

IRB Member Manual

A basic training guide designed to support board members as they learn the IRB process.

Board Member Handbook: A Basic Training Guide to Assist New Board Members with the IRB Process Provided by:

Case Western Reserve University Institutional Review Board

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Welcome

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Dear IRB Board Member,

The Case Western Reserve University (CWRU) Institutional Review Board is pleased to welcome you as you begin your service on the IRB. We hope that you will enjoy an interesting and fulfilling term with us.

This document is designed to guide you through membership expectations and related information for your service on the IRB at the CWRU. New CWRU IRB members always have many questions regarding IRB practices and the use of SpartaIRB, our electronic research submission software. We encourage you to let staff know about your training needs as a new Board member.

Over time, you will be exposed to a multitude of differing research studies--some with unique sets of circumstances that require use of additional federal guidelines. At IRB meetings you will learn about regulations that pertain to vulnerable subjects such as children, pregnant women and, and prisoners.

As an IRB member you are not required to become an expert in these federal regulations. The IRB Chair and administrative staff will be able to assist you with questions that you may have as a reviewer. Just remember that your expertise and unique perspective as a reviewer is valued even if you do not have experience in any of the special circumstances described.



Executive Director for the Human Research Protection Program

Chapter 1: The IRB Administrative Office

Office Location

The IRB Administrative Office is located on the 6th floor in Nord Hall, Suite 615. The IRB administrative staff is available to assist you in your role as an IRB Member.

Contact Lists

The contact lists for the IRB administrative staff may be found on the CWRU IRB website <https://case.edu/research/faculty-staff/compliance/institutional-review-board-cwru-irb>

IRB Administrative Staff

The administrative staff for the IRB consists of paid professionals who write procedures and guidance, handle correspondence with relevant federal agencies, process applications for review, request progress reports from researchers, conduct training for researchers and IRB members, arrange IRB meetings, and generally provide support services needed for the oversight of research at CWRU. The IRB, not the professional staff, makes final decisions regarding a research project that has been submitted for consideration. Thus, the IRB and the administrative staff have differing roles and responsibilities, and their relationship with researchers will therefore differ.

Chapter 2: Introduction, Definitions, and History

Introduction

The Case Western Reserve University (CWRU) Institutional Review Board (IRB) reviews social/behavioral/educational and low-risk biomedical Human Research studies conducted by CWRU faculty members, staff and students. The CWRU IRB is constituted to review research involving Human Research according to Code of Federal Regulations at 45CFR46 and the U.S. Food and Drug Administration (FDA) regulations at 21CFR Parts 50 and 56. The CWRU IRB is an appropriately constituted administrative body established to protect the rights and welfare of human subjects. The IRB functions independently. Attempts to coerce or otherwise unduly influence the actions of the IRB are forbidden. Federal regulations at 45 CFR 46.107 outline the requirements for the composition of institutional review boards:

The IRB shall have at least five members, with varying backgrounds to promote complete and adequate review of research activities commonly conducted by the institution. The IRB shall be sufficiently qualified through the experience and expertise of its members, and the diversity of the members, including consideration of race, gender, and cultural backgrounds and sensitivity to such issues as community attitudes, to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects. In addition to possessing the professional competence necessary to review specific research activities, the IRB shall be able to ascertain the acceptability of proposed research in terms of institutional commitments (including policies and resources) and regulations, applicable law, and standards of professional conduct and practice. The IRB shall therefore include persons knowledgeable in these areas. If an IRB regularly reviews research that involves a vulnerable category of subjects, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons, consideration shall be given to the inclusion of one or more individuals who are knowledgeable about and experienced in working with these categories of subjects.

Every nondiscriminatory effort will be made to ensure that no IRB consists entirely of men or entirely of women, including the institution's consideration of qualified persons of both sexes, so long as no selection is made to the IRB based on gender. No IRB may consist entirely of members of one profession.

The IRB shall include at least one member whose primary concerns are in scientific areas and at least one member whose primary concerns are in nonscientific areas.

The IRB shall include at least one member who is not otherwise affiliated with the institution and who is not part of the immediate family of a person who is affiliated with the institution.

No IRB member may participate in the IRB's initial or continuing review of any project in which the member has a conflicting interest, except to provide information requested by the IRB. The IRB may, in its discretion, invite individuals with competence in special areas to assist in the review of issues that require expertise beyond or in addition to that available on the IRB. These individuals may not vote with the IRB.

Definitions

Affiliated member is an employee or agent of CWRU (or a member of that person's immediate family) who is appointed to the IRB as a full member or alternate, either scientific or non-scientific. Affiliated members include but are not limited to individuals who are: Full- or part-time employees; current students; members of any governing panel or board of the institution; paid or unpaid consultants; CWRU pensioners; emeriti; health care providers holding credentials to practice at the institution; and volunteers working at the institution on business unrelated to the IRB.

Faculty Member is a tenured, tenure track or non-tenure track person holding a full-time academic appointment at the ranks of professor, associate professor, or assistant professor in the constituent faculty whose obligations to the University include at least two of the following: 1) teaching, 2) research and scholarship, and 3) service to the University community.

Member is a person who is appointed to the IRB with the right to participate in all discussions. A member of the IRB may be voting or ex officio.

Voting Member is a person who is appointed to the IRB with the right to vote and count in determining the quorum at a convened meeting.

Non-Affiliated Member is a person who is appointed to the IRB as a full member or alternate, either scientific or non-scientific, but not connected or associated with Case Western Reserve University or its affiliate institutions in any way other than as an IRB member or alternate. Non-Affiliated members are also not part of the immediate family of someone who is affiliated with the CWRU or its affiliates. Non-affiliated members cannot work for the university, or receive any funds from the university (i.e., pension, stipend, contract, etc.). This connection includes children, spouses, partners, and/or working relationships.



Alternate member is an individual who has the experience, expertise, background, professional competence, and knowledge comparable to that of the primary IRB member(s) whom the alternate would replace.

A Scientific member is an individual who has formal education and training as a physician or other healthcare professional, A Master’s or Doctoral-level physical, biological, or social/ behavioral scientist, or significant post-baccalaureate work experience in a physical, biological, or social-behavioral sciences.

A Non-Scientific member is an individual who may have formal education and training in a discipline generally considered to be non-scientific (e.g., humanities, law, business) and/or is engaged in an occupation or role that is generally considered to be non-scientific (e.g., law enforcement, management, minister/rabbi/imam).

A Scientific and/or Cultural Reviewer or Consultant is an individual with competence in a special area whom the IRB has invited to assist in the review of issues which require expertise beyond or in addition to that available on the IRB. These individuals may not vote with the IRB as per 45 CFR 46.107(e).

Ex Officio Member is a person who is appointed to the IRB with the right to participate in all discussions, but who does not vote or count in the quorum.

Conflicting Interest or Conflict of Interest means the existence of one or more concerns that might influence an IRB member in the performance of their Board responsibilities. Conflicting interests are factors that can cloud judgment, such as personal relationships between an IRB member and an investigator, and financial relationships with sponsor companies.

Brief History of Human Subjects Research Regulations

The modern history of ethical standards for human subject’s research began in the 1940s with the Nuremberg Code. Since then, the U.S. federal government has increased awareness for protecting the rights and welfare of human subjects by establishing regulatory codes and regulations. This section provides a brief background on the history of the regulations and ethics that are required when human subjects are involved in research.

Nuremberg Code

The Nuremberg Code was developed following the Nuremberg Military Tribunal which judged Nazi doctors conducting human experimentation. The Code encompasses many of the basic principles governing the ethical conduct of human subject’s research today. The Nuremberg Code states that “the voluntary consent of the human subject is absolutely



essential” and it further explains the details implied by this requirement: capacity of participants to consent, participants’ rights to participate or not, freedom from coercion, no penalty for withdrawal, and comprehension of the risks and benefits involved.

Declaration of Helsinki

In 1964, the World Medical Association established recommendations to guide medical doctors in biomedical research involving human subjects. The Declaration governs international research ethics and defines rules for "research combined with clinical care" and "non-therapeutic research." The Declaration of Helsinki was revised in 1975, 1983, 1989, 1996, 2000, and 2008 and is the basis for Good Clinical Practices used today.

Issues addressed in the Declaration of Helsinki include:

- Research involving medical interventions with humans should be based on the results from laboratory and animal experimentation.
- Research protocols should be reviewed by an independent committee prior to initiation.
 - Informed consent from research participants is necessary.
- Research should be conducted by medically/scientifically qualified individuals.
- Risks should not exceed benefits.

Belmont Report

In 1978, the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research wrote “The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research.” The Belmont Report sets forth the basic three ethical principles expected to be followed when doing research involving human subjects: respect for persons (autonomy), beneficence, and justice.

Respect for Persons: “Respect for persons incorporates at least two ethical convictions: first, individuals should be treated as autonomous agents, and second, persons with diminished autonomy are entitled to protection. The principle of respect for persons thus divides into two separate moral requirements: the requirement to acknowledge autonomy and the requirement to protect those with diminished autonomy.” In short, this states that the person must be capable of making the decision on whether or not to participate in a human subject’s research project.

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



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

Federal Policy for the Protection of Human Subjects (Common Rule)

In 1981, the Department of Health and Human Services codified the Policy for the Protection of Human Subjects (Title 45, Part 46). These regulations, called the “Common Rule,” provide for the basic foundation of Institutional Review Boards. This Federal Policy has been codified by the 18 federal agencies that conduct, support, or otherwise regulate human subjects research, hence the title “Common Rule.” The Policy also provides additional protections to specific populations, such as pregnant women, fetuses, and neonates (Subpart B), prisoners (Subpart C), and children (Subpart D) involved in human subjects research. In January 2019, a revised Common Rule went into effect.

United States Food and Drug Administration Regulations The U.S. Food and Drug Administration, within the Department of Health and Human Services, regulates drugs, medical devices, and biologics. FDA regulations 21 CFR Part 50 (Protection of Human Subjects), and 21 CFR Part 56 (Institutional Review Boards) must be adhered to when studies are conducted using drugs, medical devices, or biologics. Although FDA regulations are similar to the regulations found in the Common Rule, there are some differences.

Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule The Health Insurance Portability and Accountability Act Privacy Rule (HIPAA) is a federal law that generally prohibits health care providers (such as physicians or other health care practitioners, hospitals, nursing facilities and clinics) from using or disclosing “protected health information” (PHI) without written authorization from the patient. If an investigator intends to create, use, or release to others (e.g., sponsors, other investigators, collaborators) any identifiable health information in connection with their research, he/she must indicate that in the IRB application. When reviewing proposed research, the IRB serves as the Privacy Board and can approve waivers or alterations of HIPAA authorization for use of PHI. Protected Health Information (PHI) is health information

transmitted or maintained in any form or medium that includes ALL of the three following parts:

- identifies or could be used to identify an individual; and
- is created or received by a healthcare provider, health plan, or healthcare clearinghouse; and
- relates to the past, present, or future physical or mental health or condition of an individual.

The provision of healthcare to an individual; or the past, present, or future payment for the provision of healthcare to an individual. The full text of the updated HIPAA Privacy Rule can be found at the Office for Civil Rights (OCR) website:

<http://www.hhs.gov/ocr/privacy/hipaa/administrative/privacyrule/index.html>.

Chapter 3: Board Composition

All standard operating procedures and policies apply to all members and alternates of the CWRU IRB.

The Case Western Reserve University Institutional Review Board (CWRU IRB) will be constituted according to the federal regulations governing IRB membership, as outlined in 45 CFR 46.107.

Composition of IRB

The CWRU IRB is a board comprised of faculty members, a prisoner representative, a non-scientist, and a non-affiliated member.

On an annual basis, the IRB Chair and the Executive Director for the Human Research Protection Program shall review the membership and composition of the IRB to determine if they continue to meet regulatory and institutional requirements. Members will receive documented feedback on their performance as reviewers following this annual review.

Who Cannot Sit on the IRB and IRB Member Conflict of Interests

University Faculty, Deans, Administrators or Other Personnel with on-going conflict of interests cannot sit as IRB members. Individuals from the CWRU Office of Research and Technology Management may not serve as voting members of the IRB. Individuals from these offices may provide information to the IRB and attend IRB meetings as guests or ex officio members. No individual with responsibility for the business and financial interests of the organization may serve on the IRB.

No IRB member may participate in the review (initial, continuing, or modification) of any project in which the member has a conflicting interest, except to provide information requested by the IRB. It is the responsibility of each IRB member to disclose any COI in a protocol submitted for review and recuse him/herself from the deliberations and vote by leaving the room.

All members and alternate members of the IRB who are affiliated with the University CWRU annual COI Disclosure form, those who are not affiliated complete the CWRU Outside Interests Disclosure Form - Community Partners and annually thereafter. These forms are submitted to the Executive Director for HRPP or an Associate Director for the IRB who shares information regarding IRB member COIs with IRB staff. The IRB staff, in turn, ensure that IRB members and alternates are not assigned to conduct reviews of

protocols for which they have a conflict and to ensure appropriate recusal during convened meetings.

An IRB member, alternate, or consultant may be considered to have a conflicting interest requiring recusal when they, or immediate member of their family, have any of the following:

1. Substantive involvement in the design, conduct, and reporting of the research.
2. Significant financial interests (See 2012 Policy on Individual Conflict of Interests and Institutional Conflict of Interests for a definition of significant financial interests) related to the research being reviewed
3. Any other situation where an IRB member believes that another interest conflicts with his or her ability to deliberate objectively on a protocol.

The IRB Chair will query IRB members at each convened meeting to determine if a COI exists regarding any research protocols to be considered during the meeting and remind them that they should recuse themselves by leaving the room during the discussion and vote of the specific research study. If a conflicted member is participating by conference call, videoconference or web meeting the member's participation is terminated for discussion and voting.

IRB members with a conflicting interest are excluded from being counted towards quorum. All absences of members with COIs are recorded in the minutes.

If the Conflict of Interests status of an IRB member changes during the course of a study, the IRB member is required to declare this to the IRB Chair and/or Executive Director for HRPP.

Consultants and the investigator-as-member cannot participate in the review and approval process for any project in which he or she has a present or potential conflict of interests. Where the investigator-member has a conflicting interest, he or she should be present only to provide information requested by the IRB. He or she should be absent from the meeting room during the discussion and voting phases of the review and approval process; IRB minutes will reflect whether or not these requirements have been met.

Appointment of IRB Members

Members are appointed annually by the Senior Vice President for Research and Technology Management.

The qualities considered for leadership appointments [Chair and Vice-chair] include academic status and record of leadership; academic expertise; willingness to commit the time required; experience with IRB and human research protection issues; administrative



abilities; and personal capacity to listen and guide multiple opinions expressed in a meeting format. Appointments may be renewed annually. Continuing membership is contingent upon satisfactory performance on the IRB, which includes, but is not limited to, reliable attendance and participation.

Non-Affiliated IRB Members

As with Affiliated members, Non-Affiliated members are questioned about whether their immediate family members are affiliated with the institution. They are interviewed by the Executive Director for HRPP or an Associate Director of the IRB and/or IO to inform them about the obligations of being a Board member and to determine suitability for Board membership.

Alternates

All alternates must be officially appointed and their role as a substitute member must be listed on the membership roster. Each alternate is only permitted to substitute for a specific IRB member or a class of IRB members for whom they are listed and have similar background and expertise.

Alternate members will be subject to the same appointment, terms of service, conflict of interest review and responsibilities as regular voting members of the IRB. If an IRB member cannot attend a meeting, his or her alternate will be contacted by the IRB member he/she represents to determine if he or she can attend. When an alternate member substitutes for a primary member, the alternate member receives and reviews the same material that the primary member receives.

Prisoner Representative

When the IRB reviews research that involves prisoners, at least one voting member present at the convened IRB meeting must be a prisoner representative with the appropriate background and expertise to serve in that capacity. If a prisoner representative is selected to serve on the IRB, the person must have a close working knowledge, understanding and appreciation of prison conditions from the perspective of a prisoner.

Suitable individuals could include present or former prisoners; prison chaplains; prison psychologists, prison social workers, or other prison service providers; persons who have conducted advocacy for the rights of prisoners; or any individuals who are qualified to represent the rights and welfare of prisoners by virtue of appropriate background and experience. The prisoner representative must be officially appointed and be listed on the membership roster, and will be subject to the same appointment, terms of service, conflict of interests review and responsibilities as regular voting members of the IRB.

Terms and Conditions of Service

Members of the IRB may be reappointed annually by the Senior Vice President for Research and Technology Management. Upon appointment to the IRB, a current copy of each member's Curriculum Vitae (CV) must be provided to the IRB and maintained on file. Updated copies of members' CVs are requested at the beginning of each academic year and as re-appointments are made to the IRB.

Members of the IRB are expected to attend all scheduled meetings of the IRB and participate in the discussion and review of all protocols. Members of the IRB who are not able to attend a scheduled meeting of the IRB should provide sufficient advance notice (at least five working days) to an Associate Director of the CWRU IRB of the intended absence(s). If an IRB member is to be absent for an extended period of time, such as for a sabbatical, he or she should notify the IRB at least 30 days in advance so that an appropriate replacement can be obtained. If the member has a designated alternate, the alternate can serve during the primary member's absence.

Orientation and Education of IRB Members

The Office of Research Administration and the IRB office have qualified IRB leadership and said leadership are annually reviewed and reappointed. New members of the IRB will receive a letter of appointment and meet with Executive Director for HRPP or an Associate Director of the IRB (or designee). The orientation session will review the functions of IRB members, discuss the confidentiality rules of the IRB, and review the member conflict of interest policy. Each new member is provided with an extensive outline of important topics and given various references for information on those topics. IRB members will receive training in the use of the IRB electronic submission and review system.

Opportunities for additional education are also provided. Until new IRB members have been sitting on the IRB for 6 months they will not be assigned as a primary or secondary reviewer for protocols. Prior to the new IRB member's first review presentation, the member will maintain an on-going relationship to meet with and work with the IRB staff to discuss the review process, to answer any questions prior to the scheduled IRB meeting, to discuss any concerns, to review policies and review processes.

IRB members must have Human Subjects' Protection or CREC certification. Relevant articles are routinely distributed to IRB members to further their knowledge and educational opportunities are provided by the CWRU Continuing Research and Education Credit (CREC) Program and the IRB Advisory Committee to enhance members' knowledge of regulations and information relating to protection of human

subjects. IRB members who have served for 1 year are awarded Continuing Research Education Credits applicable toward Human Subjects' Protections recertification.

What are the expectations for an IRB Member?

As an IRB Member, you are expected to do the following:

- Prepare for IRB meetings by reviewing all agenda items.
- Utilize this manual and other HRPP Toolkit documents in preparation for IRB meetings.
- Contribute to the collegial discussion of agenda items at IRB meetings.
- Confirm attendance for and attend approximately 85% of scheduled IRB meetings.
- Communicate well in advance to your assigned IRB Analyst when you cannot attend an IRB meeting or when you need assistance with accessing or interpreting submission or review materials.
- Report any Conflicting Interest for IRB Members to your assigned IRB Analyst, IRB Chair or Panel Chair, and the HRPP Director (see "SOP: Definitions (HRP-001)" for a definition).
- Become a designated reviewer at the time of 1 year of service or sooner if requested due to gaps in expertise.
- Stay current with all training requirements.
- Treat all oral and written information obtained as part of the review process as confidential; IRB members must not disclose or use confidential information without prior authorization, which includes refraining from communicating review results to Investigators separately from any official IRB communication.
- Unless asked to do so by the Executive Director or Institutional Official, refrain from issuing statements about HRPP or IRB operations, policies, tools, systems, or other related topics in a manner that would appear to be speaking on behalf of the HRPP or IRB.

IRB Performance and Evaluation

The IRB is routinely assessed for performance, composition, and attendance. Annual reappointment of the Chair and Vice Chair is contingent upon satisfactory review by the Associate Vice President for Research.

IRB members are sent a self-evaluation form annually. IRB Member performance is reviewed by the Associate Vice President for Research and the Executive Director for HRPP on an annual basis. The major criteria for the assessment are knowledge of IRB regulations, attendance at Board meetings and other IRB committees, leadership, and ability to conduct expedited reviews.

If a performance review identifies a problem, which cannot be resolved, a replacement will be appointed.

Chair of the IRB

CWRU's Institutional Official (IO), in consultation with the Executive Director for HRPP, appoints a Chair and Vice Chair of the IRB to serve for renewable annual terms. Any change in appointment, including reappointment or removal, requires written notification.

Roles and Responsibilities

- The IRB Chair should be a highly respected individual, from within CWRU, fully capable of managing the IRB, and the matters brought before it with fairness and impartiality. The task of making the IRB a respected part of the institutional community will fall primarily on the Chair.
- The IRB Chair will represent the CWRU IRB as a voting member of the IRB Advisory Committee (IAC).
- The IRB Chair is responsible for conducting the meetings and may serve as signatory for correspondence generated by the IRB.
- The IRB Chair is authorized to take immediate action to suspend a study or studies if information is presented regarding subject safety or for any other reason where such action would be deemed appropriate, pending review by the convened IRB.
- The IRB Chair advises the Institutional Official and the Executive Director for HRPP about IRB member performance and competence.

The performance of IRB Chair will be reviewed on an annual basis by the Executive Director for HRPP in consultation with the IO. Feedback from this evaluation will be provided to the Chair. If the Chair is not acting in accordance with the IRB's mission, following these policies and procedures, has an undue number of absences, or not fulfilling the responsibilities of the Chair, he/she may be removed.

Vice Chair of the IRB

The Vice Chair serves as the Chair of the IRB in the absence of the Chair and has the same qualifications, authority, and duties as Chair.

IRB Members

The role of an IRB member is to ensure that human research activities comply with federal regulations, state and local laws, and institutional policies and procedures, by:

1. Completing member education and training, both initial and on-going.
2. Maintaining the confidentiality of IRB deliberations and the research reviews.
3. Conducting and documenting reviews of research as assigned in a timely fashion.

4. Attending IRB meetings as scheduled.
Members should attend all meetings for which they are scheduled. If a member is unable to attend a scheduled meeting, they should inform the IRB Chair, Vice Chair, or an IRB Office staff member. If an IRB member is to be absent for an extended period of time, such as for a sabbatical, he or she should notify the IRB at least 30 days in advance so that an appropriate replacement can be obtained. If the member has a designated alternate, the alternate can serve during the primary member's absence.
5. Participating in subcommittees of the IRB if requested and available.
6. Conduct him/herself in a professional and collegial manner.

The performance of IRB members will be reviewed on an annual basis by the Research Compliance Officer. IRB members will receive formal documented feedback on the results of this review. Members who are not acting in accordance with the IRB's mission or policies and procedures or who have an undue number of absences may be removed.

Alternate Members

The appointment and function of alternate members is the same as that for primary IRB members, and the alternate's expertise and perspective are comparable to those of the primary member. The role of the alternate member is to serve as a voting member of the IRB when the regular member is unavailable to attend a convened meeting. When an alternate member substitutes for a primary member, the alternate member will receive and review the same materials prior to the IRB meeting that the primary member received or would have received. The IRB roster identifies the primary member(s) or class of members (e.g., physician scientist) for whom each alternate member may substitute. The alternate member will not be counted as a voting member unless the primary member is absent. The IRB minutes will document when an alternate member replaces a primary member.

Scientific and/or Cultural Reviewers/Consultants

If a primary or secondary reviewer with the appropriate scientific, scholarly, or cultural expertise and background is not available, the IRB office will seek out a reviewer within or outside of CWRU to serve as a consultant and utilize that person as the appropriate reviewer. The IRB utilizes non-IRB or CWRU reviewers or consultants when it is determined that members do not have the expertise necessary to review a particular protocol.

When the need for a consultant is established, the Executive Director for HRPP or an Associate Director of the IRB will identify an appropriate consultant, arrange for the review, and ask the consultant to provide written documentation of his/her review. A copy of the written communication is provided to each Board member prior to the meeting for their review. In addition, all written communications between the consultant and the IRB are included in the protocol file.

When a consultant is scheduled to review a protocol, they are asked by the Executive Director for HRPP or an Associate Director of the IRB, to disclose to the IRB any conflict of interests related to the protocol. If a conflict exists, the consultant will be excused from the review of the protocol and the IRB will identify another consultant without a conflict.

Written comments of consultants will be kept in IRB records. Key information provided by consultants at meetings will be documented in the minutes. Written reviews provided by the outside reviewer also will be filed with the study application. While it is often sufficient for a consultant to provide his/her comments in writing after reviewing the protocol, the IRB may request a consultant's presence at a full board meeting. If in attendance, these individuals will provide consultation to IRB members but may not participate in the vote.

Liability Coverage for IRB Members

The insurance coverage that CWRU carries that applies to employees and any other person authorized to act on behalf of CWRU for acts or omissions within the scope of their employment or authorized activity applies to IRB members conducting their normal duties.

Reporting and Investigation of Allegations of Undue Influence

If an IRB chair, member, or staff person feels that the IRB has been unduly influenced by any party, they shall make a confidential report to the Executive Director for HRPP or Institutional Official (IO) depending on the circumstances. The IO will ensure that a thorough investigation is conducted and, if the allegation is determined valid, that corrective action is taken to prevent additional occurrences. In the event that the allegation is regarding the IO, the matter will be referred to the President for investigation and any necessary action.

Undue influence means attempting to interfere with a normal functioning and decision making of the IRB or to influence an IRB member, or staff outside of the establish processes or normal and accepted methods in order to obtain a particular result, decision or action by the IRB or one of its members or staff.

IRB Member File Documentation

A file (hard copy and/or electronic) on each member of the IRB, including consultants, will be maintained and kept in the IRB Administrative Office. These files will be maintained indefinitely.

Each IRB member's file will include the following information or documentation:

- Updated Curriculum Vita or resume
- Appointment/Reappointment Letters
- Documentation of Human Subjects Regulation Training and Certification

- Documentation of Continuing Education
- Related Correspondence

IRB Registration Updates

Changes in CWRU IRB will be reported to the OHRP as follows:

1. Within 90 days after changes regarding the IRB chairperson or the contact person who provided the IRB registration information.
2. Within 90 days of a change in the membership roster.
3. Within 30 days after CWRU's decision to disband as a registered IRB or permanent cessation of the IRB's review of HHS-conducted or -supported research.
4. Promptly to register any additional IRB before it is designated under an FWA and reviews research conducted or supported by HHS.

Chapter 4: IRB Meetings

Overview

The CWRU IRB usually meets on the first Wednesday of each month. The agenda, along with meeting materials, is available to IRB members five to seven days in advance of the meeting via SpartaIRB. Protocols may be submitted to the IRB at any time via SpartaIRB. Protocols that require Full Board review must be submitted to the IRB office at least two weeks before the next meeting (i.e., approximately the middle of the month before the meeting date). Deadline dates are listed on the [CWRU IRB website](#). If an investigator does not submit a protocol requiring full board review before the monthly deadline date, the review will automatically be placed on the agenda for the following month's meeting. It is important to keep the deadline dates in mind to avoid delays.

Some protocols are delayed because they require multiple full board reviews due to protocols that require substantial revision or additional information. The IRB cannot approve protocols that are lacking required information or that are unclear. Careful preparation of the application by the investigator helps to avoid such delays. Protocols are not reviewed unless the submission is complete.

All research not falling into an expedited, exempt or not human subject research category requires full board review and approval (i.e., review and vote by a majority of members of the IRB at a convened meeting). Research involving children, pregnant women, fetuses, prisoners, the cognitively impaired, the educationally and economically disadvantaged may require full board review and approval. Other areas requiring full board review include initial and continuing review of research that is determined to involve greater than minimal risk, and any other continuing review, change requests or adverse event that the Chair or expedited reviewer requests receive full board review.

The Research Compliance Officer or the Associate Director, IRB is responsible for tracking quorum and, in conjunction with the IRB chair, determines whether meetings are appropriately convened.

Reviewer System

The IRB Office administrators will assign a primary reviewer to each protocol based upon expertise. The IRB Office is responsible to ensure that at least one reviewer has the required scientific and scholarly expertise required to review the protocol. If the research involves prisoners, the IRB staff will assign a prisoner representative as the primary reviewer. If a primary or secondary reviewer with the appropriate scientific, scholarly, or cultural expertise and background is not available, the IRB office will seek out a reviewer within or outside of CWRU to serve as a consultant and utilize that person as the appropriate reviewer.

The primary reviewer is responsible to review all materials in depth and present the research proposal at the convened meeting of the IRB. A secondary reviewer is responsible to review all materials in depth, substitutes for the primary reviewer if the latter is absent at the meeting, and otherwise provides an additional level of review and discussion. After the primary and secondary reviewers have presented their comments, all Board members discuss the documents received for review and add their comments.

Meeting Procedures

The IRB Chair (or Vice-chair in the Chair's absence) calls the meeting to order, once it has been determined that a quorum is in place (educational presentations may commence before a quorum is established). The Chair will check for and remind IRB members to recuse themselves from the discussion and vote by leaving the room where there is a conflict of interest. The IRB will review and discuss the IRB Minutes from the prior meeting.

The IRB uses technology in its meetings to assist the Board in meeting regulatory requirements. As each protocol is considered/presented, appropriate sections of the IRB application, protocol/study design, consent forms and other documents are projected for members' information and discussion. The IRB reviewers' comments pertaining to the review of the IRB submission can be viewed by the full board via the projected documents. The reviewers are also able to review any necessary checklist pertaining to the review of the IRB submission.

The IRB reviews all submissions for initial and continuing review, as well as requests for amendments. The Primary and Secondary Reviewer present an overview of the research and lead the IRB through the completion of the regulatory criteria for approval in the "Institutional Review Board - Protocol Review/Initial Review" checklist. In order for the research to be approved, it must receive the approval of a majority of those voting members present at the meeting. Before closing the meeting, the Chair will ensure that the members have the opportunity to comment on the monthly report of the actions taken by the IRB using the expedited review procedures, which includes a listing of the approved protocols (new studies; continuing reviews; and amendments to approved protocols).

Quorum and Voting

A majority of IRB members including at least one member whose primary concerns are in nonscientific areas must be present at a convened IRB meeting. A protocol must receive approval of a majority of the IRB members present at a meeting for it to be approved. The IRB Office staff is responsible for monitoring the members present at convened meetings to determine that the meetings are appropriately assembled and remain appropriately convened. When quorum is lost during a meeting, the IRB must not take further actions or votes until the quorum is restored. If the quorum cannot be restored, the meeting adjourns. Abstentions count toward the quorum but not toward the required voting majority. The Chair counts towards meeting quorum.

Minutes of a Convened Board Meeting

Procedures for Documentation of IRB meeting Minutes:

An IRB non-voting staff member will attend each committee meeting and will draft detailed notes to document the discussions and determinations of the Board for each agenda item. The Minutes of each IRB meeting will document the separate deliberations, actions, and votes for each protocol undergoing initial or continuing review by the convened IRB, and the vote on all IRB actions including the number of members voting for, against, and abstaining. The minutes must be sufficient in detail to demonstrate:

- The IRB Chair, with the assistance of the Research Compliance Officer or Associate Director, IRB, will confirm that quorum is present before calling the meeting to order. The Research Compliance Officer or Associate Director, IRB, will be responsible to ensure that the IRB meeting remains appropriately convened. The Research Compliance Officer or Associate Director, IRB will document the time of arrival and departure for all IRB members and notify the IRB Chair if a quorum is not present.
- Minutes of IRB meetings will contain sufficient detail to show the presence of a quorum throughout the meeting. The attendance list shall include those members present at the beginning of the meeting. The minutes will indicate, by name, those members who enter or leave the meeting. The vote on each action will reflect the numbers of members present for the vote on that item. Members who recuse themselves because of conflict of interest are listed by name and the reason documented.
- Attendance at the meeting for each IRB action, to include:
 - If an alternate is present and who they are representing.
 - The initial and continued presence of a majority of members (quorum), including at least one non-scientist.
 - If a consultant is present for each protocol discussed, the minutes must document his or her attendance and protocol comments.
 - Attendance of unaffiliated member(s) is documented at convened meetings.
- If a Committee Member is excused from the meeting due to a conflict of interest during the discussion and vote on the study. The name of the committee member is also recorded.
- Actions taken by the IRB (e.g. approved; modifications required to secure approval; deferred; and disapproved)
- The discussion of any controversial issues and their resolutions, and documentation of a consultant's findings.
- Discussion and resolution of any issues with human research protection language in research contracts and funding agreements including, but not limited to, provision of and payment for research-related injury.
- If the IRB reviews research that involves categories of subjects vulnerable to coercion or undue influence, one or more individuals who are knowledgeable about or experienced in working with such subjects are present.
- The basis for required changes in research.
- The basis for disapproving research.

- The level of risk involved in the research (i.e., minimal or greater than minimal risk).
- Mechanisms to mitigate any researcher Conflicts of Interest, including the requirement of additional terms (modifications) to ensure the COI is managed for the specific IRB protocol.
- The approval period for initial and continuing review.
- Justification for any change in study design or risk level for amendments, including those submitted with the continuing review.
- The vote on the actions including the number of voting “for; against; and abstaining.” In order to document the continued existence of a quorum, votes should be recorded in the minutes using the following format: Total = xx, For: xx, Against: xx, and Abstained: xx.
- Determinations required by the regulations (e.g., waiver or alteration of informed consent; research involving pregnant women, human fetuses, or neonates; research involving prisoners; research involving children); and protocol specific findings justifying those determinations.
- Justification for deletion or substantive modification of information concerning risks or alternative procedures contained in any HHS-approved sample informed consent document.
- When the suspension of an approved protocol is considered, documentation of the discussion on whether to allow for continued treatment of enrolled subjects must be included.

Notice of Committee Reports

The Notice of Committee is a monthly report of the actions taken by the IRB using the expedited review procedures; and includes a listing of the approved protocols (new studies; continuing reviews; and changes to approved protocols). Each month, the report is generated by the IRB staff and sent to all IRB members.

Distribution of the Minutes

Draft minutes will be prepared by the IRB Office Administrators and forwarded to the IRB for review. The Board members will receive copies of the minutes electronically.

The minutes will be reviewed by the Board members and will send any requested revisions to the IRB Office Administrators. These will be reviewed by the IRB Office Administrators and IRB Chair or Vice-Chair incorporated in the final version of the minutes. The Chair will review the minutes each month to finalize them.

Notification of Action and Review of Responses

The IRB office reviews exempted protocols and sends investigators exemption notices via the electronic IRB system. However, the full IRB reviews all studies in need of full review and one or more IRB members review all studies eligible for expedited review. When Full and Expedited reviews involve major or minor modifications to secure approval, written notification of the IRB’s action, together with the reason(s) for its decision are provided to the Principal Investigator. The results of IRB actions are conveyed in writing usually within one week of a convened IRB meeting at which the protocol was considered. Furthermore, when a primary

reviewer (either through Full Board or expedited review) determines that additional modifications or clarifications are required, these are also forwarded in writing to the Principal Investigator. All communications are sent by the IRB Administrative staff.

The investigator must respond to all IRB requests and enquiries in writing or in person. When an investigator responds to the IRB actions, these correspondences are reviewed by the IRB members to determine whether the information provided satisfies the Board's requests and the criteria for IRB approval. The information can be reviewed by expedited review (when the investigator has agreed to the changes requested by the IRB or the protocol is eligible for review using the expedited procedure). Otherwise, the modifications are reviewed by the convened IRB.

When the IRB disapproves a protocol, the Principal Investigator is provided with written notification for the reason(s) for the disapproval; however, a detailed critique of the protocol is not provided. The investigator is instructed to contact the IRB office with any questions and may attend an IRB meeting to discuss the study. An investigator may rewrite and submit the study as a new protocol if they wish but must take into account the Board's concerns and reason(s) for the disapproval of the protocol.

Chapter 5: Records

By federal regulation, the IRB is required to keep paper / electronic copies of all approved protocols on file or in the SpartaIRB electronic database and available for inspection by authorized representatives of the DHHS, the Office for Human Research Protections (OHRP) and other regulatory agencies. The IRB is also required to maintain files indicating documentation of all actions taken by the IRB, membership of the IRB and attendance records for at least three years. IRB documentation includes the following:

- Minutes of IRB meetings.
- A list of IRB members in the same detail as described in [45 CFR 46.103\(b\)\(3\)](#).
- Written procedures for the IRB in the same detail as described in [45 CFR 46.103\(b\)\(4\)](#) and [45 CFR 46.103\(b\)\(5\)](#).
- Statements of significant new findings provided to subjects, as required by [45 CFR 46.116\(b\)\(5\)](#).
- Reports of injuries to subjects.

Overview

The IRB will maintain protocol files (paper and/or electronic) on each study as stipulated by DHHS regulations at [45 CFR 46.115\(a\)\(1\),\(3\),\(4\)](#), and [\(7\)](#). The minutes of IRB meetings will include all the information stipulated by DHHS regulations [45 CFR 46.115\(a\)\(2\)](#).

The federal regulations require all IRB protocol records related to research which is conducted, to be retained for at least three years after study completion; and all other IRB records to be retained for three years ([45 CFR 46.115\(b\)](#)). The CWRU IRB shall maintain records according to the above regulation and will keep paper copies secure in lockable filing cabinets or storage rooms and all electronic submission secure in the SpartaIRB electronic database. At present, the IRB will keep all IRB protocol records (paper and electronic) as well as other IRB records indefinitely. These records are available to the IRB at any time upon request.

When CWRU is engaged in human subjects research subject to the revised Common Rule, the following records will be maintained in addition to those described in the CWRU HRPP/IRB SOP Manual

1. Institutional Records –

For nonexempt research involving human subjects covered by the Common Rule that takes place at an institution in which IRB oversight is conducted by an IRB that is not operated by the institution, the institution and the organization operating the IRB shall document the institution's reliance on the IRB for oversight of the research and the responsibilities that each entity will undertake to ensure compliance with the requirements of this guidance document (e.g., in a written agreement between the

- a. institution and the IRB, by implementation of an institution-wide directive providing the allocation of responsibilities between the institution and an IRB that is not affiliated with the institution, or as set forth in a research protocol)

2. IRB Records –

- a. The rationale for conducting continuing review of research that otherwise would not require continuing review
- b. The rationale for a determination that research appearing on the expedited review list published in the Federal Register is more than minimal risk

IRB Meeting Agenda

The following are the basic elements of the IRB Meeting Agenda for each full review meeting:

- Date, Time and Location of IRB Full Review meeting
- Motion to approve the IRB minutes from the previous IRB full review meeting
- New Protocols
 - Protocol Number and Title
 - Protocol Responsible Investigator and Academic Department
 - IRB Primary Reviewer(s)
- Continuing Review Protocols
 - Protocol Number and Title
 - Protocol Responsible Investigator and Academic Department
 - IRB Primary Reviewer(s)
- Other Protocol Actions (i.e., Modifications, Protocol Deviations)
- New Business/Other Items
- Educational Articles and/or Discussions
- Located on every agenda: IRB Conflict of Interest definitions and standard operating procedures on identifying COIs, presenting COIs to full board, recusal and abstention from voting on protocol with the conflict.

IRB Protocol SpartaIRB File for Protocols Approved via Full or Expedited Review

In order to allow a reconstruction of a complete history of IRB actions related to the review and approval of the protocol, the IRB records include copies of:

- Completed IRB application(s).
- Complete approved protocol.
- Signed IRB approval letters, which also denotes the frequency for the next continuing review.
- All approved versions of consent/assent forms (with IRB stamp), including copies of DHHS-approved sample consent documents.
- Copy of federal grant application, if applicable.
- Scientific and ethical evaluations (e.g., consultant's reports and Department approvals).



- Progress reports/continuing review.
- Modifications to protocol.
- Advertising or recruiting materials, if any.
- Reports of injuries to study participants and associated adverse events.
- Results of any Quality Improvement Program (auditing) activities, if any.
- Documentation, as required by 45 CFR 164(i)(2), indicating the approval of a waiver or alteration of the HIPAA Authorization.
- Documentation of project closeout.
- Correspondence between IRB and investigator.
- Correspondence between IRB staff and IRB reviewers, including notification of researcher Conflict(s) of Interest, COI management plans, and research contract/funding agreement HRP language discrepancies, if applicable.
- Administrative actions.
- Documentation of IRB determinations required by the regulations and protocol-specific findings supporting determinations.
- The justification for using the expedited procedure.
- Statements of significant new findings provided to subjects, as required by [45 CFR 46.116\(b\)\(5\)](#).
- Copies of approved recruiting advertisement/ brochures/materials.
- Data and safety monitoring reports, if any.
- File Checklists items submitted with a File Checklist.
- Reports of internal/external unanticipated problems.
- Local context review information from investigator and/or consultant (if applicable).
- Translated consent forms (if applicable).
- Closure Checklist and final report, or other relevant information (e.g., IRB Continuing Review reminder notices, notice of study archive for failure to submit continuing review).
- If a protocol is cancelled without subject enrollment, IRB records are maintained for at least three years after cancellation.

IRB SpartaIRB File for Protocols determined to be Exempt

The following are the basic elements of the IRB protocol file for Exempt research protocols:

- Request for Exemption application and includes the specific approved exemption category for the research.
- The justification for exempt determinations.
- Any researcher Conflict of Interest and COI management plans, if applicable, including Ancillary Review by the Outside Interests Committee (CWRU COI).
- Any research contract/funding agreement HRP language discrepancies,
- Signed approval letter stating the specific category under which the study was determined to be exempt.
- Department review and approval.

- Any changes or revisions to the exempt protocol, and affirmation of continued exempt status via Modification requests.

IRB SpartaIRB Minutes

The minutes of the meetings of the fully convened IRB are confidential and are available only for inspection by authorized representatives of CWRU, DHHS, OHRP and other regulatory agencies. Organizations that conduct ethical consultations and national accreditations may also review meeting minutes when contracted by the university to do so. Documentation of compliance with the federal regulations is noted in the minutes. Electronic versions of the meeting minutes are maintained by the IRB Office.

Minutes will document required determinations and protocol-specific findings justifying those determinations for:

- Attendance recorded for each IRB action;
- Quorum requirements. A majority of IRB members and at least one member, whose primary concerns are in nonscientific areas, must be present at convened meetings. A protocol must receive approval of a majority of the members present at a meeting for it to be approved. When quorum is lost during a meeting, the IRB must not take further action or vote until quorum is restored;
- Actions taken by the full IRB on the initial or continuing review of research; review of protocol or informed consent modifications or modifications; unanticipated problems involving risks to study participants or others; adverse event reports; reports of noncompliance with the human study participant regulations or IRB determinations; suspensions or terminations of research; requirements of any researcher COI management plans, including but not limited to elements of the protocol and informed consent; human research protection language in contracts and funding agreements; review of and required actions regarding HRP-related discrepancies regarding contracts and funding agreements; and other actions;
- Protocol-specific votes (for, against, or abstained) for any action involving the review of research protocols;
- Separate votes for other IRB actions;
 - Waiver or alteration of the consent process.
 - Research involving pregnant women, fetuses, and neonates.
 - Research involving prisoners.
 - Research involving children.
 - Research involving subjects with diminished capacity.
- The basis for requiring changes in or disapproving research;
- Summary of controverted issues and their resolution;
- Name of persons who excused themselves from the discussion and vote on the study due to a conflict of interest.

IRB Membership Rosters

The IRB Office maintains electronic lists of IRB members that include name, earned degrees, scientific status, representative capacity, indications of experience, relationship with CWRU, affiliation status, office, membership status, and alternate status. The IRB membership lists will be retained permanently. The IRB will neither provide nor publish the names of the members of the IRB except to authorized representatives of CWRU, DHHS, OHRP and other regulatory agencies. Organizations that conduct ethical consultations and national accreditations may also review membership rosters when contracted by the university to do so.

IRB Policies and Procedures

The IRB Office maintains current guidance documents reflecting the procedures to implement federal regulations for protection of human subjects by the CWRU IRB. These documents are maintained electronically and are available for review on the CWRU IRB website.

IRB Database

IRB Office maintains an electronic database of studies reviewed by the CWRU IRB with relevant information relating to the status of each protocol and IRB actions. As of January 2012, the CWRU IRB required that all new protocol submissions be submitted to the IRB Office electronically, using the new electronic system (SpartaIRB). The SpartaIRB system allows for documents to be submitted to the IRB electronically. In addition, research-related documents, board/committee meetings and review records are uploaded and managed electronically.

This database resides on a server that is housed within the Office of Research Administration and is secured and maintained by the IRB Office as well as the Office of Research Administration IT Unit. Investigators can access SpartaIRB via university ID and password by asking the IRB Office to add them as a user. Once a user, investigators can enter SpartaIRB and submit IRB forms. Information on the server is backed up according to the Office of Research Administration IT Unit's practices.

Non-Compliance Information

Any information related to allegations of non-compliance with institutional policies or federal regulations pertaining to human subject protections are maintained with the CWRU IRB Office. Copies of relevant information related to compliance investigations, including compliance summaries, IRB findings and letters to investigators, OHRP, etc., are maintained in the IRB protocol file.

Format and Retention Period for IRB Records

Currently all IRB records are maintained in either hard (paper) copy, the IRB database, or in the SpartaIRB system. Federal regulations require that the IRB protocol file be maintained for three years after completion of the study; and other IRB records be maintained for three years. The IRB complies with the regulations and maintains complete records of all protocols that have been

completed; or canceled without participant enrollment. It is the current practice of the CWRU IRB to retain all IRB protocol files and IRB records indefinitely. Inactive paper IRB records are maintained and archived in an off-site facility staffed by Cintas.

Access to IRB Records

All IRB records, in any format, are considered confidential and may be accessed only by authorized individuals or regulatory agencies as required by law. Access to IRB records is limited to the IRB, IRB Office, authorized IRB representatives, CWRU officials (e.g., IO, legal office, University audit) and officials of federal and state regulatory agencies. Investigators or their designated staff shall be provided reasonable access to files related to their research. Department Chairs can access the files of faculty or staff in their departments. All other access to IRB records is limited to those who have legitimate need for access, as determined by the IRB Office and the CWRU Associate Vice President for Research Administration. All records shall be accessible for inspection and copying by authorized representatives of CWRU, DHHS, OHRP and other regulatory agencies. Organizations that conduct ethical consultations and national accreditations may also review IRB records when contracted by the university to do so.

Investigator Records

Each investigator is required to maintain accurate and complete files for each IRB approved protocol. Investigators must maintain original signed consent forms in their study files. Investigators' files must be available upon request for IRB review via Quality Assurance Audit. Investigators must maintain their study files in a secured and confidential manner to protect subject confidentiality and sponsor confidential information. Investigator records must be kept for a minimum of three years following the end of the study.

Chapter 6: Non-compliance Involving Human Research

This guidance describes the process that the IRB follows to manage allegations and findings of non-compliance with human subject protection regulations.

Definitions Pertinent to Non-compliance

Allegation of Non-Compliance: An unproven assertion of non-compliance; suspected non-compliance with human subject protection regulations, CWRU policies, or IRB requirements and determinations.

Continuing Non-Compliance: A pattern of non-compliance that, in the judgment of the CWRU IRB Chair or convened IRB, indicates a lack of understanding of the regulations or institutional requirements that may affect the rights and welfare of subjects, would have been foreseen as compromising the scientific integrity of a study such that important conclusions could no longer be reached, suggests a likelihood that non-compliance will continue without intervention, or frequent instances of minor non-compliance. Continuing non-compliance also includes failure to respond to a request to resolve an episode of non-compliance with human subject protection regulations.

Non-Compliance: Any action or activity associated with the conduct or oversight of research involving human subjects that fails to comply with federal regulations or the requirements or determinations of the CWRU IRB. Non-compliance actions may range from minor to serious, be unintentional or willful, and may occur once or more than once. The degree of non-compliance is evaluated on a case-by-case basis and will take into account such considerations as to what degree subjects were harmed or placed at an increased risk and willfulness of the noncompliance. Examples include, but are not limited to:

- Failure to obtain CWRU IRB approval prior to recruitment and involvement of human subjects;
- Inadequate or non-existent procedures for the informed consent process;
- Inadequate supervision;
- Failure to follow recommendations made by the CWRU IRB;
- Failure to report adverse events or protocol changes;
- Failure to disclose Conflict of Interests
- Failure to provide ongoing progress reports; or protocol deviations.

Serious Non-Compliance: An action or omission in the conduct or oversight of research involving human subjects that affects the rights and welfare of subjects, increases risks to subjects, decreases potential benefits or compromises the integrity or validity of the research. Examples of serious non-compliance include, but are not limited to:

- Conducting non-exempt research without CWRU IRB approval;

- Enrollment of subjects that fail to meet the inclusion or exclusion criteria of the protocol
- Enrollment of subjects that increase the risk to the subject;
- Enrollment of subjects while study approval has lapsed;
- Major protocol deviations that may place subjects at risk from the research.

Minor Non-Compliance: Non-compliance that is neither serious nor continuing. An example of minor non-compliance includes failure to comply with IRB policies that are administrative in nature (for example, turning in a report of an unanticipated problem late, or failure to date a consent form).

What is the IRB Oversight Responsibilities to Evaluate Allegations of Non-compliance?

The IRB, as part of their oversight responsibilities, must evaluate all non-compliance with human subject protection regulations and institutional policies, promptly report any serious or continuing non-compliance with federal regulations or institutional policies. The IRB requires investigators to report all matters of potential non-compliance. If an allegation of non-compliance is reported from any source (including monitoring/auditing reports, subject complaints, internal allegation or investigator self-reporting), the IRB Office in consultation with the IRB, and the University Compliance Officer will make an initial assessment to determine:

- Whether there is sufficient information present to verify and determine if the allegation is true;
- Whether additional information is needed to make a determination; and
- Whether a determination of non-compliance is serious or continuing.

All reports of alleged non-compliance are investigated by the CWRU Office of Research Administration. If it is determined that the non-compliance might be serious or continuing, the suspected non-compliance is forwarded to a convened meeting for full Board review and determination.

Goals of investigating and managing issues of potential noncompliance include:

- Assuring the safety, rights and welfare of human research subjects;
- Developing action plans to prevent recurrence, and promote a culture for future compliance;
- Educating research staff to assure the understanding of HHS regulations and guidelines and IRB Guidance; and
- Reporting serious or continuing non-compliance to the appropriate regulatory agencies and institutional officials.

Identification and Investigation of Non-Compliance

An allegation of non-compliance will result in the Research Compliance Officer conducting an investigation of the suspected non-compliance. Allegations and/or findings of non-compliance are identified in a variety of ways including notification by investigators, research team members, regulatory bodies, sponsors, research subjects, institutional personnel or committees, the public or anonymous sources. The initial allegation may be presented orally. Findings of non-compliance may also be identified during quality assurance visits.

Unsolicited or Voluntary Notifications of Allegations or Findings of Non-Compliance

When findings and allegations of non-compliance are reported to the IRB, it is initially reviewed by the Research Compliance Officer. The Office will review documentation and request additional information, as needed. The Office of Sponsored Projects will be notified of the investigation if that office is responsible for managing any related federal funding to the protocol in question. If a detailed explanation does not accompany the report, the IRB Office or the Research Compliance Officer will contact the investigator to request additional information. The investigation will begin within 5 working days of learning of the recognized concern. The purpose of the investigation is fact-finding and may involve examination of study records and discussion with investigators, the research team, other personnel, research subjects, and others as appropriate. A communication will be sent to the investigator describing the issue or allegations, any interim immediate action, and a request for additional information.

If requested by the individual reporting the allegation, the IRB will attempt to keep his or her identity confidential; however, confidentiality cannot be assured. If an anonymous allegation is made, the IRB will decide if sufficient detail is available to determine if non-compliance occurred and whether the allegation can be investigated in the absence of an identified complainant.

Allegations or Findings Identified by the IRB

Allegation or findings of non-compliance identified during monitoring visits conducted by the Research Compliance Officer are reviewed with the IRB. The IRB Office or the Research Compliance Officer will prepare a written summary of the observations and a proposed action plan for the investigator. The IRB will review the summary at the next full review meeting.

The action plan may include any, or all of the following:

- Asking the investigator to submit or revise an Unanticipated Problem, Adverse Event and Protocol Deviation Form to the IRB via SpartaIRB for further review;
- Identifying the finding as minor non-compliance and request a thorough action or COI management plan to correct and/or prevent the event from occurring again;
- Require Human Subject Protection Education;
- Require additional monitoring for the study in question and/or other studies conducted by the investigator.

Once the IRB is in agreement with the proposed action plan, the investigator will receive a determination letter that includes all monitoring observations, proposed action items, recommendations, educational requirements, and additional monitoring requests.

Minor Non-Compliance

The IRB staff will try to resolve reports of minor non-compliance with the investigator and research team. If the IRB staff cannot work out a corrective action plan with the investigator, then the report will be referred to the IRB for review and recommendations.

Allegations of minor non-compliance will be investigated by the IRB Office by contacting the investigator and research team for verification. The IRB Office receives allegations or reports of non-compliance and will conduct the initial fact-finding and compile information. If non-compliance is clearly minor and the proposed action plan seems adequate, the IRB Office may handle the allegation or report by documenting the event and the proposed corrective action and reporting the incident to the IRB with no further action required. If, in the course of handling the allegation or report of non-compliance, the IRB Office becomes concerned that the non-compliance may be serious or continuing, the matter will be referred to the Associate Vice President for Research, IRB Chair and Vice Chair for further action.

Upon completion of the initial fact-gathering process, the IRB will issue one of the following determinations:

Not Non-Compliance

When the Chair/designee determines that the facts do not support a finding of non-compliance as defined in this guidance, the report of non-compliance will be dismissed and no further action will be taken. The affected investigator(s) will be notified in writing of the determination.

Minor Non-Compliance

When the IRB determines that the facts support a finding of minor non-compliance, the IRB will either approve the research to continue with no further action required or require modifications.

The affected investigator will be notified in writing of the determination and the facts supporting the determination. No further action will be taken unless the investigator refuses to cooperate with the corrective action. Any required changes or modifications submitted by the investigator in response to the determination shall be reviewed by the IRB according to applicable policies on review of proposed changes in approved research. It is generally expected that these changes will be eligible for review according to the procedures on review of minor changes in approved research using the expedited review process.

Serious or Continuing Non-Compliance

When the information regarding an alleged report of non-compliance indicates serious non-compliance, the information is forwarded to the full IRB for review, consideration of suspension criteria, or consideration of termination. An investigation by the IRB Office and the Research Compliance Officer can occur simultaneously with IRB review for consideration of suspension.

Review of Non-Compliance Reports by the IRB

To assist in making a determination, a report outlining the facts surrounding the allegation and appropriate supporting documentation will be forwarded to all members of the IRB for review prior to the meeting. The following documents will be forwarded/accessible to all IRB members:

- A statement of the non-compliance allegation;
- Supporting documents including a copy of the current IRB approval letter, protocol, and consent form (as applicable to the investigation);
- A statement of previous IRB administrative actions related to the non-compliance;
- Any relevant additional information or special circumstances;
- Assessment of increased risk (if any) to subjects resulting from the non-compliance;
- Recommendations for possible actions or resolution;
- Review of the status of the investigator's other IRB-approved protocols;
- The Grant, if applicable; and
- Any other pertinent information (e.g., questionnaires, DSMB/audit reports, etc.)

Any voting member of the IRB may serve as primary and secondary reviewers. The Research Compliance Officer or Associate Director, Research Compliance will present the materials at the convened IRB meeting. The IRB will then:

1. Review the information;
2. Vote on the information provided, or defer the vote and gather additional information if needed from the investigator or others involved;
3. Vote on whether the non-compliance is serious; and
4. Vote on whether the non-compliance is continuing

The discussion, determination, and vote will be recorded in the IRB meeting minutes. The minutes must also include a description of the non-compliance issue and allegations and also document the vote as to whether the study is to continue with or without change, is suspended, or is terminated and whether corrective action is required.

Unless otherwise approved by the IRB, no guests/visitors may be present during the portion of the IRB meeting when a non-compliance matter is discussed. If an IRB member has or declares a conflict of interest regarding a specific investigator or protocol scheduled for a compliance discussion, he or she will leave the meeting while the non-compliance issue is discussed and will not vote on the issue.

After voting, the IRB may require:

- No action, protocol continues as previously approved;
- Modification of the study protocol;
- Modification of study documents;
- Modification of the informed consent process;
- Re-consent of subjects;
- Providing information about the non-compliance to current study subjects;
- Additional information be provided to past subjects;
- Obtaining more information pending a final decision;
- Modification of the continuing review schedule;
- Additional training of the investigator and research team;
- Monitoring the research;
- Monitoring the consent process;
- Suspension of the research;
- Termination of the research;
- Destruction of data collected at the time the non-compliance event occurred;
- Withdrawing or limiting the privileges of the investigator to conduct human research;
- Referral to other organizational bodies, as appropriate; and/or
- Other actions deemed appropriate.

The investigator will receive written notification from the IRB regarding the non-compliance issue, including recommendations for corrective actions. The IRB will maintain a file via SpartaIRB, including documentation and correspondence, on each non-compliance issue brought to the IRB for review. A report outlining any IRB determination of serious or continuing non-compliance will be submitted to the appropriate regulatory agencies and copied to the CWRU Institutional Official.

The IRB Chair or Vice Chair, using the expedited review process, may review and approve all minor modifications to previously approved research received in response to non-compliance. All modifications that are determined to be more than minor will be reviewed at a convened IRB meeting.

Suspension or Termination

If the allegation concerns non-compliance that might be serious or continuing, the IRB may suspend research activities immediately until such time that the full IRB can convene if they believe that research subjects may be exposed to immediate harm. If in the opinion of the HRPP Organizational Official or the Institutional Official, the allegation concerns non-compliance that might be serious or continuing, they may suspend institutional permission to conduct the research activities immediately until such time that the full IRB can convene if it is believed that research subjects may be exposed to immediate harm.

Suspension or termination of IRB approval of research will be reported to the appropriate regulatory agencies and institutional officials.

Non-Compliance with HIPAA (Privacy Language Requirement)

Failure to comply with HIPAA (Privacy Rule) requirements for research studies will be co-investigated by the Research Compliance Officer and the CWRU Director of Privacy Management. Instances of non-compliance with HIPAA requirements that also constitute non-compliance with human subject research regulations will be reviewed by the IRB under non-compliance procedures.

Chapter 7: Receiving and Reviewing Subject Complaints, Concerns and Questions

It is the right of research subjects to provide input, complain, voice a concern, or ask a question about a research study and to have the complaint, concern or question resolved in a timely manner.

The CWRU IRB Office recognizes that all research subjects have the following rights:

1. Subjects should know that taking part in a research study is always a choice.
2. Subjects have the right to know the purpose of the research.
3. Subjects should be told about every procedure he/she will need to follow and that he/she can ask questions at any time during the study.
4. Subjects should be told of any possible risks, side effects, or problems from being in the study.
5. Subjects should be told of any possible benefits of being in the study.
6. Subjects should be told whether there are costs of being in the study and whether he/she will be paid for your participation.
7. Subjects should be told who will see information collected about/from him/her and how it will be kept confidential.
8. Subjects should be told about any other choices available to him/her other than being in the study. Alternatives must be presented if they exist.
9. Subjects should be told if medical care is available and who will pay for such care if injuries occur to him/her as a result of the study.
10. Subjects have the right to refuse or withdraw from a study at any time.
11. Subjects have the right to know if a Principal Investigator and/or study team members have a COI pertaining to the study they are being asked to participate in.

Complaints, concerns, or questions may be raised by research subjects (past, present and potential), family members, designated spokespersons or anyone interested in research to the CWRU IRB phone, in writing or in person. IRB-approved consent documents include information for contacting the Principal Investigator and the CWRU IRB office should the subject have questions about the subject's rights and responsibilities and/or to report research-related problems. Each CWRU Office of Research Administration webpage includes the opportunity to provide feedback, input, and suggestions. CWRU also implements an Integrity Hotline, which is managed by an external entity that allows for reporting of any complaints about university processes.

IRB Responsibilities and Procedures

1. The IRB Office is responsible for initial review of the complaint, concern, or question and communicating with the person with the complaint, concern, or question. The IRB Office will obtain and document the following information, as appropriate:



- a. The person's name and contact information. However, if the person wishes to remain anonymous, the person will be advised that a thorough review may not be possible and that without this information, follow-up with the person would not be possible. Information will not leave the office and will be handled confidentially.
 - b. The protocol number and title, and Principal Investigator and staff names.
 - c. The person's relationship to the study such as past subject, present subject, potential subject, subject family member, etc.
 - d. A detailed explanation of the complaint, concern, or question.
 - e. Who the person has contacted regarding the complaint, concern, or question such as the PI, research staff or anyone else and when such contact was made?
 - f. A description from the person of a proposed resolution of the complaint/concern, if the person has such a proposal.
2. The IRB Office will communicate to the person that he/she will inquire into the circumstances associated with the complaint, concern, or question and that a response regarding the resolution of or a determination about the complaint, concern, or question will be provided promptly. The IRB Office will also inform the person about the limits of confidentiality in regard to the inquiry including who may be informed, what information may be reviewed, etc.
 3. The IRB Office will review study documents and other relevant information to begin the initial review of the complaint, concern, or question. The Research Compliance Officer or an Associate Director, IRB may also contact the Principal Investigator, either orally or in writing, to obtain information in association with the initial review.
 4. After performing the initial review, the IRB Office will determine whether the complaint, concern, or question is minor and can be handled administratively or whether the complaint, concern, or question needs to be reviewed by the IRB Chair and/or the IRB.
 - a. If the complaint, concern, or question is determined to be minor including those that do not involve potential risk to subjects or others or cause a change in the risk/benefit ratio associated with the study such as the subject not receiving approved compensation for participation, the review and response for such complaints, concerns, or questions may be done at the administrative level by the IRB Office. The report associated with the complaint, concern, or question and response including corrective action will be made a part of the project file and need not be provided to the IRB Chair for review unless deemed appropriate by the Research Compliance Officer or an Associate Director, IRB.
 - b. If the complaint, concern, or question is determined to involve potential risk to subjects or others or cause a change in the risk/benefit ratio associated with the study, the written report will be provided to the IRB Chair or Vice Chair for review.

- c. If the complaint, concern, or question is determined to be an allegation of noncompliance, the complaint, concern, or question will be reviewed as outlined in the Non-Compliance SOP.

IRB Chair/IRB Review Procedures

After the IRB Office has provided the report and response regarding the complaint, concern, or question to the IRB Chair, the IRB Chair will do the following:

1. If the IRB Chair determines that the complaint, concern, or question does not involve potential risk to subjects or others or cause a change in the risk/benefit ratio associated with the study, the Chair may accept the report and inform the IRB Office of said acceptance. Any report and acceptance of the report will be made a part of the project file.
2. If the IRB Chair determines that the complaint, concern, or question does involve potential risk to subjects or others or cause a change in the risk/benefit ratio associated with the study, the IRB Chair may determine the complaint, concern, or question requires review by the full Committee and the IRB Office will place the issue on the next appropriate meeting agenda for IRB review.
3. If the IRB Chair determines that the complaint, concern, or question would have an immediate effect to the health, welfare and/or rights of subjects, the IRB Chair will instruct the IRB Office to contact the Principal Investigator of the study to establish procedures for the protection of subjects pending review by the IRB.
4. If the complaint, concern, or question is reported to the IRB by the Principal Investigator, the complaint, concern, or question will be reviewed as outlined in the Event Reporting SOP.
5. If the IRB determines that the complaint, concern, or question is an unanticipated problem(s) involving risks to others; serious or continuing noncompliance; or results in suspension or termination of IRB approval, the determination and appropriate information must be reported to the Institutional Official and all other pertinent agencies.
6. The Principal Investigator will be informed in writing of the results of the review of the complaint, concern, or question by IRB promptly.

Chapter 8: Event Reporting

Federal regulations [45 CFR 46.108\(a\)\(4\)\(i\)](#) require IRBs to have written procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, and the federal department or agency head of any unanticipated problems involving risks to subjects or others. The IRB complies with all applicable local, state, and federal regulations in the conduct of human research studies. In keeping with these regulations, investigators are required to promptly report any unanticipated problem, adverse event or protocol deviation, with special attention to deviations involving risks to subjects or others. The IRB reviews the reports and fulfills all applicable reporting requirements to the appropriate institutional officials and federal departments or agencies.

The IRB has the authority to suspend or terminate a protocol that has been associated with unexpected serious harm to subjects or others.

Unanticipated Problem is an event that could adversely affect the rights, safety or welfare of the participants, or others (e.g., family members, by-standers, and researcher/team) or which significantly impacts the integrity of research data.

An example would be a breach of confidentiality or unintentional destruction of study records.

Adverse Event is any unintended negative experience associated with the study materials or research procedures. Adverse events include both physical and psychological harms; although they most commonly occur in the context of biomedical research, they also can occur in the context of social and behavioral research.

Serious Adverse Events are adverse events that result in any of the following outcomes: death; a life-threatening experience; inpatient hospitalization or prolongation of existing hospitalization; a persistent or significant disability/incapacity; or a congenital anomaly/birth defect.

In addition, events that may not result in death, be life-threatening, or require hospitalization may be considered serious when, based upon appropriate medical judgment, they may jeopardize the subject and may require medical or surgical intervention to prevent one of the outcomes listed above.

Non-Serious Adverse Event is any event that causes interference with routine daily activities without major discomfort and these interferences do not persist.

Non-serious events also include events that are easily tolerated and do not affect participation in routine daily activities.

Protocol Deviation is any alteration/modification to the IRB-approved protocol, whether intentional or inadvertent, that is not approved by the IRB prior to its initiation or implementation.

Minor Protocol Deviation is an incident involving noncompliance with the protocol but one that typically does not have a significant effect on the subject's rights, safety, welfare, or on the integrity of the resultant data.

Major Protocol Deviation is a more serious incident involving noncompliance with the protocol usually involving critical study parameters. Major protocol deviations generally affect the subject's rights, safety, or welfare, or the integrity of the study data.

Protocol Exception is a temporary deviation from the protocol that has been approved by the IRB before its initiation. Protocol exceptions are usually for a specific subject (e.g., allowing enrollment of a subject who is close to, but outside of, the age eligibility).

Minimal Risk means that both 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 ([45 CFR 46.102 \(j\)](#)).

IRB Review of Adverse Events and Unanticipated Problems

All adverse event or unanticipated problem reports are initially reviewed by the Chair or a Vice-Chair of the IRB before submitted to the full board to determine whether the problem is an unanticipated problem involving risks to subjects or others based on whether the problem is:

1. Unexpected (in terms of nature, severity, or frequency) given:
 - a. The research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and
 - b. The characteristics of the subject population being studied; and
2. Suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.
3. Related (or probably/possibly related) to the study procedures/interventions.

If the IRB Chair or Vice Chair determines that the problem is NOT an unanticipated problem involving risks to subjects or others, it will be reported to the IRB in the monthly notice to committee report.

If the IRB Chair or Vice Chair determines that the problem IS an unanticipated problem involving risks to subjects or others, the problem is reviewed by a convened IRB as described below.

All unanticipated problems reviewed at full Board will be assigned a primary and secondary reviewer. The reviewers will usually be the Chair and Vice Chair; however, another IRB member may also be assigned to review. If possible, the information about the event will be distributed with the meeting packets; however, if time does not allow it, it will be distributed in advance to the primary and secondary reviewers and to the other Board members at the meeting.

The primary and secondary reviewers and the rest of the full IRB will have access to the completed RNI form and any other related document deemed necessary. The complete IRB file is available to all members in SpartaIRB before, during and after the IRB meeting.

When unanticipated problems are reviewed at an IRB meeting and determined by the Board to be an unanticipated problem, the IRB will consider whether any corrective actions or substantive changes to the research are required. At its discretion the IRB may request outside consultation to assist in its review. The IRB may consider any of the following and determine that corrective actions or substantive changes are required.

- Review changes to the research protocol initiated by the investigator prior to obtaining IRB approval to eliminate apparent immediate hazards to subjects.
- Request further information from the investigator.
- Request modification of inclusion or exclusion criteria to mitigate the newly identified risks.
- Implementation additional procedures for monitoring subjects such as additional monitoring by an independent monitor.
- Suspension of enrollment of new subjects.
- Suspension of research procedures in currently enrolled subjects.
- Modification of informed consent documents to include a description of newly recognized risks.
- Require notification of additional information about newly recognized risks to current and previously enrolled subjects.
- Increase the frequency of continuing review.
- Halt new enrollment in the study pending a revised approved consent form and require currently active subjects to be re-consented using the revised consent form.
- Referral to other organizational entities.
- Terminate all study activities.
- Accept the report with no changes to the risk/benefit ratio or the informed consent documents.

The minutes must document the IRB's discussion, determinations and actions. This includes but is not limited to:

- Whether the report is determined to be an unanticipated problem.
- Whether the study is to continue as written and approved.

- Whether the protocol and/or consent form needs to be revised to address any additional risks.
- Whether subjects need to be re-consented.
- Whether additional information about the event needs to be provided.
- Whether the protocol is to be suspended or terminated.

The IRB will communicate its determination and finding to the Principal Investigator by sending a letter outlining the findings of the IRB and any required actions of the Principal Investigator. The IRB Office will report any event that has to be reported to Regulatory Agencies, Department Heads and Institutional Officials.

Protocol Deviations

An investigator with an IRB-approved protocol must conduct the protocol under the terms and specifications of the study as approved by the IRB. An investigator may not deviate from the approved procedures without prior IRB authorization except to avoid an immediate apparent hazard to subjects. Protocol Deviations must be reported by the investigator to the IRB within three (3) business days.

All protocol deviations are initially reviewed by the IRB Office. Deviations that result in harm to the subject are presented at a convened Board meeting and reviewed.

Deviations are reported using the RNI form via SpartaIRB. The investigator should explain the corrective actions taken to avoid future deviations. Protocol deviations that result in a change in the protocol, consent form or the risk/benefit ratio for the study should be reported to the IRB within 3 business days and a Modification must be completed and submitted in SpartaIRB. The Principal Investigator must be sure to upload and attach the amended protocol, consent form, along with other revised study documents.

Failure to report a protocol deviation in a timely manner may constitute non-compliance and will be referred to the IRB for review as possible non-compliance, which will be processed as described in the CWRU IRB Non-Compliance document.

Examples of Deviations

- Informed consent obtained by someone not approved to obtain consent for the protocol.
- Use of invalid consent form, e.g., consent form without IRB approval; or outdated/expired consent form.
- Enrollment of a subject who was ineligible for the study.
- Performing a research procedure not in the approved protocol.
- Study medication dispensing or dosing error.
- Use of recruitment procedures that have not been approved by the IRB.
- Enrolling significantly more subjects than proposed in the IRB protocol.

- Failure to follow the approved study protocol that does not affect subject safety (e.g., study procedure conducted out of sequence, failure to perform a required test, missing laboratory results, study visit conducted outside of required timeframe).

Chapter 9: Administrative Hold, Suspension or Termination of IRB-approved Protocols

Definitions Pertinent to IRB Oversight

Administrative Hold is a voluntary action by an investigator or departmental chair to temporarily or permanently stop some or all research activities as a modification to approved research. Examples when this would be appropriate include the following: unanticipated problem, investigator going on a sabbatical leave or leave of absence. Although the investigator may discuss this action beforehand with the IRB chair, Executive Director for the Human Research Protection Program or Vice President for Research, the hold must be initiated voluntarily by the investigator and must not be used to avoid IRB mandated suspension or termination or reporting requirements. During administrative hold, the research remains subject to continuing review and requirements for reporting non-compliance and unanticipated problems involving risks to subjects or others. Administrative holds must not be used to avoid reporting deficiencies or circumstances that otherwise require reporting by federal agencies. Administrative holds are not considered suspensions or terminations, and do not meet reporting requirements to OHRP, FDA and other federal agencies.

Administrative Termination of non-approved protocol/protocol submission is an action by the IRB on research which has been reviewed and given contingent approval (minor modification required to secure approval), and the investigator does not respond.

Suspension is when research on an approved protocol is partially or completely stopped pending future action by the IRB. Examples include: an unanticipated problem in research involving greater than minimal risks to subjects or others; unexpected serious harm to subjects; or when the IRB is investigating a research protocol for possible issues of human subject non-compliance or continuing non-compliance with federal regulations, or with the determinations of the IRB. Suspended protocols remain open and require continuing review.

Termination of IRB approval is defined as a permanent halt in IRB approval of all research activities.

Overview

The IRB has the authority and responsibility to suspend or terminate approval of research that is not being conducted in accordance with the IRB policies and procedures, or that has been associated with unexpected harm to subjects or others. The IRB has the ability to temporarily or permanently suspend or terminate approval for some or all research activities. Depending on the circumstances surrounding the suspension or termination action, the investigator may be required to submit a report to the IRB, detailing any adverse events and/or study outcomes that were previously unreported to the IRB for consideration. Any letter of suspension or termination

of approval to an investigator must include a statement of the reasons for the action by the IRB, which is outlined in HHS regulations under ([45 CFR 46.113](#)) and FDA regulations under ([21 CFR 56.113](#)).

The IRB Chair, Vice-Chair, or the Vice President for Research is authorized to suspend or terminate the enrollment of subjects; and the ongoing involvement of subjects in research, as it deems necessary to protect the rights and welfare of subjects. This also includes compelling and urgent instances when subject safety is of concern. The IRB will review such suspensions and terminations at a subsequent convened meeting. A plan will be developed that takes into account the rights and welfare of currently enrolled subjects and those subjects who may need to be withdrawn from the study. If the agreed upon plan of action involves withdrawal of enrolled subjects, the IRB will take into account their rights and welfare (e.g., transfer to another researcher, and continuation in the research under independent monitoring). If the IRB determines that a suspension or termination of the research will place subjects at risk of harm, the investigator will be requested to submit a proposed script or letter for subjects for IRB review and approval. The IRB determines the information that is to be provided to subjects and the method of their notification e.g., in writing or by telephone. This includes appropriate subject follow-up and notification of the reasons for the action. All protocol suspensions or terminations are reviewed at a subsequent IRB meeting.

When study approval is suspended or terminated, the IRB or the person ordering the suspension or termination considers:

- actions to protect the rights and welfare of currently enrolled subjects.
- informing current subjects of the termination or suspension.
- if any adverse events or outcomes have been or need to be reported to the IRB.

The IRB has the authority to allow the continued participation of subjects in research for which IRB approval has lapsed while the continuing review process occurs, only if there are overriding safety concerns or ethical issues that indicate it is in the best interest of the subjects to continue, for example when the research interventions have the prospect of direct benefit to subjects or when withholding the study interventions poses an increased risk to subjects. In such cases, the study will be closed to new enrollment and all data analysis must stop until the IRB completes the review process.

If an investigator makes a determination that immediately stopping all or some of the research activities would not be in a subject's best interest, the investigator must inform the IRB via SpartaIRB. This formal request should be made as a Modification and must include the rationale and justification as to why the research activities should be allowed to continue. It should also include a confidential list of the research subjects (identified by study number or initials only) for whom suspension of the research interventions would potentially increase risk or deny benefits. The determination by the IRB may be made by the IRB chairperson, by another IRB member or

group of IRB members designated by the IRB chairperson, or at a convened meeting of the IRB. Furthermore, this determination may be made for all enrolled subjects as a group or for each individual subject. If the investigator or IRB determines that it is not in the best interests of already enrolled subjects to continue to participate, investigators must stop all human subjects research activities, including intervening or interacting with subjects and obtaining or analyzing identifiable private information about human subjects ([45 CFR 46.109](#)(a) and (e)).

Reporting to Regulatory Agencies, Department Heads and Institutional Officials

The IRB will report all suspensions or terminations of IRB approval to Regulatory Agencies, Department Heads and Institutional Officials as required.

Chapter 10: Reporting to Regulatory Agencies, Department Heads and Institutional Officials

This document establishes guidelines to ensure prompt reporting by the Office of Research Compliance in response to findings of the CWRU IRB of those events listed in federal regulations. These regulatory requirements may be found in [45 CFR 46.103](#)

Definitions Pertinent to the IRB Oversight

Continuing Non-Compliance: A pattern of non-compliance that, in the judgment of the CWRU IRB Chair or convened IRB, indicates a lack of understanding of the regulations or institutional requirements that may affect the rights and welfare of subjects, would have been foreseen as compromising the scientific integrity of a study such that important conclusions could no longer be reached, suggests a likelihood that non-compliance will continue without intervention, or frequent instances of minor non-compliance. Continuing non-compliance also includes failure to respond to a request to resolve an episode of non-compliance with human subject protection regulations.

Non-Compliance: Any action or activity associated with the conduct or oversight of research involving human subjects that fails to comply with federal regulations or the requirements or determinations of the CWRU IRB. Non-compliance actions may range from minor to serious, be unintentional or willful, and may occur once or more than once. The degree of non-compliance is evaluated on a case-by-case basis and will take into account such considerations as to what degree subjects were harmed or placed at an increased risk and willfulness of the noncompliance. Examples include, but are not limited to:

- Failure to obtain CWRU IRB approval;
- Inadequate or non-existent procedures for the informed consent process;
- Inadequate supervision;
- Failure to follow recommendations made by the CWRU SBER IRB;
- Failure to report adverse events or protocol changes;
- Failure to provide ongoing progress reports; or protocol deviations.

Serious Non-Compliance: An action or omission in the conduct or oversight of research involving human subjects that affects the rights and welfare of subjects, increases risks to subjects, decreases potential benefits or compromises the integrity or validity of the research. Examples of serious non-compliance include, but are not limited to:

- Conducting non-exempt research without CWRU SBER IRB approval;
- Enrollment of subjects that fail to meet the inclusion or exclusion criteria of the protocol;
- Enrollment of subjects that increase the risk to the subject;
- Enrollment of subjects while study approval has lapsed;
- Major protocol deviations that may place subjects at risk from the research.

Suspension is a formal partial or complete interruption of research on an approved protocol pending future action by the CWRU IRB. Examples include:

- An unanticipated problem in CWRU IRB Policies and Procedures research involving greater than minimal risks to subjects or others;
- Unexpected serious harm to subjects;
- When the IRB is investigating a research protocol for possible issues of human subject non-compliance or continuing non-compliance with federal regulations, or with the determinations of the IRB.

Suspended protocols remain open and require continuing review.

Termination is when the CWRU IRB permanently withdraws study approval.

Unanticipated Problem involving risks to subjects includes any incident, experience, or outcome that meets **all** of the following criteria:

1. It is related to the research;
 - a. Unexpected (in terms of nature, severity, or frequency) given: the research procedures that are described in the protocol-related documents, such as the CWRU IRB-approved research protocol and informed consent document; and
 - b. the characteristics of the subject population being studied; and
2. Suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

Overview

It is the responsibility of the Human Research Protection Program Office at CWRU to assure reporting occurs according to the federal regulations, institutional policy and CWRU IRB guidance when the CWRU IRB determines that an event represents:

1. An unanticipated problem involving risks to subjects or others;
2. A serious or continuing noncompliance with research regulations or determination of the CWRU IRB; or
3. A suspension or termination of CWRU IRB approval.

In these instances, the IRB Research Compliance Officer or IRB Office Administrator will prepare a draft report within ten (10) working days after the IRB meeting at which the determination occurred or after which time an appropriate administrative action was taken outside of a Full Board meeting of the CWRU IRB.

Any concerns regarding data integrity outside of the jurisdiction of the Human Research Protection Program Office or the CWRU IRB will be referred to the Research Integrity Officer,

the Office of Research Compliance at Case Western Reserve University (CWRU) or the respective Dean's Office at CWRU for further consideration/action.

Procedures

The contents of the required reporting will include:

1. The nature of the event (unanticipated problem involving risks to subjects or others, serious or continuing non-compliance, suspension or termination of approval of research);
2. Name of the institution conducting the research and the awardee institution as applicable;
3. Protocol title;
4. Name of the Principal Investigator;
5. CWRU IRB number and identification numbers of any applicable federal or non-federal award(s) (grant, contract, or cooperative agreement, etc.);
6. A detailed description of the issue including the findings of the institutions involved and the reasons for the Research Compliance Office's investigation and the CWRU IRB's decision;
7. Actions the Research Compliance Office, the institution or the CWRU IRB is taking or plans to take to address the problem (e.g., revise the protocol, suspend subject enrollment, terminate the research, revise the informed consent document, inform enrolled subjects, increase monitoring of subjects, etc.); and
8. Plans, if any, to send a follow-up or final report by the earlier of: a specific date, when an investigation has been completed or a corrective action plan has been implemented.

The Research Compliance Officer or an IRB Office Administrator, in consultation with the CWRU IRB Chair, Vice Chairs (designees) will review and finalize the report within fifteen (15) working days after the IRB meeting at which the final determination occurred. The reporting will take place within 30 days of the completion of an investigation and/or determination has been reached.

The Research Compliance Officer will send the report to the following as applicable:

1. The CWRU IRB (as an information item with the agenda, or as an administrative action report);
2. OHRP, per the CWRU Federalwide Assurance*;
3. UHCMC Office of Research Compliance* whenever the research involves the use of shared facilities or employees or agents with appointments at both CWRU and UHCMC and by awardee institution, as applicable);
4. Other federal agencies* that are a signatory to "The Common Rule" who conduct or oversee the research, including the FDA;
5. Principal Investigator and other members of the research team, as applicable;

If deemed appropriate by the Research Compliance Officer, the report will also be forwarded to the following:

1. Department(s) chair(s), program director and supervisor(s) of the investigator and employee;
2. Other organizations and departments involved with the research;
3. The sponsor or funding agency; and/or
4. The applicable Grants and Contracts offices.

*Reporting is not required if the agency has already been made aware of the event through other mechanisms, such as reporting by the investigator, sponsor, or another Organization.