have a medical condition or disease. In research involving devices, a human subject means a human who participates in an investigation, either as an individual on whom or on whose specimen an investigational device is used or as a control (21 CFR 812).

Note: The terms “subject” and “participant” are used interchangeably in this document and have the same definition.

Research. Research as defined by the Common Rule means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalized knowledge (45 CFR 46.102(d)).

Research as defined by FDA regulations means any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the Food and Drug Administration under section 505(i) or 520(g) of the Federal Food, Drug, and Cosmetic Act, or need not meet the requirements for prior submission to the Food and Drug Administration under these sections of the Federal Food, Drug, and Cosmetic Act, but 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. The terms research, clinical research, clinical study, study, and clinical investigation are synonymous for purposes of FDA regulations. [21 CFR 50.3(c), 21 CFR 56.102(c)]

- Experiments that 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” means any use of a drug other than the use of an approved drug in the course of medical practice. [21 CFR 312.3(b)]
- Experiments that 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” means any activity that evaluates the safety or effectiveness of a device. [21 CFR 812.2(a)]
- Any activity in which results are being submitted to or held for inspection by FDA as part of an application for a research or marketing permit is considered to be FDA-regulated research. [21 CFR 50.3(c), 21 CFR 56.102(c)]”

Test Article. A test article is a drug, device, or other article including a biological product used in clinical investigations involving human subjects or their specimens.

Institutional Review Board (IRB). An IRB is a board established in accordance with and for the purposes expressed in the Common Rule (45 CFR 46.102(g)).

Institutional Official (IO). The IO is the University official responsible for ensuring that the HRPP at the facility has the resources and support necessary to comply with all federal regulations and guidelines that govern human subjects research.

Principal Investigator (PI). A PI is an individual who conducts a research investigation, i.e., under whose immediate direction research is conducted, or, in the event of an investigation conducted by a team of individuals, is the responsible leader of that team. FDA considers PI and investigator as being the same.

Co-Investigator (Co-I). A Co-I is an individual who, under the direction of the PI, is involved in some or all aspects of the research project, including the: design of the study, conduct of the study, analysis and interpretation of identifiable data, and writing of manuscripts resulting from the project.

Research under the Auspices of the UCD. Research considered under the auspices of UCD and its affiliated entities includes research conducted at the institution, conducted by or under the direction of any employee or agent of the institution (including students) in connection with his or her institutional responsibilities, conducted

by or under the direction of any employee or agent of the institution using any property or facility of the institution, or involving the use of the institution's non-public information to identify or contact human subjects.

4 Ethical Principles

The UCD is committed to conducting research with the highest regard for the welfare of human subjects. It upholds and adheres to the principles of *The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects in Research* by the National Commission for the Protection of Human Subjects in Biomedical and Behavioral Research (1979). These principles are:

1. **Respect for Persons**, which is ensured by obtaining informed consent, consideration of privacy, confidentiality, and additional protections for vulnerable populations.
2. **Beneficence**, which is assured by ensuring that possible benefits are maximized and possible risks are minimized to all human subjects.
3. **Justice**, the equitable selection of subjects.

The UCD HRPP, in partnership with its research community, is responsible for ensuring the ethical and equitable treatment of all human subjects in research conducted under its auspices.

5 Regulatory Compliance

The HRPP is responsible for ensuring compliance with federal regulations, state law, and the policies of the Department of Veterans Affairs. All human subjects research at UCD and its affiliate institutions will be performed in accordance with the Department of Health and Human Services (HHS) policy, and regulations at 45 CFR 46 (also known as the "Common Rule"), the Food and Drug Administration (FDA) 21 CFR 50 and 21 CFR 56, the Department of Veterans Affairs policies for human research protection, including the regulations at 38 CFR 16, and the VHA Handbook 1200.5, and to all other applicable federal, State, and local laws and regulations. The UCD commitment to the protection of human participants applies to all UCD research, regardless of whether the research is funded by federal, state, non-profit, industry sponsors or internal funds and regardless of the location of the research.

6 State Law

UCD and its HRPP elements rely on the counsel of the University of Colorado Office of the General Counsel for the interpretation and application of Colorado State law and the laws of any other jurisdiction where research is conducted as they apply to human subjects research.

The exception is research conducted by Eastern Colorado Health Care System which relies on the VA Regional Council for legal interpretation and application.

7 Institutional Authority

The UCD HRPP operates under the authority of UCD's policy on Human Research Protections Program (HRPP) adopted February 2008. As stated in that policy, the operating procedures in this document "...serve as the governing procedures for the conduct and review of all human research conducted under the auspices of the UCD." The HRPP Policy and these operating procedures are made available to all UCD investigators and study staff and are posted on the UCD website.

8 Institutional Official

UCD Chancellor has designated the Vice Chancellor for Research as the Senior Research Officer that has overall responsibility for research conducted at UCD or by UCD faculty and staff. In this role, the Vice Chancellor has been delegated authority to represent UCD with the University of Colorado System Offices, research sponsors, regulatory agencies and affiliated programs for all aspects of UCD research program.

UCD Chancellor and Vice Chancellor for Research have designated the Assistant Vice Chancellor for Regulatory Compliance as the Institutional Official (IO) who has overall responsibility for the UCD HRPP. The duties of the Institutional Official are as follows:

1. Be responsible for compliance with institutional policies and all applicable regulations for the protection of human subjects.
2. Be the signatory authority for the Federal-wide Assurance to the Office of Human Research Protections.
3. Provide support to the human research protections program within the means of the institution.
4. Implement quality assurance and quality improvement programs as necessary for the protections of human subjects.
5. Suspend or terminate approval of research not being conducted in accordance UCD or regulatory requirements, policies, procedures, and guidance documents and research that has been associated with unexpected serious harm to participants.

In the performance of these duties, the IO has the authority to delegate such activities as may be necessary in order to fulfill these duties.

The UCD IRBs report their decisions to the IO and the Vice Chancellor for Research through standing reports. Approvals, favorable actions and recommendations made by the IRBs may be subject to review and further restriction by institutional administration. The IO will work with the Vice Chancellor for Research and the appropriate individuals at UCD to determine any administrative restrictions that may be necessary. For example, protocols could be approved by the IRBs on a scientific and ethical basis but be restricted or disapproved by institutional administration due to potential for adverse public/community reaction or because the research activities do not fit with institutional objectives. Protocol disapproval, restrictions or conditions imposed by the IRBs upon

any activity involving human subjects may not be rescinded or removed by the IO or institutional administration.

Additionally, the Assistant Vice Chancellor for Regulatory Compliance is the designated Compliance Officer for UCD and has the authority to investigate and manage matters of non-compliance or allegations of such as part of the UCD's Compliance Program. The Office of Regulatory Compliance is under the direction of the Assistant Vice Chancellor for Regulatory Compliance and is tasked with the development, implementation and management of UCD'S Compliance Program, including topics of conflict of interest, environmental health and safety, animal research, human subjects' research, research misconduct, research billing, HIPAA, privacy and data security. The offices supporting the Colorado Multiple Institutional Review Board (COMIRB), the Human Subjects Research Committee (HSRC), the Institutional Animal Care and Use Committee (IACUC), HIPAA Office and Environmental Health and Safety (EHS) are divisions structured under the Office of Regulatory Compliance.

9 Affiliated Hospitals and Research Centers

UCD and the affiliated hospital and research centers listed herein have established the responsibilities and authority of the components of the HRPP under Memorandums of Understanding between UCD-Anschutz Medical Campus and the individual affiliated hospital or research centers. Accordingly, each affiliated hospital or research center manages its administrative processes for reviewing and approving research protocols that involve human subjects, including the management of research funding and requirements set forth by research sponsors. In the course of this process, the affiliated hospitals and research centers have agreed to adhere to the standards set forth in the UCD HRPP. As needed, each affiliated hospital or research center conduct scientific reviews for purpose of conducting ethical research.

The Strategic Advisory Committee is a committee formed from representatives of UCD and it affiliated hospitals and research center to ensure a dialogue is maintained between UCD and the joint Human Research Protective Program with each Affiliate. Membership is comprised of senior administrative representation from each Affiliate, the compliance officer from each Affiliate, faculty representative, IRB staff representation and senior research coordinator representative. The committee will act in an advisory capacity to the Assistant Vice Chancellor for Regulatory Compliance, monitoring the effectiveness of existing compliance programs, developing new or revised policies as changes in requirements occur, and disseminating compliance information to the research community.

The Office of Regulatory Compliance addresses issues of non-compliance with the associated compliance or regulatory office of the affiliated hospital or research center as appropriate if concerns or non-adherence to UCD's HRPP arise. On a regular basis, the Office of Regulatory Compliance and the affiliated hospitals and research centers meet to discuss programmatic concerns as well as prospective ways to ensure the safety and well-being of human research participants.

Affiliated hospitals and research centers are as follows: the University of Colorado Hospital (UCH), The Children's Hospital (TCH), Denver Health Medical Center (DHMC), and the Denver Veteran's Affairs Medical Center (DVAMC).

10 Federalwide Assurance (FWA)

UCD holds two Federal Wide Assurances (FWA) from the Office of Human Research Protections (OHRP) in the Department of Health and Human Services (DHHS):

COMIRB - FWA# FWA00005070
HSRC – FWA# FWA00000066

In its FWA's with DHHS, UCD has elected to extend the applicability of OHRP's authority to all human subjects research conducted at UCD.

11 Written Policies and Procedures

Under the UCD HRPP Policy, the IO and the IRBs "...shall adopt operating procedures to implement this policy. These procedures shall serve as the governing procedures for the conduct and review of all human research conducted under the auspices of UCD." The present document serves as the written policies and procedures for the UCD HRPP. The IRBs each have developed written policies and procedures governing the conduct and review of human research.

These policies and procedures present the most current information for reference by potential investigators and their staff. They are not however, static documents. The policies and procedures are reviewed for adequacy annually by IO and the Director of the IRB Offices. Revisions to these policies and procedures are made by the Director of the IRB Offices, reviewed, and approved by the IRBs, and final approval is given by the IO. The Director of the IRB Offices will keep the research community apprised of new information that may affect the human research protection program, including laws, regulations, policies, procedures, and emerging ethical and scientific issues on its website.

12 HRPP Organization

12.1 Institutional Review Board (IRB)

UCD has two Institutional Review Boards (IRBs) as part of its human research protection program that are established to protect the rights and welfare of human research subjects recruited to participate in research activities conducted under the auspices of participating institutions.

UCD-Anschutz Medical Campus and a consortium of affiliated hospitals and research centers in Colorado together participate in the Colorado Multiple Institutional Review

Board (COMIRB). In addition to UCD-Anschutz Medical Center, the consortium includes: The Children's Hospital, Colorado Prevention Center, Denver Health Medical Center, the VA Eastern Colorado Health Care System, and the University of Colorado Hospital. COMIRB provides IRB review for human subjects research under this consortium under Memorandums of Understanding between UCD-Anschutz Medical Campus and the individual affiliated hospital or research center. COMIRB comprises of four individual review panels (biomedical and social / behavioral panels). Each COMIRB panel consists of nine standing members and their designated alternates.

The Human Subject Research Committee (HSRC) based at the UCD - Downtown Campus is responsible for social and behavioral research at that campus. HSRC consists of nine standing members and their designated alternates.

UCD-Anschutz Medical Campus investigators and its affiliated hospitals and research centers may elect to utilize WIRB (Western IRB) for a limited set of industry sponsored protocols in accordance with COMIRB policies and procedures. COMIRB will continue to have full jurisdiction over the WIRB protocols and has the authority to refuse to allow initial submission to WIRB or to suspend or terminate a study if it is deemed necessary. COMIRB will coordinate any activities with WIRB but retains the responsibility for reporting non-compliance issues or unanticipated problems in accordance with its policy (described later in this document).

COMIRB retains responsibility for ensuring that investigators and staff are appropriately trained and continues to act as the privacy board for all WIRB studies.

The IO, the Director of the IRB Offices, and the Chairs of the IRBs will review the activity of the IRBs on at least an annual basis and make a determination as to the appropriate number of IRBs that are needed for UCD and evaluate whether or not the IRBs have appropriate membership to be able to review the types and volume of the proposed research. The IO and the Director will also annually review the use of WIRB and determine whether that option will continue to be offered to investigators.

As part of the annual review, the IRB members will be asked to complete a relatively brief evaluation of the effectiveness of IRB processes, suggestions for appointment of members with specific training, and the effectiveness of the chairs and will be asked to comment on the IRBs' related training that they feel will add to their ability to contribute to assuring human subject protections. In addition, each member will be evaluated by their appropriate chair and each chair will be evaluated by the Director of the IRB Offices and the IO.

The IRB Board Meeting is a monthly meeting of the panel Chairs, senior IRB administrative staff and the IO to establish policy for the IRBs, evaluate systems, raise issues and assess compliance concerns.

12.1.1 Authority of the IRBs

IRBs are empowered to act by the UCD Chancellor. IRBs review and have the authority to approve, require modifications in, or disapprove all research activities conducted under the auspices of the participating institutions. The IRB panels also has the authority to suspend, place restrictions, or terminate approval of research activities that fall within its jurisdiction that are not being conducted in accordance with IRB requirements or that have been associated with unexpected serious harm to subjects.

In the review of research, actions by IRBs will be guided by the principles (i.e., respect for persons, beneficence, and justice) set forth in the ***Ethical Principles and Guidelines for the Protection of Human Subjects of Research*** (often referred to as the Belmont Report) and will performed in accordance with the Department of Health and Human Services (HHS) policy, and regulations at 45 CFR 46 (also known as the “Common Rule”). The actions of IRBs will also conform to all other applicable federal, State, and local laws and regulations.

IRBs ensure that appropriate safeguards exist to protect the rights and welfare of research subjects [45 CFR 46.111]. In fulfilling these responsibilities, the panel reviews all the research documents and activities that relate directly on the rights and welfare of the subjects of proposed research. The protocol, the consent/assent document(s), the investigator's brochure when applicable, tests, surveys, questionnaires and similar measures, and recruiting documents are examples of documents that each panel uses to conduct its review.

Before any human subject is involved in research in relationship to this institution, a panel will give proper consideration to:

1. the risks to the subjects;
2. the anticipated benefits to the subjects and others;
3. the importance of the knowledge that may reasonably be expected to result;
and
4. the informed consent process to be employed.

IRBs have the authority to suspend, place restrictions, or terminate approval of research activities that fall within its jurisdiction that are not being conducted in accordance with panel requirements or that have been associated with serious harm to subjects. IRBs have the authority to observe or have a third party observe the consent process and the research if the panel determines it to be indicated.

12.1.2 Autonomy of the IRBs

IRBs are under the authority of the Chancellor, but function independently. IRBs also function in coordination with UCD officials, including the IO, and other committees. UCD officials, investigators, employees and sponsors of research are prohibited from attempting to unduly influence or to interfere with the normal function or decision-making -- as established by accepted methods and regulatory requirements—of the

IRBs, any of its members or staff, or any member of the research team to obtain a particular result, decision or action. A decision by IRBs to not approve research is final and may not be overruled.

If a panel chair, member, or staff person feels that the panel has been unduly influenced by any party, they shall make a confidential report to the Assistant Vice Chancellor for Regulatory Compliance and/or Chancellor, depending on the circumstances. The institution will conduct a thorough investigation and corrective action will be taken to prevent additional occurrences.

Research that has been reviewed and approved by IRBs may be subject to review and disapproval by officials of the institution. However, those officials may NOT approve research if it has been disapproved by one of the IRBs panels.

12.1.3 Jurisdiction of the IRBs

IRBs together have jurisdiction (as defined above) over all human subject research conducted under the auspices of UCD and its affiliated entities. Research under the auspices of the institutions includes research conducted at the institution, conducted by or under the direction of any employee or agent of the institution (including students) in connection with his or her institutional responsibilities, conducted by or under the direction of any employee or agent of the institution using any property or facility of the institution, or involving the use of the institution's non-public information to identify or contact human subjects.

All institutional and non-institutional performance sites for participating institutions, domestic or foreign, will be obligated by this institution to conform to ethical principles which are at least equivalent to those of this institution, as cited in the previous paragraph or as may be determined by the Department of Health and Human Services (DHHS) Secretary.

12.1.4 IRB Relationships

The IRBs panels function independently of, but in coordination with, other institutional regulatory committees. The panels, however, makes its independent determination whether to approve or disapprove a protocol based upon whether or not human subjects are adequately protected. The panels have review jurisdiction over all research involving human subjects conducted, supported, or otherwise subject to regulation by any federal department or agency that has adopted the human subject regulations.

IRBs may choose, on a case-by-case basis, to provide human research protection oversight for another institution. In order for the panel to provide this oversight, a formal relationship (cooperative agreement) must be established between the COMIRB or HSRC and the other institution through either a Memorandum of Understanding or an IRB Authorization Agreement. This relationship must be formalized before the panels will accept any human research proposals from the other institution.

In the conduct of cooperative research projects, COMIRB or HSRC acknowledge that each institution is responsible for safeguarding the rights and welfare of human subjects

and for complying with applicable federal regulations. When a cooperative agreement exists, COMIRB or HSRC may enter into a joint review arrangement, rely on the review of another qualified IRB, or make similar arrangements for avoiding duplication of effort.

When COMIRB or HSRC relies on another IRB, the Director of the IRB Offices (or designee) will review the policies and procedures of the IRB to ensure that they meet COMIRB and/or HSRC standards. If the other IRB is part of an accredited HRPP, then it will be assumed that the IRB standards are being met.

No Eastern Colorado Health Care System research will be reviewed by another outside IRB.

When IRBs review research conducted at another institution, the particular characteristics of each institution's local research context must be considered, either (i) through knowledge of its local research context by the IRB or (ii) through subsequent review by appropriate designated institutional officials, such as the Chairperson and/or other IRB members.

When UCD is the coordinating center for a multi-center protocol, the IRB will require the local PI to ensure that IRB approval has been obtained at each participating site prior to initiation of the research at that site. At the time of initial review, the IRB will assess the procedures for dissemination of protocol information (e.g. unanticipated problems involving risks to participants or others, protocol modifications, interim findings) to all participating sites.

12.1.5 IRB Offices

The IRB Offices (COMIRB and HSRC) report directly to the Assistant Vice Chancellor for Regulatory Compliance of UCD (who also serves as the Institutional Official and the Signatory Official on the Federalwide Assurances for UCD) and both are supervised by the Director of the IRB Offices (Director). The Director has expert knowledge in regulatory issues regarding human subjects and serves as the Human Protections Administrator and is the primary contact at COMIRB and HSRC for the Office for Human Research Protections, Department of Health and Human Services.

The Director is a member of the staff of the Assistant Vice Chancellor for Regulatory Compliance and has day-to-day responsibilities for the operation of the two IRBs. This includes responding to faculty, student, and staff questions about human subjects research as well as organizing and documenting the review process. The Director works closely with the Assistant Director, the Expedited/Exempt Manager, and the Chairs of the panels in the development of policy and procedures.

Each panel at COMIRB has support staff: a panel coordinator, regulatory analyst and administrative assistant. The panel at HSRC has a panel coordinator and regulatory analyst. More detailed descriptions of the staff of each office are included in the written policies and procedures for each IRB.

Both offices share additional support personnel as outlined in the current organizational charts for the IRB Offices. The duties and responsibilities for all staff are found in their respective job descriptions, and their performance is evaluated on an annual basis.

The IRB Offices provide the staff and space for the IRB functions and serve as the initial point of contact for faculty, staff, students, and outside agencies. The IRB Offices maintain communications by distributing newsletters, maintaining websites and distributing directed mailings as needed.

12.2 Other Related Units

12.2.1 Institutional Biosafety Committee

Research involving the deliberate transfer of DNA (or DNA of RNA derived from recombinant DNA) into one or more human participants requires initial and continuing review by the Institutional Biosafety Committee (IBC). COMIRB panels will not issue final approval for protocols requiring approval from the IBC until the IBC has reviewed and approved the protocol. SAEs that occur in these protocols require reporting to the IBC and the COMIRB Office simultaneously and COMIRB approval of SAEs will be held contingent upon IBC approval. IBC approval and will be documented in the protocol file as well as in the IBC files.

12.2.2 Committee for Ionizing Radiation

Committee for Ionizing Radiation (CIR) Research involving the administration of therapeutic radiation doses using sealed sources that the participant would not otherwise receive as part of his/her medical care requires review by the CIR. Protocols should be submitted to the COMIRB Office and the CIR simultaneously. COMIRB will not approve submissions requiring approval from the CIR without documentation of CIR review and approval in the protocol file.

12.2.3 Radioactive Drug Research Committee

The Radioactive Drug Research Committee (RDRC) is authorized by the FDA to approve research which involves the use of certain “non-approved” radioactive drugs for pre-Phase I research. Protocols should be submitted to the COMIRB Office and the RDRC simultaneously. The COMIRB will not approve submissions requiring approval from RDRC without documentation of RDRC review and approval in the protocol file.

12.2.4 Pharmacy

Research involving administration of an FDA designated test article that is non-formulary or for which use is restricted at an affiliated hospital or research center requires review by the affiliated hospital or research center. COMIRB will not approve submissions requiring approval from the affiliated hospital or research center without documentation of its review and approval in the protocol file.

Research involving administration of a test article that is not been stored, dispensed and managed by an affiliated hospital or research center requires protocol specific approval of the investigator’s plan to control the test article by COMIRB. The Clinical Research Quality Assurance and Education Program will provide additional training and oversight.

12.2.5 Grants and Contracts

The Office of Grants and Contracts (OGC) establishes contracts and other funding agreements to ensure that the research conducted at UCD is conducted in accordance with the written protocol and applicable law, as well as within UCD's Policy on Clinical Trial Agreements, 4-1. OGC has pre-defined the contract standards that it incorporates into the agreements with research sponsors. These standards have been established in coordination with the IO, Director of the IRB Offices, and the affiliated hospitals and research centers.

OGC establish accounts in the financial system for extramural research awards. OGC will only release funds for expenditure on research awards involving human research upon certification of IRBs approval of the research. OGC may freeze funds at any time during the sponsored project period, upon notification by the IRB Offices of a research protocols' non-compliance with human participant research policies and procedures. Funds may continue to be frozen until the issue is resolved.

12.3 Relationship among Components

In order to ensure dialogue is maintained between the various compliance divisions, the Assistant Vice Chancellor for Regulatory Compliance has a series of standing meetings. The Assistant Vice Chancellor for Regulatory Compliance meets monthly with the Directors that report directly to her (i.e., the Director of the IRB Office, the Compliance and Privacy Officer, the Environmental Health and Safety Director, and the Institutional Animal Care and Use Committee Director). On a quarterly basis, the standing meetings also include the Biosafety Officer and the Radiation Safety Officer. Additionally, the Assistant Vice Chancellor for Regulatory Compliance meets quarterly with the Office of Legal Counsel and the Assistant Director for Contracts Division of the Office of Grants and Contracts. Finally, the Assistant Vice Chancellor for Regulatory Compliance hosts compliance meetings across the affiliated hospitals 3-4 times per year to discuss compliance and privacy issues.

With respect to UCD's Compliance Program, a Research Compliance Committee is being established as part of the overarching compliance program that UCD is implementing. Membership will be comprised of all areas related to research and the Vice Chancellor for Research will serve as the chair. The committee will act in an advisory capacity to the Vice Chancellor for Research and the Assistant Vice Chancellor for Regulatory Compliance. The purpose of the committee is to:

- Identify emerging research compliance risks;
- Identify and share best practices;
- Exchange information and resources;
- Assess research compliance needs and opportunities; and
- Oversee and implement research compliance initiatives.

Protocol-specific coordination

Research that has been reviewed and approved by the IRBs may be subject to review and disapproval by officials of UCD or the affiliated hospital or research center. However, those officials may NOT approve research if it has been disapproved by the IRBs.

The application forms for IRBs, which must be submitted with every protocol, requires PIs to indicate institutional support required for the research with the signature and submission of the protocol. Additionally, signatures and approvals from the Department Chair or their designee must also be completed prior to IRB review. The protocol will be reviewed in the IRB Offices to ensure that all necessary signatures are included and any additional reviews by additional research committees are completed.

12.4 HRPP Resources

The IO is charged by the Chancellor and Vice Chancellor for Research to provide administrative, programmatic and financial leadership and oversight for the HRPP. Additionally, the Vice Chancellor for Research and the IO accomplishes this responsibility in providing:

- educational programs (initial and continuing) for IRB members, staff, and researchers;
- space for HRPP functions;
- sufficient personnel to support the HRPP;
- sufficient equipment to aid administrative offices and IRBs in the HRPP (computers, information software system);
- space and material for required record keeping; and
- direct financial support (salaries, supplies, equipment).

The adequacy of personnel and non-personnel resources of the HRPP program is assessed on an annual basis by the IO with the Director of the IRB Offices and are reviewed and approved as part of the annual UCD budget review process.

The IO ensures that the HRPP funding allocation is conducted on a timely and appropriate basis.

With designated funds, the IO provides funds for travel and registration fees to human subject protection related educational meetings and seminars (e.g. PRIM&R, etc.).

13 Conflict of Interest

UCD encourages and supports outside interactions of its faculty and student employees with federal, state and local governments, and with the business community and industry as important parts of their research, education and public service activities. Since outside interactions also carry with them an increased potential for conflict of

interest and/or commitment, either actual or perceived, UCD has developed procedures for identifying potential conflicts through annual disclosure, and ensure rigorous and consistent review of such disclosures.

General Conflict Management

To meet the above stated goals, UCD has centralized the Conflict of Interest and Commitment (COIC) Management program within the Office of Regulatory Compliance. A standing committee is charged to review the annual disclosure forms submitted by faculty and employees and to make recommendations on how to manage, mitigate or eliminate individual conflicts of interest and commitment as they arise. The COIC Committee exists to protect the integrity of all faculty and investigators at UCD, and maintain the public trust in UCD as a state institution that serves the citizens of the State of Colorado. Because serious financial and other conflicts of interest and commitments can harm the reputation of UCD, as well as adversely affect its ability to fulfill its missions in education, patient care and research, these conflicts should be subject to the oversight and recommendations of duly-constituted and broadly representative committees. The COIC Committee carries out this charge in a manner that is intended to foster, not hinder, research and other entrepreneurial faculty relationships.

UCD and IRBs require all “covered individuals” to comply the University of Colorado Administrative Policy Statement for Conflicts of Interest and Commitment, UCD’s COIC Procedures, disclosure process and management plans, as applicable; sponsor requirements and federal regulations concerning conflict of interest and commitment management. Covered individuals include faculty, individuals who are responsible for the design, conduct and reporting of basic or clinical research, this includes anyone who obtains informed consent, those who determine eligibility, those who review data or conduct data analysis, Research Committee Members (i.e. IRB members, DSMB Members and/or other research review committees), staff who negotiate or execute research agreements on behalf of UCD Area/Program Administrators, Staff of Grants and Contracts, Technology Transfer Office. Covered individuals include non-UCD employees that participate in human subjects research protocols under the authority of IRBs. Where a non-UCD employee is an employee of an affiliated hospital or research center that has a separate conflict of interest program, the Office of Regulatory Compliance will coordinate with the respective office at the affiliated hospital or research center. Disclosures are required on an annual basis and within 30 days of a change. Management plans are project specific and will be reviewed at a minimum of an annual basis.

As part of its general financial disclosure, UCD will ask if any related research involves human subjects. If yes, any conflict management plan which is developed will be forwarded to the panel for review prior to approval. IRBs have the final say for a management plan that involves human subjects.

The IRBs Chair (or designee for Expedited) or Full Board will review the conflict management plan to determine if the conflict will adversely affect the protection of human subjects and if the management plan is adequate. Based on the significance of the conflict and the potential adverse effects on the protection of subjects, conflict management plans can include:

- Disclosure to subjects through the consent process;
- Modifications in the research plan;
- Monitoring by independent reviewers;
- Divestiture of financial interests;
- Appointment of a non-conflicted Principal Investigator; or
- Prohibition of the conduct of research at UCD.

The IRBs Chair (or designee) or Full Board can

- Accept the management plan and recommend approval;
- Recommend changes in the management plan; or
- Refer the review to the Full Board.

A copy of the final, approved conflict management plan will be kept on file in the IRB Offices, as well as in the Office of Regulatory Compliance.

Protocol-Specific Conflict Management

The IRBs application asks protocol-specific questions regarding conflict of interest for investigators and key personnel.

As part of its review process, the IRBs panel will make a determination as to whether the conflict adversely affects the protection of human subjects. If the answer is yes and an approved conflict management plan exists, the IRBs panel will review to determine if it adequately protects the human subjects in that protocol.

If no approved conflict of interest management plan exists, the IRBs panel will forward the conflict information to the COIC Management Program and an appropriate conflict management plan will be developed according to the procedures described above.

Review of conflict management plans are documented in the panel minutes for full board review and in the protocol file for expedited review. If a conflict of interest exists, final IRBs approval cannot be given until an approved conflict management plan that adequately protects the human subjects in the protocol is in place.

If the conflict of interest status of an investigator or key personnel changes during the course of a study, the individual is required to notify the IRB Offices and the COIC Management Program within 30 days of the change. The IRBs panel will review the change as a modification to the protocol.

At the time of continuing review, the investigator and key personnel will be asked whether there has been any change in the conflict of interest status relating to the research. The IRBs panel will review conflict of interest as part of its continuing review.

With respect to Institutional Conflicts of Interest, the University of Colorado System is currently drafting a policy that will parallel the policy and campus requirements for individual conflicts of interest. UCD's Assistant Vice Chancellor for Regulatory Compliance is chairing and representing UCD on this working group. Where institutional conflicts may arise from royalties or intellectual property rights associated with a technology that is the subject of the research, UCD manages these potential institutional conflicts of interest as an extension of the individual conflict of interest on a protocol specific basis. UCD anticipates that it will integrate the institutional conflict of interest management program with its existing program that has been described herein.

Additionally, UCD is currently evaluating how it interacts with the pharmaceutical and biotechnologies industries to assess potential institutional conflicts and determine any necessary policy or programs to address these interactions.

14 Research Quality Assurance and Education Program

As part of UCD's HRPP, UCD will be implementing a Research Quality Assurance and Education Program. The program is aimed at providing quality assurance/quality improvement reviews, education and feedback to researchers and to research committees for research projects conducted at UCD and its affiliated hospitals and research centers. Under the program, UCD will develop a regulatory team that will perform quality assurance/quality improvement reviews for research projects where a request for review has been made. The Research Quality Assurance and Education Program has three ways a review can be initiated. The first is at the request of the principal investigator or department that wishes to receive training or have its research projects proactively reviewed. Requests for review are made to the Office of Regulatory Compliance. Under the second track, the Office of Regulatory Compliance will randomly select research projects which it has identified as having an increased risk factor as part of risk based matrix and conduct the review. Finally, the third track is for the Office of Regulatory Compliance to conduct a for-cause-audit. The results of the reviews conducted will be provided to the principal investigator, IRBs, other UCD offices, sponsors and/or federal agencies as necessary.

In determining risk priority, we would consider the factors listed in the following table and classify each level of risk. Evaluation factors are grouped by 1) Subject Evaluation, 2) PI Evaluation, 3) Research Evaluation and 4) Oversight Evaluation. The Office of Regulatory Compliance will develop weighted measures and more delineated factors within the groups so that it can quantify a risk for purposes of prioritizing the order of reviews.

	NA	Minimal	Low	Moderate	High
Subject Evaluation					
Population					
Vulnerability					
Size					
PI Evaluation					
Level of Experience					
Volume of Protocols					
Audit History					
Staff Levels					
COI					
Research Evaluation					
Procedures					
Anticipated Adverse Events					
Status of drug/device (IND holder)					
Psycho-Social Impacts					
Knowledge Base (Literature)					
Gene Therapy					
Privacy/Data Security					
Consent Issues					
Oversight Evaluation					
Location of Research					
Study Sponsor					
Audit History					
COI					

Reviews would be conducted in a manner similar to model that pharmaceutical and device companies utilize to ensure GxP standards. A review would consist of an entrance interview with the research personnel, review of the study documentation (including medical records where appropriate), a review of the IRB documentation and files, and an exit interview the research personnel. Certain reviews may include the witnessing the informed consent process. As part of the exit interview, the principal investigator would be provided a summary report of the review. When needed, the Office of Regulatory Compliance will assist the principal investigator with drafting a notice to IRBs of any reportable findings and an action plan that addresses such.

In conducting the review, the following factors will be considered:

- Review of regulatory and study binder (including IRB documentation)
- Serious adverse event, audit and monitoring reports
- Adherence to written procedures (UCD, sponsor and federal requirements)
- Adherence to protocol
- Adequate source documents/case report forms
- Informed consent documents and process (as appropriate)

Where a specific report would be made to IRBs, the responsible IRBs panel shall determine the appropriate improvements to be implemented by the principal investigator and any required follow-up actions. Additionally, the Office of Regulatory Compliance will provide summary and trend reports that reflect the overall monitoring program to IRBs on a periodic basis. IRBs will utilize these reports to assess the research project's compliance with policies and procedures, federal regulations and guidelines; to provide the requisite oversight; and to identify areas for quality improvement.

15 Education

As part of its commitment to human subject protection, UCD has educational requirements for staff of the IRB Offices, IRB members and for individuals engaged in the conduct of human subjects research.

15.1 IRB Members

IRBs policies require an orientation for new COMIRB or HSRC members (IRB members). New members, including alternate members and consultant members will meet with the appropriate panel Chair and Director of the IRB Offices for an informal orientation session. At the session, the new member will be given an IRB Handbook (binder) that includes:

- Belmont Report;
- UCD COMIRB or HSRC Policies and Procedures for the Protection of Human Subjects;
- Federal Regulations relevant to the IRB

New members are required to complete the Initial Education requirement for IRB members before they may serve as Primary Reviewer.

For initial education, IRB members will complete the following web based training:

- IRB Member Module - "What Every New IRB Member Needs to Know" at the CITI site.
- UCD HIPAA Research Module (COMIRB members only)

To ensure that oversight of human research is ethically grounded and the decisions made by IRBs is consistent with current regulatory and policy requirements, training is

continuous for IRB members throughout their service. Educational activities include, but are not limited to:

- Training workshops;
- Copies of appropriate publications;
- Identification and dissemination by the Director of new information that might have affected the human research protection program, including laws, regulations, policies, procedures, and emerging ethical and scientific issues to panel members via email, mail, or during panel meetings;
- Completion of two CITI modules annually or the equivalent.
- Lay persons annual education day (lay members only)

The IO will provide support to send as many members of IRBs as possible to attend the annual PRIM&R/ARENA conference or regional OHRP conferences on human research protections.

15.2 IRB Offices Staff

The IRB Offices Professional Staff is required to complete the entire CITI Course in the Protection of Human Research Subjects and the UCD HIPAA Research module. Staff will be expected to attend PRIMR or OHRP training on a rotating basis.

The IRB Offices Professional Staff will be expected to become CIP-certified.

15.3 Researchers

Affiliated/local principal investigators, co-investigators, and research coordinators listed on human research protocols must successfully complete the CITI Basic course in human subject protections and the HIPAA Research Course (COMIRB protocols only) prior to submitting a protocol. Until both courses are completed an investigator and/or coordinator may not be assigned or request participation on a research project. To reiterate the importance of human subject protection, all affiliated/local principal investigators, co-investigators, and research coordinators listed on human research protocols must successfully complete the CITI refresher course every three years.

As a cornerstone of UCD's HRPP, UCD will provide support and coordination of Clinical Trials Training for Investigators and Coordinators (CTTIC). The Office of Regulatory Compliance worked with various affiliates and divisions at UCD to develop a basic curriculum for principal investigators (PIs) and research study coordinators that consists of 24 hours of content designed and largely delivered by staff at UCD. The goals of the program:

- PIs will develop a better understanding of their role and responsibilities;
- PIs and their coordinators will establish better communication;
- Compliance with regulatory standards will be improved, including reducing the number of protocol violations; and

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The need for increased education for research coordinators is a primary focus of the educational initiatives since they are integral part of the clinical research team and have a lead role in handling and maintaining the regulatory documents.

Additionally, UCD's HRPP will utilize training strategies utilizing modalities other than traditional classroom or online settings to engage various groups: researchers, research participants, community groups, technology transfer office and pharmaceutical and device companies. UCD will target a broad range of regulatory and ethical areas that lend themselves to topic specific educational programs. Community engagement forums, such as hosting films, grand rounds or other cross-disciplinary formats, coupled with an informal session for networking are good ways to engage different sectors for topics that are relevant to all. Additionally, coupling the "science" with "regulatory" provides a format that shows how the two must be integrated to have quality research.

Finally, UCD's HRPP will engage with UCD's Bioethics Center to coordinate for educational programs that promote the Responsible Conduct of Research (RCR). With the RCR program, UCD would seek to provide learning opportunities by providing access to all students and trainees to comprehensive ethics curricula that will foster a commitment on the part of trainees to:

- the ethical conduct of research,
- continuous professional development, and
- thoughtfulness regarding the broad societal implications of their work.

The curriculum highlights will include:

- Ethics mentoring
- Development by trainees of a statement on professional ethics that will be continually revised during their training
- Formal course work in the responsible conduct of research, demarcated by topics that address:
 - Boundaries of ethical behavior
 - The role of scientific, political and commercial entities in research as compared to research in the academic environment
 - Discussions and questions involving major policy and social issues
 - "Informal curriculum" consisting of brown bag luncheon discussions, guest lectures, journal clubs, etc.

16 Reporting Violations or Suspected Non-Compliance by Employees

16.1 Employee's Responsibility

UCD faculty and employees are obligated by University of Colorado policies to promptly report fiscal misconduct and fraudulent acts, as well as incidents of suspected misconduct. CU System has established methods for employees to report, confidentially and anonymously, any questionable conduct or possible violation(s). Individual employees may discuss concerns with their supervisor, directly with the Office of Regulatory Compliance or with the IRB Offices.

16.2 EthicsLine

CU EthicsLine allows individuals to anonymously report concerns involving a possible violation of law, regulation, policy, or report issues that cannot be handled or reported through normal channels. The employee may complete a report via a toll-free phone number (800) 677-5590 or a web-based reporting system at www.ethicspoint.com. This reporting service is provided by EthicsPoint, an independent company. The service provides a communication option available seven days a week, 24-hours a day. By calling the toll-free number, the employee will be assisted with completing the report. The on-line option involves completing an interactive form. The University of Colorado Internal Audit Department or other designated contact receives notifications of reports filed and will conduct the investigation or assign the report to another individual qualified to investigate the concern. The CU employee who reported the concern may access the report periodically through EthicsPoint using an assigned report number and a password to determine the status, report additional information regarding the issue, or to answer questions the investigator has posted. For UCD, all reports are managed through the Office of Regulatory Compliance. In this role, the IO reviews and ensures that all matters related to the human subjects protections are reviewed in accordance with UCD's HRPP plan and/or policies and procedures.

16.3 Confidential and Anonymous

UCD strives to ensure the anonymity, to the extent allowed by law, for all persons who choose to report violations or questionable conduct. All allegations or concerns received through reports will be investigated confidentially.

16.4 Protection for Reporting

Employees of the State of Colorado, including its institutions of higher education, have protections under Title 24, Article 50.5 of the Colorado Revised Statutes against disciplinary action or any retaliation for good faith reporting of fraud, waste, and abuse.

16.5 Reports by Research Participants

Participants in research will be provided contact information for questions, concerns or reporting complaints to the research staff or IRB Offices within the informed consent document. Additionally the websites for IRBs provide contact information, as well as a way to anonymously report to the respective IRBs any questions, concerns or complaints that they may have. Finally, participants in research can contact the IO through the Office of Regulatory Compliance or through Ethicsline as outlined above.

17 Response to Allegations, Identified Problems, and Audit Outcomes

17.1 Investigation

All reports of potential violations of laws, regulations, policies or questionable conduct, from any source, shall be reported to the Office of Regulatory Compliance, IRB Offices. Until the QA Program is implemented within the Office of Regulatory Compliance, investigations will be handled in accordance with the COMIRB or HSRC policies and procedures. A summary report of all investigations will be provided to the appropriate COMIRB or HSRC panel. Investigations resulting in corrective action and/or disciplinary action shall be reviewed and approved by the appropriate IRBs panel in addition to the appropriate UCD Official prior to implementation. The IO will provide UCD leadership with reports of all investigations and ensure that any necessary actions at an institutional level are managed accordingly.

17.2 Recommendations

17.2.1 Corrective Action

When an instance of non-compliance has been determined, a corrective action plan will be implemented by the respective IRBs panel and IO. The corrective action plan may include one or all of the following elements:

- correcting the non-compliance, including any necessary disciplinary action, further investigation, or external reporting;
- requirement of additional training or education to the affected individuals or units; and
- implementing changes in internal processes to improve, prevent, or detect compliance inadequacies and/or policies and procedures.

17.2.2 Disciplinary Action

Disciplinary action may be imposed as a part of a corrective action plan for all UCD administration, faculty and employees in accordance with UCD policy and procedures and federal or state law.

17.2.3 Obligation to Report

If the investigation produces credible evidence that provides a reasonable basis to conclude that a violation of law may have occurred, UCD shall promptly provide all information to the appropriate authorities for a determination. Further, UCD will refund overpayments to payers identified through compliance monitoring activities, through investigations, or other reviews as legally required. All reporting obligations shall be administered through legal counsel for UCD.

18 HIPAA Privacy and Security

The Health Insurance Portability and Accountability Act of 1996, 45 CFR 160, 164, (HIPAA) was enacted to create national standards for protecting personal health information by healthcare entities. The HIPAA regulations set requirements and standards for privacy, security and electronic transactions by a “covered entity” – an entity that is a health plan, healthcare clearinghouse or healthcare provider that conduct certain financial and administrative transactions electronically”. Under HIPAA, UCD is considered a “hybrid entity” which can be defined as a covered entity that is a single legal entity that performs both covered and non-covered functions under HIPAA. As such, UCD has identified which of its organizational units are considered healthcare components and therefore must comply with HIPAA Privacy and Security Rules.

Human subjects research conducted within the UCD organizational units that have been designated as healthcare components and that use “protected health information” (PHI) must comply with the HIPAA Privacy and Security Rule. Additionally, human subject research conducted within UCD organizational units that have been designated as non-healthcare components are not required to comply with the HIPAA Privacy and Security Rule.

In consultation with UCD’s Privacy Officer and Security Officer and affiliated covered entity, COMIRB serves as the Privacy Board for human subject research projects. All human subjects research protocols that arise for organizational units that have been designated as UCD healthcare components or for UCD affiliated hospitals or research centers are within the jurisdiction of COMIRB.

18.1 HIPAA Security Rule

The HIPAA Security Rule requires that reasonable and appropriate technical, physical, and administrative safeguards be taken with electronic individually identifiable health information. Specifically, the UCD must ensure the confidentiality, integrity, and availability of all electronic protected health information we create, receive, maintain or transmit.

18.2 HIPAA Education

In order to be compliant with HIPAA educational requirements, researchers must complete the general UCD or affiliated hospital HIPAA course and the UCD HIPAA Research course. Training must be completed prior to final approval of the IRB protocol or before the person becomes engaged in human subject research. The courses outline the requirements of HIPAA, specific UCD and/or affiliated hospital requirements.

19 FERPA

The Family Educational Rights and Privacy Act (FERPA) (See 20 U.S.C. § 1232g; 34 CFR Part 99) governs the disclosure of student records and access to student records by parents and eligible students. FERPA applies to all public elementary and secondary schools as well as post-secondary institutions that receive federal funding through the Department of Education. UCD is subject to FERPA. As such, UCD requires research involving students or student records to be compliant with FERPA and the IRBs policies and procedures.