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1. INTRODUCTION

1.1 UNIVERSITY AT BUFFALO HUMAN RESEARCH PROTECTION PROGRAM (HRPP)

This manual describes policies and procedures of the University at Buffalo (UB) Human Research Protection Program (HRPP). The purpose of the program is to protect the rights, dignity, welfare, and privacy of human research subjects at the University and its affiliates by adhering to the highest ethical standards and by complying with applicable federal and state regulations.

UB’s HRPP achieves its purpose through:
- Establishment and support of UB’s Institutional Review Boards (IRBs) responsible for the review and approval of all research involving human subjects
- Development and implementation of initial and continuing training and education of those involved in UB’s Human Research Protection Program: investigators, research staff, HRPP and IRB Administrators, and IRB members.
- Ongoing evaluation of the HRPP through a Quality Assurance/Quality Improvement component
- Effective communication with internal and external constituencies

1.2 ETHICAL PRINCIPLES

The University at Buffalo’s Human Research Protection Program is grounded in foundational ethical principles. These guiding ethical principles are embodied in the Nuremberg Code of 1947, the Declaration of Helsinki of 1964 and its subsequent revisions (World Medical Association), and particularly in the Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research issued by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research in 1979. The Belmont Report’s principles of respect for persons, beneficence and justice are accepted as critical for the ethical conduct of human subject research:
- Respect for Persons – Individuals should be treated as autonomous agents. They should voluntarily participate in research only after being fully informed of the benefits and risks of participation. Special protection should be given to individuals with diminished autonomy.
- Beneficence – Researchers are obligated to maximize possible benefits and reduce or eliminate possible risks to subjects.
- Justice – The risks of research should be equitably distributed and should not unduly involve persons from groups unlikely to be among the beneficiaries of subsequent applications of the research.

1.3 COMPLIANCE WITH FEDERAL REGULATIONS

All human subject research conducted by or under the auspices of the University at Buffalo will be performed in accordance with Department of Health and Human Services (DHHS) regulations contained in Title 45 Code of Federal Regulations, Part 46 including subparts B-D that afford additional protections to vulnerable populations as well as Food and Drug Administration (FDA) regulations contained in Title 21 Code of Federal Regulations Parts 50, 56, 312, and 812. In
addition, the conduct of the University at Buffalo Human Research Protection Program will conform to all other applicable federal, state, and local laws and regulations as well as applicable UB Institutional policies.

1.4 FEDERALWIDE ASSURANCE

The University at Buffalo is considered to be “engaged” in human research as defined by the Office of Human Research Protection (OHRP) and has an OHRP approved Assurance of Compliance with the DHHS regulations for the protection of human subjects [45 CFR 46.103].

The University maintains a Federalwide Assurance (FWA) that has been in effect since July 22, 2005. The Assurance certifies that UB will comply with the DHHS regulations for the protection of human research subjects for all research reviewed by UB IRBs. The Assurance also defines other responsibilities of the Institution including: the provision of sufficient institutional support for the HRPP; the authority of UB’s IRBs to approve, require modification in, or disapprove human subject research; the existence of written procedures describing the IRB’s process for the review of research projects; and the reporting to OHRP of certain research outcomes (e.g., serious events/problems [SEPs] that are unanticipated and related to participation in the research or are otherwise associated with the research).

1.5 COMPLIANCE WITH STATE LAW

New York State legally addresses research involving human subjects in Public Health Law Section 24-A. Protection of Human Subjects. This law defines human research differently from the federal regulations and as a result, only research that involves medical experimentation, medical procedures, or therapeutic intervention on human volunteers is covered. Behavioral, social science, and epidemiological research are not regulated by New York State law unless such research involves medical experimentation or procedures or therapeutic intervention. With respect to the laws’ applicability, Subsection 2445 notes that “the provisions of this article shall not apply to the conduct of human research which is subject to, and which is in compliance with, policies and regulations promulgated by any agency of the federal government for the protection of human subjects.” As all UB research, whether funded or unfunded, is covered under the University’s Federalwide Assurance (FWA), the University’s legal counsel has determined that the provisions of 24-A are not legally binding.

For research that takes place in jurisdictions other than the State of New York, the IRB will ask the PI to provide information concerning any laws related to human subject research conducted within the jurisdiction. When there are differences between federal regulations and the jurisdiction’s applicable law, the more restrictive code will be applied. In this regard, UB IRBs will seek guidance from university general counsel as needed.

1.6 AFFILIATIONS

1.6.1 Local Affiliated Hospitals

The University at Buffalo has formal institutional affiliation agreements with regional hospitals where UB clinical departments and researchers are based. The following characterizes UB’s relationship with its hospital affiliates with respect to research involving human subjects:
The Kaleida Health System’s Federalwide Assurance (FWA) designates UB IRBs as the IRBs of record for all research carried out in Kaleida Health facilities. The Kaleida Health System includes Buffalo General Hospital, Milliard Fillmore Hospital-Gates Circle, Millard Fillmore Hospital-Suburban, Women and Children’s Hospital of Buffalo, and other Kaleida facilities.

Erie County Medical Center (ECMC) has an FWA that designates UB IRBs as IRBs of record for all research conducted at the hospital.

Roswell Park Cancer Institute has its own FWA and IRBs. RPCI and UB have IRB Authorization Agreements for cancer-related research involving both RPCI and UB or its affiliates. For pediatric oncology protocols, a joint review process is carried out by UB’s Children & Youth IRB and RPCI IRB for studies conducted at both RPCI and Kaleida Health’s Women & Children’s Hospital of Buffalo. For adult oncology studies involving both RPCI and UB, UB IRB chairs have the option to accept sole review by the RPCI IRB as the IRB of record or to have the UB IRB review the study as well. Nursing research at RPCI that involves non-therapeutic studies such as patient surveys are reviewed by the UB Social & Behavioral Sciences IRB.

Veterans Administration Hospital of Western New York (VAWNY) has its own FWA and is AAHRPP accredited. UB and VAWNY have a memo of understanding (MOU) in place for conducting collaborative human research. The MOU allows for approval from either one or both IRBs under the following circumstances:
1. Only VA-IRB approval is needed when a research study is to be conducted at the VAWNY regardless of the funding source.
2. Dual review and approval from the VA-IRB and a UB-IRB will be needed when a study is to be conducted at the VAWNY and also at a UB facility.

UB IRBs provide monthly updates regarding IRB activities to affiliated hospital administrators (e.g., Kaleida’s Chief Medical Officer).

1.7 INTRA-INSTITUTIONAL RELATIONSHIPS

The HRPP coordinates its activities with other units and individuals within the Institution and its affiliates, as follows:

**Sponsored Projects Services**

The Sponsored Projects Services (SPS) Office is responsible for assisting faculty in the preparation and submission of research grant proposals and management of post award activities. Once a project has been approved, UB IRBs provide SPS with information from the HS-1A Application Form that contains basic information about the investigator, the research project, sponsor, and research staff. SPS is notified of any suspensions, terminations, or closures of sponsored research projects for which the Research Foundation or the University at Buffalo Foundation are fiscal agents.

**Dean and Vice President’s Offices**

The IRB office staff contacts the appropriate Dean or Vice President’s Office with information about the proposed sponsored research and requests a financial conflict-of-interest determination for PIs, co-PIs and other key study personnel. Final approval by the IRB is contingent upon receiving notification from the Dean’s office that there is no financial conflict-of-interest or that any conflict has been managed.

**UB Director of HIPAA Compliance**
UB IRBs administratively review research protocols for HIPAA compliance on behalf of the University. HIPAA forms and guidance were developed in collaboration with the UB Director of HIPAA Compliance, who is responsible for Institutional compliance with HIPAA regulations. When a non-routine HIPAA issue arises, IRB administrators consult with the Director of HIPAA Compliance regarding appropriate procedures.

- **University Biosafety Committee**
  Investigators that are using agents that are infectious, or potentially infectious, to humans, animals, or plants, or are using recombinant DNA (or RNA) for the introduction into humans, must have the project reviewed by the University Biosafety Committee (UBC) before it can be conducted. The investigator is responsible for submitting the project information to the UBC for review.
2. INSTITUTIONAL AUTHORITY

2.1 ORGANIZATIONAL STRUCTURE OF THE UB HUMAN RESEARCH PROTECTION PROGRAM (HRPP)

2.1.1 Vice President for Research and Economic Development-HRPP Oversight

The Vice President for Research and Economic Development (VPRED) is the senior executive who has oversight of the University’s HRPP. The VPRED has designated the Associate Vice President for Research as both the Institutional Official (IO) and the HRPP Administrator. The IO has the authority to establish the Institution’s IRBs as well as to dissolve the IRB operations. The IO’s responsibilities include:

- Serve as signatory for UB’s Federalwide Assurance as well as other Institutional documents related to UB’s HRPP including inter-institutional IRB Authorized Agreements, Certificates of Confidentiality, IRB appointment letters, reports to regulatory agencies, and Department of Defense addenda.
- Appoints IRB Chairs and Members in consultation with the VPRED
- Assure that UB IRBs comply with applicable ethical principles, federal and state laws and institutional policies and procedures for the protection of human research subjects
- Ensure the independence of the IRB, including the authority to act without undue influence
• Support IRB authority and decisions
• Support investigators in their right to a fair and impartial IRB review
• Provide final approval for the hiring and appointment of HRPP staff
• With the VPRED, set the tone for an Institutional culture of respect for human research subjects by ensuring the standing of the IRB within the institution
• Ensure effective institution-wide communication and guidance on human research
• Receive reports of alleged undue influence on the IRB process and intervene as needed
• Receive and respond to concerns from investigators that could not be resolved by processes within the HRPP
• Provide sufficient financial and administrative support to the HRPP

2.1.2 Human Research Protection Program Administrator

The IO is also the Human Research Protection Program Administrator (hereafter designated IO/HRPP Administrator) who provides administrative oversight for the HRPP. The IO/HRPP Administrator reports directly to the VPRED.

The responsibilities of the Human Research Protection Program Administrator function are:

• Create, establish, and maintain the policies and procedures for the HRPP in collaboration with the, IRB Chairs, IRB Administrators, and others as appropriate
• Provide interpretation and application of federal regulations and institutional policies and procedures
• Interact with federal authorities (e.g., OHRP, FDA) concerning HRPP issues
• Oversee the implementation of the HRPP including conducting periodic program assessments
• Assess the HRPP's human resource needs and capabilities including the creation of new positions, support for ongoing staff development and annual evaluations of HRPP personnel
• Ensure that the HRPP's fiscal needs are addressed through annual budget requests to the VPRED and through the management of the HRPP's IRB review fee fund
• Set standards for human subject research education requirements in collaboration with the, IRB Chairs, IRB Administrators, and others, as appropriate
• Interact with other organizations with respect to human subject research and develop, as needed, intra-organizational IRB Authorization Agreements that allow one organization to rely on another organization's IRB
• Coordinate UBs efforts in matters relating to accreditation through the Association for the Accreditation of Human Research Protection Programs (AAHRPP)
• Support the independence of the IRB, including the authority to act without undue influence
• Receive and respond to reports of alleged undue influence on the IRB process
• Support IRB authority and decisions
• Prepare documents necessary to fulfill certain federal reporting requirements, as mandated in 45 CFR 46.103 and FDA 21 CFR 56.113 involving:
  o Any suspensions or terminations of IRB approval
  o Instances of serious or continuing non-compliance
  o Serious events/problems (SEPs) that are unanticipated and related to participation in the research (or are otherwise associated with the research)
  o Any changes in IRB membership
- Ensure that open channels of communication are maintained between the components of the HRPP (i.e., that staff, subjects, and other interested parties have a means of communicating information about the conduct of research directly to the appropriate institutional officials, and that individuals with responsibility for the oversight of research have open and ready access to the highest levels of authority)
- Receive responses to HRPP customer service surveys
- Respond to questions, concerns or complaints from research subjects and investigators
- Facilitate communication though writing and disseminating the HRPP News Bulletin which provides timely coverage of important HRPP topics

2.1.3 HRPP Quality Assurance/Quality Improvement Administrator

The goal of the QA/QI program is to promote Institutional and investigator compliance with human subject protection regulations and requirements in order to ensure long-term program success and credibility of UB’s HRPP (see Section 19: Quality Assurance/Quality Improvement Activities). The HRPP QA/QI Administrator collaborates with members of UB’s research community to improve the Institution’s efforts to uphold high ethical standards, to meet regulatory requirements, and to improve research practices for the protection of subjects participating in the research. The QA/QI Administrator reports to the IO/HRPP Administrator.

The responsibility of the QA/QI Administrator is to provide QA/QI support for the HRPP program that includes, but is not limited to:

- Conducting investigations and audits of research:
  - When the IRB, IRB chair, IO/HRPP Administrator, or VPRED directs that an audit be conducted, including in response to a complaint or allegation of non-compliance (i.e., fact-finding or for-cause audits)
  - For purposes of program quality improvement (i.e., routine/not-for-cause audits)
- Developing and providing training and education opportunities based on concerns identified from sources that include: the HRPP staff, IRB members, researchers, and the site visit process
- Facilitating the sharing of best practices, identified through the site visit process, with the research community, usually through the use of training and education materials
- Developing and encouraging the use of tools for investigators that facilitate compliance with government regulations, ethical principles and Institutional and IRB policies
- Implementing QA/QI programs

2.1.4 Institutional Review Boards (IRBs)

The University at Buffalo has four Institutional Review Boards: the Children & Youth IRB, Health Sciences IRB Committee A, Health Sciences IRB Committee B, and the Social and Behavioral Sciences IRB. Each committee has a Chair or Co-Chairs, members, and alternate members. Committees may also have a Vice-Chair.

2.1.4.1 IRB Chairs/Co-Chairs

The IRB Chairs are responsible for assuring that the IRB operates in accordance with federal regulatory requirements governing IRB functions. The Chairs work with IRB members, the OVPRED, and investigators to ensure that the rights and welfare of research subjects are
adequately and appropriately protected. (For more information, see Section 5.1: Responsibilities of the IRB Chair/Co-Chairs.)

The IRB Chairs/Co-Chairs are selected through an internal search process. Individuals under consideration for appointment as an IRB Chair or Co-Chair must meet the following requirements:

- Have a comprehensive understanding of human subject research in order to best lead and coordinate committee review of research protocols
- Previous experience as an IRB member preferred
- Meet HRPP training and education requirements
- Display adequate knowledge of ethical principles, professional standards, federal regulations, and other applicable law, through attendance and participation at IRB meetings
- Demonstrate professional competence necessary to review specific research activities

The term of appointment ranges from one to three years and may be renewed; the term of the appointment will be specified in a letter from the IO/HRPP Administrator. The IO/HRPP Administrator may reappoint an incumbent IRB Chair or Co-Chair to serve for additional terms of one to three years. The IO/HRPP Administrator will make the final decision regarding renewal of all appointments in consultation with the VPR/ED.

The IO/HRPP Administrator through the UB performance appraisal program evaluates Chairs and Co-Chairs annually and submits such appraisals to the VPR/ED. Each Chair/Co-Chair is provided with a copy of his/her appraisal either electronically or on paper when submitted to the VPR/ED. The IRB Chairs routinely report to the IO/HRPP Administrator, but in addition, have direct access to UB’s VPR/ED as needed.

2.1.4.2 IRB Vice-Chair

The Vice-Chair assumes the responsibility of the Chair or Co-Chair in his/her absence, in instances when the Chair has a conflict of interest, or at the discretion of the Chair/Co-Chair. (For more information, see Section 5.2: Responsibilities of the IRB Vice-Chairs.)

A Vice-Chair may be appointed by the IO/HRPP Administrator upon recommendations from the IRB Chair. The same requirements for selecting a Chair or Co-Chair are used when selecting a Vice-Chair. These individuals must meet the following requirements:

- Have previous experience as an IRB member
- Meet HRPP training and education requirements
- Display adequate knowledge of ethical principles, professional standards, federal regulations, and other applicable law, through attendance and participation at IRB meetings
- Demonstrate professional competence necessary to review specific research activities

The IRB Chair evaluates the Vice-Chair at the time of re-appointment. Evaluations are based on the Vice-Chair’s attendance at meetings, participation at meetings, and thoroughness of reviews. The Vice-Chair reports to the Chair and the IO/HRPP Administrator.

2.1.4.3 IRB Administrators

IRB Administrators are responsible for the day-to-day operations of the IRB. They work in collaboration with the IRB Chairs to manage the institutional review and approval process of all
proposed research activities involving human subjects. (For more information regarding responsibilities of IRB Administrators, see Section 5.3: Responsibilities of the IRB Administrators.)

The IO/HRPP Administrator through the UB performance appraisal program evaluates administrators annually. The IRB Administrators report to their respective IRB Chairs and to the IO/HRPP Administrator.

2.1.4.4 IRB Members and Alternate Members

IRB Members may be either affiliated or unaffiliated with the institution. Members and alternates are appointed based on the recommendations of the IRB Chair. The following criteria may be taken into account when an individual is considered for appointment as an IRB member:

- educational background
- experience in research activities
- areas of expertise

In order to document qualifications of IRB members, a CV or résumé is obtained. The term of appointment ranges from one to three years and may be renewed.

The IRB Chair evaluates members and alternate members on an annual basis. Evaluations are based on the member’s attendance at meetings, participation at meetings, and thoroughness of reviews. Members are provided with the Chair’s written evaluation either electronically or on paper once they have been completed.

For more information regarding membership composition of the IRB and responsibilities of members and alternate members, see Section 5.4: IRB Membership Composition and Responsibilities of IRB Members.

2.1.4.5 IRB Ex Officio Members

The IO/HRPP Administrator may appoint ex officio members from among the academic or administrative staff of the University at Buffalo or its affiliated Institutions. An ex officio member is designated as an IRB member by virtue of that individual’s role, function, or office. If an ex officio member leaves his/her position, the IO/HRPP Administrator will determine whether to appoint another individual to that position; the membership does not remain with the individual who has left that position. A UB IRB ex officio member may not vote on any IRB action or determination.

2.2 REMOVAL FROM SERVICE TO THE IRB

The IO/HRPP Administrator may act to remove a member of the IRB, including an IRB Chair, before the end of his/her term if his/her participation in IRB activities is deemed to be inadequate, inappropriate, or damaging to the reputation of the University and its research activities. Removal of an IRB member from IRB service requires the concurrence of the IRB Chair and the IO/HRPP Administrator. Removal of an IRB Chair requires the concurrence of the IO/HRPP Administrator and VPR ED.
Members cannot be removed from the IRB because of their voting record, or in an attempt to alter the IRB's membership for purposes of obtaining approval for a certain protocol or class of protocols.

2.3 IRB MEMBER LIABILITY COVERAGE

Appointment to the IRB by the IO/HRPP Administrator qualifies members as State "employees" for purposes of personal liability and indemnification coverage. The SUNY Office of University Counsel has reviewed the question of IRB member liability and determined that all IRB members are protected in the event of a civil lawsuit under Section 17 of New York State's Public Officers Law. Coverage extends to non-University members as the Public Officers Law includes under definition of an employee "...a volunteer expressly authorized to participate in a state-sponsored volunteer program." The Public Officers Law provides for both the defense and indemnification of state "employees."

2.4 HRPP PROGRAMMATIC EVALUATION & SUPPORT

The VPR and the IO/HRPP Administrator review the status of the program on an on-going basis through regularly scheduled meetings. The IO/HRPP Administrator prepares an annual report which reviews and evaluates the HRPP with respect to the adequacy of financial, personnel and physical resources, IRB structure and membership, educational, QA/QI, access to legal counsel, conflict of interest procedures and outreach activities. The annual report to the Association for the Accreditation of Human Research Protection Programs that is prepared by the IO/HRPP Administrator also provides valuable information concerning the status of the HRPP.

The core HRPP budget covers most full-time personnel costs and is part of the OVPRED budget. IRB review fees provide critical supplemental funding in support of the HRPP program. Fees are charged for both initial and continuing review of corporately sponsored research. IRB review fees provide compensation for all part-time personnel and cover all other than personnel expenses. These expenses include, but are not limited to, equipment purchase and maintenance, facilities maintenance, purchase of books and subscription to periodicals, attendance at educational conferences for professional staff, professional organizational membership fees (e.g., PRIM&R), support for professional certification (e.g., Certified IRB Professional certification), and stipends for guest speakers.
3. EDUCATION AND TRAINING

3.1 EDUCATION OF PRINCIPAL INVESTIGATORS AND RESEARCH STAFF

3.1.1 Initial Education of Principal Investigators and Research Staff

Federal regulations require that research staff involved in human research projects complete an initial educational program in the protection of human research subjects before initiating their research involving humans. Research staff includes principal investigators, co-investigators, faculty sponsors for student investigators, all individuals who will obtain consent, study/research coordinators, study/research managers, data collectors, recruiters, interviewers, and statisticians.

To meet initial education requirements, research staff must:

- Successfully complete the biomedical and/or the social and behavioral research track of the Collaborative Institutional Training Initiative (CITI) Course in the Protection of Human Research Subjects which includes:
  - Various modules on human subject protection
  - The Belmont Report
  - The UB HRPP Investigator's FAQs
  - The UB Human Research Protection Program Policy and Procedures Manual (UB SOP)

3.1.2 Continuing Education of Principal Investigators and Research Staff

After meeting initial educational requirements, investigators and research staff are required to meet a continuing education requirement every three years. Continuing education requirements may be met either by completing a CITI refresher course or other training required by the Human Subject Protection Program (HRPP).

As part of the continuing education process, the HRPP provides investigators and research staff with the following continuing education resources:

- **HRPP Topics** - a periodic newsletter advising investigators on best practices
- **HRPP News Bulletin** - focusing on a time-sensitive or critical issue
- Various Human Subject Protection training opportunities including:
  - Departmental "brown bag" sessions
  - HRPP training sessions
  - Presentations to research methods classes
  - Issue-specific presentations for specific research groups following site visits by the QA/QI Administrator
  - Educational resources on the Research Subjects Protection (RSP) website
  - Continuing education opportunities provided through CITI (e.g., HIPAA, Good Clinical Practices)
  - HRPP Distinguished Speakers Series (presentations by experts in the field of human subject protection)

3.1.3 Monitoring of Educational Requirements for Principal Investigators and Research Staff
The IRB staff has access to the online record of CITI completion reports and may also maintain local records of completion dates. Whenever a protocol initial submittal or renewal is submitted to the IRB for review, approval will not be granted until educational requirements are up to date for all members of the research team.

3.2 EDUCATION OF IRB CHAIRS, MEMBERS, AND ALTERNATES

3.2.1 Initial Education Program of IRB Chairs, Members, and Alternates

The initial education program of IRB Chairs, members, and alternates requires that they:

- Successfully complete the biomedical and/or the social and behavioral research track of the Collaborative Institutional Training Initiative (CITI) Course in the Protection of Human Research Subjects which includes:
  - Various modules on human subject protection
  - The Belmont Report
  - The UB HRPP Investigator’s FAQs
  - The UB Human Research Protection Program Policy and Procedures Manual (UB SOP)
- Read the UB IRB Member Handbook
- Review Protecting Study Volunteers in Research: A Manual for Investigative Sites (Dunn & Chadwick)
- Review the Institutional Review Board Member Handbook (Amdur)
- Receive orientation from the current IRB Chair or IRB Administrator

3.2.2 Continuing Education of IRB Chairs, Members, and Alternates

After meeting initial educational requirements, IRB Chairs, members, and alternates are:

- Required to meet a continuing education requirement every three years; Continuing education requirements may be met either by completing a CITI refresher course or other training required by the UB HRPP
- Encouraged to read monthly publications devoted to research ethics and human research subjects protection including: Human Research Report and IRB Ethics & Human Research
- Encouraged to attend UB HRPP Distinguished Speakers Series presentations

IRB Chairs/Co-Chairs are also encouraged to attend a professional conference annually.

3.3 EDUCATION OF HRPP AND IRB ADMINISTRATORS

3.3.1 Initial Education of HRPP and IRB Administrators

The initial education process for HRPP and IRB administrators requires that they:

- Successfully complete the biomedical and the social and behavioral research tracks of the Collaborative Institutional Training Initiative (CITI) Course in the Protection of Human Research Subjects which includes:
  - Various modules on human subject protection
  - The Belmont Report
  - The UB HRPP Investigator’s FAQs
o The *UB Human Research Protection Program Policy and Procedures Manual (UB SOP)*

- Read *Protecting Study Volunteers in Research: A Manual for Investigative Sites (Dunn & Chadwick)*
- Read the *Institutional Review Board Member Handbook (Amdur)*

Further, IRB Administrators are encouraged to become familiar with the textbook, *Institutional Review Board: Management and Function* (Bankert & Amdur) and use it as a day-to-day resource.

### 3.3.2 Continuing Education of HRPP and IRB Administrators

After meeting initial educational requirements, HRPP and IRB Administrators are:

- Required to meet a continuing education requirement every three years; Continuing education requirements may be met either by completing a CITI refresher course or other training required by the UB HRPP.
- Encouraged to:
  - Use the textbook *Institutional Review Board: Management and Function* (Bankert & Amdur) as both a day-to-day as well as a continuing education resource
  - Review monthly publications devoted to research ethics and human research subjects protection including: *Human Research Report* and *IRB Ethics & Human Research*
  - Attend a professional conference when possible
  - Pursue certification as an IRB professional (CIP) through the Council for Certification of IRB Professionals

### 3.4 EDUCATIONAL RESOURCES FOR RESEARCH VOLUNTEERS AND THE COMMUNITY-AT-LARGE

The UB HRPP website provides links to a number of general educational and informational resources developed for individuals considering participation in a research study as well as for interested members of the community-at-large that includes the following:

- UB HRPP brochures:
  - *So you're thinking about being in a research study. Here are a few things you ought to know.*
  - *Questions a prospective research participant might ask the researcher and themselves*

- *Clinical Trials:*  a National Institutes of Health sponsored website that provides information to the public about active clinical research studies.

- *Should I Enter a Clinical Trial -- A Patient Reference Guide for Adults with a Serious or Life-Threatening Illness:* prepared by the Emergency Care Research Institute

- *A Bill of Rights for Research Participants*

- *Becoming a Research Volunteer- It's Your Decision:* a brochure from the federal Office of Human Research Protection (OHRP)

- The National Cancer Institute (NCI) *Clinical Trials Education Series* providing resources to help understand cancer related clinical trials

- Information about the UB HRPP Distinguished Speakers Series – presentations by experts in the field of human research subject protection that are free and open to the public
4. THE SCOPE AND AUTHORITY OF UB IRBs

4.1 DIVISION OF IRB RESPONSIBILITY

The University at Buffalo has four IRBs that serve researchers across the University and its affiliated institutions. The determination of which IRB will be responsible for project review is based on the nature of the research and the prospective subject population. In instances when more than one IRB may review a project, the Chairs will confer to determine which IRB will conduct the review.

In general, the IRBs review projects within their areas of expertise as described below:

4.1.1 Children & Youth IRB (CYIRB)

The Children & Youth IRB (CYIRB) is responsible for reviewing any research projects involving biomedical interventions principally involving children, regardless of the source of funding or the departmental affiliation of the investigator. The CYIRB meetings are held at Kaleida Health’s Women & Children's Hospital of Buffalo that also houses the CYIRB administrative office.

[Note: Investigators conducting clinical research at Kaleida-Women and Children's Hospital of Buffalo (WCHOB) must also obtain approval from the WCHOB Investigational Drug Subcommittee for use of an investigational drug(s) proposed for use in a non-approved patient population.]

4.1.2 Health Sciences IRBs (HSIRB Committee A and Committee B)

The Health Sciences IRBs review biomedical research projects principally involving adults. There are two Health Sciences committees, HSIRB Committee A and HSIRB Committee B. HSIRB meetings are held on the UB’s South Campus in 150 Parker Hall where the HSIRB administrative offices are located.

4.1.3 Social & Behavioral Sciences IRB (SBSIRB)

Social & behavioral research projects involving human subjects are reviewed by the Social & Behavioral Sciences IRB (SBSIRB). This includes health-related research projects involving surveys and other non-invasive interventions. SBSIRB meetings are held on UB's Amherst Campus. The SBSIRB administrative office is located in 515 Capen Hall.

4.2 IRB SCOPE OF RESPONSIBILITY

All human research projects covered by UB’s HRPP must be reviewed and approved by a UB IRB prior to initiation. The State University of New York’s Policy on Unrestricted Disclosure of Research Activities does not allow restriction on the dissemination of research findings. UB’s IRBs may only approve projects that comply with this policy. UB does not have any further restrictions on types of human research permitted under federal and state law. Human research projects requiring review by a UB IRB include:

- Research conducted by or under the direction of any member of the University or its affiliates in connection with his/her institutional responsibilities
• Research conducted using any property or facility of the University or its affiliates
• Research involving the use of the University's non-public information to identify or contact human subjects
• Research for which the University has accepted responsibility for review under the terms of an IRB Authorization Agreement after verifying that the collaborating organization has an approved FWA and has designated a UB IRB as the IRB of record
• Research for which the University has accepted responsibility for review under the terms of an Individual Investigator Agreement that designates a UB IRB as the IRB of record

In order for a site to rely upon UB’s IRB as the IRB of record, the site must first have an approved FWA or be entering into an individual investigator agreement. The site must then complete and send a signed IRB authorization agreement to the IO/HHRP Administrator. Upon review, the IO/HHRP Administrator may agree to allow a UB IRB to act as the IRB of record for the site by signing the agreement form. A copy of the signed agreement will be sent to the site. The site may then designate a specific UB IRB as the IRB of record in accordance with the authorization agreement. Any protocol determinations or approvals made by the IRB then extend to the site. Any necessary institutional communication between UB and an external site related to the authorization agreement will be sent from the IO/HHRP Administrator to the external official designated by the agreement.

4.3 AUTHORITY OF THE IRB

The operations of the IRB are governed by federal regulations for the protection of human subjects [DHHS 45 CFR 46 and FDA 21 CFR 56]. The regulations specifically grant IRBs the authority to:
• Determine whether a project meets the criteria for human subject research
• Determine whether a project causes the Institution to become engaged in human subject research
• Approve research activities
• Require amendments/modifications in research activities
• Disapprove any research activities overseen by the University at Buffalo or its affiliates
• Suspend or terminate approval of research that is not being conducted in accordance with the IRB's requirements or federal regulations
• Suspend or terminate approval of research that has been associated with serious events/problems (SEPs). This includes the authority of the Chair to take immediate action to suspend a research project to protect research subjects from serious risks.
• Observe, or have a third party observe, the consent process
• Observe, or have a third party observe, the conduct of the research

The UB IRBs make their independent determinations whether to approve or disapprove a project based upon whether human subjects are adequately protected. Research that has been reviewed and approved by an IRB may be subject to further review by officials of the Institution who may determine, for a number of reasons that the research project cannot commence. Those officials may not, however, override the IRB’s decision to disapprove a project [DHHS 45 CFR 46.112 and FDA 21 CFR 56.112].

4.3.1 Undue Influence on IRB Authority
Any offer of special monetary incentives, favors in kind, or other rewards by investigators to IRB members or staff in return for approval of a research study is presumed to be an attempt at undue influence. IRB staff or members, who perceive that a person has attempted to unduly influence the actions of IRB members, should report any such attempts promptly to the IRB Chair. IRB Chairs are then responsible for conveying this allegation to the Human Research Protection Program Administrator. In cases where the IRB Chair or Vice Chair is perceived as acting as an agent of an investigator attempting to unduly influence IRB staff or members, such attempts should be reported to the IO/HRPP Administrator directly. If the IO/HRPP Administrator is the alleged source of undue influence the Chair should report this allegation directly to the VPRED.

In instances where the faculty member is the alleged source of undue influence, the IRB Chair and IO/HRPP Administrator will work together to complete an initial assessment of the allegation and report their preliminary findings to the VPRED. If there appears to be evidence to substantiate that inappropriate and unethical inducement by an investigator occurred, the VPRED in consultation with the IRB Chair and IO/HRPP Administrator, will determine the appropriate course of action. This course of action may include formation of an ad hoc committee comprised of faculty, administrators and IRB members to review the allegation. In instances where the IRB Chair or IO/HRPP Administrator are the alleged sources of undue influence, the VPRED will determine how the initial assessment and further investigation will proceed.

### 4.4 Determination Whether UB is “Engaged” in Human Subject Research

The IRB Chair or designee determines when a project “engages” the University in human subject research and therefore requires UB IRB review. OHRP has provided guidance on engagement of institutions in human subject research that may be used by the IRB chair or designee when making his/her determination whether a project engages the University in human subject research.

In general, an institution is considered to be “engaged” in a particular non-exempt human subject research project when its employees or agents for the purposes of the research project obtain:

1. data about the subjects of the research through intervention or interaction with them;
2. identifiable private information about the subjects of the research; or
3. the informed consent of human subjects for the research

If the IRB determines that a project does not engage the University in human subject research as described above, notification from the Chair or Chair’s designee to the investigator shall be made as indicated in Section 6.4: Notifications of IRB Determinations.

### 4.5 Determination of “Human Subject Research”

#### 4.5.1 Overview

The determination whether a project qualifies as human subject research rests with the IRB. The decision by the Chair or Chair designee is based on whether the activity represents “research” and involves “humans” as subjects (as defined in DHHS 45 CFR 46) and, when applicable, whether the activity represents a “clinical investigation” of a “test article” involving one or more humans as subjects (as defined in FDA 21 CFR 50).
The IRB staff assists with the determination as to whether the project is research or involves human subjects. The IRB staff may ask the investigator to provide additional information regarding the activity in writing so a formal determination can be made. Once all requested information has been received, the IRB will make and convey a determination to the investigator in a timely manner.

4.5.2 Procedures for Determination of “Human Subject Research”

When a project is submitted to the IRB for review, the Chair or Chair designee makes the determination whether the research is subject to IRB review, i.e., whether the DHHS or FDA criteria for IRB review apply. The IRB Chair or designee will make the determination as follows:

A. Determination of Whether the Research Meets the Department of Health and Human Services Definition for “Research”

The IRB Chair or designee will determine whether the activity is “research” under the following DHHS 45 CFR 46.102 definition:

Research is a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. A "systematic investigation" is an activity that involves a prospective plan that incorporates data collection, either quantitative or qualitative, and data analysis to answer a question.

Generalizable knowledge is knowledge that is expressed in theories, principles, and statements of relationships that can be widely applied to our experiences. Generalizable knowledge is usually created to share with others through presentations and publications and typically requires that the results or conclusions of the activity are intended to be extended beyond a single individual or an internal program. Examples include activities where there is an intent to publish the results in a peer-reviewed journal or to present at a regional or national meeting, as well as, theses or dissertation projects conducted to meet the requirements of a graduate degree.

Master’s theses and PhD dissertations are examples of generalizable knowledge.

B. Determination of Whether the Research Meets the Department of Health and Human Services Definition for “Human Subjects”

If the activity is determined to be research, the IRB Chair or designee will then determine whether the research involves “human subjects” according to the following DHHS 45 CFR 46.102 definitions:

- **Human subject**: a living individual about whom an investigator (whether professional or student) conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information.
- **Intervention** includes both physical procedures by which data are gathered (e.g., venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.
- **Interaction** includes communication or interpersonal contact between investigator and subject.
C. Determination of Whether the Research Meets the Food and Drug Administration Definitions for “Clinical Investigation” and “Human Subject Research”

When a planned activity meets the definitions of “clinical investigation” involving a “human subject”, the FDA regulations [21 CFR 50 and 21 CFR 56] regarding the protection of human subjects also apply. The IRB Chair or designee will then determine whether the research involves “human subjects” according to the following FDA definitions:

- **Clinical investigation** means any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the Food and Drug Administration under section 505(i), 507(d), or 520(g) of the act, or need not meet the requirements for prior submission to the Food and Drug Administration under these sections of the act, but the results of which are intended to be later submitted to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit. The term does not include experiments that must meet the provisions of part 58, regarding non-clinical laboratory studies. The terms research, clinical research, clinical study, study, and clinical investigation are deemed to be synonymous for purposes of this part [21 CFR 56.102(c)].

- **Test article** means any drug (including a biological product for human use), medical device for human use, human food additive, color additive, electronic product, or any other article subject to regulation under the act or under sections 351 and 354-360F of the Public Health Service Act [42 U.S.C. 262 and 263b-263n] and 21 CFR 50.3(j))

- **Human subject** means an individual who is or becomes a participant in research, either as a recipient of the test article or as a control [21 CFR 50.3(g)]. In the case of research involving a device, a human subject includes an individual on whom or on whose specimen a device is used. [21 CFR 812.3(p)].

If the IRB determines that a project does not meet the definition for human subject research as described above, notification from the Chair or Chair’s designee to the investigator shall be made as indicated in Section 6.4: Notifications of IRB Determinations.

D. Determination of Whether Research Meets the Definition of Department of Defense Regulations for Experimental Subject

For projects subject to a DOD Addendum, research involving a human being as an “experimental subject” means an activity, for research purposes, where there is an intervention or interaction with a human being for the primary purpose of obtaining data regarding the effect of the intervention or interaction. [32 CFR 219]

4.5.3 Other Definitions for “Human Subject Research”

When research studies are sponsored by, or fall under the jurisdiction of, federal, state or other organizations that have their own definitions of "research" involving "human subjects", the IRB will assess the protocol in light of those definitions but will not abide by definitions that are less comprehensive than the DHHS and FDA definitions. (See also, Section 1.5: Compliance with State Law).
5. RESPONSIBILITIES OF IRB CHAIRS, ADMINISTRATORS, MEMBERS, and OUTSIDE REVIEWERS

The UB IRBs have qualified IRB Chairs, administrators, members, and staff whose membership and composition are periodically reviewed. The IRB Chair, administrators, staff, and members have knowledge, skills, and abilities appropriate to their respective roles.

5.1 RESPONSIBILITIES OF THE IRB CHAIRS AND CO-CHAIRS

The IRB Chair or Co-Chair is responsible for overseeing all aspects of IRB review of projects. The IRB Chair or Co-Chair shall:

- Apply the basic ethical principles of respect for persons, beneficence and justice as articulated in the Belmont Report
- Uphold federal, state, and local regulations, University policies and procedures and with regard to the protection of human research subjects.
- Be knowledgeable about, and have understanding of, ethical issues, federal research regulations, applicable state law, and Institutional policies
- Represent the IRB in discussions with federal authorities
- Work with IRB members, IO/HRPP Administrator, and investigators to ensure that the rights and welfare of research subjects are appropriately protected
- Identify the expertise needed to comprise the IRB and recommend potential members
- Direct the discussion and proceedings of the full-committee meetings, with the assistance of the IRB Administrator, to keep discussion focused on the established agenda and ensure that guidelines for IRB meeting procedures are followed
- Review protocols submitted for initial and continuing reviews as well as any amendments submitted
- Determine whether a project “engages” UB in human subject research
- Determine whether a project qualifies as human subject research, and if it does, whether it qualifies for exempt status, meets criteria for expedited review, or requires a full board review. This task may be delegated to another member or IRB staff, based on his/her expertise and experience
- Determine the potential scientific validity of the proposed project by evaluating the soundness of the research design with input from IRB members and outside reviewers as needed
- Review projects that qualify as expedited or exempt. This task may be delegated to other members of the IRB, based on their expertise and experience
- Review serious events/problems (SEPs) and take-appropriate action as needed. This includes the authority of the Chair to take immediate action to suspend a research project to protect research subjects from serious risks
- Act on the committee’s behalf, when appropriate, to suspend research pending IRB review of serious events/problems (SEPs) and determine immediate actions
- Review and take action on protocol deviations and make recommendations as necessary
- Ensure prompt reporting to the IRB, IO/HRPP Administrator, and others, as needed, regarding serious events/problems (SEPs), serious or continuing non-compliance with UB HRPP policy or the requirements or determinations of the IRB, and any suspension or termination of IRB approval
- Schedule emergency meetings or cancel meetings, when necessary
Assign primary and secondary reviewer responsibilities, when appropriate, to ensure that individuals who review protocols have sufficient familiarity and expertise in the area of research under review; This task may be delegated to another member or IRB staff, based on his/her expertise and experience

Determine if an outside reviewer is needed to supplement the expertise of the IRB; This task may be delegated to another member or IRB staff, based on expertise and experience

Evaluate prospective and current IRB members and provide recommendations to the IO/HRPP Administrator regarding IRB member appointment or re-appointment

Vote at full board meetings

Assist in preparing correspondence to researchers

Serve as the official signatory for IRB correspondence. This responsibility may be delegated to an IRB Administrator

Represent the IRB in discussions with researchers

Participate in the investigation of suspected non-compliance and the development of a plan of action to address the non-compliance

Report attempts of alleged undue influence on the IRB process to the IO/HRPP Administrator and the VPR ED

Designate individuals who have the expertise and experience to review protocols as sole designee for expedited reviews and exemption determinations based on their experience with human subject research activities, credentials, and their experience reviewing protocols. (A member is considered “experienced” and may serve as the Chair’s designee once the Chair is satisfied that the member has sufficiently demonstrated an understanding of human subject protection, ethics, and regulations. The Chair makes this determination by reviewing the member’s contributions in terms of written reviews and meeting discussions. The Chair communicates these determinations to the IRB administrator so they can be noted in the IRB records. An IRB member must have served for at least 3 months or fulfilled primary review duties in conjunction with experienced reviewers for a minimum of five protocols before they can be considered experienced.)

Perform related duties as needed

5.2 RESPONSIBILITIES OF THE IRB VICE-CHAIRS

The Vice-Chair assumes the responsibility of the Chair or Co-Chair in the Chair’s absence, in instances when the Chair has a conflict of interest, or at the discretion of the Chair.

5.3 RESPONSIBILITIES OF THE IRB ADMINISTRATORS

The IRB administrators work collaboratively with the IRB chair(s) to manage the daily activities of the IRB. The IRB administrators shall:

- Support the Chair(s), HRPP, and the IO/HRPP Administrator’s objectives for human subject protection
- Facilitate the review and approval process through independent review and interpretation and application of relevant federal and state laws, regulations, and institutional policies and guidelines
- Serve as an alternate member on the IRB applying the basic ethical principles of respect for persons, beneficence and justice as articulated in the Belmont Report
- As a designee of the Chair(s):
5.4 IRB MEMBERSHIP COMPOSITION AND RESPONSIBILITIES OF IRB MEMBERS

5.4.1 IRB Membership Composition

The membership of UB Institutional Review Boards (IRBs) shall comply with federal regulations regarding membership composition [DHHS 45 CFR 46.107; FDA 21 CFR 56.107] as follows:

- Each IRB shall be composed of no less than five members who are qualified through their experience and expertise to review research projects in terms of regulations, ethical principles, applicable laws, standards of professional conduct and practice, and Institutional commitment.
- Each IRB shall consist of members of various professions including at least one scientist, one non-scientist, and one member who is not otherwise affiliated with the Institution (e.g., a community member), and who is not part of the immediate family of a person who is affiliated with the institution.
- Each IRB shall reflect diversity in its membership in terms of experience and expertise and consider race, gender, cultural backgrounds, and sensitivity to such issues as community attitudes as factors in membership selection.
- No IRB shall consist entirely of men or entirely of women.
- No IRB will consist entirely of members of one profession.
- Each IRB shall include, as either alternates or full board members, representatives who are knowledgeable about and experienced in working with various vulnerable populations/groups such as children, prisoners, pregnant women or mentally or physically challenged individuals if research involving such populations is regularly reviewed.
- Each IRB shall include representation from affiliated institutions as appropriate.
• Individuals who are responsible for business development such as employees of the Office of Sponsored Projects Services may not serve as members of the IRB or carry out day-to-day operations of the review process.

5.4.2 Responsibilities of IRB Members

IRB members shall:
• Apply the basic ethical principles of respect for persons, beneficence and justice as articulated in the Belmont Report
• Be familiar with specific human subject protection regulations including DHHS 45 Code of Federal Regulations 46 and its subparts and FDA 21 Code of Federal Regulations Parts 50, 56, 312, and 812
• Read all materials provided in advance of IRB meetings and be prepared to discuss issues related to human subject protections
• Conduct project reviews as requested by the Chair and provide feedback on all assigned review materials
• Communicate directly with investigators as needed
• Attend IRB meetings and participate in the discussion
• Notify the IRB office as soon as possible if unable to attend an upcoming meeting so an alternate can be selected and provided with meeting materials in a timely manner.
• Report attempts of alleged undue influence on the IRB process to the IRB Chair
• Meet HRPP education requirements (initial or continuing, as appropriate)

5.4.3 Responsibilities of Alternate IRB Members

When called upon, alternate members have all the responsibilities of regular members. Alternates may be designated as a replacement for a specific member with particular expertise or may be appointed for their general area of competency. Alternate members are encouraged to attend all committee meetings, but are not required to do so unless they are called upon by the Chair(s). If both the designated alternate and the regular member attend the same meeting, only the regular member may vote unless the Chair has designated the alternate as an additional voting member. When both the regular member and the alternate are present at a meeting, the minutes shall reflect who is in attendance as a voting member.

5.5 SELECTION AND RESPONSIBILITIES OF OUTSIDE REVIEWERS

UB IRBs have a process for obtaining additional expertise when needed for reviewing specific protocols. The IRB Chair will determine whether the IRB has the required expertise to review the research or whether an outside reviewer is required. The outside reviewer may be from within or outside UB and its affiliates. Consideration in the selection of an outside reviewer may include his/her ability to evaluate the scientific design of the project, the scientific novelty of the project, ethical concerns inherent in the project, the potential risks or benefits of the project procedures, or concerns relative to the study population particularly when vulnerable subjects are involved.

The IRB Chair or IRB staff will make initial contact with the proposed outside reviewer and notify him/her of the IRB conflict of interest policy. If the outside reviewer has a conflict of interest, he/she may not conduct the review and another outside reviewer will be sought. In instances when an outside reviewer has a conflicting interest but his/her expertise is necessary, he/she may
provide information to the IRB provided certain requirements are met (see Section 16.8: Member and Outside Reviewer Conflict of Interest or Significant Obligation).

The IRB may prepare a written set of questions for the outside reviewer’s response. The responses will be provided to the IRB for review prior to, or at the time of, the full board meeting. For issues requiring more than simple clarification, at the discretion of the chair, the outside reviewer may be invited to attend the board meeting when the study is reviewed. The outside reviewer will have access to all documents submitted to the IRB relevant to the specific study under review, participate in the deliberations and make recommendations regarding the study, but may not vote. Documentation including the attendance of and discussion with the outside reviewer will be included in the meeting minutes or protocol record as appropriate.
6. FUNCTIONS OF THE IRB ADMINISTRATIVE OFFICE

The IRB administrative office staff provides support to the IRB in fulfilling their responsibilities and roles in the protection of human research subjects. The office staff serves as the point of contact between the IRB and the research community, is a resource for investigators regarding general regulatory information, and provides guidance to investigators in the preparation of submissions for IRB review.

6.1 PRELIMINARY SCREENING OF PROJECT SUBMISSIONS

The office staff performs initial screenings of submissions for completeness. This process includes checking that:

- Appropriate documents have been submitted (e.g., protocol, consent document, investigator brochure)
- Application forms are completely filled out
- Investigators and their research staff have completed education and training requirements

6.2 PREPARATION FOR IRB MEETINGS

In preparation for IRB meetings, the office staff shall:

- Prepare the meeting agenda
- Send a copy of the agenda together with appropriate submittal materials to reviewers in advance of the meetings. All materials designated to be provided to board members are distributed at least three days prior to a scheduled meeting. These may be accessible via hard copy, projection, or electronic medium.
- Ensure that copies of applicable regulations, including DHHS 45 CFR 46 and FDA 21 CFR 50, 56, 312 and 812 are available for reference at all IRB meetings. These may be accessible via hard copy, projection, or electronic medium.
- Ensure that copies of Reviewer Evaluation/Guides are available for reference at all IRB meetings. These may be accessible via hard copy, projection, or electronic medium.

6.3 MEETING MINUTES

An administrative staff member who is trained in the functions of the IRB is responsible for taking minutes at full board and other meetings. That individual assists in the preparation and distribution of the minutes to IRB members, alternates who attended the meeting, and to the Human Research Protection Program Administrator. Prior to distribution, the IRB Administrator and IRB Chair review the meeting minutes to ensure that the minutes reflect the proceedings of the full board (see Section 8.9: Meeting Minutes: Documentation of IRB Findings and Actions).

6.4 NOTIFICATIONS OF IRB DETERMINATIONS

6.4.1 Notifications to Investigators

The administrative office staff prepares notification of IRB determinations to Investigators as follows:
6.4.1.1 Notification of Approval

Notification of approval or exempt status from the Chair(s) or Chair designee to investigators shall include the following information, as appropriate:

- Project title
- IRB assigned number
- Type of review (new/initi al or continuing)
- Level of review (exempt status, expedited, full-board)
- Statement that the project was approved
- Period of approval and expiration date
- Indication of documents/materials approved by the IRB (e.g., complete protocol, consent form document, investigator brochure, advertisements, questionnaires, or surveys)
- Approval of HIPAA mechanisms or statement that the project is exempt from HIPAA requirements
- Statement of any waivers of requirements - including an indication of the type of waiver and regulatory citation permitting the waiver
- For studies meeting requirements for exempt status: citation of the specific regulatory category under which the exempt status was granted
- Reminder that any changes to the approved project must be submitted to the IRB for review and approval prior to implementation of the changes
- Reminder that any serious events/problems (SEPs) must be reported promptly to the IRB
- Reminder that the study may not be conducted beyond the expiration date without re-approval by the IRB
- Any other information deemed appropriate

6.4.1.2 Notification that Modifications are Required in Order to Secure Approval

When projects require modifications in order to secure approval, notification from the Chair(s) or Chair designee to investigators shall include the following information, as appropriate:

- Project title
- IRB assigned number
- Statement that the project requires modifications in order to secure approval
- Indication of issues that must be addressed before approval may be granted
- For projects undergoing continuing review, a reminder that the study may not be conducted beyond the current expiration date unless all pending issues have been resolved and IRB approval is obtained
- Any other information deemed appropriate

6.4.1.3 Notification Regarding Deferred/Tabled Projects

When it is determined at a full board meeting that the IRB does not have sufficient information required to conduct a thorough review, if information has not been presented to the IRB in a clear, complete, and easily understood manner, the project will be deferred or tabled. A project may also be tabled if its review is beyond the range of the IRB’s expertise; in such cases, the IRB will engage an outside reviewer to review the project.
Notification from the Chair(s) or Chair designee to the investigator shall include the following information:

- Project title
- Statement that the project was deferred/tabled
- Date of full-board meeting at which the project was tabled
- Reason(s) for tabling the project and measures needed to resolve the issues
- Any other information deemed appropriate

6.4.1.4 Notification of Disapproval

Notification of disapproval of a project from the Chair(s) or Chair designee to an investigator shall include the following information:

- Project title
- Statement that the project was disapproved
- Date of full-board meeting at which the determination was made
- Reason(s) for disapproval
- Any other information deemed appropriate
- Notification that the Researcher has the right to respond in person or in writing by contacting the IRB administrator

6.4.1.5 Notification of Suspension of Previously Approved Research

Federal regulations grant the IRB authority to suspend approval of some or all activities in previously approved research that is not being conducted in accordance with IRB requirements or has been associated with serious events/problems [45 CFR 46.113, 21 CFR 56.113].

Notification from the Chair(s) or Chair designee to the investigator shall include:

- Project title
- IRB assigned number
- Statement that the determination of the IRB is to suspend some or all project activities. If only some activities have been suspended, an indication of which activities have been suspended
- Indication of reasons for the suspension
- Actions required of the investigator when it involves the withdrawal of current subjects from the research
- Actions required of the investigator to have the suspension lifted
- Indication of other individuals or agencies that will be notified of the IRB action
- Any other information deemed appropriate

6.4.1.6 Notification of Termination of Research Activities

Federal regulations grant the IRB authority to terminate approval of previously approved research that is not being conducted in accordance with IRB requirements or has been associated with serious events/problems [45 CFR 46.113, 21 CFR 56.113].

Notification from the Chair(s) or Chair designee to the investigator shall include:

- Project title
- IRB assigned number
- Statement that the determination of the IRB is to terminate all project activities
• Indication of reasons for the termination
• Actions required of the investigator when it involves the withdrawal of current subjects from the research
• Indication of other individuals or agencies that will be notified of the IRB action
• Any other information deemed appropriate

6.4.1.7 Notification of Expiration of IRB Approval

If the investigator has not submitted a completed an Application for Continuing Review or a Completed/Closed Notification – Final Report to the IRB by the project’s expiration date, the IRB will notify the investigator that IRB approval has expired. The notification shall include a reminder that no further human subject research activities may be conducted until IRB approval is obtained. No new subjects may be contacted, recruited, or enrolled in the study until the investigator obtains current IRB approval. For therapeutic studies where subject safety is a concern, federal regulations allow some flexibility towards the continued treatment for currently enrolled subjects (the determination will be made by the IRB).

In cases of externally funded research projects administered by a University fiscal agent, UB Sponsored Projects Services (SPS) will be notified of the expiration of IRB approval.

Once a study has been closed due to expiration of approval, it must be resubmitted for review and approved before any further research may continue. When the IRB makes such a determination, notification from the Chair or Chair designee to the investigator shall include:
• Project title
• IRB assigned number
• Statement that the project expired and the date of expiration
• A reminder that no new subjects may be contacted, recruited, or enrolled in the study until the investigator obtains current IRB approval
• Any other information deemed appropriate

6.4.1.8 Notification of Determination that the Project Does Not Meet the Definition for “Human Subject Research” or “Engage” the University in Human Subject Research

If the IRB determines that a project does not qualify as human subject research or “engage” UB in human subject research (see Section 4.4: Determination Whether UB is “Engaged” in Human Subject Research and Section 4.5: Determination of “Human Subject Research”), notification from the Chair or Chair’s designee to the investigator shall include the following:
• Project title or reference to a description of the project
• Statement of the determination that the project does not meet the definition for human subject research” or does not “engage” the University in human subject research
• Basis for the determination
• Any other information deemed appropriate

6.4.2 Notification of IRB Findings to Organizational Offices and Officials

Routine IRB determinations are communicated to the IO/HRPP Administrator by providing him/her with a copy of the IRB meeting minutes and interim business reports. Sensitive determinations or other information of particular importance will be communicated either verbally
or through e-mail as soon as possible after the IRB determination is made. The IO/HRPP Administrator, as a member of the OVPRD, keeps the VPRED informed of all pertinent IRB determinations. The office of Sponsored Projects Services is notified regarding IRB actions for externally funded projects. Appropriate affiliated hospital officials are notified regarding research in their organization.

No other Institutional office is individually responsible for further review of research that has been approved by the IRB.

6.5 RECORDS MAINTENANCE

6.5.1 IRB Project Files

The IRB office staff maintains files on human subject research reviewed under the UB’s HRPP. These files include project documents, copies of correspondence between the IRB and investigators, as well as any other appropriate information. Paper and/or electronic records on human subject research are required to be maintained by the IRB offices while the project is active and for a minimum of three years after study completion or after study cancellation [45 CFR 46.115, 21 CFR 56.115]. All IRB records are kept in secured filing cabinets or storage rooms. Access to electronic files is restricted to appropriate personnel and may be encrypted.

Access to the IRB records is limited to authorized representatives of the Institution, officials of federal and state regulatory agencies including the Office for Human Research Protection (OHRP) and the Food and Drug Administration (FDA). Research investigators are provided reasonable access to files related to their research. Accreditation bodies and sponsors may also be permitted access to research records. Records will be made available for inspection and copying by authorized personnel in a reasonable time and manner.

Generally, UB IRB’s research project records include the following IRB-specific material:

- Complete protocol
- Grant application, when applicable
- HS-1A Application Form(s)
- Abstract/protocol summary
- Consent/permission/assent document(s), when applicable
- DHHS-approved sample consent document and protocol, when they exist
- Questionnaires, when applicable
- Recruitment materials, when applicable
- Investigator’s brochure, when applicable
- Scientific evaluations, if any
- Reviewer’s written comments or assessments
- Findings required under the regulations including
  - protocol-specific findings supporting determinations for waiver or alteration of the consent process
  - protocol-specific findings supporting those determinations for research involving pregnant women, fetuses, and neonates
  - protocol-specific findings supporting those determinations for research involving prisoners
6.5.1 Protocol-Specific Correspondence

- Applications for Continuing Review and related materials
- Serious Events/Problems - Initial Reports and Follow-Up Reports, if any
- Statements of significant new findings provided to subjects
- Amendment Forms or equivalent amendment information
- Protocol specific correspondence between the IRB and the Investigator
- Approval and expiration dates for initial and continuing reviews
- Data and safety monitoring reports, if any
- Documentation of non-compliance
- Any significant new findings
- All other related documents

Additionally, expedited and exempt status review project records include the following IRB specific material:
- An indication of the specific permissible category for expedited review or exempt status
- A description of the action taken by the reviewer (approval, approval contingent upon minor changes)
- Any additional justifications deemed to be necessary

6.5.2 Administrative Files

Records not related to research projects (e.g., member rosters, minutes of full board meetings, and correspondence not related to a particular research study) are retained in secured filing cabinets or storage rooms and are retained for a minimum of three years.

6.5.3 Database of IRB Projects

Office staff at each IRB office maintains a database of current IRB approved projects. The database also retains information regarding completed studies for a period of at least three years after study completion or closure.

6.5.4 Membership Information and Rosters

Each IRB office maintains current membership information including notification of appointment and re-appointment from the IO/HRPP Administrator that includes the member’s terms of service. Membership information is updated as changes occur. Copies of updated rosters are filed with the OVPRED. The roster includes:
- Member’s name
- Degree(s)
- Scientific status (scientist or non-scientist)
- Employment or other relationship between each IRB member and UB and its affiliates
- Indications of experience sufficient to describe each IRB member’s chief anticipated contribution
- Indication whether the IRB member or any of the member’s immediate family is affiliated with the organization
- Indication of whether the individual is Chair, Vice-Chair, or Co-Chair.
- Membership status (e.g., member, alternate, or non-voting. If a member serves ex-officio, indicate whether the member is a voting member)
• For alternate members, information regarding for whom, or what class of members, the alternate can substitute

6.5.5 Education and Training Records

Each IRB office maintains records confirming that IRB members and alternates, as well as researchers and research team members have successfully met HRPP required training and education requirements.

6.6 IRB RESPONSE TO SUBJECTS’ CONCERNS AND COMPLAINTS

It is the right of a research subject to voice a concern or complaint, to be assured that the concern/complaint is taken seriously, and that the complaint is addressed in a timely manner. In the consent document, the IRB may be listed as a contact when the subject wants to speak with someone not directly associated with the research regarding concerns about their rights as research subjects or concerns/complaints regarding their experience as a research subject. Concerns/complaints may also be received from others concerned about the research being conducted (e.g., subject’s family member, research staff, or another investigator).

IRB staff members will respond to subject (or other person) inquiries and provide assistance. In cases where further action is required, the matter will be managed as described below:

When the IRB is contacted with a subject concern/complaint the procedures are generally as follows (concerns/complaints voiced by individuals other than research subjects and written concerns/complaints will generally be handled in the same manner):

A. Upon receipt of a subject concern/complaint, the notice or call will be directed to the IRB Administrator. The IRB Administrator will attempt to obtain as much of the following information as possible:
   o Date concern/complaint was received
   o Name, address, and phone number of caller (if the caller wishes to report the issue anonymously, the administrator will try to obtain as much information as possible while respecting the caller’s wish to remain anonymous. The caller will be advised that without adequate information, a thorough review may not be possible and follow-up responses to the subject are not feasible.
   o Caller’s relationship with the research study (e.g., current or past subject, relative of a subject, or research staff)
   o Study protocol title or acronym – or other identifying description of the study
   o Name of PI
   o Date(s) of the occurrence, if appropriate
   o Explanation of the concern or complaint

B. The IRB Administrator will assure the subject that inquiry will be made into the matter and that appropriate measures will be taken to address the issue. Concerns/complaints that do not involve harm or potential risk of harm to subjects or others will be investigated and corrective action taken at an administrative level by the IRB Administrator.

C. The IRB Chair will be informed of any concerns/complaints that involve harm or potential risk of harm to subjects (e.g., those that require possible immediate action pending investigation and review by the full board).
D. The Chair and the IRB will be advised of all complaints, corrective actions, and resolutions.

E. The IRB Administrator will document receipt of concerns/complaints

F. When a written concern/complaint is received that includes contact information, the IRB Administrator will acknowledge receipt of the concern/complaint

G. Concerns/complaints meeting criteria for serious or continuing non-compliance will be managed as described in Section 18: Non-Compliance with HRPP Requirements

H. Concerns/complaints meeting criteria for serious events/problems (SEPs) will be managed as described in Section 17: Reportable Events and Problems

I. Upon resolution of the concern/complaint, the complainant (unless anonymous) and the PI will receive correspondence from the IRB

J. Concerns/complaints pertaining to the HRPP program or which otherwise cannot be managed using the above procedures will be referred to the IO/HRPP Administrator.
7. LEVELS AND TYPES OF IRB REVIEW

7.1 OVERVIEW

All human research activities that fall under the authority of the University at Buffalo’s Human Research Protection Program must be reviewed by a UB IRB prior to initiation of the research. When a project is submitted to the IRB for review, the Chair or Chair designee makes the determination whether the research involves human subjects and is subject to IRB review, i.e., whether the DHHS or FDA criteria for IRB review apply, as described in Section 4: The Scope and Authority of UB IRBs.

If it is determined that IRB review is required, the level (exempt status, expedited, or full board) as indicated on the application form by the PI will be considered for approval. The level of IRB review a project receives is determined by the risks the research poses to its subjects. The final determination regarding level of review rests with the Chair/designee or full IRB. All applications will be reviewed by the full board unless they meet the criteria for exempt status or expedited review.

The three levels of IRB review are:
- Exempt status (initial review by Chair or Chair designee but does not require continuing review)
- Expedited (review by Chair or Chair designee and requires continuing review)
- Full Board (review by full board and requires continuing review)

Types of project submissions include:
- New/Initial
- Continuing/Renewal
- Amendment/Modification (to an already approved project)
- Final/Closure

7.2 LEVELS OF IRB REVIEW

7.2.1 Overview

In general:
- New/initial submissions may qualify for exempt status, expedited, or full board review.
- Continuing/renewal and amendment/modification submissions may qualify for expedited or full board review.
- Final submissions are administratively reviewed by the IRB Administrative Staff

Federal regulations with respect to research that qualifies for exempt status review or review by the expedited process are considered by UB IRBs as a minimum standard of compliance. IRB determinations with respect to human subject protection may exceed those permissible under federal regulations.
7.2.2 Exempt Status Review

The IRBs are the only UB offices given the authority for determining that research involving no more than minimal risk to human subjects may be exempt from having to meet all the requirements of DHHS 45 CFR 46 and DHHS 21 CFR 56. Such research is not exempt from IRB review and approval prior to initiation. An investigator may only initiate exempt status research after receiving the corresponding written exempt status determination (approval) from the IRB.

In order for the IRB to determine whether a project qualifies for exempt status and whether any further protections are necessary for the subjects involved in the research, the investigator must submit the materials specified for initial review in Section 7.3.1: New/Initial Review: Submission Materials/Documents. The Chair or designee will conduct a review of these materials in the same manner that primary reviewers conduct review for full board projects. In order for exempt status to be granted, the Chair or designee must, as a part of their review, determine that the project is not greater than minimal risk, represents one or more approvable exempt status categories of research, and meets the institutional standards for exempt status determination. Before granting an exempt status determination, the IRB may determine that additional protections be implemented in order to protect the research subjects. The investigator is notified in writing of the determination of the Chair or designee (see Section 6.4: Notifications of IRB Determinations). When the Chair or designee requests modifications, the investigator may respond in writing indicating that the requested modifications have been made or provide justification for not doing so. The Chair or designee will then review the investigator’s response and may at that time approve the project as submitted, request further modifications or deny the exemption by stating the regulatory reason(s) for doing so at which point the investigator may request that the full board review the protocol for exemption.

The exempt status determination is valid for the life of the proposed research as submitted and approved by the IRB. If a change to the approved exempt status research is desired, an amendment must be submitted to the IRB and approval must be obtained prior to initiation of the change. It is possible that an amendment will alter the research such that it no longer qualifies for a determination of exempt status. In these cases, the modified protocol will be reviewed using the procedures for expedited or full board review, as applicable, and from that point forward, the project will be treated as non-exempt.

All IRB members periodically receive a written report of projects granted exempt status between convened meetings. These reports are typically distributed with meeting minutes or agendas.

7.2.2.1 Regulatory Applicability

The regulations permit an exempt status to be considered when human subject involvement is restricted to the following types of research:

- Research activities that: (1) present no more than minimal risk to human subjects, and (2) involve only procedures identified in one or more categories in the regulations at DHHS 45 CFR 46.101(b)(1-6) or FDA 21 CFR 56.104(a-d) may be reviewed by the IRB and granted exempt status. Exempt status projects are "exempt" from annual renewal requirements. An activity should not be deemed to be of minimal risk simply because it is identified in one of the exempt regulatory categories. Inclusion in the regulations merely means that the activity is eligible for exempt status upon concurrence of the IRB Chair/designee.
- The categories in the regulations apply regardless of the age of subjects, unless noted in the federal regulations.
• Exempt status may not be granted where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects’ financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.
• Exempt status may not be granted for classified research involving human subjects.
• The standard requirements for informed consent may be waived or otherwise altered for exempt status research but justification for doing so must be provided to the IRB.

DHHS regulations permit an exempt status to be considered when human subject involvement is restricted to the following types of research:

1. Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as (i) research on regular and special education instructional strategies, or (ii) research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

2. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless:
   - (i) information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and (ii) any disclosure of the human subjects’ responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects’ financial standing, employability, or reputation.

3. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under paragraph (b)(2) of this section, if:
   - (i) the human subjects are elected or appointed public officials or candidates for public office; or (ii) federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.

4. Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

5. Research and demonstration projects which are conducted by or subject to the approval of department or agency heads, and which are designed to study, evaluate, or otherwise examine:
   - (i) Public benefit or service programs; (ii) procedures for obtaining benefits or services under those programs; (iii) possible changes in or alternatives to those programs or procedures; or (iv) possible changes in methods or levels of payment for benefits or services under those programs.

6. Taste and food quality evaluation and consumer acceptance studies, (i) if wholesome foods without additives are consumed or (ii) if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

DHHS 45 CFR 46.101(b)
7.2.2.2 Special Considerations

- Research Involving Children: Research that involves children and meets requirements in DHHS 45 CFR 46.101(1–6) may qualify for exempt status. However, the exempt status category at DHHS 45 CFR 46.101(b)(2) pertaining to survey or interview procedures or observations of public behavior, does not apply to research involving children, except for research involving public behavior when the investigator does not participate in the activities being observed.
- Research Involving Prisoners: The exempt status categories do not apply to prisoners.
- For category #5 exempt status research:
  - The program under study must deliver a public benefit (e.g., financial or medical benefits as provided under the Social Security Act) or service (e.g., social, supportive, or nutrition services as provided under the Older Americans Act)
  - The research or demonstration project must be conducted pursuant to specific federal statutory authority
  - There must be no statutory requirement that the project be reviewed by an IRB
  - The project must not involve significant physical invasions or intrusions upon the privacy of subjects
  - The exempt status determination should have authorization or concurrence by the funding agency

7.2.2.3 Institutional Standards for Exempt Status Determination

In order to meet the Institution’s standards for exempt status, the project must:
- Not be greater than minimal risk.
- Meet the regulatory criteria for exempt status research
A study qualifying for exempt status may need to meet additional requirements as determined by the IRB including but not limited to the following:
- Demonstrate to the IRB that an adequate standard of informed consent is achieved, when applicable
- Demonstrate to the IRB that adequate confidentiality of data will be maintained
- Demonstrate to the IRB that adequate provisions to maintain the privacy interests of subjects will be adhered to
- Demonstrate to the IRB that selection of subjects is equitable
- Utilize a consent process when there are interactions with subjects that includes the following (except in cases where consent can be waived if the project was not exempt status):
  - A statement that the activity involves research
  - A description of the procedures
  - A statement that participation is voluntary
  - Name and contact information for the investigator
  - Any other elements required by the IRB
- Meet any further requirements of the IRB for additional protections

7.2.3 Expedited Review
Research activities designated in one of more categories in DHHS 45 CFR 46.110 or FDA 21 CFR 56.110 may qualify for expedited review. All studies submitted to the IRB are evaluated for possible expedited review. Studies that qualify for expedited review require the approval, at a minimum, of a single reviewer (i.e., the Chair or the Chair’s designee). Materials provided to the Chair or designee will be identical to those provided to the primary reviewer for full board review. The Chair or designee will conduct a review of these materials in the same manner that primary reviewers conduct review for the full board. In order for expedited approval to be granted, the Chair or designee must, as a part of his/her review, determine whether the research meets all applicable criteria and represents one or more approvable expedited categories of research. The Chair or designee may approve research projects as submitted or require modifications prior to approval but cannot disapprove research projects through the expedited process. The investigator is notified in writing of the determination of the Chair or designee (see Section 6.4: Notifications of IRB Determinations). When the Chair or designee requests modifications, the investigator may respond in writing indicating that the requested modifications have been made or provide justification for not doing so. The Chair or designee will then review the investigator’s response and may, at that time approve the project as submitted, request further modifications or recommend referral to the full board for review.

All IRB members periodically receive a written report of expedited actions that occur between convened meetings. These reports are typically distributed with meeting minutes or agendas.

### 7.2.3.1 Applicability

- Applicable to research projects that present no more than minimal risk to human subjects and involve only procedures identified in categories 1-7 in the table below [DHHS 46.110(a) and FDA 21 CFR 56.110(a)]. Research activities that meet this criteria may be reviewed by the IRB through the expedited review procedure authorized by DHHS 45 CFR 46.110 and FDA 21 CFR 56.110. The activities listed should not be deemed to be of minimal risk simply because they are included on the list. Inclusion on this list merely means that the activity is eligible for review through the expedited review procedure when the specific circumstances of the proposed research involve no more than minimal risk to human subjects.
- The categories in this list apply unless noted in the regulations.
- The expedited review procedure may not be used where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects’ financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.
- The expedited review procedure may not be used for classified research involving human subjects.
- IRBs are reminded that the standard requirements for informed consent (or its waiver, alteration, or exception) apply regardless of the type of review (i.e., expedited or full board) utilized by the IRB.
- Categories 1 through 7 pertain to both initial and continuing IRB review.
- Expedited review of research involving prisoners may be used provided that the IRB prisoner representative participates in the review.

The following are the only acceptable criteria for expedited review:
1. **Clinical studies of drugs and medical devices when an investigational new drug (IND) application is not required, an investigational device exemption (IDE) application is not required, or the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.**

2. **Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture from healthy non-pregnant adults who weigh at least 110 lbs. and does not exceed 550 ml in an 8 week period and collection cannot occur more frequently than 2 times per week, or from other adults or children the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.**

3. **Prospective collection of biological specimens for research purposes by noninvasive means.**

4. **Collection of data through noninvasive procedures (not involving anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves.**

5. **Research involving materials (data documents, records, specimens) that have been collected or will be collected solely for non-research purposes (such as medical treatment or diagnosis).**

6. **Collection of data from voice, video, digital, or image recordings made for research purposes.**

7. **Research on individual or group characteristics or behavior or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.**

8. **Continuing review of research previously approved by the convened IRB where research is permanently closed to enrollment of new subjects, all subjects have completed all research-related interventions, and the research remains active only for long-term follow-up of subjects or where no subjects have been enrolled and no additional risks have been identified or where the remaining research activities are limited to data analysis.**

9. **Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where categories two (2) through eight (8) do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.**

### 7.2.4 Full Board Review

Full board review is required for:

- Initial applications that are not eligible for exempt status or expedited review procedures
- Any substantive changes that increase risks to subjects or others
- Renewals of projects that do not qualify for expedited review
- Disapproval of a project
- Suspension or termination of a project
- All research projects involving the use of investigational drugs, devices, or biologics for which an IND/IDE is required
- Findings of serious or continuing non-compliance

When full board review is required, a project must be presented for consideration at a full board meeting. At the meeting, the board will discuss the project and determine what action to take (see Section 8.7: IRB Determinations). In its deliberations, the IRB will allow adequate time for
discussion of all project-related issues with sensitivity to the level of risk under consideration. The investigator is notified in writing of the determination of the board (see Section 6.4: Notifications of IRB Determinations). When modifications are requested, the investigator may be required to respond in writing or, at the discretion of the Chair, in person at a convened meeting.

When a response is provided in writing, the following procedures will be employed:

- Specific modifications that require only the concurrence of the investigator may be reviewed by the Chair or designee before approval is granted. In these cases, the Chair or designee reviews the modifications made by the investigator to see that the board’s requests have been met. When the Chair or designee determines that all requested modifications have been made and no further human subject protection issues exist, the project may be approved.
- Projects requiring substantive clarifications or modifications that are directly relevant to the determinations required by the IRB and investigator’s justifications for not making requested modifications will be tabled or deferred. These projects will be brought to a subsequent full board meeting for review before approval may be granted.
- Appeal of IRB determinations will be managed as described in Section 8.7.5: Appeal of IRB Determinations.

7.3 TYPES OF PROJECT SUBMISSIONS

7.3.1 New/Initial Review

7.3.1.1 New/Initial Review: Submission Materials/Documents

For new submissions, whether exempt, expedited or full board, the investigator is responsible for submitting all materials necessary for the IRB to evaluate the research project. An IRB number will be assigned to the project that will be referenced in future communications between the IRB and the investigator.

The investigator must provide the IRB with copies of the following application documents, as applicable:

- HS-1A Application Form
- Full protocol
- Grant application
- All consent/permission/assent documents
- All HIPAA documents
- Recruitment materials and advertisements for initial recruitment into a study
- Investigational Drug Brochure or Device Information
- Copy of the signed FDA 1572 form submitted to the sponsor
- Authorization of Fee Collection for IRB Review
- Previous determinations of other IRBs
- Description of any retention incentives
- For DHHS-supported multicenter clinical trials, the DHHS-approved sample consent document and the complete DHHS-approved protocol when these documents exist
- Any other documents that the IRB might require

Investigators are responsible for checking their specific IRB website for submission requirements.
Submissions that are incomplete, or for which the investigator is non-responsive to IRB requests, may be withdrawn from consideration for IRB approval at the discretion of the IRB Administrator. The Administrator will notify the investigator of the project’s withdrawal from consideration. If the Investigator decides to proceed with the project, the project must be submitted to the IRB as a new/initial submission and be given approval prior to initiation of the research.

7.3.1.2 New/Initial Review: IRB Considerations

DHHS and FDA regulations set forth criteria for IRB approval of a research project. The criteria for initial review include a determination by the IRB that the regulatory criteria for approval are met. The full board or the reviewer using the expedited procedure uses the Guide/Evaluation for Initial Review to determine whether the regulatory criteria are met (see Section 9: Criteria for IRB Approval of Research Projects).

7.3.1.3 New/Initial Review: Approval Date and Expiration Date

DHHS and FDA regulations require that the IRB conduct continuing review of previously approved research at intervals appropriate to the degree of risk, but not less frequently than once per year. The IRB may determine that a project requires review at more frequent intervals than annually or after a specified number of subjects have completed certain procedures in order to ensure the continued protection of the rights and welfare of research subjects. The IRB makes this determination after discussion at a convened meeting based on factors such as the risk level of the protocol, the experience of the research team, and the nature of the research.

When research is reviewed and approved through an expedited review process, the date that approval is granted by the Chair or his/her designee is the IRB approval date. When research is reviewed and approved through a full board review process, the period of approval for research starts on the date of the full board meeting at which the IRB approved the protocol or for the date that all minor or prescriptive changes or conditions were determined to be met. For projects reviewed by the expedited process, the expiration date for new approvals will be calculated by adding the approval period to the approval date. For full board reviews, the expiration date will be calculated by adding the approval period to the meeting date of the full board at which the project was approved. The expiration date may not be greater than one year from the approval date.

7.3.1.4 Notifications of IRB Determinations

Investigators will be notified of IRB determinations as indicated in Section 6.4: Notifications of IRB Determinations.

7.3.2 Continuing/Renewal Review

The purpose of continuing review is to review the progress of the entire study including any changes to it since the last review. All expedited or full board approved projects are required to undergo continuing review at intervals appropriate to the degree of risk, but not less than once per year. The IRB may require more frequent IRB review based on known or potential study risks to subjects.

Continuing review must occur for all non-exempt human subject research including research that remains active for long-term follow-up of subjects, even when the research is permanently closed to enrollment of new subjects and all enrolled subjects have completed all research-related
interventions. Continuing review must also occur for research that includes the collection or analysis of privately identifiable information.

Continuing reviews that meet the requirements for expedited review may be renewed by the IRB Chair or Chair designee using expedited procedures. All other projects will be reviewed by the full board. Generally, if research did not qualify for expedited review at the time of initial review, it will not qualify for expedited review at the time of continuing review except in limited circumstances as follows:

- When the research is permanently closed to the enrollment of new subjects, all subjects have completed all research-related interventions, and the research remains active only for long-term follow-up of subjects, or
- When no subjects have been enrolled and no additional risks have been identified, or
- When the remaining research activities are limited to data analysis only, or
- For research not conducted under an investigational new drug application or investigational device exemption where the IRB has determined and documented at a full board meeting that the research involves no greater than minimal risk and no additional risks have been identified.

### 7.3.2.1 Continuing/Renewal: Submission Materials/Documents

The IRB office will notify investigators when it is time to submit their project for continuing review and specify a deadline by which documents must be submitted.

At the time of Continuing Review, whether expedited or full board, the Investigator must provide the IRB with copies of application documentation as follows:

- Application for Continuing Review including all associated documents listed on the form
- All Consent/Permission/Assent Documents, when applicable
- Any other documents that the IRB might require

### 7.3.2.2 Continuing Review: IRB Considerations

The convened IRB, or the reviewer using the expedited process, uses the *Guide/Evaluation for Continuing Review* in making the determination whether the regulatory criteria for approval continue to be met. In particular, the IRB needs to determine whether any new information has emerged – either from the research itself or from other sources – that could alter the IRB’s previous determinations, mainly with respect to risks to subjects. Information regarding any serious events/problems (SEPs) and amendments that have occurred since the previous review are included in the IRB’s considerations. When reviewing the current consenting documents, the IRB will consider: a) whether the currently approved or proposed consent/permission/assent document is still accurate and complete, and b) whether any significant new findings that may relate to a subject’s willingness to continue participation are included in the document.

If there are any significant new findings that may relate to subjects’ willingness to continue participation, the IRB will consider whether appropriate and adequate information has been provided to enrolled subjects in accordance with federal regulations DHHS 45 CFR 46 .116(b)(5) and FDA 21 CFR 50.25(b)(5).

The IRB may determine that a project requires review at more frequent intervals than annually or after a specified number of subjects have completed certain procedures in order to ensure the continued protection of the rights and welfare of research subjects. The IRB makes this
determination after discussion at a convened meeting based on factors such as the risk level of the protocol, the experience of the research team, and the nature of the research.

(See also Section 9: Criteria for IRB Approval of Research Projects, Section 14: The Informed Consent Process, and Section 17: Reportable Events and Problems)

7.3.2.3 Continuing Review: Approval Date and Expiration Date

DHHS and FDA regulations require that the IRB conduct continuing review of previously approved research at intervals appropriate to the degree of risk, but not less frequently than once per year.

When research is reviewed and approved through an expedited review process, the date that approval is granted by the Chair or his/her designee will be the of IRB approval date. When research is reviewed and approved through a full board review process, the period of approval for research starts on the date of the convened meeting at which the IRB approved the project or the date that all minor or prescriptive changes or conditions were determined to be met.

The HSIRB calculates the expiration date for all renewal approvals by adding the approval period to the approval date (e.g., the current expiration date is 8/2/2008 -- the project is approved on 7/16/2008 for a one year period -- the new approval period will be from 7/16/2008 to 7/15/2009). The SBSIRB and CYIRB use the same method as the HSIRB to calculate expiration dates when approval does not take place within 30 days prior to expiration. However, when approval takes place within 30 days prior to expiration, the SBSIRB and CYIRB calculate the expiration date by adding the approval period to the previous expiration date (e.g., the current expiration date is 8/2/2008 -- the project is approved on 7/16/2008 for a one year period -- the new approval period will be from 7/16/2008 to 8/2/2009). These procedures are consistent with OHRP guidance that provides for expiration “anniversary dates” to be retained when approval takes place within 30 days prior to expiration.

(See also Section 9: Criteria for IRB Approval of Research Projects and Section 15: Responsibilities of Investigators and Faculty Sponsors.)

7.3.2.4 Projects Needing Verification from Sources Other Than the PI

UB’s Federalwide Assurance requires that the IRB have written procedures describing the basis upon which the IRB will verify “from sources other than the [PI] that no material changes have occurred since [the] previous IRB review.” The IRB may conduct such verification at the time of continuing review, or at any other time during the course of the project, in order to verify that the research remains in compliance with applicable regulations and policies.

Examples of criteria that may be used by the IRB to initiate such verification include:

- Allegations of investigator misconduct
- Complaints from a subject or a third party "whistle-blower"
- Complex research protocols involving unusual levels or types of risk to subjects
- Research protocols conducted by an investigator who previously failed to comply with the required regulations or the requirements or determinations of the IRB
- Research projects where there is concern that changes have been made without IRB approval based upon information provided in the continuing review report or from other sources
In addition, the QA/QI function of the HRPP includes random assessments of projects. These assessments may assist the IRB in providing verification from sources other than the PI that no material changes have occurred over the course of the research.

### 7.3.2.5 Expiration of IRB Approval

The expiration date is the last day of the approval period. The regulations make no provision for any grace period extending the conduct of research beyond the expiration date of IRB approval. DHHS 45 CFR 46.108(b) and 109(e). Continuing review and re-approval must occur on or before the date when IRB approval expires. While the IRBs provide reminder notices, investigators are responsible for maintaining IRB approval for their projects and for submitting the application for continuing review for all active projects in a timely manner.

When continuing review of a research protocol does not occur prior to the end of the approval period specified by the IRB, IRB approval expires automatically. Research activity must stop -- enrollment of new subjects may not occur. Subject follow-up, study interventions, and data collection and analysis must also stop. Research conducted during a lapse in approval constitutes non-compliance with federal, institutional, and IRB policy and may result in closure of the study, invalidation of the collected data, and reporting to the Office of Human Research Protection (OHRP). An expired project must be submitted to the IRB for review, and receive IRB approval prior to resumption of the research project.

In rare circumstances, when the investigator is actively pursuing renewal with the IRB and the IRB believes that an over-riding safety concern or ethical issue may be involved, the IRB may permit study activities to continue during the time required to complete the review process.

Continuing instances of expiration of IRB approval may be managed under HRPP Non-Compliance procedures. (See Section 19: Non-Compliance with HRPP Requirements.)

### 7.3.2.6 Continuing Review: Notification of IRB Determinations

Investigators will be notified of IRB determinations as detailed in Section 6.4: Notifications of IRB Determinations.

### 7.3.3 Amendments/Modifications to an Approved Project

#### 7.3.3.1 Overview

During the conduct of the study, amendments/modifications to the protocol may be proposed or unplanned changes may be discovered that require IRB notification. Amendments/modifications to the IRB-approved project, whether planned or otherwise, are governed by federal regulations and IRB policies and procedures. Any proposed amendment/modification to an IRB-approved research project or consent document must be submitted to the IRB using the Amendment Form and be approved by the IRB prior to implementation. Any amendment/modification not prospectively approved by the IRB is considered a protocol violation and must be reported to the IRB. The only exception to this requirement is a change in procedure that may be necessary to eliminate an apparent immediate hazard to a research subject or study personnel. Such events must be reported to the IRB by completing both the Amendment Form and the Serious Events/Problems – Initial Report.
IRB approval of amendments/modifications to research protocols and consent documents can be requested at any time. Amendments/modifications require either expedited or full board review, as determined by the IRB Chair or designee. The full board or the reviewer using the expedited procedure may use the Guide/Evaluation for Amendments/Modifications to determine whether the regulatory criteria for approval are met.

In order to ensure that investigators do not implement protocol changes without prior IRB review and approval, except when necessary to eliminate apparent immediate hazards to subjects, the UB HRPP has put the following procedures in place:

- Inclusion in approval documents of a statement informing researchers that changes in research procedures, recruitment, or consent processes shall not be initiated by research investigators without IRB review and approval, except where necessary to eliminate apparent immediate hazards to subjects
- Conduct of random quality assurance/quality improvement review of approved studies
- Inclusion in its educational program (CITI) for all research staff information on the need to get prior IRB approval for any amendments/modifications prior to implementation of changes

The IRB Chair or designee can review and approve minor amendments/modifications to an IRB-approved project or consent document through the expedited process when the change(s) will not adversely affect the risk/benefit assessment of the project or substantially change the specific aims or design of the study (i.e., the change or modification involves no more than minimal risks to subjects and does not increase the overall risks of the study).

Examples of such minor amendments/modifications may include:

- An increase/decrease in proposed enrollment supported by a statistical justification
- Changing the inclusion or exclusion criteria where risks do not increase
- Alterations in payment or liberalization of payment schedule with proper justification
- Changes to improve the clarity of statements or to correct typographical errors, provided that such a change does not alter the content or intent of the statement
- The addition/deletion of qualified investigators/research personnel or study sites

Amendments/modifications to an IRB-approved project and/or consent form document that affect the risk/benefit assessment of the project or substantially changes the specific aims or design of the study are considered major amendments/modifications must undergo full board review.

Examples of such major amendments/modifications may include:

- Changing the inclusion or exclusion criteria such that it increases risk
- Alterations in the dosage or route of administration of an administered drug
- Extending substantially the duration of exposure to the test material or intervention
- The deletion of laboratory tests, monitoring procedures, or study visits directed at the collection of information for safety evaluations
- A project change in response to a serious event/problem (SEP)
- Changes which, in the opinion of the IRB Chair or designee, should be referred to the full board

7.3.3.2 Amendments/Modifications: Submission Materials/Documents
The Investigator may submit to the IRB a completed Amendment Form and all associated documents whether the amendment is being submitted for expedited or full board review.

When a change in procedure is necessary to eliminate an apparent immediate hazard to a research subject or others without prospective IRB approval, the change represents a response to a serious event/problem (SEP) -- (see Section 17: Reportable Events and Problems). Therefore, both an Amendment Form and a Serious Event/Problem–Initial Report must be submitted to the IRB within 7 days of occurrence unless a death is involved in which case the report must be made within 24 hours.

7.3.3.3 Amendments/Modifications: IRB Considerations

The IRB will consider all information provided by the investigator, with particular attention to:

- What part of the research is being revised
- Whether the revision affects potential risks to subject
- Whether the currently approved consent, or revised consent submitted with the amendment, reflects any potential increase in risk indicated by the amendment

After consideration of these items, the Chair or designee will then determine if the amendment involves a change that will adversely affect the risk/benefit assessment of the project or substantially change the specific aims or design of the study. If the Chair or designee determines that the amendment may adversely affect the risk/benefit assessment of the project or substantially change the specific aims or design of the study, the amendment is considered to be “major” and must be referred to the full board for review. If not, the amendment is considered to be “minor” and the Chair or designee may review the amendment using the expedited process. In these case, the Chair or designee may approve the amendment, request modifications be made to the protocol or consent form in order to secure approval, or refer the amendment to the full board when approval cannot be recommended. When the Chair or designee requests modifications in order to secure approval of the amendment, the investigator’s response will be reviewed by the Chair or designee to determine whether approval will be granted.

When an amendment is reviewed by the full board, the IRB considers:

- Whether, with the amendments, the study continues to meet the regulatory criteria for approval. If the determination is that the amended protocol no longer meets the regulatory criteria for approval, the board will request further modification necessary to approve the amendment. If the amended project cannot be modified to meet the regulatory requirements, the board will disapprove the amendment request
- Whether the currently approved or proposed consent/permission/assent document is still accurate and complete
- Whether any significant new findings that may relate to the subject’s willingness to continue participation need to be provided to the subject in accordance with federal regulations DHHS 45 CFR 46 .116(b)(5) and FDA 21 CFR 50.25(b)(5).

When reviewing a change in procedure made without prospective IRB approval in order to eliminate an apparent immediate hazard to a research subject or study personnel, the IRB will consider the changed procedure as a response to a serious event/problem (SEP). In addition to the review required for serious/events problems (SEPs) (see Section 17: Reportable Events and Problems) the IRB will determine whether the change was consistent with ensuring the subjects’ continued welfare. The IRB may request further modifications as appropriate.
When an amendment to research is reviewed and approved through an expedited review process, the date that approval is granted by the Chair or his/her designee will be the of IRB approval date. When research is reviewed and approved through a full board review process, the period of approval for research starts on the date of the convened meeting at which the IRB approved the project or the date that all minor or prescriptive changes or conditions were determined to be met. An amendment/modification to a project ordinarily does not alter the date by which continuing review must occur.

(See also Section 9: Criteria for IRB Approval of Research Projects.)

7.3.3.4 Amendments/Modifications: Enrollment Exceptions

Enrollment exceptions are rare occurrences which will be reviewed as amendments. For more information, see Section 13.15: Special Topics-Enrollment Exceptions.

7.3.3.5 Amendments/Modifications: Notification of IRB Determinations

Investigators will be notified of IRB determinations as indicated in Section 6.4: Notifications of IRB Determinations

7.3.4 Final/Closure

According to Federal Regulations, DHHS 45 CFR 46.115, the IRB is charged with maintaining adequate documentation and records of continuing activity. If a study is completed, closed, or discontinued, the IRB must be informed in order to administratively review and close out the study. If an Application for Continuing Review or a Completed/ Closed Notification – Final Report has not been received by the IRB and the expiration date has been reached, the study is administratively closed.

A study is considered to be completed when subjects are no longer being recruited, no longer being followed, and data analysis has been completed or data has been completely de-identified. If a project is “closed to enrollment,” it is considered to be active as long as study subjects are undergoing intervention, follow-up, or analysis of identifiable data is taking place.

A Completed/Closed Notification – Final Report should be submitted to the IRB as soon as possible, but no later than the expiration date of the study if it is not being renewed, when the study has:

- been completed, or
- been denied funding, or
- not been conducted, or
- been closed prematurely for any reason, or
- been closed by the study sponsor, or
- been discontinued because the PI left the institution without provision for continuation

If the study is sponsored and a close-out visit is conducted, a Completed/Closed Notification – Final Report should be submitted to the IRB when the close-out visit has been completed.

Once a study is completed or closed, no further collection or analysis of data is permitted and all study activity must cease. If the study being closed was a sponsored study using one of UB’s fiscal agents, Sponsored Projects Services will be notified of the closure.
Investigators are responsible for maintaining study records for at least 3 years after closure. An IRB closure date serves as the starting point for this requirement.

The IRB will be in contact with the investigator as required by the particular situation. At minimum, the IRB staff will acknowledge receipt of the Completed/Closed Notification – Final Report.

7.3.5 When an Investigator Leaves the Institution

When a Principal Investigator plans to leave the institution, he/she is responsible for notifying the IRB of her/his departure and the arrangements that have been made for continuation or closure of the study. The PI is responsible for taking appropriate steps to do one of the following:

a. Terminate or Close the Study: The PI should complete and submit the Completed/Closed Notification – Final Report to the IRB

b. Transfer the Study to another UB PI who will take responsibility for the research. The IRB must be notified of this change, as follows:
   - The PI must complete and submit an Amendment Form to the IRB at the time of the transfer. Information provided in the Amendment Form must clearly indicate the transfer of the study to another UB PI and include the name of the new PI, and
   - The individual who will be taking over the PI responsibilities must notify the IRB in writing of her/his acceptance of PI responsibilities for the study

c. Take the data or biological specimens to the next institution: The PI is responsible for closing the study at UB by completing and submitting to the IRB a Completed/Closed Notification – Final Report (Note: The PI is also responsible for making necessary arrangements to obtain the appropriate IRB approvals at the next institution.)
d. The investigator may arrange to continue the research as an investigator from an unaffiliated institution or as an unaffiliated investigator

If it is discovered that any investigator has left the institution without making the required notifications to the IRB, the IRB may unilaterally close the study.

The IRB will be in contact with the investigator as required by the particular situation.

7.4 Reviews Involving Unaffiliated Institutions and Investigators

7.4.1 Overview

Research often involves collaboration among investigators from different institutions and individual studies may have multiple study sites. The UB HRPP and IRBs work closely with UB investigators and with researchers and administrators from other institutions that are unaffiliated with UB in order to address these situations in a manner that most effectively and efficiently fulfills each site’s ethical, regulatory, and organizational requirements for the protection of research subjects.

UB’s IRBs have the authority to determine if/when a project “engages” the Institution in research and if/when an unaffiliated Investigator’s involvement in a protocol is acceptable. When a UB IRB makes the determination that a research project meets the definition of “engaging” UB or its
affiliates in research, that IRB has assumed responsibility to review a project unless an IRB authorization agreement designates an external IRB as the IRB of record for the project.

7.4.2 Research Involving Unaffiliated Institutions

When a research project involves an unaffiliated institution that has its own FWA and IRB, the following options are available:

- Both the UB IRB and the unaffiliated institution’s IRB review the project (dual review), or
- The unaffiliated institution enters into an IRB Authorization Agreement with UB and designates UB’s IRB as the IRB of record for the specific project, or
- UB enters into an IRB Authorization Agreement with the unaffiliated institution, and designates the unaffiliated institution’s IRB as the IRB of record for the specified project.

When the unaffiliated institution does not have its own FWA or IRB:

- The unaffiliated institution must obtain an FWA and enter into an IRB Authorization Agreement with UB designating a UB IRB as the IRB of record for the specific project, or
- An Individual Investigator Agreement may be entered into by UB and the unaffiliated institution that designates UB as the IRB of record for the specific project when an investigator from an unaffiliated institution:
  - is not otherwise an employee or agent of UB or its affiliates;
  - is conducting collaborative research activities outside the facilities of UB of its affiliates;
  - is acting as an employee or agent of a non-assured institution with respect to his or her involvement in the research being conducted by UB or its affiliates; and
  - is employed by, or acting as an agent of, a non-assured institution that does not routinely conduct human subject research.

7.4.3 Research Involving Unaffiliated Investigators

Research projects involving a single investigator without institutional affiliation are considered on a case-by-case basis and typically will not be reviewed by a UB IRB. Cases where the UB HRPP may accept responsibility for providing IRB review include:

- When UB enters into an Individual Investigator Agreement with an unaffiliated investigator to allow a UB IRB to act as the IRB of record as permitted by UB’s FWA. The project must be submitted to a UB IRB for review.
- When a research project meets the definition of “engaging” UB or its affiliates in research.

7.4.4 Designation of UB as the IRB of Record

In order for an external site that is engaged in research to rely upon UB’s IRB as the IRB of record, the site must first have an approved FWA or the site (or the individual investigator) must be entering into an individual investigator agreement with UB. The site or the investigator, as applicable, must then complete and send a signed copy of the agreement to the IO/HRPP Administrator. Upon review, the IO/HRPP Administrator may agree to allow a UB IRB to act as the IRB of record for the site or individual by signing the agreement form. A copy of the signed agreement will be sent to the site.
A specific UB IRB may be designated as the IRB of record in accordance with the authorization agreement. Any protocol determinations or approvals made by the UB IRB then extend to the site. Any necessary institutional communication between UB and an external site related to the authorization agreement will be sent from the IO/HRPP Administrator to the external official designated by the agreement.

7.5 MULTI-SITE RESEARCH

7.5.1 Overview

Multi-site research refers to projects involving sites outside of UB and its affiliates such as company sponsored clinical trials and projects involving collaborators. There may be multiple IRBs involved when research is conducted at multiple sites.

As described in Section 4.2: IRB Scope of Responsibility, UB IRBs are responsible for the review of all research conducted by an employee or agent of UB or its affiliated institutions whether the research is conducted at UB, a UB affiliated institution or another site outside of UB. UB IRBs are also responsible for reviewing research using University or affiliates’ facilities.

Regardless of how many research sites are involved in the study, the investigator serves as the single liaison among participating sites.

7.5.2 When UB Serves as the Coordinating Site

When the investigator indicates on the HS-1A Application Form–Supplemental Information for Multi-Site Research that UB is the coordinating site, the investigator must provide to the IRB:

- A list of participating sites and provide the name of a contact person and his/her contact information
- For sites that have their own IRB, indication of the project’s approval status by the IRB
- An indication of sites that do not have an IRB or sites whose IRB will defer review to a UB IRB. (When applicable, the investigator will be provided with information on how to request that a UB IRB serve as the IRB of record.)
- A description of the procedures that will be used to communicate information among participating sites relevant to the protection of subjects (e.g., serious events/problems (SEPs), interim results, or protocol modifications)

If a participating site does not have an IRB, that site may request that a UB IRB serve as the IRB of record. See Section 7.4.4: Designation of UB as the IRB of Record.

7.5.3 When UB Serves as a Participating Site

When UB is serving as a participating site, the UB IRB will review only the research to be conducted at UB or its affiliated institutions.

7.5.4 Management of Information in Multi-Site Research

Investigators are required to describe their plans for communicating information relevant to the protection of human subjects among participating sites on the HS-1A Application Form-Supplemental Information for Multi-Site Research. This includes the communication of serious
events/problems (SEPs), protocol modifications, and interim results, etc. The investigator is responsible for maintaining documentation of regular communication with participating sites that provides them with this information.

For multi-site research studies, the IRB considers as one of the criteria for approval whether or not management of information that might be relevant to the protection of participants is adequate. This requirement is a part of the reviewer guides for use in the review of new submissions, continuing reviews and amendments.
8. IRB MEETINGS

8.1 TIME AND LOCATION OF MEETINGS

Each UB IRB holds regularly scheduled meetings. The agenda, research proposals, and other appropriate documents for review are distributed to reviewers and members in advance of the scheduled meeting allowing sufficient time for review. The agenda indicates the date, time, and location of the meeting as well as the projects to be reviewed. Information regarding meeting dates, times, locations, and project submission timing for each IRB can be found on their respective websites.

Scheduled meetings may be cancelled by the Chair due to:
- Lack of applications requiring full board review
- Holiday
- Inability to secure a quorum for attendance, or
- Other reasons as may arise that make a scheduled meeting unnecessary or otherwise inappropriate

Scheduled meetings that have been cancelled will be re-scheduled by the Chair as necessary.

8.2 EMERGENCY AND SPECIAL MEETINGS

The IRB Chair, Co-Chair, or Vice-Chair may call an emergency or special meeting as needed. For emergency and special meetings, materials will be distributed as they become available. A quorum must be present in order to conduct the meeting. Records are kept of any emergency or special meetings and copies of the minutes are sent to IRB members and the IO/HRPP Administrator.

8.3 INFORMATION/MATERIALS PROVIDED TO REVIEWERS

The information/materials that board members receive may vary between boards because reviewer systems vary and the SBSIRB uses an electronic submission process while the CYIRB and HSIRB rely on paper submissions.

Information/materials provided to primary reviewers are available to other board members at the full board meeting. Board members who wish to review those materials outside of the full board meeting may contact the IRB staff and the materials will be made available to them.

8.3.1 Social & Behavioral Sciences IRB (SBSIRB): Information/Materials Provided to Reviewers

The SBSIRB utilizes an electronic submissions system and a primary reviewer system. Individuals who will be attending the meeting as voting members will receive information/materials as follows:
### SBSIRB: Initial/New Submissions

<table>
<thead>
<tr>
<th>Primary Reviewers</th>
<th>Non-Primary Reviewers</th>
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<tbody>
<tr>
<td>o HS-1A Application Form</td>
<td>o HS-1A Application Form</td>
</tr>
<tr>
<td>o Full research protocol</td>
<td>o Study synopsis or full research protocol</td>
</tr>
<tr>
<td>o All consenting documents</td>
<td>o All consenting documents</td>
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<tr>
<td>o Advertising and recruitment materials</td>
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<tr>
<td>o Data &amp; Safety Monitoring Plan (DSMP)</td>
<td>o Any other documents that might be required depending on the proposed research</td>
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<td>o All HIPAA documents (when applicable)</td>
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<tr>
<td>o Investigational drug brochure or device information (when applicable)</td>
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<tr>
<td>o Grant application (when applicable)</td>
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<tr>
<td>o FDA 1572 form (when applicable)</td>
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<tr>
<td>o For DHHS-supported multi-center clinical trials, the DHHS-approved sample</td>
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<td>consent document and the complete DHHS-approved protocol when these documents</td>
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<td>exist</td>
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### SBSIRB: Continuing Review Submissions

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<tr>
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<tr>
<td>o Any other documents that might be required depending on the research</td>
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### SBSIRB: Amendments to Projects Approved by the Full Board

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<thead>
<tr>
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<tbody>
<tr>
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<tr>
<td>o Any materials that may have been updated as a result of the amendment request</td>
<td>o Any materials that may have been updated as a result of the amendment/modification</td>
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<td>amendment and the research being conducted</td>
<td>o Any other documents that might be required depending on the proposed research</td>
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8.3.2 Health Sciences IRB (HSIRB): Information/Materials Provided to Reviewers

The HSIRB utilizes a paper submissions system and a primary reviewer system. Individuals who will be attending the meeting as voting members will receive information/materials as follows:

<table>
<thead>
<tr>
<th>HSIRB: Initial/New Submissions</th>
<th>HSIRB: Continuing Review Submissions</th>
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</thead>
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<tr>
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<td>o Any other documents that might be required depending on the proposed research</td>
</tr>
</tbody>
</table>

| o Application for Continuing Review | o Application for Continuing Review or summary of pertinent information provided in the form |
| o Full research protocol including any protocol modifications previously approved by the IRB | o Protocol synopsis |
| o All consenting documents | o All consenting documents |
| o Advertising and recruitment materials | o Comments of the primary reviewer |
| o Investigational drug brochure or device information (when applicable) | o Any other documents that might be required depending on the proposed research |
| o Grant application (when applicable) | o Any other documents that might be required depending on the proposed research |
| o SEPs submitted with the continuing review application (when applicable) | o Any other documents that might be required depending on the proposed research |
| o FDA 1572 form (when applicable) | o Any other documents that might be required depending on the proposed research |
| o Any other documents that might be required depending on the proposed research | o Any other documents that might be required depending on the proposed research |
8.3.3 Children & Youth IRB (CYIRB) Information/Materials Provided to Reviewers

The CYIRB utilizes a paper submission system.

A. New Projects
   All individuals who will be attending the meeting as voting members will receive the following information/materials:
   o HS-1A Application Form
   o Full research protocol
   o All consenting documents
   o Advertising and recruitment materials
   o Data & Safety Monitoring Plan (DSMP)
   o All HIPAA documents (when applicable)
   o Investigational drug brochure or device information (when applicable)
   o Grant application (when applicable)
   o FDA 1572 form (when applicable)
   o For DHHS-supported multi-center clinical trials, the DHHS-approved sample consent document and the complete DHHS-approved protocol when these documents exist
   o Any other documents that might be required depending on the proposed research

B. Continuing Renewals
   Primary Reviewer receives the following:
   o HS-1A Application Form
   o Application for Continuing Review
   o Full research protocol including any protocol modifications previously approved by the IRB
   o All consenting documents
   o Advertising and recruitment materials
   o Investigational drug brochure or device information (when applicable)
   o SEPs submitted with the continuing review application (when applicable)
   o Any other documents that might be required depending on the research

   All individuals who will be attending the meeting as voting members will receive the following information/materials:
   o Application for Continuing Review or summary of pertinent information provided in the form
   o Protocol synopsis
   o Comments of the primary reviewer
Any other documents that might be required depending on the proposed research

C. Amendments to Projects Approved by the Full Board

All individuals who will be attending the meeting as voting members will receive the following information/materials:
- Amendment Form
- Any materials that may have been updated as a result of the amendment request
- Any other documents that might be required depending on the nature of the amendment and the research being conducted

8.4 PREPARATION FOR THE IRB MEETING

8.4.1 Responsibilities of the IRB Members

In preparation for the IRB meetings, IRB members, including alternates who will be attending, shall:
- Review all the application submission documents/materials provided to them in enough depth to discuss the information when they are present at the convened meeting and determine if the project fulfills or continues to fulfill the criteria for approval
- If designated as a primary reviewer: to review materials prior to the meeting and provide any written reviews to the IRB staff for distribution to other board members either in advance of or at the full board meeting
- Be prepared to discuss any questions regarding submissions with the Chair and/or investigators, as appropriate
- Identify changes that may be needed in the application, protocol or consent document for presentation to the board for discussion

8.4.2 Selection and Responsibilities of Primary Reviewers

IRB Chairs may determine when a primary reviewer system will be utilized. When a primary reviewer system is used, primary reviewers are assigned in advance of a full board meeting. The Chair may, at his/her discretion, serve as the primary reviewer. Considerations when selecting a primary reviewer are that the individual will be knowledgeable about the subject area and issues involved with the study’s special populations or experienced in working with such populations. The primary reviewer is responsible for an in-depth review of all materials in preparation for the meeting. When a primary reviewer system is not used, all members are responsible for an in-depth review of all materials.

The primary reviewer may not have a conflict of interest regarding the research project under review. If the primary reviewer is unable to conduct review of an assigned project due to conflict of interest or for any other reason, the IRB Office should be notified as soon as possible so another primary reviewer can be identified.

The conflict of interest policy requires any member with a conflict of interest to disclose that information to the IRB Chair and leave the room during discussion of the project and related vote. This policy applies to all projects reviewed by the IRB, regardless of the level or type of review.

8.4.3 Selection and Responsibilities of Outside Reviewers
If the Chair determines that no IRB member has adequate knowledge or experience to provide an in depth review of a project, the Chair may engage an outside reviewer with appropriate expertise and experience to conduct the review. Outside reviewers will receive all documentation associated with the project submission. If the Chair is unable to identify a reviewer with appropriate expertise or obtain appropriate consultation, the IRB Chair will defer review of the project until an individual with the appropriate expertise is identified.

One or more outside reviewers may be consulted in order to obtain the expertise to adequately review a project. Outside reviewers may not vote. The responsibilities of outside reviewers include the following:

- To disclose any potential conflict of interest related to the project to the IRB Chair as soon as it is identified. If a conflict of interest exists, the chair will generally engage another outside reviewer. In instances when an outside reviewer has a conflicting interest but his/her expertise is necessary, he/she may provide information to the IRB provided certain requirements are met (see Section 16.8: IRB Member and Outside Reviewer Conflict of Interest or Significant Obligation)
- To review the application submission documents/materials regarding the assigned project review prior to the convened meeting
- To discuss any questions regarding the submission with the chair and/or investigator
- To identify changes that may be needed in the application, protocol or consent document for presentation to the board for discussion
- To provide any written reviews to the IRB staff for distribution to board members either in advance of or at the full board meeting
- At the request of the chair, to present a summary of findings and any concerns at the full board meeting

When an outsider reviewer is needed the Chair may ask IRB members or staff to provide names of potential persons who may have the expertise needed. Occasionally, other sources may be utilized to determine potential outside reviewers with necessary expertise. The Chair or a designee will select a person or persons to contact. An IRB member or IRB staff member will then be asked to initiate contact with the potential outside reviewer(s), notify them of the specific expertise needed and request that they provide the following information related to the project:

- Their willingness to provide the outside review in a timely manner
- A disclosure of any potential conflicts of interest that the outside reviewer may have
- Information related to their ability to provide the necessary expertise (e.g. a statement of their credentials/experience in the area or a CV)

This information will then be provided to the Chair or designee who will make a preliminary determination as to the suitability of the outside reviewer for providing the review needed. If the reviewer is suitable, the applicable protocol materials will be provided to the reviewer along with any specific questions or areas that the Chair or designee would like addressed. The outside reviewer will then be asked to provide his/her review of the materials either in writing or at a convened meeting.

8.5 IRB MEETING AGENDA

IRB meetings are conducted by the IRB Chair. In the absence of the Chair, the Vice-Chair or Chair designee may conduct the meeting. The meeting agenda includes, but is not limited to:
At the discretion of the Chair, or at the request of the IRB, investigators may be invited to attend meetings for purposes of additional clarification or discussion of their proposed research. In these instances, the presentation/discussion by the investigator is included in the agenda. Guest investigators are required to leave the meeting prior to subsequent discussion and voting.

8.6 ESTABLISHING A QUORUM

The IRB may not take any official action at a full board meeting unless a quorum is established. [45 CFR 46.108(b) and 21 CFR 56.108] A quorum consists of more than half of the total number of full voting members listed on the IRB roster including at least one member whose primary concern is non-scientific, and at least one member who represents the general perspective of participants. If the IRB regularly reviews research that involves categories of participants vulnerable to coercion or undue influence (e.g. children), one or more individuals who are knowledgeable about or experienced in working with such participants must also be present. An unaffiliated member is not required to be in attendance in order to attain quorum, but the unaffiliated members must contribute to the function of the board by taking part in either the written review of protocols or through meeting attendance. An alternate member may only count towards meeting quorum requirements when present as voting member. Outside reviewers do not count as voting members for purposes of determining a quorum.

Members may be present in person or via audio or video conference. Such members who will not be physically present at a meeting, must be provided with all materials available to members who will be in attendance at the meeting and are responsible for review of those materials prior to the meeting. These members may vote and shall be noted in the meeting minutes as being present via audio or video conference.

The IRB meeting is called to order when a quorum of members that includes a non-scientist is in attendance. The meeting ends when business has been completed or a quorum is lost. Upon loss of a quorum, no further official business is conducted. Loss of a quorum and reason for the loss shall be noted in the meeting minutes. The IRB Chair is responsible for ensuring that no vote takes place without a quorum present and the meeting recorder(s) will document that quorum is present and if/when quorum is lost as a part of the minutes.

8.7 IRB DETERMINATIONS

8.7.1 Overview

Research projects reviewed at the full board level must be reviewed, discussed, and voted on by the IRB membership at convened meetings. The Chair or primary reviewer, if that system is used, will present a summary of their review and provide recommendations. IRB members present at
the meeting may ask questions about and discuss each project presented. The board, as a part of their deliberation, may also consider written comments from members who are not present.

Other reviews requiring a vote at full board meetings include, but are not limited to, review of continuing projects as well as substantive revisions to previously approved projects where the changes include a potential increased risk to subjects.

(For details of considerations for IRB approval, see Section 9: Criteria for IRB Approval of Research Projects.)

8.7.2 Voting

The IRB may not take any official action at a full board meeting unless a quorum is established. If a quorum is present, IRB members may cast a vote for or against a motion or abstain. At the discretion of the Chair, vote may be indicated by show of hands, voice vote, or written ballot. The official minutes will reflect, without individual identification, the number of votes to approve, disapprove, or to abstain. Abstentions will be noted.

Only individuals listed as voting members on the official IRB membership roster may vote. Alternate members hold full voting rights only when the regular member they are authorized to replace is not present at the meeting. An alternate may cast only one vote even if he/she is authorized to replace two regular members and both of the regular members are absent. Members who are unable to physically attend a meeting may be present via audio or audio-visual teleconference, and vote.

8.7.3 IRB Motions

Following presentation and discussion of a project submission, the IRB will make a motion for each application request. All voting members present shall vote on the following types of motions: A majority vote of the members present at the meeting is required for a motion to pass. Proxy votes are not permitted.

Possible Voting Motions Include:

- To approve the project as reviewed: The IRB may vote to approve the project as reviewed.
- To approve upon verification of non-substantive or specific changes requiring only the concurrence of the researcher: Such changes may be accepted by the Chair/designee on behalf of the IRB once a revision is provided that meets the board’s requirements and any additional items then identified by the reviewer.
- To table/defer due to a need for substantive changes (e.g., when the project is incomplete in some significant way, when risks are significant and have not been minimized, or there are questions raised by the IRB that await the response of the investigator). The IRB may vote to require changes to the project and/or to the consent document that are considered substantive. When this occurs:
  - For an initial review project: the research may not commence until the investigator has submitted a response to the concerns raised by the IRB and the revised project is reviewed again and is approved by the IRB
  - For a continuing review project: the research may not continue past the expiration date unless the investigator has submitted a response to the concerns made by the IRB and the revised project is then reviewed again and approved by the IRB
o (In specific instances, certain study activities necessary to protect the safety and welfare of the subjects may be permitted to continue past the expiration date while the PI is actively seeking to obtain continuing approval)

o For an amendment to a previously approved project: the amendment may not be initiated until the investigator has submitted a response to the concerns raised by the IRB and the revised project is then reviewed again and approved by the IRB

- To table/defer because the IRB does not have appropriate scientific expertise available to make a determination at the full board meeting

- To suspend or terminate: The IRB may suspend or terminate approval of research that is:
  o Not being conducted in accordance with HRPP or regulatory requirements, or
  o That has been associated with serious events/problems (SEPs)

- To disapprove: The IRB determines that the research cannot be conducted in its present form or that it is inappropriate in its present design

8.7.4 Suspensions and Terminations of IRB Approval

8.7.4.1 Overview

- Suspension: A “suspension” is the temporary or permanent stoppage of some or all of a research project or an investigator’s privilege to conduct research imposed by the IRB (or in specific instances, the IRB Chair)

- Termination: A “termination” of IRB approval is a directive from the IRB to permanently stop all previously approved research activities.

The IRB has the authority to suspend or terminate approval of previously approved research that is not being conducted in accordance with the IRB’s requirements or federal regulations that has been associated with unexpected serious harm to subjects or others or when there are immediate serious risks to subjects or others. The IRB Chair has the authority to take action to suspend some or all research activities to protect research subjects from immediate hazards and risks when there is insufficient time to have the full board review the situation.

When a suspension involves the withdrawal of current subjects from research interventions or interactions, the Chair considers actions to protect the rights and welfare of currently enrolled participants and whether measures need to be taken to protect the currently enrolled subjects from any harm that may result from such withdrawal. Such considerations may include the need to arrange for clinical care outside the research, the continuation of some research activities under the supervision of an independent monitor, or permitting or requiring the follow-up of subjects for safety reasons.

With the exception of the authority granted to the IRB Chair to take immediate action to suspend a project, as described below, the authority to suspend or terminate previously approved research rests with the full board. This applies to projects originally approved under expedited procedures or by the full board.

Occasionally an entity that is not affiliated with the HRPP (such as the study sponsor or other university or hospital administrative office) will suspend or terminate a research project. In these cases, the suspension or termination must be reported to the IRB and reviewed by the convened IRB.
8.7.4.2 Procedures for Suspension of IRB Approval

A. Suspension of IRB Approval by the IRB Chair
The IRB Chair has the authority to take action to suspend all or some research activities to protect research subjects from immediate hazards and risks when there is insufficient time to have the full board review the situation. When the IRB Chair suspends some or all aspects of IRB approval, the Chair will document which activities will be suspended and the reason for the suspension. The IRB members are notified of the suspension and the IRB reviews the suspension at a full board meeting where the action may be approved, modified, or rescinded. The OVPRED will be notified immediately of the suspension. The Chair or designee will notify the investigator in writing of the suspension.

When a suspension involves the withdrawal of current subjects from research interventions or interactions, the Chair considers actions to protect the rights and welfare of currently enrolled participants and whether measures need to be taken to protect the currently enrolled subjects from any harm that may result from such withdrawal. Such considerations may include the need to arrange for clinical care outside the research, the continuation of some research activities under the supervision of an independent monitor, or permitting or requiring the follow-up of subjects for safety reasons.

Notification from the Chair(s) or Chair designee to investigators shall include the following information, as appropriate:
- Project title
- IRB assigned number
- Statement that research activities have been suspended. When only some research activities have been suspended, the notice will indicate which activities have been suspended.
- Effective date of the suspension
- Any action that the investigator must take to protect subjects
- Indication of any corrective actions needed for the IRB to consider lifting the suspension
- Any other information deemed appropriate

B. Suspension of IRB Approval by the Full Board
When the full board determines that approval of some or all aspects of a research project will be suspended, the minutes will document the reason(s) for the suspension, any information needed from the PI, and any corrective actions needed for the IRB to consider lifting the suspension.

When a suspension involves the withdrawal of current subjects from research interventions or interactions, the IRB considers actions to protect the rights and welfare of currently enrolled participants and whether measures need to be taken to protect the currently enrolled subjects from any harm that may result from such withdrawal as noted in A above. The IRB will also consider informing current participants of the suspensions and of the procedures for the research subjects to report any adverse events or outcomes to the IRB.

Notification from the Chair(s) or Chair designee to investigators shall include the following information, as appropriate:
- Project title
- IRB assigned number
• Statement that the full board has suspended research activities. When only some research activities have been suspended, the notice will indicate which activities have been suspended (e.g., enrollment, recruitment, interventions, interactions, or data analysis)
• Date of the full board meeting when the project was suspended
• Any action that the investigator must take to protect subjects including, as appropriate, whether follow-up of subjects who may need to be withdrawn due to the suspension for safety reasons is permitted or required
• Indication of any corrective actions needed for the IRB to consider lifting the suspension
• Any other information deemed appropriate.

C. Further Reporting of Suspensions of IRB Approval
All suspensions initiated by the IRB will be reported immediately to the IO/HRPP Administrator who is responsible for promptly notifying the following agencies within 10 business days of receipt of notification regarding the suspension of the IRB approved research:
  o OHRP
  o FDA, when the research is FDA regulated
  o Any other federal agencies when the research is overseen by those agencies and they require a direct report
  o The University Office of Sponsored Projects Services in instances where the project is externally funded and using a University fiscal agent

D. Responsibilities of the Principal Investigator When a Project is Suspended
The PI is responsible for:
  o notifying enrolled subjects of the suspended research activities
  o considering, when applicable, procedures for the withdrawal of enrolled subjects, taking into account their rights and welfare
  o complying with IRB policies, requirements, procedures, decisions, and conditions

8.7.4.3 Procedures for Termination of IRB Approval
A. When the full board determines that approval for the conduct of a research project will be terminated, the minutes will document the reason(s) for the termination.

B. When a termination involves the withdrawal of current subjects from research interventions or interactions, the IRB considers actions to protect the rights and welfare of currently enrolled participants and whether measures need to be taken to protect the currently enrolled subjects from any harm that may result from such withdrawal. Such considerations may include the need to arrange for clinical care outside the research, the continuation of some research activities under the supervision of an independent monitor, or permit or require the follow-up of subjects for safety reasons. The IRB will also consider informing current participants of the termination and procedures for having any adverse events or outcomes reported to the IRB.

C. The IRB notifies the principal investigator, in writing, of the termination. The notice shall include:
  • Project title
  • IRB assigned number
University at Buffalo
Human Research Protection Program
Policies and Procedures Manual

- Statement that research activities have been terminated
- Date of the full board meeting when the project was terminated
- Any action that the investigator must take to protect subjects including, as appropriate, whether follow-up of subjects for safety reasons is permitted or required
- Any other information deemed appropriate

D. Further Reporting of Terminations of IRB Approval

All terminations initiated by the IRB will be reported immediately to the IO/HRPP Administrator who is responsible for promptly notifying the following agencies within 10 business days of receipt of notification regarding the suspension of IRB approved research:
- OHRP
- FDA, when the research is FDA regulated
- Any other appropriate federal agencies, when the research is overseen by those agencies and they require reporting separate from that to OHRP
- The University Office of Sponsored Projects Services, in instances where the project is externally funded and using a University fiscal agent

E. The PI is responsible for:
- notifying enrolled subjects of the terminated research activities
- considering, when applicable, procedures for the withdrawal of enrolled subjects, taking into account their rights and welfare
- complying with IRB policies, requirements, procedures, decisions, and conditions

8.7.5 Appeal of IRB Determinations

When an investigator disagrees with a determination of the IRB, a written appeal may be submitted to the IRB requesting reconsideration of the decision. The request will be discussed at a full board meeting and either the previous determination will be affirmed or a further determination will be issued. At the discretion of the Chair, the investigator may be invited to attend the open portion of the IRB meeting in order to provide information in support of his/her position.

In the case of a decision by the IRB to disapprove, suspend, or terminate a project, the decision may not be reversed by the IO/HRPP Administrator or any other officer or agent of the University at Buffalo, state or federal regulatory agencies.

8.8 IRB MEMBER AND OUTSIDE REVIEWER CONFLICT OF INTEREST

IRB members and outside reviewers may not participate in the review of the research project in which they have a conflict of interest or significant obligation except to provide information requested by the IRB. Any member or outside reviewer with a conflict of interest or potential conflict of interest must disclose that information to the IRB Chair. This policy applies to all types of projects reviewed by the IRB, regardless of level or type of IRB review. (See Section 16.8: IRB Member and Outside Reviewer Conflict of Interest or Significant Obligation.)
8.9 **MEETING MINUTES: DOCUMENTATION OF IRB FINDINGS AND ACTIONS**

Federal regulations require that for research approved by the convened IRB, all required findings be fully documented in the minutes of the IRB meeting, including project-specific information justifying each IRB finding.

Meeting minutes shall document the following, as appropriate:

- Attendance regarding voting members, non-voting members, guests, and members excused or absent, and when an alternate replaces a primary member
- Approval of the minutes of the previous meeting
- Separate specific comments and actions taken by the full board on each project for initial and continuing review of research including:
  - A written summary of the discussion (e.g., the basis for requiring changes in or disapproving research and any controverted issues and their resolution)
  - Level of risk of the research
  - Approval period for the research including identification of research that warrants review more often than at least annually
  - Identification of any research for which there is a need for verification from sources other than the investigator that no material changes are made in the research
  - Justification for any deletion or substantive modification of information concerning risks or alternative procedures contained in a DHHS-approved sample consent document
- Protocol-specific information justifying findings for approval of the following:
  - A procedure which does not include, or which alters, some or all of the required elements of informed consent or when waiving the requirement to obtain informed consent
  - A procedure which waives the requirement for the investigator to obtain written documentation of consent
  - Research involving pregnant women, human fetuses, or neonates
  - Research involving prisoners
  - Research involving children
  - Research involving vulnerable populations/groups requiring special consideration
  - The rationale for significant/non-significant risk device determinations
- Specific comments and actions taken by the full board regarding amendments or modifications
- Actions taken by the IRB with respect to serious events/problems (SEPs)
- Specific comments regarding suspension or termination of research
- Record of vote on actions taken that includes the number voting for, against, and abstentions, as well as any recusal
- Record of whether the project was approved, disapproved, tabled/deferred, or approved upon verification of non-substantive changes. The minutes shall reflect the reason(s) for requesting changes, tabling or disapproval
- When a member recuses him/herself due to a personal conflict of interest with respect to a particular project and when the member returns
- When a member leaves the room for reasons other than a conflict of interest and when the member returns
- When a quorum is lost during the meeting and when a quorum is restored
• That the IRB members received a written report of expedited actions that occurred since the last full board meeting including new applications, continuing reviews, and amendments. These reports are typically distributed with the meeting minutes or agendas.
• Any other business considered by the convened IRB.
9. CRITERIA FOR IRB APPROVAL OF RESEARCH PROJECTS

9.1 INTRODUCTION

The IRB shall conduct a systematic review of project materials and shall consider the same principles and criteria in all project deliberations as established by the federal regulations DHHS 45 CFR 46.111 and FDA 21 CFR 56.111. DHHS and FDA regulations are essentially equivalent with the exception that the FDA requires additional protections for children involved in clinical research [21 CFR 50 subpart D].

45 CFR 46.111: Criteria for IRB approval of research.

a. In order to approve research covered by this policy the IRB shall determine that all of the following requirements are satisfied:

(1) Risks to subjects are minimized: (i) By using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and (ii) whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.

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

(3) Selection of subjects is equitable. In making this assessment the IRB should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons.

(4) Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by 45 CFR 46.116.

(5) Informed consent will be appropriately documented, in accordance with, and to the extent required by 45 CFR 46.117.

(6) When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.

(7) When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

b. When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects.

In order to ensure that the criteria for approval of research including those applicable to informed consent are systematically reviewed and met, reviewers are provided with guides for use in the review of new submittals, continuing reviews and amendments. The federal criteria for approval of research are listed in the reviewer guides.
9.2 MINIMIZATION OF RISK

- **Risk** is the probability of harm or injury occurring as a result of participation in a research study.

9.2.1 Types of Risks

The IRB shall identify potential risks to human subjects, both physical and non-physical, associated with the research project under review. Types of risks considered include:

- **Physical**
  Physical risks involve the potential for physical discomfort, pain, injury, illness or disease brought on as a result of methods or procedures involved in the research. These risks to subjects cover a wide range and may be minor and transient or may hold the prospect of permanent injury or death. Risk of physical harm caused to the subject by another human being may also be considered, e.g., in retaliation for participation in the research.

- **Psychological**
  Psychological risks involve the potential for undesired changes in thought processes and emotion including episodes of depression and confusion resulting from feelings of stress, guilt, or loss of self-esteem. As is the case with physical risks, these effects are usually, but not always, transient. Psychological effects may be experienced at the time of research participation or later, as a result of participation.

- **Social**
  Social risks involve the potential for causing embarrassment or stigmatization to the subject or others, or loss of respect of others within a social group or place of employment.

- **Legal**
  Legal risks involve the potential for putting the subject or others at risk of civil liability or criminal prosecution if information collected as part of the research is revealed.

- **Economic**
  Economic risks include the potential for subject loss of employment or the inability of the subject to work due to serious injury as a result of participation in the research. Less severe economic risks include loss of wages and failure of medical insurance companies to cover costs for participation in investigational therapies.

- **Risk Associated with the Invasion of Privacy and Breaches of Confidentiality**
  Risk associated with the invasion of privacy involves the intrusion of the research or researcher into information or behavior that the subject considers to be private, without their consent. Confidentiality of data concerns the safeguarding of information that has been voluntarily given by one person to another. Invasions of privacy and breaches of confidentiality have the potential for effecting psychological, social, economic, and legal risks described above.

9.2.2 Minimal Risk vs. Greater Than Minimal Risk

- **Minimal risk** means that the probability and magnitude of harm or discomfort anticipated in the proposed 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. [DHHS 45 CFR 46.102 (i); FDA 21 CFR 50.3 (k)]
Once risks have been identified, the IRB shall determine whether the research risks to subjects are no more than minimal risk or are greater than minimal risk. This determination is critical in the IRB’s review of any project. (See also, Section 7: Levels and Types of IRB Review.)

Further, DHHS regulations for research involving fetuses, pregnant women, prisoners, and children, strictly limit research that presents more than minimal risk. For such subjects, the IRB will consider “minimal risk” in the context of the population’s general conditions or disabilities.

9.2.3 Sound Research Design

In the assessment of a project’s research design, the IRB shall consider the purpose of the research, scientific methodology, qualifications of the research personnel, and adequacy of resources to conduct the research. The IRB evaluates the purpose of the research including the hypothesis and anticipated outcomes. The IRB will utilize at least one reviewer with appropriate scientific or scholarly experience to conduct an in-depth review of the protocol including:

- **Scientific Design**
  The IRB evaluates the scientific design of each project for its adequacy in producing valid scientific data and considers whether the design is adequate to answer the hypothesis posed and has sufficient statistical power.

- **Research Team Qualifications**
  The IRB considers the capability of the investigator and research team to conduct the proposed study. The investigator and research team's professional credentials and experience are considered in relation to the complexity of the study and the scientific training and technical skills needed to bring the study to completion. Projects that, in the estimation of the IRB, require capabilities beyond those held by the principal investigator and research team may need to be modified or have additional qualified personnel added prior to IRB approval. The IRB may require less experienced research investigators to work with a more experienced researcher.

- **Adequacy of Resources**
  The IRB may consider and request assurance that sufficient resources exist with respect to personnel, space, equipment, time, and finances to successfully carry the project to its completion and protect participants. This includes access to population that will allow recruitment of the necessary number of participants and availability of medical or psychosocial resources that participants may need as a consequence of the research.

9.2.4 Risk/Benefit Assessment

All protocols submitted must detail the procedures to be performed as a part of the study, indicate any foreseeable risks, and describe procedures to manage and minimize those risks. The IRB considers whether risks identified in the protocol have been minimized to the extent possible. The IRB may identify additional risks and require that the investigator develop a plan to minimize those risks. The IRB will consider the range of risks described in Section 9.2.1: Types of Risks, in terms of their potential likelihood, frequency, magnitude, and duration as well as the adequacy of procedures to minimize those risks. Further, the IRB will consider whether a study’s research design maximizes any potential benefits and determine whether exposure to a study’s risks is justifiable when considered in relation to any potential benefits. When no direct benefits to the
subject are anticipated, the IRB must evaluate whether the risks presented by procedures performed solely to obtain generalizable knowledge are ethically acceptable.

In conducting a risk/benefit assessment, the IRB shall:

- Evaluate the purpose of the research including the hypothesis and the anticipated outcomes
- Identify the potential risks to subjects associated with the research, as distinguished from the risks of therapies the subjects would receive if not participating in the research
- Determine that the risks to subjects are minimized by the research design. This includes consideration of whether studies are reducing risk to subjects by incorporating procedures already being performed on subjects for diagnostic treatment purposes or by using results already obtained from tests or treatments for diagnostic purposes
- Identify the probable benefits derived from the research and consider that they are maximized
- Determine that the risks are reasonable in relation to benefits to the subjects, if any, and the knowledge to be gained
- Assure that subjects are provided with an accurate and fair description of the risks or discomforts and any anticipated benefits
- Determine the appropriate intervals for periodic review in light of the risk/benefit assessment
- Determine that adequate provisions are in place for monitoring the data collected,
- Determine the adequacy of the provisions to protect the privacy of subjects and to maintain confidentiality of the data
- When subjects are likely to be members of a vulnerable population/group, determine that appropriate additional safeguards are in place to protect the rights and welfare of those subjects

9.3 EQUITABLE SELECTION OF SUBJECTS

While taking into account the purpose of the research and setting for the research, the IRB will consider whether the ethical principle of justice, which requires fairness in distribution of both risk and benefit across the study population, is reflected in the composition of the proposed study population(s) in terms of age, gender, social group and physical or psychological condition. The IRB will further consider whether the protocol adequately describes and provides the rationale for inclusion of the proposed population including:

- That selection of the proposed study population(s) is not solely based on their easy availability, compromised position, or susceptibility to manipulation
- That the research does not unduly involve individuals from populations unlikely to benefit from any subsequent beneficial applications of the research
- Where there is the prospect of significant benefit, that participation is as broad as possible across various populations
- That vulnerable populations/groups are included only when needed to answer the scientific hypothesis posed
- When vulnerable populations/groups are included in the study, that the possibility for coercion or undue influence are appropriately addressed
9.4 RESEARCH INVOLVING VULNERABLE POPULATIONS/GROUPS

Additional expertise or knowledge may be required when a research project involves any population requiring special protections. In these cases, the IRB chair may request that an IRB member or outside reviewer who is knowledgeable about and has experience with the specific group be involved in the review process when necessary to ensure that adequate provisions have been made to protect the safety, rights, and welfare of the subjects and to minimize risks unique to the population. In its review, the IRB shall consider:

- Whether the inclusion of that population is justified
- Whether there is risk of coercion or undue influence
- The ability of subjects to provide informed consent
- Whether adequate safeguards are provided for risks unique to that population
- The regulatory requirements specific to the vulnerable population/group, if any

For research falling under 45 CFR 46 subparts B, C, and D (research involving pregnant women, fetuses, or neonates, prisoners, and children), the IRB follows the regulatory criteria for approval for such research to determine whether adequate safeguards are in place to protect the specific subject group.

Although federal regulations identify special protections only for specified populations, each project reviewed by the UB IRBs is evaluated for circumstances that may place subjects in vulnerable situations that call for special consideration. (For additional details, see Section 10: Vulnerable Populations/Groups Requiring Special Consideration.)

9.5 THE INFORMED CONSENT PROCESS

9.5.1 Overview

The IRB considers informed consent to be an ongoing process that begins with the first contact between the research team and the prospective subject and continues throughout the course of the research project. (For a full discussion of the Informed Consent Process, see Section 14: The Informed Consent Process.)

The investigator’s description of the consent process in the application documents must provide sufficient information for the IRB to consider the following:

- The adequacy of the consent document or other forms of communication used to obtain consent in terms of content including: the information to be communicated to the prospective subject, language understood by prospective subjects if other than English, and language to be used by those obtaining consent
- That the required elements of consent will be provided to each subject or a legally authorized representative in accordance with the regulations
- Whether information in the consent document will be presented in a manner appropriate to the subject population (e.g., level of complexity or need for non-English translation)
- Who will present the research information to the subject
- Who will obtain consent from the subject
- Who will provide consent or permission
- When consent will be obtained including whether there will be a waiting period between presenting information to the subject and obtaining consent
- Where and how consent will be obtained
• How documentation of consent will be accomplished, unless the requirement for documentation is waived
• Provision by investigators to inform enrolled subjects of any new information relating to the research that might affect their willingness to continue participation in the study
• That the consent process will not include exculpatory language through which the subject or the legally authorized representative is made to waive or appear to waive any of the subject’s legal rights or appears to release the investigator, the sponsor, the institution, or its agents from liability for negligence.
• Any steps that need to be taken to minimize the possibility of coercion or undue influence so that the IRB can determine that these factors have been minimized
• Any special protections when a research project involves populations subject to vulnerabilities (for more information, see Section 14: The Informed Consent Process)

After consideration of the above, the IRB will determine whether the investigator will be obtaining the legally effective consent of the subject or the subject’s legally authorized representative.

(For additional details, see Section 14: The Informed Consent Process.)

9.5.2 The Consent Document
A consent document that will be signed by the subject or the subject’s legally authorized representative is required for all human subject research unless the research activity meets regulatory criteria for waiver or alteration of informed consent. The IRB and/or IRB staff will review consent documents to verify that all of the basic elements of consent required by federal regulations are contained in the document. The consent document will also be evaluated for its readability and its congruence with the research study. (For details, see Section 14: The Informed Consent Process.)

9.5.3 Waiver or Alteration of Informed Consent
When specific criteria are met, the IRB may approve a consent procedure which does not include, or which alters, some or all consent requirements in DHHS 46.116(a)(b), or waive the requirement to obtain informed consent (see Section 14.7: Waiver of Consent Requirements).

9.5.4 Documentation of Consent
Unless the research activity meets regulatory criteria for waiver of consent, the IRB shall require that informed consent be documented by the use of an IRB approved written consent document that will be signed by the subject or the subject’s legally authorized representative and that a copy of the document is given to the person signing the document (see Section 14.8: Documenting Consent).

9.5.5 Waiver of Documentation of Consent
When specific criteria are met, the IRB may waive the requirement for written documentation of consent for some or all subjects (see Section 14.8.3: Waiver of Written Documentation of Consent).
9.6 DATA AND SAFETY MONITORING

The IRB will consider the investigator’s plan for collection, monitoring, storage, and analysis of data. The level of monitoring required is related to the degree of risk posed by the research.

9.6.1 Data and Safety Monitoring Plan (DSMP)

At minimum, all investigators involved in non-exempt research must provide a “plan” for ensuring data integrity and safety monitoring for human subjects who are involved in the research. The level of detail in the plan should be based on the degree of risk to research subjects. Low risk studies, for example, may have simple plans. The plan may be included in the submission documents or provided as an appendix to the protocol.

The IRB shall determine, that the submitted project documents (or other documentation) includes adequate plans for monitoring the data collected, i.e., for analyzing the data during the collection process to enable the identification of problems regarding data integrity and reevaluation of risks to subjects to assure that they are no greater than initially predicted. The IRB will determine whether the DSMP is adequate for the nature, size, and complexity of the research project, the expected risks of the research and the type of population being studied. When a reviewer considers a DSMP to be inadequate, he/she shall indicate this concern either in writing as a part of his/her review or during the board’s discussion of the project at a board meeting.

The DSMP shall include information regarding:

- The type of data or events that will be monitored
- The frequency of review
- The individual responsible for monitoring the plan including the data collected
- The individual(s) responsible for monitoring serious events and problems (SEPs) and the responsible party to whom such events or problems should be reported and the timeframe for reporting them
- Specific stopping rules or triggers used to determine when the study should be stopped or altered
- Procedures for communicating the outcome of DSMP reviews to the study sponsor, and others, when appropriate (the investigator provides this information to the IRB at the time of Continuing Review on the Application for Continuing Review).
- What safety information will be collected, including serious adverse events.
- How the safety information will be collected (e.g., with case report forms, at study visits, by telephone calls with participants).
- The frequency of data collection, including when safety data collection starts.
- The frequency or periodicity of review of cumulative safety data.
- The plan might include establishing a data monitoring committee and a plan for reporting data monitoring committee findings to the IRB and the Sponsor.
- For studies that do not have or are not required to have a data monitoring committee and are blinded, have multiple sites, enter vulnerable populations, or employ high-risk interventions, the IRB needs to carefully review the data and safety monitoring plan and determine whether a data monitoring committee is needed.
- If not using a data monitoring committee, and if applicable, statistical tests for analyzing the safety data to determine whether harm is occurring;
- Provisions for the oversight of safety data (e.g., by a data monitoring committee).
• Conditions that trigger an immediate suspension of the research, if applicable.

9.6.2 Data and Safety Monitoring Board (DSMB)

Data and Safety Monitoring Plans may fall anywhere along a continuum from monitoring by the principal investigator or group of investigators to the establishment of an independent Data and Safety Monitoring Board (DSMB) or Data Monitoring Committee (DMC). When a DSMB is utilized, the IRB considers the DSMB’s findings in its determination regarding continuing approval of research.

9.7 PROTECTING THE PRIVACY OF SUBJECTS AND MAINTAINING THE CONFIDENTIALITY OF DATA

9.7.1 Protecting the Privacy of Subjects

Privacy is defined in terms of having control over the extent, timing, and circumstances of sharing oneself (physically, behaviorally, or intellectually) with others. The right to privacy is highly valued in the United States and is secured by laws other than those for protecting research subjects including the Family Educational Rights and Privacy Act (FERPA) designed to protect the privacy of students’ educational records and the Health Insurance Portability and Accountability Act (HIPAA) protecting access to private health information.

Submitted project documents must describe how recruitment procedures adequately protect the privacy of participants as well as any provisions for ensuring that data is collected in a manner the protects participants’ privacy. The IRB must evaluate if the research plan makes adequate provisions to protect the privacy interests of subjects before approving a project. IRB considerations with respect to privacy may include:

• Whether the research will involve observation or intrusion in situations where the subjects have a reasonable expectation of privacy
• The availability of alternative ways to do the research
• If privacy is to be invaded, whether the importance of the research justifies the intrusion and the provision for informing the subject of the invasion of privacy or justification for not doing so
• When investigators want to review existing records to select subjects for the project, how this will be accomplished

In general, identifiable information may not be obtained from private (non-public) records without the approval of the IRB and the informed consent of the subject. This includes activities intended to identify potential subjects who will later be approached to participate in research.

9.7.2 Maintaining the Confidentiality of Data

Confidentiality pertains to the treatment of information that an individual has disclosed in a relationship of trust and with the expectation that it will not be divulged to others in ways that are inconsistent with the original disclosure.

When information linked to individuals will be recorded as part of the research design, the IRB will consider whether adequate precautions will be taken to safeguard the confidentiality of the
information. The IRB will take into account the nature, probability, and magnitude of harms that would likely result from a disclosure of confidential information obtained through the research to unauthorized individuals or organizations.

IRB considerations regarding adequate provision for protecting confidentiality of the data shall include, as appropriate, whether:

- The data can be collected anonymously
- The data will be stored in a secure area
- Electronic files will be coded or encrypted
- Subject identifiers will be destroyed as soon as possible
- Access to the data will be limited
- A Certificate of Confidentiality should be considered to protect the identity of subjects from subpoena (e.g., in research where information obtained about subjects might interest law enforcement or other government agencies)
- Disclosures to subjects about confidentiality are adequate and that the confidentiality of identifiable data will be maintained in accordance with agreement between investigators and subjects
- Documentation of consent should be waived in order to protect subject confidentiality
- Any combination of data presents the risk of subject identification

9.8 FUNDING SPECIFIC APPROVAL CRITERIA

When a federal agency funds or oversees research, the agency may impose additional requirements above those required by the common rule. The specific agency’s requirements must then be met in order to approve the project. Reviewer guide sheets that parallel the following policies and procedures are used by the HRPP to ensure that agency specific requirements and guidance are applied before approval is granted. The reviewer Guides are accessible to investigators via the IRB websites and are also provided to researchers pursuing funding from agencies with funding specific approval criteria to aid them in preparation of a project.

9.8.1 Department of Defense (DoD)

Additional criterion for meeting DoD requirements and guidance are as follows. While the IRB may use of the following criteria as a guide in approving projects not funded by the DoD, they must be applied to projects funded by the DoD. The IRB will verify that the project meets the appropriate requirements by using the DoD Reviewer Guide before approving research.

Reporting Requirements

When following Department of Defense (DoD) regulations and requirements, in addition to any other required reporting, the HRPP will also promptly report to the DoD human research protection officer:

- Any serious or continuing non-compliance.
- When significant changes to the research protocol are approved by the IRB.
- The results of the IRB continuing review.
- Change of reviewing IRB.
- When the organization is notified by any Federal department, agency or national organization that any part of the HRPP is under investigation for cause involving a DoD-supported research protocol.
• Any unanticipated problem involving risks to participants or others.

Records maintained that document compliance or non-compliance with DoD regulations shall be made accessible for inspection and copying by representatives of the DoD at reasonable times and in a reasonable manner as determined by the supporting DoD component.

Experimental Subject

An activity involving an “experimental subject” is defined as an activity, for research purposes, where there is an intervention or interaction with a human being for the primary purpose of obtaining data regarding the effect of the intervention or interaction (DoDD 3216.02).

When a project is DoD funded, if the research participant meets the definition of “experimental subject,” a waiver of the consent process is prohibited unless a waiver is obtained from Secretary of Defense or, the Secretary of the DoD component when the project is to advance the development of a medical product necessary to the Armed Forces and the research project may directly benefit the subject. In these cases the project may be approved by the IRB but the PI will be informed that the waiver must be obtained before research commences. If the research participant does not meet the definition of “experimental subject,” the IRB may waive the consent process. The IRB may approve a consent procedure which does not include, or which alters, some or all of the elements to be disclosed as a part of the informed consent process without approval from the Secretary.

Minimal Risk

When following Department of Defense regulations and requirements, the definition of minimal risk based on the phrase “ordinarily encountered in daily life or during the performance of routine physical or physiological examination or tests” shall not be interpreted to include the inherent risks certain categories of human subjects face in their everyday life. For example the risks imposed in research involving human subjects focused on a special population should not be evaluated against the inherent risks encountered in their work environment (e.g., emergency responder, pilot, soldier in a combat zone) or having a medical condition (e.g., frequent medical tests or constant pain.)

Applicability of Subparts B, C and D to DoD Research

When following Department of Defense (DoD) regulations and requirements, research involving pregnant women, prisoners, and children are subject to the DHHS Subparts B, C. and D with the following modifications:

• For purposes of applying Subpart B, the phrase “biomedical knowledge” shall be replaced with “generalizable knowledge.”
• The applicability of Subpart B is limited to research involving pregnant women as participants in research that is more than minimal risk and included interventions or invasive procedures to the woman or the fetus or involving fetuses or neonates as participants.
• Fetal research must comply with the US Code Title 42, Chapter 6A, Subchapter III, Part H, 289g.
• Research involving prisoners cannot be reviewed by the expedited procedure.
When the IRB reviews research involving prisoners, at least one prisoner representative must be present for quorum.

In addition to allowable categories of research on prisoners in Subpart C, epidemiological research is also allowable when:

- The research describes the prevalence or incidence of a disease by identifying all cases or studies potential risk factor association for a disease.
- The research presents no more than minimal risk.
- The research presents no more than an inconvenience to the participant.

When a prisoner becomes a subject, if the researcher asserts to the IRB that it is in the best interest of the prisoner-participant to continue to participate in the research while a prisoner, the IRB chair may determine that the prisoner-participant may continue to participate until the convened IRB can review this request to approve a change in the research protocol and until the organizational official and DoD Component office review the IRB’s approval to change the research protocol. Otherwise, the IRB chair shall require that all research interactions and interventions with the prisoner-subject (including obtaining identifiable private information) cease until the convened IRB can review this request to approve a change in the research protocol. The convened IRB, upon receipt of notification that a previously enrolled human participant has become a prisoner, shall promptly re-review the research protocol to ensure that the rights and wellbeing of the human subject, now a prisoner, are not in jeopardy. The IRB should consult with a subject matter expert having the expertise of a prisoner representative if the IRB reviewing the research protocol does not have a prisoner representative. If the prisoner-participant can continue to consent to participate and is capable of meeting the research protocol requirements, the terms of the prisoner-participant’s confinement does not inhibit the ethical conduct of the research, and there are no other significant issues preventing the research involving human participants from continuing as approved, the convened IRB may approve a change in the study to allow this prisoner-participant to continue to participate in the research. This approval is limited to the individual prisoner-participant and does not allow recruitment of prisoners as participants.

Research involving a detainee as a human participant is prohibited. This prohibition does apply to research involving investigational drugs and devises when the same products would be offered to US military personnel in the same location for the same condition.

Research involving children cannot be exempt.

**Additional Educational Requirements**

When a project is to be funded by DoD, initial and continuing research ethics education is required for all personnel who conduct, review, approve, oversee, support, or manage human participants research. These requirements are typically met through the initial and continuing educational programs described in sections 3.1.1 and 3.1.2. Whenever specific DoD educational requirements or certifications are required, the IRB will not approve a study submittal until all are met.

The IRB staff, chair, and members as well as Researchers and Research Staff become aware of and educated about the specific requirements contained in Department of Defense regulations and requirements when appropriate. This occurs by providing appropriate personnel with the UB IRB Guide/Evaluation for Review of Department of Defense (DoD) Additional Criteria.
Scientific Review
All substantive amendments to approved research undergo scientific review as a part of the review conducted by the IRB.

International Populations
In addition to the safeguards included in the criteria for approval of other projects involving international populations (See Section 10.6: International Research), when following DoD regulations, the IRB will ensure that the researcher has permission to conduct research in that country by certification or local ethics review. The researcher will also be required to provide the IRB with an assurance that the proposed project will follow all local laws, regulations, customs, and practices.

Survey Research with DoD Personnel
Surveys which are intended specifically to be performed on Department of Defense personnel must be submitted, reviewed, and approved by the Department of Defense after the research project is reviewed and approved by the IRB.

Multi-Site Research
When conducting multi-site research, a formal agreement between organizations is required to specify the roles and responsibilities of each party.

Research Monitors
The IRB will consider the appointment of a research monitor. A research monitor is required for research involve greater than minimal risk. The IRB can also require a research monitor for a portion of the research or studies involving no more than minimal risk, when appropriate.

The research monitor may be a member of the IRB or another individual designated by the IRB. The monitor may be an ombudsman or a member of the data safety monitoring board. There may be more than one research monitor (e.g. if different skills or experience are needed but any/all research monitors shall be independent of the team conducting the research.

The independent research monitor must be appointed by name. While the duties of the research monitor are determined on the basis of specific risks or concerns about the research a research monitor generally has the authority to:
- Stop a research study in progress.
- Remove individuals from study.
- Take any steps to protect the safety and well being of participants until the IRB or EC can assess the situation.
- Perform oversight functions (e.g. observe recruitment, enrollment procedures, and the consent process, oversee study interventions and interactions, review monitoring plans and unanticipated problems involving risks to participants or others, oversee data matching, data collection and analysis).
- Discuss the research protocol with researchers, interview human subjects, and consult with others outside of the study.
- Report observations and findings to the IRB or other designated official.

The IRB must approve a written summary of the monitors’ duties, authorities, and responsibilities and shall communicate with research monitors to confirm their duties, authorities, and responsibilities.
Research with Military Personnel
When research is intended to involve U.S. military personnel as the principal participants, the project must include additional protections for military research participants to minimize undue influence. These protections must include the following procedures:

- Officers are not permitted to influence the decision of their subordinates.
- Officers and senior non-commissioned officers may not be present at the time of recruitment.
- Officers and senior non-commissioned officers must have a separate opportunity to participate.
- When recruitment involves a percentage of a unit, an independent ombudsman is present.
- When research involves U.S. military personnel, policies and procedures require limitations on dual compensation:
  - Prohibit an individual from receiving pay of compensation for research during duty hours.
  - An individual may be compensated for research if the participant is involved in the research when not on duty.

Consent Disclosure Requirements
The IRB will determine that the consent disclosure includes that provisions for research-related injury follow the requirements of the DoD component.

The exception from consent in emergency medicine research is prohibited unless a waiver is obtained from the Secretary of Defense.

If consent is to be obtained from the experimental subjects’ legal representative, the research must intend to benefit the individual participant. The determination that research is intended to be beneficial to the individual experimental subject must be made by an IRB.

Prisoners of War
Research involving prisoners of war is prohibited and may not be approved. The IRB will be made aware of the definition of “prisoner of war” for the DoD component granting the addendum.

Prisoner of War (POW) is generally defined as a detained person as defined in Articles 4 and 5 of the Geneva Convention Relative to the Treatment of Prisoners of War of August 12, 1949. In particular, one who, while engaged in combat under orders of his government, is captured by the armed forces of the enemy.

9.8.2 Department of Justice (DoJ)
Additional criterion for meeting DoJ requirements and guidance are as follows. While the IRB may use of the following criteria as a guide in approving projects not funded by the DoJ, Section 9.8.2.1 must be applied to projects funded by the National Institute of justice and Section 9.8.2.2 must be applied to projects which are both funded by the DOJ and conducted within the Bureau
of Prisons. The IRB will verify that the project meets the appropriate requirements by using the DOJ Reviewer Guide before approving research.

9.8.2.1 When a project is funded by the National Institute of Justice (NIJ):

- All Researchers and Research Staff are required to sign employee confidentiality statements, which are maintained by the responsible Researcher.
- All projects are required to have a privacy certificate approved by the NIJ human subject protection officer.
- Under a privacy certificate, Researchers and Research Staff do not have to report child abuse unless the participant signs another consent document to allow child abuse reporting.
- The confidentiality statement on the consent document must state that confidentiality can only be broken if the participant reports immediate harm to participants or others.
- A copy of all data must be de-identified and sent to the National Archive of Criminal Justice Data, including copies of the informed consent document, data collection instruments, surveys, or other relevant research materials.

9.8.2.2 When DOJ funded research is conducted within the Bureau of Prisons:

- Implementation of Bureau programmatic or operational initiatives made through pilot projects is not considered to be research.
- The Organization, IRB, and Researchers and Research Staff must follow the requirements of 28 CFR 512, including:
  - The project must not involve medical experimentation, cosmetic research, or pharmaceutical testing.
  - The research design must be compatible with both the operation of prison facilities and protection of human participants.
  - The Researcher must observe the rules of the institution or office in which the research is conducted.
  - Any Researcher who is a non-employee of the Bureau must sign a statement in which the Researcher agrees to adhere to the requirements of 28 CFR 512.
  - All research proposals will be reviewed by the Bureau Research Review Board.
- The project must have an adequate research design and contribute to the advancement of knowledge about corrections.
- The Researcher must have academic preparation or experience in the area of study of the proposed research.
- The Researcher must assume responsibility for actions of any person engaged to participate in the research project as an associate, assistant, or subcontractor to the Researcher.
- The selection of participants within any one organization must be equitable.
- Incentives may not be offered to help persuade inmate participants to participate. However, soft drinks and snacks to be consumed at the test setting may be offered.
- Reasonable accommodations such as nominal monetary recompense for time and effort may be offered to non-confined research participants who are both:
  - No longer in Bureau of Prisons custody.
  - Participating in authorized research being conducted by Bureau employees or contractors.
• A non-employee of the Bureau may receive records in a form not individually identifiable when advance adequate written assurance that the record will be used solely as a statistical research or reporting record is provided to the agency.

• Except as noted in the consent statement to the participant, the Researcher must not provide research information that identifies a participant to any person without that participant’s prior written consent to release the information. For example, research information identifiable to a particular individual cannot be admitted as evidence or used for any purpose in any action, suit, or other judicial, administrative, or legislative proceeding without the written consent of the individual to whom the data pertain.

• Except for computerized data records maintained at an official Department of Justice site, records that contain non-disclosable information directly traceable to a specific person may not be stored in, or introduced into, an electronic retrieval system.

• If the Researcher is conducting a study of special interest to the Office of Research and Evaluation (ORE) but the study is not a joint project involving ORE, the Researcher may be asked to provide ORE with the computerized research data, not identifiable to individual participants, accompanied by detailed documentation. These arrangements must be negotiated prior to the beginning of the data collection phase of the project.

• Policies and procedures indicate that for research conducted within the Bureau of Prisons required elements of disclosure include:
  o Identification of the Researchers.
  o Anticipated uses of the results of the research.
  o A statement that participation is completely voluntary and that the participant may withdraw consent and end participation in the project at any time without penalty or prejudice (the inmate will be returned to regular assignment or activity by staff as soon as practicable).
  o A statement regarding the confidentiality of the research information and exceptions to any guarantees of confidentiality required by federal or state law. For example, a Researcher may not guarantee confidentiality when the participant indicates intent to commit future criminal conduct or harm himself or herself or someone else, or, if the participant is an inmate, indicates intent to leave the facility without authorization.
  o A statement that participation in the research project will have no effect on the inmate participant's release date or parole eligibility.

• When submitting a research project, the applicant shall provide the following information:
  o A summary statement, which includes:
    ▪ Names and current affiliations of the Researchers.
    ▪ Title of the study.
    ▪ Purpose of the study.
    ▪ Location of the study.
    ▪ Methods to be employed.
    ▪ Anticipated results.
    ▪ Duration of the study.
    ▪ Number of participants (staff or inmates) required and amount of time required from each.
    ▪ Indication of risk or discomfort involved as a result of participation.
  o A comprehensive statement, which includes:
    ▪ Review of related literature.
    ▪ Detailed description of the research method.
Significance of anticipated results and their contribution to the advancement of knowledge.

Specific resources required from the Bureau of Prisons.

Description of all possible risks, discomforts, and benefits to individual participants or a class of participants, and a discussion of the likelihood that the risks and discomforts will actually occur.

Description of steps taken to minimize any risks.

Description of physical or administrative procedures to be followed to:
- Ensure the security of any individually identifiable data that are being collected for the study.
- Destroy research records or remove individual identifiers from those records when the research has been completed.

Description of any anticipated effects of the research study on organizational programs and operations.

Relevant research materials such as vitae, endorsements, sample consent statements, questionnaires, and interview schedules.

A statement regarding assurances and certification required by federal regulations, if applicable.

- At least once a year, the Researcher shall provide the Chief, Office of Research and Evaluation, with a report on the progress of the research.
- At least 12 working days before any report of findings is to be released, the Researcher shall distribute one copy of the report to each of the following: the chairperson of the Bureau, Research Review Board, the regional director, and the warden of each institution that provided data or assistance. The Researcher shall include an abstract in the report of findings.
- In any publication of results, the Researcher shall acknowledge the Bureau's participation in the research project.
- The Researcher shall expressly disclaim approval or endorsement of the published material as an expression of the policies or views of the Bureau.
- Prior to submitting for publication the results of a research project conducted under this subpart, the Researcher shall provide two copies of the material, for informational purposes only, to the Chief, Office of Research and Evaluation, Central Office, Bureau of Prisons.

### 9.8.3 Department of Education (DoEd)

Additional criterion for meeting DoEd requirements and guidance are as follows. Sections 9.8.3.1-9.8.3.3 apply only to projects directly funded by the U.S. Department of Education or otherwise subject to the U.S. Department of Education regulations and guidance. The IRB will verify that the project meets the requirements of the Department of Education Reviewer Guide before approving research.

#### 9.8.3.1 Inclusion of Children with Disabilities

When the project purposefully requires inclusion of children with disabilities or individuals with mental disabilities as research participants that is funded by the National Institute on Disability...
and Rehabilitation Research, the IRB will include at least one person primarily concerned with the welfare of these research participants. At least one of these members must contribute to the project review either by attendance at the convened meeting where the protocol is voted on or via providing their written review of the protocol to the IRB.

The IRB will ensure that research projects comply with the Family Educational Rights and Privacy Act (FERPA) with respect to access to Educational Records.

**9.8.3.2 Access to Educational Records**

Access to education records for research purpose will typically require authorization. In the case of post secondary records, the authorization may be granted by the student. In other cases, the parent or guardian must authorize access of the records. The authorization may be a part of the consent document or may be a separate document.

The IRB is authorized to grant exceptions to parental or student authorization to release student records for research. These determinations must fall into one of the following categories:

A. An educational agency or institution associated may disclose personally identifiable information from an education record of a student without consent if the disclosure is to a researcher conducting studies for, or on behalf of the educational agency or institution to:
   - Develop, validate, or administer predictive tests
   - Administer student aid programs
   - Improve instruction.

A school district or postsecondary institution that uses this exception is required to enter into a written agreement with the Organization or Researcher conducting the research that specifies:
   - The determination of the exception.
   - The purpose, scope, and duration of the study.
   - The information to be disclosed.
   - That information from education records may only be used to meet the purposes of the study stated in the written agreement and must contain the current requirements in Department of Education regulations on redisclosure and destruction of information.
   - That the study will be conducted in a manner that does not permit personal identification of parents and students by anyone other than representatives of the Organization with legitimate interests.
   - That the Organization is required to destroy or return all personally identifiable information when no longer needed for the purposes of the study.
   - The time period during which the Organization must either destroy or return the information.

B. Education records may be released without consent under FERPA if all personally identifiable information has been removed including:
   - Student’s name and other direct personal identifiers, such as the student’s social security number or student number.
• Indirect identifiers, such as the name of the student’s parent or other family members; the student’s or family’s address, and personal characteristics or other information that would make the student’s identity easily traceable; and date and place of birth and mother’s maiden name.

• Biometric records, including one or more measurable biological or behavioral characteristics that can be used for automated recognition of an individual, including fingerprints, retina and iris patterns, voiceprints, DNA sequence, facial characteristics, and handwriting.

• Other information that, alone or in combination, is linked or linkable to a specific student that would allow a reasonable person in the school community, who does not have personal knowledge of the relevant circumstances, to identify the student with reasonable certainty.

9.8.3.3 Access to instructional material

Instructional material used in a research or experimentation program that is funded by the U.S. Department of Education must meet the following:

• All instructional material—including teachers’ manuals, films, tapes, or other supplementary instructional material—which will be used in connection with any research or experimentation program or project must be available for inspection by the parents or guardians of the children engaged in such research.

• Research or experimentation program or project means any program or project in any research that is designed to explore or develop new or unproven teaching methods or techniques.

• Children are persons enrolled in research not above the elementary or secondary education level, who have not reached the age or majority as determined under state law.

The IRB will ensure that research projects comply with the following Protection of Pupil Rights Amendment for projects directly funded by the U.S. Department of Education.

No student will be required, as part of any research project, to submit without prior consent to surveys, psychiatric examination, testing, or treatment, or psychological examination, testing, or treatment, in which the primary purpose is to reveal information concerning one or more of the following:

• Political affiliations or beliefs of the student or the student’s parent.
• Mental or psychological problems of the student or the student’s family.
• Sex behavior or attitudes.
• Illegal, anti-social, self-incriminating, or demeaning behavior.
• Critical appraisals of other individuals with whom respondents have close family relationships.
• Legally recognized privileged or analogous relationships, such as those of lawyers, physicians, and ministers.
• Religious practices, affiliations, or beliefs of the student or student’s parent.
• Income (other than that required by law to determine eligibility for participation in a program or for receiving financial assistance under such program.

Prior consent means:

• Prior consent of the student, if the student is an adult or emancipated minor.
9.8.3.4 Research not directly funded by the U.S. Department of Education and conducted in a school that receives funding from the U.S. Department of Education

For research projects not directly funded by the U.S. Department of Education and conducted in a non-postsecondary school that receives funding from the U.S. Department of Education: The IRB will require that the researcher provides evidence to verify compliance with U.S. Department of Education regulations that schools are required to develop and adopt policies in conjunction with parents regarding the following:

- The right of a parent of a student to inspect, upon the request of the parent, a survey created by a third party before the survey is administered or distributed by a school to a student.
- Any applicable procedures for granting a request by a parent for reasonable access to such survey within a reasonable period of time after the request is received.
- Arrangements to protect student privacy that are provided by the agency in the event of the administration or distribution of a survey to a student containing one or more of the following items (including the right of a parent of a student to inspect, upon the request of the parent, any survey containing one or more of such items):
  - Political affiliations or beliefs of the student or the student’s parent.
  - Mental or psychological problems of the student or the student’s family.
  - Sex behavior or attitudes.
  - Illegal, anti-social, self-incriminating, or demeaning behavior.
  - Critical appraisals of other individuals with whom respondents have close family relationships.
  - Legally recognized privileged or analogous relationships, such as those of lawyers, physicians, and ministers.
  - Religious practices, affiliations, or beliefs of the student or the student’s parent.
  - Income (other than that required by law to determine eligibility for participation in a program or for receiving financial assistance under such program).
  - The right of a parent of a student to inspect, upon the request of the parent, any instructional material used as part of the educational curriculum for the student.
- Any applicable procedures for granting a request by a parent for reasonable access to instructional material received.
- The administration of physical examinations or screenings that the school or agency may administer to a student.
- The collection, disclosure, or use of personal information collected from students for the purpose of marketing or for selling that information (or otherwise providing that information to others for that purpose), including arrangements to protect student privacy that are provided by the agency in the event of such collection, disclosure, or use.
- The right of a parent of a student to inspect, upon the request of the parent, any instrument used in the collection of personal information before the instrument is administered or distributed to a student.
Any applicable procedures for granting a request by a parent for reasonable access to such instrument within a reasonable period of time after the request is received.

9.8.4 Department of Energy (DoE)

Additional criterion for meeting DoE requirements are as follows:

In order for a project to be approved when following Department of Energy requirements and guidance, the organization must periodically conduct self-assessments to ensure compliance with the HRPP procedures and other requirements. This requirement is met through the AAHRPP accreditation process. The IRB of record for the specific project will contact the IO/HRPP Administrator to verify that the self assessment for AAHRPP is current before approving the specific project.

When a project utilizes personally identifiable information (PII), researchers will be provided with the “DOE CHECKLIST FOR USE BY RESEARCHERS CONDUCTING HUMAN SUBJECTS RESEARCH THAT UTILIZES PERSONALLY IDENTIFIABLE INFORMATION (PII)” to be used in protocol design. The IRB will verify that the protocol meets the requirements of the “DOE INSTITUTIONAL REVIEW BOARD TEMPLATE FOR REVIEWING HUMAN SUBJECTS RESEARCH PROTOCOLS THAT UTILIZE PERSONALLY IDENTIFIABLE INFORMATION (PII)” before approving research.

Researchers must also promptly (within 3 days of learning of the occurrence) report the following to the human subject research program manager:

- Any significant adverse events, unanticipated risks; and complaints about the research, with a description of any corrective actions taken or to be taken.
- Any suspension or termination of IRB approval of research.
- Any significant non-compliance with HRPP procedures or other requirements.

Any compromise of personally identifiable information must be reported to the human subject research program manager immediately (within one (1) business day of learning of the occurrence).

9.8.5 Environmental Protection Agency (EPA)

Additional criterion for meeting Environmental Protection Agency (EPA) requirements and guidance apply only to research conducted or supported by the EPA or intended to be submitted to the EPA. In these cases, the provisions of 40 CFR 26 are extended to human research involving the intentional exposure of non-pregnant, non-nursing adults to any substance. Therefore, before approving research the IRB will ensure that:

- Research will not involve the intentional exposure of pregnant women, nursing women, or children to any substance.
- 40 CFR 26 Subparts C and D will be applied in order to provide additional protections to pregnant women and children as participants in observational research, i.e., research that does not involve intentional exposure to any substance.
Documentation of IRB determinations and approval will be provided to the investigator who must provide them to the EPA human subject research review official for final review and approval before the research can begin.

While the intentional exposure of pregnant women, nursing women, or children to any substance is not allowed under EPA regulations and guidance, observational research is permissible for these populations as long as the research adheres to the following additional requirements.

Observational research involving pregnant women may only be approved if it meets the requirements of 40 CFR 26 and 45 CFR 46 Subpart B as follows:

§ 26.301 To what does this subpart apply?
(a) Except as provided in paragraph (b) of this section, this subpart applies to all observational research involving human subjects who are pregnant women (and therefore their fetuses) conducted or supported by the Environmental Protection Agency (EPA). This includes research conducted in EPA facilities by any person and research conducted in any facility by EPA employees.
(b) The exemptions at §26.101(b)(1) through (b)(6) are applicable to this subpart.
(c) The provisions of §26.101(c) through (i) are applicable to this subpart. References to State or local laws in this subpart and in §26.101(f) are intended to include the laws of federally recognized American Indian and Alaska Native Tribal Governments.
(d) The requirements of this subpart are in addition to those imposed under the other subparts of this part.

§ 26.302 Definitions.
The definitions in §§26.102 and 26.202 shall be applicable to this subpart as well. In addition, observational research means any human research that does not meet the definition of research involving intentional exposure of a human subject in §26.202(a).

§ 26.303 Duties of IRBs in connection with observational research involving pregnant women and fetuses.
The provisions of 45 CFR 46.203 are applicable to this section.

§ 26.304 Additional protections for pregnant women and fetuses involved in observational research.
The provisions of 45 CFR 46.204 are applicable to this section.

§ 26.305 Protections applicable, after delivery, to the placenta, the dead fetus, or fetal material.
The provisions of 45 CFR 46.206 are applicable to this section.

Observational research involving children may only be approved if it falls into one of the following two categories:

A. Observational research involving children that does not involve greater than minimal risk may be approved only if the IRB finds that adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians, as set forth in 40 CFR 26.406.

B. Observational research involving children that involves greater than minimal risk but presenting the prospect of direct benefit to the individual participants if the IRB finds and documents that:
   i. The intervention or procedure holds out the prospect of direct benefit to the individual participant or is likely to contribute to the participant's well-being.
ii. The risk is justified by the anticipated benefit to the participants.
iii. The relation of the anticipated benefit to the risk is at least as favorable to the participants as that presented by available alternative approaches.
iv. Adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians, as set forth in 26.406.
10. VULNERABLE POPULATIONS/GROUPS REQUIRING SPECIAL CONSIDERATION

10.1 OVERVIEW

Vulnerable subjects in research: individuals who lack the capacity to provide informed consent or whose willingness to participate in research may be unduly influenced by others.

Because the ongoing informed consent process is the primary means for subjects to protect themselves in research, vulnerability pertains above all to threats to an individual’s ability to grant voluntary informed consent.

The investigator is required to indicate the involvement of potentially vulnerable populations/groups to the IRB in the application documents (usually in the protocol) and provide a description of safeguards to protect the rights and welfare of vulnerable subjects. The IRB may require further protections for safeguarding those subjects as a condition of approval.

Although federal regulations only identify special protections for specific populations, (i.e., children, prisoners, pregnant women and fetuses, and neonates), each project reviewed by the IRB is evaluated for circumstances that may place subjects in vulnerable situations that call for special consideration. If the IRB identifies such circumstances, additional protections for safeguarding those subjects may be required as a condition of approval.

Generally, approval for research projects involving vulnerable populations/groups may be considered if one of the following conditions is met:

- The research does not involve more than minimal risk to the subject
- The research is likely to benefit the subject directly, even though the risks are considered to be more than minimal
- The research involves greater than minimal risk with no prospect of direct benefit to individual subjects but is likely to yield generalizable knowledge about the subject’s disorder or condition

10.2 RESEARCH INVOLVING PREGNANT WOMEN, HUMAN FETUSES AND NEONATES

10.2.1 Overview

DHHS regulations at 45 CFR 46 Subpart B covers research involving pregnant women, human fetuses, neonates, human in vitro fertilization as well as human fetal tissue, and placenta or post-delivery fetal material. DHHS conditions for approval of research involving these subject populations include the:

- Scientific appropriateness of the research,
- Acceptability of potential risks and benefits,
- Compliance with additional informed consent provisions,
- Absence of any inducements to terminate a pregnancy, and
- Confirmation of the independence of the researchers from the decisions related to pregnancy termination or any decisions related to the determination of viability of a neonate.
In general, the IRB shall consider:

- For all studies, whether women will be appropriately represented
- For all studies, whether there is reason to exclude pregnant or lactating women and, if so, how strict the screening measures should be
- For studies involving pregnant women, whether appropriate studies on animals and non-pregnant humans have been conducted
- For studies directed toward maternal health, whether risks to the fetus are minimized
- For studies directed toward maternal health, whether the mother will be adequately informed of the potential risk to the fetus as well as of any alternative treatments and their risks and benefits
- For studies of pregnancy, labor, or delivery, whether the risk to the fetus is no greater than minimal
- For studies of pregnancy, labor, or delivery, whether the father's consent is required
- For studies of lactating women, whether the supply and content of breast milk is adequately protected
- For studies of conception or contraception, whether the risks, benefits, reversibility, and alternatives are adequately explained in the consent document
- For contraceptive studies, whether there is adequate explanation of possible failure and of the options available for dealing with unintended pregnancies

### 10.2.2 IRB Requirements for Approval of Biomedical Research Involving Pregnant Women and Fetuses

The IRB shall only approve biomedical research involving pregnant women or fetuses if the conditions outlined in DHHS regulations 45 CFR 46 Subpart B are met. IRB requirements for approval are summarized below according to the subject populations defined by OHRP:

- **Research Involving Pregnant Women or Fetuses Prior to Delivery** [45 CFR 46.204]
  
  Pregnant women or fetuses prior to delivery may be involved in research if all of the following conditions are met:
  
  - Where appropriate, prior animal studies and clinical studies with non-pregnant women have been conducted and provide data for assessing potential risks to pregnant women and fetuses;
  - Any risk is the least possible for achieving the objectives of the research;
  - The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus, or, if there is no such prospect of benefit, the risk to the fetus is not greater than minimal, and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means.
  - No inducements, monetary or otherwise, will be offered to terminate a pregnancy;
  - Investigators will have no part in decisions about the timing, method, or procedures used to terminate a pregnancy or decisions regarding the viability of a fetus.
  - The consent form clearly explains the reasonably foreseeable impact of the research on the fetus, and
  - Consent will be obtained from the appropriate individuals (see Section 14: The Informed Consent Process)
  - For children who are pregnant, assent and permission are obtained in accord with the provisions of the DHHS 45 CFR 46 Subpart D: Protections for Children Involved as Participants (for details see Section 14: The Informed Consent Process)
• **Research Involving Fetuses after Delivery [45 CFR 46.205]**
  o Fetuses of Uncertain Viability: After delivery, and until it has been ascertained whether a fetus is viable, a fetus may not be involved in research unless all of the following conditions are met:
    - The research holds out the prospect of enhancing the probability of survival of the fetus to the point of viability, and any risk is the least possible for achieving that objective, or
    - The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means and there will be no added risk to the fetus resulting from the research
  For informed consent requirements, see Section 14: The Informed Consent Process.
  o Nonviable fetuses: After delivery, a nonviable fetus may not be involved in research unless all of the following conditions are met:
    - Vital functions of the fetus will not be artificially maintained
    - The research will not terminate the heartbeat or respiration of the fetus
    - There will be no added risk to the fetus resulting from the research, and
    - The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means
  For informed consent requirements, see Section 14: The Informed Consent Process.

  o Viable fetuses and neonates
    - A fetus, after delivery, that has been determined to be viable, is a child as determined by DHHS 45 CFR 46.402(a) and may be included in research only to the extent permitted by, and in accord with, the requirements of DHHS 45 CFR 46 both subparts A and D, special protections for children, and FDA 21 CFR 50 subpart D, special protection for children in clinical investigations.

• **Research Involving, After Delivery, the Placenta, the Dead Fetus or Fetal Material [45 CFR 46.206]**
  o Research involving (after delivery), the placenta, the dead fetus, macerated fetal material, or cells, tissue, or organs excised from a dead fetus, shall be conducted only in accord with any applicable federal, state, or local laws and regulations regarding such activities.
  o If identifying data are associated with the material in a manner that living individuals can be identified, directly or through identifiers linked to those individuals, those individuals are considered to be research subjects and all pertinent privacy protection measures are applicable.

• **Research Involving Human *in vitro* Fertilization**
  o DHHS regulations require that all research involving human *in vitro* fertilization or embryo transfer to be reviewed by a national Ethics Advisory Board before it can be funded by the Department [45 CFR 46.204(d)]. The lapse in the Board has precluded federal funding of human *in vitro* fertilization research, which plans to establish guidelines for research in this area.
  o When a project is submitted for review involving privately funded *in vitro* fertilization research, the IRB shall consult with the American College of Obstetricians and Gynecologists (ACOG) and the American Fertility Society (AFS) National Advisory Board on Ethics in Reproduction.
10.2.3 IRB Requirements for Approval of Behavioral Research Involving Pregnant Women

The following requirement of Subpart B for the involvement in research of Pregnant Women or Fetuses Prior to Delivery [45 CFR 46.204] that “the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means” cannot be met in most social, behavioral and educational research. In addition, when there is no reasonably foreseeable risk to the physical health of the mother or fetus that would be caused by participation in a study, requiring that consent be obtained from the father for the mother’s participation does not provide any additional protection for either the mother or the fetus. If these requirements were applied as written in most behavioral research, the principle of justice would be violated by causing the exclusion of pregnant women from participation in research in which there was no reasonable reason for their exclusion.

For behavioral studies, the IRB or expedited reviewers may make the following determinations:

- The IRB may determine that the Additional Protections of 45CFR46 Subpart B for Pregnant Women, Human Fetuses and Neonates Involved in Research are unnecessary for the involvement of Pregnant women in the research because the intervention or interaction is solely of a behavioral nature (i.e. involving no medical intervention and no strenuous physical activity) presenting no known risks to the fetus or newborn child. Consent of the father is not required in these cases. This determination will be documented in protocol approval documentation.
- Where behavioral studies would present risks to the mother or fetus (e.g. alcohol administration studies, studies involving significant physical activity) pregnant women must be excluded from participation based on an appropriate screening process.
- In any other cases, the requirements for approval of biomedical research involving pregnant women, fetuses and neonates will be followed.

In all cases:

- No inducements, monetary or otherwise, will be offered to terminate a pregnancy;
- Investigators will have no part in decisions about the timing, method, or procedures used to terminate a pregnancy or decisions regarding the viability of a fetus.
- For children who are pregnant, assent and permission are obtained in accord with the provisions of the DHHS 45 CFR 46 Subpart D: Protections for Children Involved as Participants (for details see Section 14: The Informed Consent Process)

10.3 RESEARCH INVOLVING PRISONERS

UB IRBs comply with the regulatory requirements for research involving prisoners as outlined in DHHS 45 CFR 46, Subpart C. The term “prisoner” includes any individual who is:
- Involuntarily confined or detained in a penal institution,
- Sentenced to serve time in a penal institution under a criminal or civil statute,
- Detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution, or is;
- Detained pending arraignment, trial, or sentencing.

The regulations that apply to prisoner enrollment in human subject research studies also apply to subjects already enrolled in a study who become incarcerated. Federal regulations do not differentiate between detention, jail, or prison. People incarcerated in any of these places are considered prisoners.
The IRB requires that, if the enrollment of prisoners is anticipated, it must be indicated in the protocol, and justification for research with this population must be provided to the IRB. If the study is not approved to recruit prisoners, the investigator may not enroll a prisoner.

For ongoing projects, if an enrolled subject becomes a prisoner and the study was not reviewed and approved by the IRB for the inclusion of prisoners, the following procedures will be followed:

A. When the investigator wishes to have the now-incarcerated prisoner-subject continue to participate in the research he/she must:
   - Notify the IRB immediately upon becoming aware of the incarceration and inform the IRB of the intent to amend the protocol to include prisoners as subjects
   - Cease all research interactions and interventions with, and obtaining private information about, the now-incarcerated prisoner-subject unless the IRB Chair determines that it is in the best interest of the individual to continue participation during the time required to meet the federal requirements of Subpart C
   - Begin the process to amend the existing protocol (using the Amendment Form) to include the enrollment of prisoners (to meet federal requirements of subpart C) and submit it to the IRB for review. Unless the IRB Chair has approved the continued participation by the now-incarcerated prisoner-subject during the time required to complete the requirements of Subpart C, all interventions and interactions with the individual must cease until requirements of Subpart C have been satisfied.

If a participant becomes a prisoner while enrolled in a research study that was not reviewed according to Subpart C if some of the requirements of Subpart C cannot be met, but it is in the best interest of the participant to remain in the study, the IRB may approve a procedure to keep the participant enrolled and will inform OHRP of the decision along with the justification if the project is DHHS-funded research project.

B. When the now-incarcerated prisoner-subject will be withdrawn from the research project and the withdrawal of the now-incarcerated prisoner-subject from the research involvement or intervention may increase risk to the subject, the investigator must:
   - Notify the IRB immediately upon becoming aware of the incarceration, and
   - Request a determination from the Chair that it is in the best interest of the now-incarcerated prisoner-subject to continue certain study interventions (e.g., drug treatment) as a non-subject for subject safety reasons until such time that he/she can be safely withdrawn from the interventions. This is accomplished through investigator submission of a Serious Events and Problems Report. (The IRB Chair may also make the independent determination that it is in the best interest of the now-incarcerated prisoner-subject to continue certain study interventions (e.g., drug treatment) as a non-subject for subject safety reasons until such time that he/she can be safely withdrawn from the interventions.)

Otherwise, the investigator will withdraw the now-incarcerated prisoner-subject from the study (where the withdrawal from the research involvement or intervention does not pose increased risk to the subject) as follows:
   - All research interactions and interventions with, and obtaining private information about, the now-incarcerated prisoner-subject must cease immediately upon becoming aware of the incarceration
   - The investigator must notify the IRB of the withdrawal at the time of continuing review on the Application for Continuing Review.

C. If a participant is incarcerated temporarily while enrolled in a study:
If the temporary incarceration has no effect on the study, the participant may remain enrolled
If the temporary incarceration has an effect on the study, handle according to the above guidance

For IRB review of research involving prisoners:
- The majority of the IRB board members (exclusive of prisoner members) shall have no association with the prison(s) involved, apart from their membership on the IRB.
- The IRB review shall include an individual with appropriate background and experience to serve as a prisoner representative, by nature of having experience or a close working knowledge, understanding and appreciation of prison conditions from the perspective of a prisoner.
- The prisoner representative must be present, as a voting member, and must present his/her review either orally or in writing at the full board meeting when the project is reviewed.
- The prisoner representative will receive all review materials pertaining to the research (i.e. the same materials as primary reviewer).
- The prisoner representative shall participate in the review of all research involving prisoners including initial reviews, continuing reviews, amendments/modifications, reportable events and problems, and other reviews that may be applicable.
- An expedited review process may be used when the research involves no greater than minimal risk, as defined for the prisoner population, only if the IRB’s prisoner representative is one of the designated reviewers.
- Research with prisoners does not qualify for exempt status review.
- The IRB shall approve only research studies involving prisoners as research subjects that meet one of the four categories described below:
  - Studies of the possible causes, effects, and processes of incarceration, and of criminal behavior, provided that the study presents no more than minimal risk and no more than inconvenience to the participants;
  - Studies of prisons as institutional structures or of prisoners as incarcerated persons, provided that the study presents no more than minimal risk and no more than inconvenience to the participants;
  - Research on conditions particularly affecting prisoners as a class (e.g., vaccine trials and other research on hepatitis which is a condition that is more prevalent in prisons than elsewhere; and research on social and psychological problems such as alcoholism, drug addiction, and sexual assaults) provided that the study may proceed only after the Department of Health & Human Services (DHHS) Secretary has consulted with appropriate experts including experts in penology, medicine, and ethics, and published notice, in the Federal Register, of the intent to approve such research; or
  - Research on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well-being of the participant. In cases in which those studies require the assignment of prisoners in a manner consistent with protocols approved by the IRB to control groups which may not benefit from the research, the study may proceed only after the DHHS Secretary has consulted with appropriate experts, including experts in penology, medicine, and ethics, and published notice, in the Federal Register, of the intent to approve such research.
  - As per DHHS Waiver, prisoners may be included in epidemiologic research in which the sole purposes are to describe the prevalence or incidence of a disease by identifying all cases or to study potential risk factor associations for a disease.
studies must pose no more than minimal risk and present no more than an inconvenience to the prisoner subjects, and prisoners must not be a particular focus of the research [Federal Register June 20, 2003 68 FR 36929].

In addition, the IRB shall only approve prisoner research studies when:

- Any possible advantages accruing to the prisoner through his or her participation in the research, when compared to the general living conditions, medical care, quality of food, amenities and opportunity for earnings in the prison, are not of such a magnitude that his or her ability to weigh the risks of the research against the value of such advantages in the limited choice environment of the prison is impaired;
- The risks involved in the research are commensurate with risks that would be accepted by non-prisoner volunteers;
- Procedures for the selection of participants within the prison are fair to all prisoners and are protected from arbitrary intervention by prison authorities or prisoners. Unless the principal investigator provides the IRB with justification in writing for following some other procedures, control participants must be selected randomly from the group of available prisoners who meet the characteristics needed for that particular research study;
- Information regarding the research is presented in a language and reading level that is understandable to the participant population;
- Adequate assurance exists that parole boards will not take into account a prisoner's participation in the research in making decisions regarding parole, and each prisoner is clearly informed in advance that participation in the research will have no effect on his/her parole; and
- When the IRB finds there may be a need for follow-up examination or care of participants after the end of their participation, adequate provision has been made for such examination or care, taking into account the varying lengths of individual prisoners' sentences, and for informing participants of this fact.

When the IRB approves a DHHS-funded research project that involves prisoners as subjects, the IO/HRPP Administrator will notify the Office for Human Research Protection (OHRP) indicating that the IRB has approved a study that will include prisoners, the category the study meets, as well as how the study satisfies the six criteria listed above. In addition to IRB approval, these research projects are not permitted to commence until written approval is received from OHRP on behalf of the DHHS Secretary.

For research that does not involve interaction with prisoners (e.g. existing data, record review) reviewed by the expedited procedure:

- The research may be reviewed by the expedited procedure, if a determination is made that the research involves no greater than minimal risk for the prison population being studied.
- Review by a prisoner representative is not required.
- The prisoner representative may review the research as a reviewer or consultant if designated by the IRB chair.
- Review of modifications and continuing review must use the same procedures as initial review.

10.4 RESEARCH INVOLVING CHILDREN

10.4.1 Overview
UB IRBs adhere to the regulatory requirements for research with children, as outlined in DHHS 45 CFR 46 Subpart D. The categories for approval of research involving children are based on the degree of risk and benefit to individual subjects as follows:

- **Research that does not involve greater than minimal risk** may be approved if the IRB finds that adequate provisions are made for soliciting the assent of the child and the permission of his/her parent(s) or guardian [45 CFR 46.404].

- **Research involving greater than minimal risk, but presenting the prospect of direct benefit to an individual participant, or a monitoring procedure that is likely to contribute to the participant's well-being**, may be approved if the IRB finds that [45 CFR 46.405]:
  - The risk is justified by the anticipated benefit to the participant;
  - The relationship of anticipated benefit to risk is at least as favorable as that presented by available alternative approaches; and
  - Adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians.

- **Research involving greater than minimal risk with no prospect of direct benefit to individual participants, but likely to yield generalizable knowledge about the participant's disorder or condition**, may be approved if the IRB finds that [45 CFR 46.406]:
  - The risk represents a minor increase over minimal risk;
  - The intervention or procedure presents experiences to participants that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations;
  - The intervention or procedure is likely to yield generalizable knowledge about the participant's disorder or condition which is of vital importance for the understanding, prevention, or alleviation of the participant's disorder or condition; and
  - Adequate provisions are made for soliciting permission of the parents or guardians and assent of the child.

- **Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children**, may be approved if the IRB finds that [45 CFR 46.407]:
  - The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children; or
  - When the study is funded by the DHHS, the DHHS Secretary has to determine either that the research in fact satisfies the conditions of 45 CFR 46.404, 46.405, or 46.406, or
  - The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children; and
  - The research will be conducted in accordance with sound ethical principles; and
  - Adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians, as set forth in 46.408.

### 10.4.2 Parental Permission and Assent of the Child

Generally, children may be subjects of research only if permission is obtained from at least one parent or a legal guardian unless the IRB determines that a study meets the requirements for waiving parental permission. The IRB will determine which of the following provisions for permission of parents and guardians must be followed:
• The permission of both parents is required if both parents are alive, known, competent, reasonably available, and have legal responsibility for the care and custody of the child. Otherwise, the permission of one parent is required.

• The permission of one parent is sufficient, even if the other parent is alive, known, competent, reasonably available, and shares legal responsibility for the care and custody of the child. (Not allowed for last two categories 45 CFR 46.406 & 45 CFR 46.407)

Generally, assent of the child will be obtained. For details regarding parental permission and child assent, see Section 14:13: Permission and Assent for Children.

10.4.3 Wards of the State

Research involving children who are wards of the state or any other agency, institution, or entity can be included in research under DHHS 45 CFR 46.406-407 only if that research is:

• Related to their status as wards, or

• Conducted in schools, camps, hospitals, institutions, or similar setting in which the majority of children involved as participants are not wards [DHHS 45 CFR 46.409]. For details, see Section 14:14: Wards of the State.

10.4.4 Children Who Reach the Age of Majority During the Course of Participation

The IRB will consider whether the project includes subjects who were enrolled in the research as children but will reach the age of majority during the course of participation and will require re-consenting as adults. The consent to continue in the research should be documented by having those subjects sign an adult consent form for continued participation at the next visit or intervention after turning 18. If subjects are undergoing any research procedure or intervention, a current, approved version of the consent form must be used. If, however, all research procedures and interventions have been completed and the subject is in long-term follow-up involving data collection only, the IRB may approve the use of an addendum to the consent for continued data collection.

10.5 OTHER GROUPS AND RESEARCH SITUATIONS REQUIRING SPECIAL CONSIDERATION

10.5.1 Overview

Every project reviewed by the IRB is evaluated for circumstances that may place subjects in vulnerable situations and call for special protection. When a subject group is identified as being “vulnerable” in a particular research setting, the IRB will consider whether the protocol provides adequate protections for those subjects. The IRB may require additional protections for safeguarding those subjects as a condition of approval. Some of the more commonly encountered groups and situations requiring special consideration are described below.

10.5.2 Adults Unable to Provide Consent

There are currently no specific federal regulations to address the needs of this vulnerable population. UB IRB policy for decisionally impaired adults who are unable to provide consent is to generally follow recommendations governing the conduct of research in children. The IRB to make the final determination on the appropriateness of involving decisionally impaired subjects.
Decisionally impaired persons are those who have a diminished capacity for judgment and reasoning due to developmental, psychiatric, organic, or other disorders that affect cognitive or emotional functions. Other individuals, who may be considered decisionally impaired (with limited decision-making capacity) are individuals under the influence of or are dependent on drugs or alcohol, those suffering from degenerative diseases affecting the brain, terminally ill patients, and persons with severely disabling physical disabilities. Decisional impairment/incapacity may be temporary, permanent, progressive, or fluctuating.

If it is anticipated that decisionally impaired subjects will be enrolled in a study, the IRB shall consider whether the investigator has provided adequate justification for the inclusion of those subjects and how adequate informed consent will be obtained. The IRB shall also consider provisions for assessment of the decision-making capacity of subjects who may require consent by the subject’s Legally Authorized Representative (LAR). The IRB may require an independent determination of the capacity of the subject.

In general, the IRB shall approve projects when the intended study population is decisionally impaired subjects only when:

- Such subjects comprise the only appropriate subject population
- The research question focuses on an issue unique to subjects in this population

Research that is greater than minimal risk may be acceptable where the purpose is therapeutic with respect to the individual subjects and where the risk is commensurate with the degree of expected benefit.

For details regarding informed consent for decisionally impaired adults, see Section 14.12: Consent Involving Adult Decisionally Incapacitated Subjects.

10.5.3 Research in Schools

When research will be conducted in schools, the IRB will consider, in addition to DHHS 45 CFR 46 subparts A and D, whether protections required by two laws that apply to research in schools, the Family Educational Rights and Privacy Act (FERPA) and Protection of Pupil Rights Amendment (PPRA), are adequately met as described below:

FERPA defines the rights of students and parents concerning the reviewing, amending, and disclosing educational records. Except under certain circumstances, FERPA requires that written permission must be obtained prior to disclosure of personally identifiable information from a student’s educational record. Researchers who wish to inspect student records must obtain parental permission if identifiers are linked to the data.

Survey research in schools is regulated under PPRA. This law states that surveys, questionnaires, and instructional materials may be inspected by parents or guardians. The law further states that parental permission must be obtained to allow children to participate in a survey revealing certain types of information, e.g., mental and psychological problems, income, sexual behavior and attitudes, illegal behavior, political affiliations, and close family relationships.

10.5.4 Students, Employees, and Others in Subordinate Positions

Students, employees and other persons in subordinate positions or positions of lesser power or status provide a pool of easily accessible research subjects. IRBs will consider whether the
autonomy and confidentiality of these individuals are adequately protected. IRB considerations may include:
- That incentives for participation do not present undue influence
- That subjects have the ability to decline participation
- That confidentiality is maintained for self-disclosures of a personal nature
- For students, if course credit is given for participation, that alternatives that are no more burdensome than the participation in research are available for receiving equal credit.

10.5.5 Economically or Educationally Disadvantaged Persons and Other Groups Requiring Special Consideration

The economically or educationally disadvantaged, homeless persons, the elderly, and members of particular minority groups are only some of the additional populations that may require special protections in the research environment. When such groups are specifically targeted as research subjects, the IRB will consider whether adequate safeguards are in place to protect such subject groups from risks unique to the population and that researchers do not use their position to unduly influence participation.

10.5.6 Minors in New York State Who May Consent for Themselves

In New York State, there are certain conditions that may permit minors to consent for themselves. Although these individuals may, in some specific instances, consent for themselves, because of their age, this subject group is considered to be vulnerable. (See also, Section 14.13.10: Minors in New York State Who May be Able to Give Legally Effective Informed Consent.)

10.6 INTERNATIONAL RESEARCH

Investigators who are conducting international research are responsible for reviewing the provisions provided in the current International Compilation of Human Subject Research Protections available through OHRP at [http://www.hhs.gov/ohrp/international/HSPCompilation.pdf](http://www.hhs.gov/ohrp/international/HSPCompilation.pdf) and incorporating local regulations into their project. They will be required to confirm compliance with these regulations as a part of the application process. Whenever possible, researchers should collaborate with a research or educational institution familiar with the local culture and research-related issues.

When reviewing international research the IRB will apply all federal regulations, guidelines and University policies as if the study were being conducted domestically. However, in performing its review of the project, the IRB will take into account the local cultural context of the location where the study will take place. This may result in different requirements than those of domestic research. While these differences may make some U.S. requirements and procedures inappropriate, they may also necessitate additional protections for research subjects. The IRB must determine that, when taken as a whole, protections afforded international subjects approximate those provided to subjects in the U.S.

Requests to waive some standard elements of U.S. approvals may be considered by the IRB. When requesting such a waiver, the investigator must provide information justifying the waiver request and, when applicable, explain what equivalent protections will be provided.
When research is sponsored by a U.S. federal agency, the regulations of that agency apply. Providing equivalent protections is unacceptable in lieu of providing the required federal protections.

For international research, research applications must include the following information either as a part of the study description or as an appendix:

- A description of the research location/population
- Information about local languages to be used in the consent process and qualification of research personnel or others to communicate with participants in those languages.
- Information about any local laws of the host country that are pertinent to the project
- Information about any cultural issues that provide context for the need for specialized procedures to either protect participants or respect their cultural standards.
- Information about local requirements or customs for obtaining appropriate access to the population.
- Information on any additional required qualifications of the Researchers and Research Staff for conducting research in the host country
- A statement confirming compliance with provisions provided in the current International Compilation of Human Subject Research Protections (available through OHRP at [http://www.hhs.gov/ohrp/international/HSPCompilation.pdf](http://www.hhs.gov/ohrp/international/HSPCompilation.pdf))

The IRB may require that this information be provided in a separate form or appendix.

When reviewing international research, the IRB or expedited reviewers use the *Reviewer Guide Sheet for International Research* to ensure that the research meets the following study specific criteria for approval:

- Equivalent levels of protections must be afforded to international research participants that would otherwise be required in this country
- Language and literacy issues relevant to the consent process must be adequately addressed.
- Local laws identified are adhered to
- Cultural norms identified are adhered to
- Local norms for securing access to the population are adhered to
- Additional required qualifications for research staff will be met
- Procedures for handling of complaints, non-compliance, and unanticipated problems involving risk to participants or others must be sufficient for protection of participants rights and welfare.

In making these determinations, the IRB may:

- Review and/or consult with University, local or national experts to determine if the research is appropriate based on the laws and knowledge of the country or community in which the research will take place
- Consult the Office of Human Research Protection (OHRP) website publication, *The International Compilation of Human Research Protections*, for in-country research information
- Consider current events and news sources as appropriate
- Communicate and/or coordinate with local IRBs or ECs when appropriate.
• Require that procedures for post-approval monitoring are included in the protocol, are appropriate to the level of risk, and will be made available to the IRB.

For issues related to language and literacy in international research see also Section 14.9 and Section 14.10

10.7 COMMUNITY BASED PARTICIPATORY RESEARCH

In some studies, principal investigators may provide members of local communities with opportunities to assist in the development of the research project and study materials, implementation of the research, and dissemination of the research results. When reviewing these studies, IRBs should consider whether the community members are provided with sufficient training to perform the research functions and whether there is a clear communication plan between the community members and the principal investigator to convey information about the conduct of the study as well as any adverse events or unanticipated problems that may be encountered.

When community members are both study team members and subjects, IRBs should examine the study protocol and informed consent materials to ensure that there is a clear delineation between each role, attendant expectations and risks, and whether community members have been provided with sufficient information to understand the difference in the nature and responsibilities of each role. IRBs should ensure that community members in this dual role have been provided the contact information for the IRB if they have questions about their rights as a study team member and/or as a subject.
11. HEALTH INSURANCE PORTABILITY AND ACCOUNTABILITY ACT (HIPAA)

11.1 DEFINITIONS FOR PURPOSES OF THIS POLICY:

- **Anonymous data**: Information recorded or collected without any of the 18 personal identifiers, or pieces of the identifiers, related to an individual, relatives of the individual, household members or employers as defined by HIPAA regulations, and no code is assigned which would permit data to be traced to an individual, relative, household member, or employer.

- **Authorization**: An individual's written permission to allow the use or disclosure of specified Protected Health Information (PHI) for a particular purpose, the contents of which comply with requirements stipulated by the HIPAA regulation.

- **Coded Data**:
  - **Identifying code**: code that explicitly contains any of the 18 identifiers defined by HIPAA regulations, or pieces of those identifiers, or any non-identifying code that could be used in combination with other information directly accessible by the researcher to identify the associated individual.
  - **Non-identifying code**: Under the Privacy Rule, a non-identifying code is one that does not contain any of the 18 identifiers defined by HIPAA regulations, or pieces of those identifiers, and cannot be used in combination with other information directly accessible by the researcher to identify the associated individual.

- **Covered entity**: A legal entity defined by HIPAA regulations as having to comply with the regulations. Currently defined as a health plan, a health care clearinghouse, or health care provider who transmits health information in connection with a transaction for which DHHS has adopted a standard, or any other entity designated as part of a covered function within a hybrid entity.

- **De-identified data**: Protected Health Information (PHI) that has been de-identified by removing all HIPAA specified identifiers related to an individual, relatives of the individual, household members, or employers.

- **Disclosure**: The release, transfer, access to, or divulging of information by a covered entity in any manner outside the entity holding the information.

- **Health information**: Information in any form or medium (paper, electronic, verbal, and images such as x-rays or sonograms) that relates to a living or deceased individual's past, present, or future physical or mental health or condition, or to the provision or payment of healthcare to an individual.

- **Hybrid Entity**: An entity comprised of functions that are considered covered by the HIPAA regulations, and other functions that are not.

- **Individually Identifiable Health Information (IIHI)**: A subset of health information that identifies the individual in a manner defined by the HIPAA regulations, or that can reasonably be used to identify the individual.

- **Protected Health Information (PHI)**: PHI is Individually Identifiable Health Information that is created or received by a covered entity and is transmitted by electronic media, maintained in electronic media, or transmitted or maintained in any other form or medium, including verbal or written form. PHI excludes education records covered by the Family Educational Rights and Privacy Act (FERPA) and Employment Records held by a covered entity in its role as employer.
11.2 OVERVIEW

The Privacy Rule, or Standards for the Privacy of Individually Identifiable Health Information, issued by the Department of Health and Human Services, implements a subset of requirements under the Health Insurance Portability and Accountability Act of 1996. It establishes a set of national standards for the protection of certain health information that apply to the use and disclosure of individuals’ health information, called Protected Health Information (PHI), for various purposes including research. It also sets standards for individuals’ privacy rights to gain access to, be informed of, and control how their health information is used.

Although the UB research function has been explicitly defined as a non-covered function under HIPAA, research involving the provision of health care, or that will be obtaining health information from a third party entity are required by UB IRBs to adhere to the HIPAA regulations as they relate to a non-covered entity for acquiring individually identifiable health information for research purposes from a covered entity.

This policy enables UB to ensure that its research activities do not generate HIPAA liabilities for entities providing information to its researchers, and further ensures that UB does not establish differential protections for human subjects based on the source of information pertaining to them.

11.3 HIPAA PRIVACY RULE AS IT PERTAINS TO UB

The University at Buffalo is a sub-component of the State University of New York (SUNY). For the purposes of HIPAA, SUNY is the covered entity. SUNY has designated itself a hybrid covered entity which means it is comprised of some functions that fall under HIPAA and other functions that do not. The University at Buffalo Director of HIPAA Compliance serves as the campus HIPAA liaison to SUNY Administration and is the individual on campus charged with reviewing and approving all aspects of campus operations impacted by HIPAA to ensure campus compliance with the regulations. UB IRBs have certain direct responsibilities as explicitly defined in the HIPAA regulations and additionally administer HIPAA policies developed by UB as they pertain to research.

11.4 THE COMMON RULE AND THE PRIVACY RULE

The Common Rule [DHHS 45 CFR 46] and the Privacy Rule differ in what is considered identifiable information. The Common Rule covers both directly and indirectly identifiable information. The Privacy Rule covers only directly identifiable health information. The Privacy Rule does not cover coded information, but it does cover the code itself as well as information associated with that code which may lead to individual identification as defined by HIPAA. Therefore, all projects involving directly or indirectly identifiable information must be submitted to the IRB for review under the Common Rule and Privacy Rule, as appropriate.
11.5 IRB REVIEW OF HIPAA INFORMATION TRANSFER MECHANISMS

11.5.1 Overview

Research projects may obtain Individually Identifiable Health Information from different sources and for different uses in various stages of the research project, e.g., identification of potential subjects, recruitment, or data collection and analysis. A project that is required to comply with UB's HIPAA research policies must have a HIPAA mechanism in place for every piece of Individually Identifiable Health Information it obtains. To ensure compliance with the requirements of HIPAA, IRB review and approval is required prior to use of any of the following transfer mechanisms:

- Authorization for the Use and Disclosure of Identifiable Health Information for Research Purposes
- Waiver of Individual Authorization for Use of Individually Identifiable Health Information
- Limited Waiver of the Authorization for Use of Individually Identifiable Health Information for Study Recruitment
- Alteration of the Authorization
- Certification of De-Identification of Health Information for Research Purposes
- Limited Data Set
- Transition Provisions

UB IRBs do not review the acquisition of PHI by researchers that may occur by way of the Research on Decedents or Reviews Preparatory to Research data transfer mechanisms. These reviews are conducted by the covered entity.

It is University policy that the Limited Data Set data use agreement, while permitted under HIPAA, will in general not be used as the mechanisms above are sufficient to enable the transfer of data from a covered entity to the UB research function.

11.5.2 Authorization for the Use and Disclosure of Identifiable Health Information for Research Purposes

Generally, projects that require compliance with Privacy Rule regulations and UB HIPAA policy must obtain from each subject a signed Authorization for the Use and Disclosure of Identifiable Health Information for Research Purposes in addition to the signed consent document. The IRB will accept either a separate consent document and separate HIPAA Authorization Form or a combined consent document/authorization form. HIPAA Authorizations prepared by the study sponsor, whether combined with the consent document or separate, may also be acceptable. Regardless of the source or type of authorization employed, the authorization must be reviewed and approved by the IRB for compliance with the requirements of HIPAA prior to use.

When the authorization is combined with the consent, or the authorization is from a source other than the UB provided Authorization for the Use and Disclosure of Identifiable Health Information for Research Purposes template, the IRB will review the authorization for compliance with HIPAA requirements using the Authorization Validity Checklist provided by the office of the UB Director of HIPAA Compliance to ensure the authorization meets HIPAA requirements.

Research subjects who signed a consent document prior to April 14, 2003, are not affected by the privacy provisions of HIPAA unless they need to be re-consented.
11.5.3 Waiver of Individual Authorization for Use of Individually Identifiable Health Information

A waiver of the authorization requirement allows use or disclosure of Individually Identifiable Health Information without securing the research subject’s signed authorization. Investigators may submit a request for a waiver of the authorization requirement to the IRB for review and approval. Examples of instances when a waiver may be appropriate include:

- Research on existing health information, e.g., medical records research
- Research where a waiver of informed consent is also being requested

Regulatory criteria for approval include:

- The research could not practicably be conducted without the waiver or alteration of authorization,
- The research could not practicably be conducted without access to and use of Individually Identifiable Health Information,
- The use or disclosure of health information involves no more than a minimal risk to the privacy of individuals, based on, at least, the presence of the following elements:
  - A brief description of the Protected Health Information for which use or access has been determined to be necessary,
  - An adequate plan to protect the identifiers from improper use and disclosure,
  - An adequate plan to destroy the identifiers at the earliest opportunity that is consistent with the conduct of the research, unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law, and
  - Adequate written assurances that the Protected Health Information will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of Protected Health Information would be permitted.

Waiver documentation issued by the IRB will contain all elements required in such documentation by the HIPAA regulations.

11.5.4 Limited Waiver of the Authorization for Use of Individually Identifiable Health Information for Study Recruitment

A request for a limited waiver may be submitted to the IRB for review and may be approved if regulatory criteria can be fulfilled. An application for limited waiver is typically used when acquiring Individually Identifiable Health Information from a covered entity as a prerequisite to identifying candidates who might participate in the proposed study.

The waiver is considered limited because the requirement to acquire an authorization or to utilize one of the other data transfer mechanisms once subjects have been recruited remains in force. If the subjects agree to participate in the research study and procedures include the use or disclosure of Individually Identifiable Health Information, then a signed Authorization for the Use and Disclosure of Identifiable Health Information for Research Purposes, or one of the other data transfer mechanisms must be implemented before any additional health information may be sought from the covered entity.

Waiver documentation issued by the IRB will contain all elements required in such documentation by the HIPAA regulations.
11.5.5 Alteration of the Authorization

An Alteration of Authorization may be granted by the IRB in order to allow a researcher to access Individually Identifiable Health Information in situations where meeting the full requirements stipulated by HIPAA for a written authorization cannot be met. The IRB may approve the alteration of specific requirements prescribed for the Authorization in the HIPAA regulations, such as permitting the authorization elements to be collected verbally rather than in written format. The criteria that must be satisfied for information to be obtained via an Alteration of Authorization are the same as those pertaining to obtaining a full or limited waiver of authorization.

Waiver documentation issued by the IRB will contain all elements required in such documentation by the HIPAA regulations.

11.5.6 Certification of De-Identification of Health Information for Research Purposes

Health information is considered "de-identified" under the HIPAA privacy regulations if specific categories of direct or indirect personal identifiers are removed from data sets. De-identified information is considered anonymous and does not fall under any of the regulatory provisions of HIPAA.

When information is not being acquired from a HIPAA covered entity, the research may be considered de-identified as long as requirements for non-permissible identifiers are met.

If information is being provided to a researcher by an entity that is covered by HIPAA, the information from that providing entity may be considered de-identified as long as none of the listed identifiers are ever disclosed to the research team (including the PI) by any means, including the formal transfer of identifiers to the researcher, or an incidental disclosure of the identifiers, such as in a conversation with covered entity staff about the research project, or the provision of an algorithm to the research by the covered entity which permits the researcher to re-identify the subject of the information.

A Certification of De-Identification of Health Information for Research Purposes may be submitted to the IRB for review when the appropriate criteria regarding identifiers are met as follows:

Permissible Identifiers: Health information is considered "de-identified" even if the following identifiers are used:

1. Gender
2. Ethnicity
3. Age (if less than 90)
4. Dates not directly related to the individual (admission and discharge dates are considered to be directly related to the individual)
5. Dates directly related to the individual that are not more specific than a year, including birth year if individual is less than 90
6. The first three digits of most zip codes (exceptions noted under #2 below)
HIPAA 18 Non-permissible Identifiers: Under de-identification rules, these identifiers must be removed:

1. Names
2. All geographical subdivisions smaller than a State, including street address, city, county, precinct, zip code, and their equivalent geocodes, except for the initial three digits of a zip code, if according to the current publicly available data from the Bureau of the Census: (1) The geographic unit formed by combining all zip codes with the same three initial digits contains more than 20,000 people; and (2) The initial three digits of a zip code for all such geographic units containing 20,000 or fewer people is changed to 000.
3. All elements of dates (except year) for dates directly related to an individual, including birth date, admission date, discharge date, date of death; and all ages over 89 and all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 or older
4. Phone numbers
5. Fax numbers
6. Electronic mail addresses
7. Social Security numbers
8. Medical record numbers
9. Health plan beneficiary numbers
10. Account numbers
11. Certificate/license numbers
12. Vehicle identifiers and serial numbers, including license plate numbers
13. Device identifiers and serial numbers
14. Web Universal Resource Locators (URLs)
15. Internet Protocol (IP) address numbers
16. Biometric identifiers, including finger and voice prints
17. Full face photographic images and any comparable images
18. Any other unique identifying number, characteristic, or code (note this does not mean the unique code assigned by the investigator to code the data)

A limited mechanism does exist for acquiring de-identified data from a HIPAA covered entity while maintaining a way to re-establish identity if necessary or required by law. In these instances, the covered entity may disclose a unique ID (non-identifying code) linked to the research subject along with their associated de-identified data to the researcher. Any such key must be generated by the covered entity, must not be based on any personal identifiers, and the algorithm for generating the key or re-linking it with the subjects identity may not be disclosed to the researcher if it would permit the researcher any means to independently re-identify the individual associated with the key. While this mechanism does not permit the researcher to re-identify the research subject directly, it does permit re-identification by the HIPAA covered entity when necessary.

11.6 REVIEWS PREPARATORY TO RESEARCH

HIPAA provides a mechanism to access personally identifiable information for the purpose of reviews preparatory to research. This provision might be used to design a research study, to assess the feasibility of conducting a study, or to assemble a database of individuals who indicate a willingness to be considered for participation in future research studies. This mechanism does not permit the collection of data for conducting actual research or the removal of information from a covered entity. In addition, if the information is being provided by a
covered entity, UB researchers who do not have staff privileges with that covered entity may not use this mechanism. Researchers in this situation require an IRB approved waiver of authorization.

This mechanism consists of representations from the researcher to the covered entity, if applicable, either in writing or orally, that:

- The use or disclosure of the Protected Health Information is solely to prepare a research protocol or for similar purposes preparatory to research,
- The researcher will not remove any Protected Health Information from the covered entity, and
- Representation that PHI for which access is sought is necessary for the research purpose

[DHHS 45 CFR 164.512(i)(1)(ii)]

The *Request to Access Protected Health Information Required for the Preparation of a Research Protocol* form does not require IRB review and may be presented directly to the covered entity by the researcher when seeking PHI to conduct reviews preparatory to research.

### 11.7 RESEARCH ON DECEDENTS

Decedents are afforded the same privacy protections as the living under HIPAA. However, HIPAA does make exceptions in the area of research on decedents. The *Request to Access Protected Health Information Required to Perform Research on Decedents* form does not require any prior approvals from the IRB. It does, however, require approval from the covered entity. The covered entity is also free to impose additional restrictions on access to information about decedents according to its own internal policies.

### 11.8 BUSINESS ASSOCIATE CONTRACTS

Situations believed to require business associate contracts are not the responsibility of the IRB and should be brought to the attention of the University’s Director of HIPAA Compliance. Since signature authority for entering into these agreements has not been delegated on campus, under no circumstances shall such an agreement be executed by an individual investigator, a department chair, or a dean, etc.

### 11.9 RESOLVING HIPAA ISSUES

HIPAA is a complex set of regulations, and there is not uniform agreement across entities on how the regulations are to be interpreted or implemented. When investigators encounter problems with an external institution regarding acceptance of documentation or approach to interpretation of HIPAA, the problem should be directed to the IRB. The IRB will then, at its discretion, work with the external entity to resolve issues that fall within the policies and guidelines established by UB, or forward the issue to the UB Director of HIPAA Compliance for resolution.

Any HIPAA specific transfer mechanism requiring contractual agreements not already in place (i.e., data use agreements or business associate contracts) require mandatory review by the UB Director of HIPAA Compliance.
12. RESEARCH USING FDA REGULATED PRODUCTS:
INVESTIGATIONAL DRUGS, AGENTS, BIOLOGICS, AND DEVICES

12.1 OVERVIEW

The Food and Drug Administration (FDA) is the federal regulatory and oversight agency responsible for protecting public health by assuring the safety, efficacy, and security of human drug, biological products, medical devices, and products that emit radiation.

12.2 INVESTIGATIONAL DRUGS, AGENTS AND BIOLOGICS

12.2.1 Overview

FDA regulations 21 CFR 312 (drugs) and 601 (biologics) contain procedures and requirements for research involving a drug or biologic. All clinical research projects involving drugs or biologics, not FDA-approved for marketing, must be reviewed by the FDA through the filing of an Investigational New Drug Application (IND).

An Investigational New Drug Application (IND) is a request for a US Food and Drug Administration (FDA) authorization to administer an investigational drug to humans. The FDA reviews the IND application for safety to assure that research subjects will not be subjected to unreasonable risk. Such authorization must be secured prior to interstate shipment and administration of any new drug that is not the subject of an approved new drug application.

12.2.2 Types of IND Applications

- **Commercially Sponsored IND**: an IND submitted primarily by a company to conduct a clinical trial with the goal to obtain marketing approval for a new product.
- **Investigator IND**: an IND submitted by a physician who initiates and conducts an investigation and under whose immediate direction the investigational drug is administered or dispensed (e.g., when a physician proposes study of an unapproved drug or of an approved product for a new indication or in a new patient population).
- **Emergency Use IND**: an IND issued by the FDA, in accordance with 21 CFR 312.23 or 312.34, to allow the use of an experimental drug or biologic for the treatment of one patient when there are no other reasonable treatment options and there is not time for submission and review of a regular IND or for IRB review. Research may not be conducted under an emergency use IND. An emergency use IND exemption may be used one time only for a particular drug or biologic at a particular institution (see Section 12.2.10: Emergency Use of an Investigational Drug or Biologic)
- **Expanded access to Investigational Drugs** (see Section 12.2.13: Expanded Access to Investigational Drugs)

12.2.3 Phases of a Clinical Trial

An IND may be submitted for one or more phases of a trial. The clinical trial of a previously untested drug is generally divided into three phases. Although, in general, the phases are conducted sequentially, they may overlap. The three phases are as follows:
• Phase 1 clinical trials include the introduction of an investigational new drug into humans. These studies are usually conducted in healthy human volunteers and are designed to determine the metabolic and pharmacological actions of the drug in humans, the side effects associated with increasing doses, and if, possible, to gain early evidence on effectiveness. Phase 1 studies also evaluate drug metabolism, structure-activity relationships, and the mechanism of action in humans. Phase 1 studies generally include 20-80 subjects.

• Phase 2 clinical trials include the early controlled clinical studies conducted to obtain some preliminary data on the effectiveness of the drug for a particular indication or indications in patients with the disease or condition. This phase of testing proposes to determine the common short-term side effects and risks associated with the drug. Phase 2 studies generally involve several hundred subjects.

• Phase 3 clinical trials are intended to gather the additional information about effectiveness and safety that is needed to evaluate the overall benefit-risk relationship of the drug. Phase 3 studies also provide an adequate basis for providing information to the general population about the drug and for development of information for physician labeling. Phase 3 studies generally include several hundred to several thousand subjects.

Phase 4 clinical drug trials are post-marketing studies of an FDA-approved drug in order to gain more information (e.g., to further study the incidence of a specific adverse reaction or the long-term effects of the drug on morbidity and mortality).

12.2.4 Requirements for Submission of an IND Application to the FDA for Research Involving Drug or Biologics that Have Not Yet Reached the Market

The FDA and the IRB require that, for clinical research involving a drug or biologic that has not yet reached the market, an IND exemption must be on file with the FDA and an IND number granted.

Examples of when an IND may be required include:

• When the principal intent of the investigational use of a test article is to develop information about the product’s safety or efficacy, including FDA approved drugs

• If the intent of the research is to generate data that will lead to a new advertising claim, a new clinical indication, or a new formulation of the product

When an IND is required, the investigator must submit to the FDA a completed and signed FDA Statement of Investigator Form 1572 in order to participate in the research investigation. Unless contacted by the FDA, an investigator may begin clinical trials 30 days after the FDA receives the IND application.

12.2.5 Clinical Investigations of Marketed Drugs Not Requiring Submission of an IND Application

Clinical investigation of a marketed drug or biologic does not require submission of an IND if all six of the following conditions are met:

• It is not intended to be reported to the FDA in support of a new indication for use or to support any significant change in the labeling for the product;

• It is not intended to support a significant change in the advertising of the product;
• It does not involve a route of administration, dosage level, use in a subpopulation, or any other factor that significantly increases the risk, or decreases the acceptability of the risks, associated with the use of the product;
• Use will be conducted in compliance with the IRB approval and informed consent procedures;
• It is conducted in compliance with the requirements concerning the promotion and sale of the drugs [FDA 21 CFR 312.7]; and
• It does not intend to request exception from informed consent requirements for emergency use [FDA 21 CFR 50.24].

12.2.6 Research Involving Combinations of FDA Approved Drugs, Agents or Biologics

Research involving combinations of FDA approved drugs, agents, or biologics that are currently approved as single use do not require an IND. However, use of these drugs, agents, or biologics in research must be prospectively reviewed and approved by the IRB.

12.2.7 Investigator Responsibilities for Research Involving Investigational Drugs, Agents and Biologics

In addition to investigator responsibilities identified in Section 15: Responsibilities of Investigators and Faculty Sponsors), when the research involves investigational drugs, agents and biologics, the investigator is responsible for:
• Providing the IRB with all applicable documentation for the investigational drugs, agents, or biologics including: the protocol, Investigational Brochure, and a copy of the FDA IND exemption letter or the IND number
• Submitting to the FDA a completed and signed FDA Statement of Investigator Form 1572 and providing the IRB with a copy when an IND is required
• Obtaining the drug, agent or biologic from the sponsor/supplier
• Providing the IRB with their plan for the storage, handling and dispensing of the investigational drug in compliance with state, federal and any site-specific requirements (e.g., specific hospital requirements) including information concerning those individuals authorized to dispense the drug and procedures to ensure that only consenting research subjects will be administered the investigational drug
• Developing a plan for the storage, handling and dispensing of the investigational drug at the site where the research will be conducted (e.g., hospital policy or local pharmacy policy)
• Ensuring that informed consent from the subject or the subject’s legally authorized representative (LAR) is prospectively obtained and meets IRB, DHHS and appropriate FDA requirements (see Section 14: The Informed Consent Process)
• Preparing and maintaining adequate and accurate case histories that record all observations and other data pertinent to the investigation for each subject
• Maintaining all study case report forms and product dispensing records as required by the sponsor, FDA, and site where the research is being conducted.
• Retaining records for a period of two years following the date the marketing application is approved for the drug for the indication for which it is being investigated; or if no application is to be filed or if not approved for such an indication, until 2 years after the investigation is discontinued and the FDA is notified by the sponsor
• Ensuring that the drug, agent, or biologic is used only in accordance with the plan of investigation as described in the FDA-approved IND application and the IRB approved protocol
• Ensuring that the drug, agent, or biologic is used only by subjects who are under the supervision of the principal investigator or under the supervision of physicians who are directly responsible to the investigator
• Notifying the FDA and sponsor of termination, suspension, discontinuation, closure or completion of the study and provide a summary report of study status and research findings, as required
• Notify the IRB of termination, suspension, discontinuation, closure or completion of the study using the Completed/Closed Notification – Final Report
• Returning any unused product per the sponsor’s instruction or otherwise provide for disposition of the unused supplies of the drug, agent or biologic

When the investigator is also the sponsor of a clinical research study, the investigator assumes all responsibilities of both the study sponsor and the investigator as stated in 21 CFR 312 and 314. Additional responsibilities include, but are not limited to:
• Submitting the IND application for FDA review
• Complying with all FDA regulatory reporting requirements including IND Safety reporting, Annual Reports, and Final Study Report
• Adhering to drug manufacturing and control standards
• Assessing safety issues
• Ensuring IRB approval from each study site prior to shipping clinical supplies to the sites
• Monitoring investigators and keeping them informed of study related issues

12.2.8 IRB Responsibilities for Research Involving Investigational Drugs, Agents and Biologics

When a project is subject to review under both DHHS and FDA regulations, the requirements of each set of regulations must be met. In addition to the criteria for IRB approval of research described in Section 9: Criteria for IRB Approval of Research Projects, the following applies to research involving investigational drugs, agents, and biologics. When IND exemptions apply, the IRB office staff will ensure that the pertinent code of federal regulations is available for reference at the full board meeting [i.e., 21 CFR 312.2(b)].

The IRB administrators, chairs, and board shall:
• Confirm that one of the following is true:
  o the drug has an IND issued by the FDA, or
  o the drug falls into one of the six IND exemption categories [21 CFR 312.2(b)(1)-(6)]
• Determine whether the investigator’s justification meets the criteria for exemption from the IND requirements if the Investigator is requesting that the drug, agent, or biologic be exempt from IND requirements. The IRB may request that the investigator contact the FDA for review of the proposed treatment to determine exemption from an IND or provide a document from the sponsor indicating an exemption from an IND. The FDA has final authority regarding determination of whether a study drug is exempt or non-exempt from an IND.
• Confirm that the IND number is consistent throughout the application materials including:
  o the IND number imprinted on the sponsor protocol
Investigator Responsibilities for Storage, Handling, and Dispensing of Investigational Drugs, Agents, and/or Biologics

All investigational drugs, agents, or biologics must be stored, handled, and dispensed in accordance with governing regulations and policies of the site where the research is being conducted.

Drug storage, handling, and dispensing may vary between institutions and research sites covered under UB’s FWA. Investigators are responsible for checking with the specific sites where the research will take place regarding investigational drug requirements (e.g., investigational drug policies of UB’s affiliated hospitals where clinical research is conducted including Erie County Medical Center’s Department of Pharmaceutical Services policy on investigational drug services and the Kaleida Health System’s policies and procedures regarding the handling of investigational drugs). The Investigator must comply with requirements of the institution where research will be conducted as well as with UB policies and procedures.

With the exception of controlled substances, an investigational drug, agent, or biologic utilized in a clinical trial may be stored in an area other than UB or its affiliated institutions if it is under the direct supervision of the PI. In such instances, the Investigator shall provide the IRB with details regarding the storage, handling, and dispensing of those products.

Emergency Use of an Investigational Drug or Biologic

It is the policy of UB IRBs that data obtained when an investigator utilizes the emergency use provisions for the administration of FDA-regulated investigational drugs, agents, biologics, or devices, the activity may not be considered research as defined by DHHS regulations, nor may any data acquired through such use be included in any report of a research activity except as required by FDA regulations.

The emergency use of an unapproved investigational drug or biologic requires an IND. If the intended subject does not meet the criteria of an existing study protocol, or if an approved study protocol does not exist, the investigator shall contact the manufacturer to determine if the drug or biologic can be made available for the emergency use under the company’s IND.

If the need for an investigational drug or biologic occurs in an emergency situation that does not allow time for submission of an IND, the investigator should contact the appropriate department of
the FDA to request an authorization for shipment of the test article in advance of the IND submission. Requests for such authorization may be made by telephone or other direct means of communication [21 CFR 312.36].

12.2.11 Emergency Exemption from Prospective IRB Approval

Emergency use is defined as the use of an investigational drug or biological product with a human subject in a life-threatening situation in which no standard acceptable treatment is available and in which there is not sufficient time to obtain IRB approval [21 CFR 56.102(d)]. The emergency use provision in the FDA regulations [21 CFR 56.104(c)] is an exemption from prior review and approval by the IRB. The exemption, which may not be used unless all of the conditions described in 21 CFR 56.102(d) exist, allows for one emergency use of a test article without prospective IRB review. FDA regulations require that any subsequent use of the investigational product at the institution have prospective IRB review and approval. FDA acknowledges, however, that it would be inappropriate to deny emergency treatment to a second individual if the only obstacle is that the IRB has not had sufficient time to convene a meeting to review the issue.

- **Life-threatening**, for the purposes of section 56.102(d), includes the scope of both life-threatening and severely debilitating, as defined below:
  - **Life-threatening** means diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted and diseases or conditions with potentially fatal outcomes, where the end point of clinical trial analysis is survival. The criteria for life-threatening do not require the condition to be immediately life-threatening or to immediately result in death. Rather, the subjects must be in a life-threatening situation requiring intervention before review at a convened meeting of the IRB is feasible.
  - **Severely debilitating** means diseases or conditions that cause major irreversible morbidity. Examples of severely debilitating conditions include blindness, loss of arm, leg, hand or foot, loss of hearing, paralysis, or stroke.

The IRB must be notified prior to such emergency use, however, this notification should not be construed as an IRB approval. Notification is used by the IRB to initiate tracking to ensure that the investigator files a report within the five day timeframe required by 21 CFR 56.104(c). The FDA regulations do not provide for expedited IRB approval in emergency situations. Therefore, "interim," "compassionate," "temporary" or other terms for an expedited approval process are not authorized. The IRB will either convene and give "full board" approval of the emergency use or, if the conditions of 21 CFR 56.102(d) are met and it is not possible to convene a quorum within the time available, the use may proceed without IRB approval.

If it is not possible to convene a quorum of the full board within the time available, the IRB may send the sponsor a written statement that the IRB is aware of the proposed use and considers the use to meet the requirements of 21 CFR 56.104(c). Although, this is not an "IRB approval", the acknowledgment letter has been acceptable to manufacturers and has allowed the shipment to proceed. When emergency medical care is initiated without IRB approval, the patient may not be considered a research participant under DHHS regulations but is a subject under FDA regulations. Under FDA regulations, the emergency use of a test article, other than a medical device, is a clinical investigation, the patient is a participant, and the FDA may require data from an emergency use to be reported in a marketing application.
12.2.12 Exception from Informed Consent Requirement

Even for emergency use, the investigator is required to obtain informed consent of the subject or the subject's legally authorized representative unless both the investigator and a physician who is not otherwise participating in the clinical investigation certify in writing all of the following [21 CFR 50.23(a)]:

- The subject is confronted by a life-threatening situation necessitating the use of the test article, and
- Informed consent cannot be obtained because of an inability to communicate with, or obtain legally effective consent from, the subject, and
- Time is not sufficient to obtain consent from the subject's legal representative, and
- No alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the subject's life, and
- No standard acceptable treatment is available, and
- The emergency use will be reported to the IRB within five working days, and
- Any subsequent use of the investigational product at the institution will have prospective IRB review and approval.

If, in the investigator's opinion, immediate use of the test article is required to preserve the subject's life, and if time is not sufficient to obtain an independent physician's determination that the conditions above apply, the clinical investigator should make the determination and, within 5 working days after the use of the article, have the determination reviewed and evaluated in writing by a physician who is not participating in the clinical investigation. The investigator must notify the IRB within 5 working days after the use of the test article [21 CFR 50.23(c)]. The report should include:

- The name of the investigational drug, agent, or biologic
- A copy of the consent document
- The conditions under which the investigational drug, agent, or biologic was administered
- The date and time the investigational drug, agent, or biologic was administered
- The subject protection measures implemented
- Any serious events/problems (SEPs)
- The outcomes, if known

The investigator is responsible for evaluating the likelihood of a similar need for the drug, agent, or biologic, and if future use is likely, immediately initiate efforts to obtain IRB approval and an FDA approved IND for the drug, agent, or biologic’s subsequent use.

(See also, Section 12.5.5: Exception from Informed Consent for Planned Emergency Research)

12.2.13 Expanded Access to Investigational Drugs

Investigational products are sometimes used for treatment of serious or life-threatening conditions either for a single subject or for a group of subjects. The procedures that have evolved for an investigational new drug (IND) used for these purposes reflect the recognition by the Food and Drug Administration (FDA) that, when no satisfactory alternative treatment exists, subjects are generally willing to accept greater risks from test articles that may treat life-
threatening and debilitating illnesses. In addition to the provision for emergency use of investigational drug or biologics (described above), the following mechanisms expand access to promising therapeutic agents without compromising the protection afforded to human subjects or the thoroughness and scientific integrity of product development and marketing approval:

- **Open Label Protocol or Open Protocol IND**
  These are usually uncontrolled studies, carried out to obtain additional safety data (Phase 3 studies). They are typically used when the controlled trial has ended and treatment is continued so that the subjects and the controls may continue to receive the benefits of the investigational drug until marketing approval is obtained. These studies require prospective IRB review and informed consent.

- **Treatment IND**
  The treatment IND [21 CFR 312.34 and 312.35] is a mechanism for providing eligible subjects with investigational drugs for the treatment of serious and life-threatening illnesses for which there are no satisfactory alternative treatments. A treatment IND may be granted after sufficient data have been collected to show that the drug "may be effective" and does not have unreasonable risks. Because data related to safety and side effects are collected, treatment INDs also serve to expand the body of knowledge about the drug.

  There are four requirements that must be met before a treatment IND can be issued:
  1. The drug is intended to treat a serious or immediately life-threatening disease, and
  2. There is no satisfactory alternative treatment available, and
  3. The drug is already under investigation, or trials have been completed, and
  4. The trial sponsor is actively pursuing marketing approval.

  Treatment IND studies require prospective IRB review and informed consent. A sponsor may apply for a waiver of local IRB review under a treatment IND if it can be shown to be in the best interest of the subjects, and if a satisfactory alternate mechanism for assuring the protection of human subjects is available (e.g., review by a central IRB). Such a waiver does not apply to the informed consent requirement. The UB IRB may require review and approval of a study even if the FDA has granted a waiver.

- **Group C Treatment IND**
  The Group C program provides a means for the distribution of investigational agents to oncologists for the treatment of cancer under protocols outside the controlled clinical trial. Group C drugs are generally Phase 3 study drugs that have shown evidence of relative and reproducible efficacy in a specific tumor type. Group C drugs are distributed only by the National Institutes of Health under National Cancer Institute (NCI) protocols. Although treatment is the primary objective and patients treated under Group C guidelines are not part of a clinical trial, safety and effectiveness data are collected. Because administration of Group C drugs is not done with research intent, the FDA has generally granted a waiver from the IRB review requirements [21 CFR 56.105]. Although the FDA has granted a waiver for these drugs, the UB IRB requires prospective IRB review and approval.

- **Parallel Track**
FDA Parallel Track policy [57 FR 13250] permits wider access to promising new drugs for AIDS/HIV related diseases under a separate "expanded access" protocol that "parallels" the controlled clinical trials that are essential to establish the safety and effectiveness of new drugs. Although the Secretary of DHHS may on a protocol-by-protocol basis, waive the provisions of 45 CFR 46 where adequate protections are provided through other mechanisms, the UB IRB requires prospective IRB review and approval as well as informed consent.

- **Single-Patient Use**
  Single patient use involves use of an investigational product outside a controlled clinical trial for a patient, usually in a desperate situation, who is unresponsive to other therapies or in a situation where no approved or generally recognized treatment is available. There is usually little evidence that the proposed therapy is useful, but may be plausible on theoretical grounds or anecdotes of success. Access to investigational products for use by a single identified patient may be gained either through a sponsor under a treatment protocol, or through the FDA, by first obtaining the product from the sponsor and then submitting a treatment IND to the FDA requesting authorization to use the investigational product for treatment use. Prospective IRB review and approval is required.

### 12.3 INVESTIGATIONAL DEVICES

#### 12.3.1 Overview

A medical device is defined, in part, as any health care product that does not achieve its primary intended purposes by chemical action or by being metabolized. An investigational device is a medical device that is the object of a clinical study designed to evaluate the effectiveness and/or the safety of the device. All investigational device use must have prior IRB review and approval by the IRB in accordance with applicable laws and regulations [FDA 21 CFR 812 and 814 Subpart H].

An initial review by IRB administrators will establish that:
- the device has an IDE issued by the FDA or
- the device fulfills the requirements for an abbreviated IDE [21 CFR 812.2(b)(1)] or
- the device falls into one of the seven IDE exemption categories [21 CFR 812.2(c)(1-7)]
- and that all written correspondence concerning the investigational device has the same IDE number (e.g., communications from the FDA or the sponsor protocol)

When IDE exemptions apply, the IRB office staff will ensure that the pertinent code of federal regulations, 21 CFR 812.2(c), is available for reference at the full board meeting.

#### 12.3.2 Investigational Device Exemption (IDE)

An investigational device exemption (IDE) allows the investigational device to be used in a clinical study in order to collect safety and effectiveness data required to support requests to legally market the device. Investigational use also includes clinical evaluation of certain modifications or new intended uses of legally marketed devices. All clinical evaluations of investigational devices, unless exempt, must have an approved IDE before the study is initiated.
In general, requirements for clinical evaluation of devices that have not been cleared for marketing include the following:

- If the study involves a significant risk device (see below), the IDE must be approved by the FDA and the IRB, and
- Informed consent must be obtained from all subjects, and
- Labeling must indicate that the device is for investigational use only, and
- Monitoring of the study, and
- Submission of required records and reports

An approved IDE permits a device to be shipped lawfully for the purpose of conducting investigations of the device without complying with other requirements of the Food, Drug and Cosmetic Act that would apply to devices in commercial distribution.

12.3.3 Exemptions from Obtaining an IDE

A device may be exempt from IDE requirements if it meets one of the seven exemption categories. The claim that the device is exempt must reference the exemption category. Full information regarding the seven exemption categories can be found in FDA 21 CFR 812.2 (c).

The first two exemption categories pertain to devices that were either manufactured before 1976 or similar products manufactured after 1976. Categories 3 and 4 are the most commonly applied exemptions (see below). Categories 5 and 6 are pertinent to the use of devices in animals. Category 7 pertains to custom devices and is rarely utilized.

The exemption category most commonly claimed for human subject use is FDA 21 CFR 812.2(c)(3) [diagnostic device]. In addition to the sponsor’s compliance with applicable requirements in FDA 21 CFR 809.10(c), the device testing must comply with the following requirements:

- Is non-invasive, and
- Does not require an invasive sampling procedure that presents significant risk, and
- Does not by design or intention introduce energy into a participant, and
- Is not used as a diagnostic procedure without confirmation of diagnosis by another, medically established diagnostic product or procedure.

The second most commonly claimed exemption category for human subject use is FDA 21 CFR 812.2(c)(4). To qualify for this exemption, the device testing must not be for purposes of determining safety and effectiveness and must not put subjects at risk. The device testing must be limited to the following:

- Consumer preference testing
- Testing of a modification
- Testing of a combination of two or more devices in commercial distribution

It is the sponsor’s responsibility to provide sufficient justification to support the exemption category being claimed. An exemption from the IDE requirement is not an exemption from the requirement for prospective IRB review and approval or informed consent.

12.3.4 Significant Risk vs. Non-Significant Risk Devices

Unless exempt from Investigational Device Exemption (IDE) regulations, an investigational device must be categorized as either a Significant Risk (SR) device or a Non-Significant Risk...
(NSR) device. The initial risk assessment is determined by the sponsor, but the IRB must review the sponsor’s SR or NSR determination and will modify the determination if the full board disagrees with the sponsor. When the FDA makes the SR or NSR determination for a study, its determination is final.

**SR device studies** must be conducted in accordance with the full IDE requirements [21 CFR part 812], and may not commence until 30 days following the sponsor's submission of an IDE application to FDA. The study may not commence until FDA has approved the IDE application and the IRB has approved the study.

**NSR device studies** do not require submission of an IDE application to FDA. Instead, the sponsor is required to conduct the study in accordance with the “abbreviated requirements” of the IDE regulations [21 CFR 812.2(b)]. Unless otherwise notified by FDA, an NSR study is considered to have an approved IDE if the sponsor fulfills the abbreviated requirements. The abbreviated requirements address, among other things, the requirements for IRB approval and informed consent, recordkeeping, labeling, promotion, and study monitoring. NSR studies may commence immediately following IRB approval.

### 12.3.5 Investigator Responsibilities for Studies Involving Investigational Devices

In addition to responsibilities identified in *Section 15: Responsibilities of Investigators and Faculty Sponsors*, the investigator is responsible for:

- Ensuring that the research meets the following requirements for use of an investigational device in research conducted under the jurisdiction of the UB HRPP:
  - The investigational device shall be used only by the investigator or under his/her direct supervision;
  - The investigational device shall be used only as specified in the IDE and as described in the currently approved IRB documents;
  - The investigator shall not supply the investigational device to any persons not authorized under the IDE; and
  - Informed consent from the subject or the subject’s legally authorized representative (LAR) must be prospectively obtained, unless waived by the IRB (for details see *Section 14: The Informed Consent Process*).

- Providing all information to the IRB regarding the use of investigational devices, as required, to include:
  - Identification of the IDE number, when applicable
  - Sending the sponsor a copy of the notification letter from the FDA
  - Providing the IRB with a copy of all correspondence from the sponsor and/or FDA regarding the determination of the device as being NSR or SR. If the sponsor considers that a study is NSR, the investigator should provide the IRB with an explanation of the determination and any other information that may assist the IRB in evaluating risks associated with the study including a description of the device, reports of prior investigations with the device, the proposed investigational plan, and a description of subject selection criteria and monitoring procedures.
  - If the FDA has made an assessment of the device’s risk, providing information regarding the FDA determination
  - Providing the plan for storage, control and dispensing of the device to the IRB and appropriate officials at the site(s) where the research is being conducted (e.g., hospital officials). The plan should describe those investigators authorized to implement the...
investigational device and the individuals who will be obtaining consent from subjects who will use the device

- Documentation that the appropriate authorities at the site where the research will be conducted have approved the plan must be provided
- Providing information as to whether another IRB has reviewed the proposed study and what determination was made
- Providing a description of any change in the device during the course of the research
- Assuring that any serious events/problems (SEPs) (including Unanticipated Adverse Device Effects) are reported to the IRB according to the requirements in Section 17: Reportable Events and Problems.

In the case of an NSR device, if the IRB determines the new information gained in the report changes its risk assessment, the IRB has the authority to reconsider its prior NSR decision and ask for FDA review

- Notifying the IRB of study closure, suspension, termination, or completion of the study

- Submitting to the sponsor, reports of any serious events/problems (SEPs) as soon as possible, but no later than 10 working days after the investigator first learns of the event
- Complying with all requirements of the site where the research is being conducted (e.g., hospital requirements) or other regulatory policy
- Notifying the sponsor of an IRB reclassification of a device from NSR to SR
- Maintaining all case report forms and records as required by the sponsor, the Institution, the site where research is being conducted (e.g., hospital), or the FDA
- Accepting responsibility for the receipt, storage, use, tracking, and disposal of the FDA-regulated devices in accordance with requirements of the site where research is being conducted (e.g., hospital), applicable Institutional, state, and federal laws and regulations.
- Submitting a final report to the sponsor and the IRB within 3 months after termination or completion of the investigator's part of the investigation
- Returning all unused products in the event of study closure, suspension, termination, or completion of the study per the sponsor's instructions

12.3.6 Responsibilities of Investigators Who Also Sponsor the Research

When an investigator is also the sponsor of a research investigation, he/she must assume all responsibilities of both the study sponsor and investigator as stated in FDA 21 CFR 812. In such instances the Investigator/Sponsor responsibilities include, but are not limited to:

- Submitting the application to the FDA for review
- Complying with all FDA regulatory reporting requirements
- Being responsible for manufacturing and control issues, and for assessing safety
- Ensuring IRB approval prior to shipping clinical supplies to sites

12.3.7 Investigator Responsibilities Involving Unanticipated Adverse Device Effects

The investigator is responsible for submitting to the sponsor and the IRB reports of unanticipated adverse device effects and any other serious events/problems. FDA regulations require that unanticipated adverse device effects must be reported to the IRB within 10 days of investigator knowledge or notification of the event; the Serious Events/Problems (SEPs) Initial Report should be used to notify the IRB. All other SEPs should be reported to the IRB according to the reporting timetable in Section 17: Reportable Events and Problems.
The investigator must ask the sponsor to conduct an evaluation of these reports. A sponsor who determines that an unanticipated adverse device effect presents an unreasonable risk to subjects must terminate or suspend all investigations or parts of investigations presenting that risk as soon as possible. Termination or suspension must occur no later than 5 working days after the sponsor makes this determination and no later than 15 working days after the sponsor first received notice of the effect.

If the event involves an SR device, the investigator may not resume a terminated or suspended investigation without IRB and FDA approval. If the device is a NSR device, the investigator may not resume a terminated or suspended investigation without IRB approval and, if the investigation was terminated or suspended for an unanticipated adverse device effect that presented an unreasonable risk to subjects, until FDA approval is obtained.

12.3.8 IRB Review of Investigational Devices in Determining SR/NSR

Device studies that are exempt from IDE requirements may qualify for expedited review [FDA 21 CFR 812]. Based on the initial expedited review, the IRB reviewer may complete the review, request that the IDE-exempt study be sent to an additional reviewer, or recommend that the study be reviewed by the full board.

Both Significant Risk (SR) and Non-Significant Risk (NSR) device studies must go to the full board for review and approval. The IRB is responsible for reviewing and determining whether it is in agreement with the sponsor's determination of NSR. The IRB may consult with the FDA for its opinion. The risk determination should be based on the proposed use of the device in an investigation and not on the device alone. In deciding if a study poses a SR, an IRB must consider the nature of the harm that may result from the use of the device.

Device studies that are considered SR are those:

- where the potential harm to subjects could be life-threatening
- that could result in permanent impairment of a body function
- that could result in permanent damage to body structure
- that could necessitate medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to body structure

In addition, if the subject must undergo a procedure as part of the investigational study (e.g., a surgical procedure), the IRB must consider the potential harm that could be caused by the procedure in addition to the potential harm caused by the device.

In determining whether a medical device is an SR, the IRB will consider if the device:

- Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject
- Is purported or represented to be for use in supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject
- Is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease or otherwise preventing impairment of human health and presents a potential for serious risk to health, safety, or welfare of a subject
- Otherwise presents a potential for serious risk to health, safety, or welfare of a subject

The FDA considers all SR studies to present more than minimal risk and therefore must receive full board review. The IRB may approve or disapprove the proposed research based on local
context and its responsibilities to protect human subjects in research even when an IDE has been granted by the FDA.

12.3.9 IRB Considerations for Approval of Studies Involving Investigational Devices

Once the SR/NSR decision has been reached, the IRB will consider whether the research study should be approved or not. The criteria for approval of SR and NSR studies shall follow the review process outlined in Section 9: Criteria for IRB Approval of Research Projects as well as specific review requirements for FDA regulated research [21 CFR 56.111]. To assure that risk to the subjects are reasonable in relation to the anticipated benefits, the risks and benefits of the investigation will be compared to the risks and benefits of alternative devices or procedures. This review for IRB approval differs from the specific determination regarding whether a study poses SR or NSR which is based solely upon the seriousness of the harm that may result from the use of the device.

The full board will review the proposed research, consent documents, and additional information, when appropriate, and determine whether the research study meets DHHS 45 CFR 46.111 and FDA 21 CFR 56.111 criteria for approval. When IDE exemptions apply, the IRB office staff will ensure that the pertinent code of federal regulations is available for reference at the full board meeting [i.e., 21 CFR 812.2(c)]. (See also Section 12.3.1: Investigational Devices: Overview and Section 12.3.3: Exemptions from Obtaining an IDE.)

When determining whether the research study can be approved, the IRB will consider the following:
- That the protocol is scientifically sound
- The study design, including study population, the trial phase and mechanisms for data analysis and surveillance
- The risks and benefits of the medical device compared to the risks and benefits of alternative devices and procedures are appropriate
- All risks and benefits of the proposed research is reviewed, not just that of the device.
- Consideration of prior reviews by the FDA, other institution reviews, scientific review committees, funding agencies (e.g., NIH), or others

The IRB will provide written documentation of its determination.

NSR investigational devices and minimal risk studies may receive expedited review at continuing review. SR investigational devices, regardless of the risk associated with the study, must be reviewed by the full board at continuing review.

12.3.10 Investigator Responsibility for Maintaining the Distinction Between Research and Therapy

Throughout clinical trials, the distinction between research and therapy must be maintained.

Investigator/Physician responsibilities:
- A physician who participates in research by utilizing a new device in consenting patients must ensure that the patients understand and remember that the device is experimental, and that its benefits for the condition under study are unproven.
• When an individual is both the investigator and the subject's treating physician, conflicting interests may exist. In such cases, the investigator is responsible for informing subjects that the person with whom he/she is dealing may have such conflicting interests.

IRB Responsibilities:
• The IRB may consider the need to inform potential subjects of possible conflicts in this area.

12.3.11 Concurrence of FDA, Sponsor and IRB Determinations for SR/NSR

The IRB’s SR/NSR determination has significant consequences for the study sponsor, FDA, and prospective research subjects:

• **When the IRB Concurs with the Sponsor’s Determination of NSR**
  If an investigator or a sponsor proposes the initiation of a claimed NSR investigation to an IRB and if the IRB agrees that the device is a NSR and approves the study, the investigation may begin without submission of an IDE application to the FDA. NSR studies must be conducted in accordance with the "abbreviated requirements" of the IDE regulations [21 CFR 812.2(b)]. NSR studies may commence following IRB approval.

• **When the IRB Disagrees with the Sponsor’s Determination of NSR**
  When the sponsor determines the investigational device to be NSR and the IRB disagrees, the proposed research shall be “tabled” by the full board. The IRB will notify the investigator of the determination and the investigator will notify the sponsor. The sponsor or investigator may then:
    o Withdraw the study and not submit the investigational device to the FDA for consideration of an IDE
    or
    o Submit a request for an IDE approval from the FDA and when received, the IRB will re-review the research.

• **When the FDA Rules Against the Sponsor and IRB Determination of NSR**
  In the event the FDA rules that the investigational device is a significant risk device after the sponsor and the IRB have determined the investigational device to be a non-significant risk device, the IRB will suspend the currently approved study detailing criteria for suspension. The study may not reopen until an IDE is granted by the FDA and the study is reviewed by the full board with appropriate changes to the IRB application, protocol and consent documents. The IRB will direct the investigator on the issue of re-consenting subjects, when appropriate.

• **When the IRB Concurs with the Sponsor Determination of SR**
  The study may not commence until 30 days following the sponsor’s submission of an IDE application to FDA and the IRB has approved the study. It must be conducted in accordance with the full IDE requirements [21 CFR 812].

12.4 HUMANITARIAN USE DEVICES

12.4.1 Overview
The purpose of the Humanitarian Use Device (HUD) classification is to encourage the development of devices to treat or diagnose conditions that occur infrequently (i.e., fewer than 4,000 individuals in the United States per year). When the market potential of a medical device is limited, the expense associated with extensive medical testing is likely to discourage product development. The HUD classification gives sponsors a mechanism for making beneficial devices available for general use without the level of testing that is required for FDA approval. To be considered for HUD status, a device sponsor must complete a humanitarian device exemption (HDE) application.

An approved HDE application authorizes the applicant to market the device and local physicians to use the device to treat or diagnose a medical condition. Research is not required for use of a HUD. This is the only situation where federal regulations require IRBs to approve and monitor an activity that is clearly not research [21 CFR 814 Subpart H].

### 12.4.2 Investigator Responsibilities for HUdS

The investigator is responsible for:

- Providing to the FDA all applicable information regarding the use of the HUD. The application must contain sufficient information for the FDA to determine whether the device poses an unreasonable or significant risk of illness or injury, and whether the probable benefit to health outweighs the risk of injury or illness from its use, when taking into account the probable risks and benefits of currently available devices or alternative forms of treatment.
- Substantiating to the FDA that no comparable devices are available to treat or diagnose the disease or condition and that he/she could not otherwise bring the device to market.
- Provide the IRB with a copy of the FDA HUD application which contains the following supplemental information:
  - The generic and trade name of the device
  - The FDA Humanitarian Device Exception (HDE) number
  - The date of HUD designation
  - The indications for use of the device
  - A description of the device
  - Contraindications, warnings, and precautions for use of the device
  - Information regarding any adverse effects of the device on human health
  - Information regarding alternative practices and procedures
  - The HUD brochure
  - Marketing history of the device
  - A summary of studies using the device
- Providing the patient with the HUD brochure prepared by the manufacturer and review it with him/her prior to use of the device
- Fulfilling continuing review requirements at the designated IRB intervals. At each continuing review, the investigator will provide a summary of any individual use of the HUD for the previous 6 months at other sites, if applicable. This summary should be available from the sponsor and will include the following:
  - The clinical indications for the use of the HUD in each patient
  - Serious events/problems (SEPs) that are possibly related to the use of the HUD
  - Clinical outcomes of each subject, if known
- Reporting any amendments and serious events/problems (SEPs) according to UB’s HRPP policies and procedures. In addition, these occurrences shall be reported to the FDA and the manufacturer as outlined in 21 CFR 830.30.
When the use of a HUD is for diagnosis or treatment, and not associated with research or data collection, HIPAA regulations for research do not apply. However, HIPAA regulations for hospital medical records per institutional policy are applicable.

12.4.3 Additional Reporting Requirements for Serious Events/Problems (SEPs) Involving HUDs

Whenever the physician or health care provider receives or otherwise becomes aware of information, from any source, that reasonably suggests that a HUD has or may have caused or contributed to the death or serious injury of a patient, the physician or health care provider must report such findings to the FDA and the IRB as soon as possible, but no later than 10 working days after the investigator first learns of the effect or problem by completing and submitting a Serious Events/Problems–Initial Report (see Section 17: Reportable Events and Problems). This reporting is in addition to, not a substitute for, FDA and/or manufacturer reporting requirements in accordance with 21 CFR 803.30. The physician or health care provider shall promptly report any FDA action(s) regarding the HUD to the IRB.

Modifications to the HUD or the clinical use of the HUD are to be promptly reported to IRB in accordance with IRB policy for amendments/modifications (see Section 7.3.3: Amendments/Modifications to an Approved Project).

12.4.4 IRB Review of HUD Use

In order for a HUD to be used in treatment, diagnosis, or research at UB or its affiliated organizations, the IRB and the FDA must approve its use and a Humanitarian Device Exemption (HDE) must be issued. The IRB approval must verify that the use of the HUD, as proposed, is congruent with current labeling of the device and does not exceed the scope of the FDA approved indication. The IRB may impose more stringent restrictions for use of the HUD in order to provide additional protections, as deemed necessary.

Initial HUD reviews shall be conducted by the full board. Continuing review will be performed at the level for which criteria is met. The IRB will verify that the provided HUD documents are congruent with the manufacturing labeling and the approved use granted by the FDA. The labeling for a HUD must state that the device is a humanitarian use device and that, although the device is authorized by Federal Law, the effectiveness of the device for the specific indication has not been demonstrated. Based on the information above, the IRB will determine if the HUD request meets the FDA criteria.

The physician utilizing the HUD for treatment, diagnosis or research must use the HUD only in accordance with the labeling of the device, intended purpose, and in the designated population for which the FDA approved its use. Only the holder of the HUD agreement with the FDA may use the HUD. An informed consent is required from a patient prior to the use of a HUD when the HUD is the subject of a clinical investigation or when the IRB requires the use of informed consent.
12.5 EMERGENCY USE OF UNAPPROVED MEDICAL DEVICES

12.5.1 Overview

While this policy applies to research utilizing unapproved medical devices, nothing in this policy shall limit the authority of a physician to provide emergency medical care for patients who need such care. UB IRBs recognize the provisions found in the Food and Drug Administration (FDA) regulations for the emergency use of investigational drugs, agents, biologics, or devices. Manufacturers or sponsors that agree to allow the use of the investigational device, but will not ship without a letter of acknowledgement from the IRB, will be provided with a written statement that the IRB is aware of the proposed use and based on the information provided by the investigator and the proposed use meets the requirements of FDA 21 CFR 56.102(d).

The Food and Drug Administration (FDA) recognizes that emergencies arise where an unapproved device may offer the only possible life-saving alternative, but an IDE for the device does not exist, or the proposed use is not approved under an existing IDE, or the physician or institution is not approved under the IDE. In such emergencies, a physician may choose to use an unapproved device. In such instances, that the physician must later justify to FDA that an emergency actually existed and the physician further complied with all other FDA and IRB requirements regarding the emergency use.

It is policy of UB IRBs that data obtained when an investigator utilizes the emergency use provisions for the administration of non-FDA regulated investigational drugs, agents, biologics, or devices, the activity may not be claimed as research, nor may any data acquired through such use be included in any report of a research activity. DHHS 45 CFR 46 does not permit research activities to be started, even in an emergency, without prior IRB review and approval. When emergency medical care is initiated without prior IRB review and approval, the patient may not be considered a research subject under DHHS regulations.

FDA regulations relevant to this section:

- **FDA 21 CFR 56.102(d).** Emergency use means the use of a test article on a human subject in a life threatening situation in which no standard acceptable treatment is available, and in which there is not sufficient time to obtain IRB approval. Emergency use does not apply to planned research in emergency settings.

- **FDA 21 CFR 56.104 Exemptions from IRB requirements.** The following categories of clinical investigations are exempt from the requirements of this part for IRB review … (c) Emergency use of a test article, provided that such emergency use is reported to the IRB within 5 working days. Any subsequent use of the test article at the institution is subject to IRB review.”

- **FDA 21 CFR 56.102(d) defines life threatening and severely debilitating:***
  - *Life threatening means disease or conditions where the likelihood of death is high unless the course of the disease is interrupted and diseases or conditions with potentially fatal outcomes, where the end point of clinical trial analysis is survival. The criteria for life threatening do not require the condition to be immediately life threatening or to immediately result in death. Rather, the subjects must be in a life-threatening situation requiring intervention before review at a convened meeting of the IRB is feasible.*
• Severely debilitating means diseases or conditions that cause major reversible morbidity. Examples of severely debilitating conditions include blindness, loss of arm, leg, hand, or foot, loss of hearing, paralysis, or stroke.

12.5.2 Requirements for Emergency Use

Each of the following conditions must exist to justify emergency use:
- The patient is in a life-threatening condition that needs immediate treatment,
- No generally acceptable alternative for treating the patient is available, and
- Because of the immediate need to use the device, there is no time to use existing procedures to get FDA approval for the use.

The physician must determine whether these criteria have been met, assess the potential for benefits from the unapproved use of the device, and have substantial reason to believe that benefits will exist. The physician may not conclude that an "emergency" exists in advance of the time when treatment may be needed based solely on the expectation that IDE approval procedures may require more time than is available.

If the criteria listed above are met, and the device is shipped to the physician, the physician must assure that the device developer notifies the FDA immediately after shipment is made and follows any other applicable FDA procedures. An unapproved device may not be shipped in anticipation of an emergency.

The FDA and the IRB require that the physician follow as many subject protection procedures as possible including:
- Obtaining an independent assessment by an uninvolved physician,
- Obtaining informed consent from the patient or a legal representative,
- Notifying institutional officials as specified by institutional policies,
- Notifying the IRB, and
- Obtaining authorization from the IDE holder, if an approved IDE for the device exists

Although FDA 21 CFR 56.104 allows for an exemption from prior review and approval by the IRB for emergency use, UB IRBs require prior notification, whenever possible, of emergency use of investigational medical devices. Further, data collected may not be used for research purposes unless prior IRB review and approval have been granted.

12.5.3 After-use Procedures

After an unapproved device is used in an emergency, the physician shall:
- If not already reported to the IRB, do so within five days [21 CFR 56.104(c)] and otherwise comply with provisions of the IRB regulations [21 CFR 56]. The report shall include:
  o The name of the investigational device
  o A copy of the consent document
  o The conditions under which the investigational device was utilized
  o The date and time utilized
The subject protection measures implemented

- Any serious events/problems (SEPs) involving the recipient or others
- The outcomes, if known

- Evaluate the likelihood of a similar need for the device occurring again, and if future use is likely, immediately initiate efforts to obtain IRB approval and an approved IDE for the device's subsequent use,
- If an IDE for the use does exist, notify the sponsor of the emergency use, or if an IDE does not exist, notify FDA of the emergency use and provide the FDA with a written summary of the conditions constituting the emergency, subject protection measures, and results.

Subsequent emergency use of the device may not occur unless the physician or another person obtains approval of an IDE for the device and its use. If an IDE application for subsequent use has been filed with FDA and FDA disapproves the IDE application, the device may not be used even if the circumstances constituting an emergency exist. Developers of devices that could be used in emergencies should anticipate the likelihood of emergency use and should obtain an approved IDE for such uses.

**12.5.4 Exception from Informed Consent Requirement for Medical Devices**

Even in situations of emergency use, the FDA and IRB require the investigator to obtain informed consent of the subject or the subject's legally authorized representative unless both the investigator and a physician (who is not otherwise participating in the clinical investigation) certify in writing all of the following [21 CFR 50.23(a)]:

- The subject is confronted by a life-threatening situation necessitating the use of the test article, and
- Informed consent cannot be obtained because of an inability to communicate with, or obtain legally effective consent from, the subject and
- Time is not sufficient to obtain consent from the subject's legal representative, and
- No alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the subject's life, and
- No standard acceptable treatment is available, and
- The emergency use will be reported to the IRB within five working days, and
- Any subsequent use of the investigational product at the institution will have prospective IRB review and approval.

If, in the investigator's opinion, immediate use of the test article is required to preserve the subject's life and if time is not sufficient to obtain an independent physician's determination that all of the conditions above apply, the clinical investigator should make the determination and, within 5 working days after the use of the article, have the determination reviewed and evaluated in writing by a physician who is not participating in the clinical investigation. The investigator must notify the IRB within 5 working days after the use of the test article [21 CFR 50.23(c)].

**12.5.5 Exception from Informed Consent for Planned Emergency Research**

The conduct of planned research in life-threatening emergency situations where obtaining informed consent has been waived is provided by 21 CFR 50.24 and 45 CFR 46.101(i).
The IRB with the concurrence of a licensed physician who is a member of, or consultant to, the IRB and who is not otherwise participating in the clinical investigation must find each of the following:

- The research activity is subject to regulations codified by the Food and Drug Administration (FDA) at Title 21 CFR part 50 and will be carried out under an FDA investigational new drug application (IND) or an FDA investigational device exemption (IDE).
- The application has clearly identified the protocols that will include subjects who are unable to consent.

Planned emergency medicine research must meet the following conditions:

1) the human subjects are in a life threatening situation, available treatments are unproven or unsatisfactory. In addition, the collection of valid scientific evidence, which may include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and efficacy of particular interventions

2) obtaining informed consent is not feasible because i) the subjects will not be able to give consent as a result of their medical condition, ii) the intervention involved must be administered before consent from the subjects’ legally authorized representative is feasible, iii) there is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the research

3) participation in the research holds out the prospect of direct benefit to the subjects because i) subjects are facing a life threatening situation that necessitates intervention, ii) appropriate animal and pre-clinical studies have been conducted, and the information derived from those studies support the potential for the intervention to provide direct benefit to the subject, iii) risks associated with the investigation are reasonable in relation to what is known about the medical condition of the potential class of participants, the risks and benefits of standard therapy, if any, and what is known about the risks and benefits of the proposed intervention or activity

4) the research could not practicably be carried out without the waiver

5) the proposed research protocol defines the length of the potential therapeutic window, and the investigator has committed to attempting to contact a legal authorized representative within that window of time

6) the IRB has reviewed and approved informed consent procedures and a consent document in accord with FDA 21 CFR 50.25. These procedures and the consent document are to be used with subjects or their legally authorized representatives in situations where use of such procedures and documented is feasible. The IRB has reviewed and approved procedures and information to be used when providing an opportunity for a family member to object to a subject’s participation in the clinical investigation consistent with 7(v) below

7) additional protections of the rights and welfare of the subjects, including i) consultation with representatives of the communities in which the research will be conducted and from which the subjects will be drawn from, ii) public disclosure to the communities in which the research will be conducted and from which the subjects will be drawn from, prior to initiation of the research, of plans for the research and its risks and expected benefits, iii) public disclosure of sufficient information following completion of the research, iv) establishment of an independent data monitoring committee to exercise oversight of the research, v) if obtaining informed consent is not feasible and a legally authorized representative is not reasonable available, the investigator has committed to attempting to
contact within the therapeutic window the subject’s family member who is not a legally authorized representative, and asking whether he or she objects to the subject’s participation in the research.

8) Procedures are in place to inform, at the earliest feasible opportunity, each subject, or if the subject remained incapacitated, a legally authorized representative of the subject, or if such a representative is not reasonably available, a family member, of the subject’s inclusion in the clinical investigation, the details of the investigation and other information contained in the consent document.

- There is a procedure to inform the subject, or if the subject remained incapacitated, a legally authorized representative of the subject, or if such a representative is not reasonably available, a family member, that he or she may discontinue the subject’s participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.
- If a legally authorized representative or family member is told about the clinical investigation and the subject's condition improves, the subject is also to be informed as soon as feasible.
- If a subject is entered into a clinical investigation with waived consent and the subject died before a legally authorized representative or family member can be contacted, information about the clinical investigation is to be provided to the subject’s legally authorized representative or family member, if feasible.

If the research activity is subject to FDA regulations, it must be carried out under an approved FDA IND or IDE and must meet the requirements under 21 CFR 50.24.

If the research activity is not subject to FDA regulation, documentation must be provided indicating that it is not subject to FDA regulations at 21 CFR 50 and must meet the above conditions.

12.5.6 Investigator Responsibilities for Conducting Planned Emergency Research

The investigator will provide to the IRB:
- all appropriate materials required by the IRB for review of new and initial submissions
- documentation of FDA approval of the research plan if the research to be conducted is to be carried out with FDA approved IND or IDE
- documentation that the research is not subject to FDA regulations at 21 CFR 50
- documentation that the above conditions for planned emergency research have been met

The investigator will provide to the IRB at time of continuing review:
- all appropriate materials required by the IRB for continuing review and approval
- a summary of the efforts made to contact legally authorized representatives to obtain consent (condition #5)
- a summary of the efforts made to contact a family member to obtain consent (condition #7)

12.5.7 IRB Review of Planned Emergency Research

The IRB or primary reviewer for initial/new submissions will:
- determine the research meets regulatory criteria under 45 CFR 46.111 and 21 CFR 56.111
determine the research is subject to FDA regulations at 21 CFR 50

determine and documented that the research is not subject to FDA regulation 21 CFR 50

review and determine that each condition for emergency research consent waiver has been met

document in the minutes the regulatory determinations and protocol specific findings justifying those determinations for emergency research consent waiver have been met

If an IRB determined that it cannot approve a clinical investigation because the investigation did not meet the criteria in the exception or because of other relevant ethical concerns, the IRB documented its findings and provided these findings promptly in writing to the clinical investigator and to the sponsor of the clinical investigation. The sponsor of the clinical investigation promptly disclosed this information to FDA and to the sponsor’s clinical investigators who are participating or are asked to participate in this or a substantially equivalent clinical investigation of the sponsor, and to other IRB’s that has been or are asked to review this or a substantially equivalent investigations by that sponsor.

For review of research that is not FDA regulated involving waiver of informed consent for planned emergency research, the primary reviewer brings to the IRB meeting a copy of the DHHS regulations at 45 CFR 46 regarding waiver of informed consent requirements in certain emergency research and takes the IRB through the determinations to determine whether the research can be approved and to make all other required determinations. The IRB provides protocol specific determinations justifying each regulatory determination to the IRB staff taking minutes and the IRB staff document in the minutes the regulatory determinations and protocol specific findings justifying those determinations. For the purposes of this waiver “family member” means any one of the following legally competent persons: spouses; parents; children (including adopted children); brothers, sisters, and spouses of brothers and sisters; and any individual related by blood or affinity whose close association with the participant is the equivalent of a family relationship.

The IRB or primary reviewer for continuing review submissions will:

- determine the research continues to meet regulatory criteria under 45 CFR 46.111 and 21 CFR 56.111
- determine that the research meets regulatory criteria under 45 CFR 46.116 (b)(5) and 21 CFR 50.25 (b)(5)
- determine that each condition for emergency research consent waiver
- determine that the efforts made to contact the subject’s legally authorized representative to obtain consent is acceptable
- determine that the efforts made to contact the subject’s family member to obtain consent is acceptable
- document in the minutes the regulatory determinations and protocol specific findings justifying those determinations for emergency research consent waiver continue to be met

**12.6 IRB RESPONSIBILITIES FOR EMERGENCY USE OF FDA REGULATED PRODUCTS**

The emergency use of FDA regulated products requires the involvement of an IRB Chair (if the Chair is a physician) or a physician designee. The IRB Chair or his/her designee will be promptly notified of the investigator’s intent for emergency use of an investigational drug, agent, biologic,
or device. If the IRB Chair was not notified prior to the emergency use, the IRB Chair shall make a determination, based upon the report provided within 5 working days, whether the criteria allowing the emergency use was met. Written notification will be sent to the physician regarding the Chair’s determination of whether the activity met the FDA criteria for emergency use. If, upon retrospective review, it is determined that the activity did not meet the criteria allowing an exemption, the action may be handled according to UB HRPP’s policies and procedures on management of non-compliance (see Section 18: Non-Compliance with HRPP Requirements).

The IRB Chair or his/her designee will review the 5-day follow-up report submitted by the investigator for adherence to FDA regulations and institutional procedures. Following the review, the IRB Chair or his/her designee may request:

- An authorization from the sponsor or manufacturer to allow the use by the investigator for the test article
- An approved IND/IDE or a letter explaining the exemption from FDA
- An adequate description of the situation regarding the use of the test article with an independent physician’s certification, if applicable
- The consent document or the certification for the exception from obtaining informed consent
- Any other materials that may aid in the evaluation of the request

The full board will be notified of the emergency use of an FDA regulated product.
13. **SPECIAL TOPICS**

13.1 Recruitment Materials and Advertising  
13.2 Payments for Purposes of Recruitment  
13.3 Subject Compensation  
13.4 Deception and Incomplete Disclosure  
13.5 Certificates of Confidentiality  
13.6 Pilot Studies  
13.7 Program Evaluation or Quality Assurance Studies  
13.8 Case Reporting  
13.9 Prospective Research Involving Retrospective Review of Medical Records  
13.10 Oral Histories  
13.11 Observational Research  
13.12 Student Practica, Internships, and Research Projects  
13.13 Surveys, Questionnaires, Interview Materials, or other Testing Instruments  
13.14 Use of Human Cadaver Tissue or Cells  
13.15 Enrollment Exceptions

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13.1 **RECRUITMENT MATERIALS AND ADVERTISING**

Recruitment is the initial step of the informed consent process. Prior IRB approval is required for any materials used for subject recruitment into a study and includes, but is not limited to:

- Recruitment letters
- Scripts for telephone or other personal contact
- Flyers, posters, newspaper ads, press releases
- TV and/or radio spots
- Websites/internet ads
- Electronic mailings

In all cases the final form of the advertisement must be provided to the IRB and approved before it may be used.

The mode of using recruitment materials must be described in the submitted project documents. Recruitment materials and advertisements must be consistent with information contained in the submitted protocol documents and consent document. Any changes to the IRB approved method of recruitment or materials used for recruitment must be submitted to the IRB for review and approval prior to their use. As recruitment materials are subject to ongoing review, they must be submitted along with other materials at the time of continuing review. These materials may be reviewed by the Chair or designee.

If an ad will be posted on the Internet, the Internet address (URL) and/or content of the webpage(s) or internet ad must be provided with the submission so that the IRB can verify the website material.

If an ad will be disseminated via audio or video, the IRB must review the final audio or video taped advertisement before it may be used.
Content Requirements
Recruitment materials and advertisements must clearly state that the purpose for recruitment is research. In addition, the materials should generally contain the following elements:

- The name of the investigator or research facility (letterhead is acceptable if it includes this information)
- The condition under study or the purpose of the research
- A brief list of participation benefits, if any
- A summary of the criteria that will be used to determine eligibility for the study
- The location where the research will be conducted
- Time or other commitments required by the study
- Compensation, if any. (The terms “compensation” or “reimbursement” should be used on recruitment and advertising materials rather than “payment.”)
- The person or office to contact for further information

Additional considerations:
- Information provided in the advertising or recruitment materials may indicate that reimbursement or compensation will be provided. Whether the amount of compensation is included in the ad is left to the discretion of the IRB
- Excessive monetary amounts or other incentives that could be interpreted as inappropriate, posing undue influence, or are coercive may not be offered
- For drug, device, or biologic studies:
  o The advertisement may not claim the superiority, safety or effectiveness of the drug or device
  o The terms “new treatment,” “new medication,” or “new drug” may not be used because it inappropriately implies that safety and effectiveness have been determined. It must be clear that the drug or biologic is investigational, meaning non-FDA approved.
  o Proprietary names of study products may not be used
  o Advertisements or recruiting tools must not include the promise of “free medical treatment” when the intent is only to say the subjects will not be charged for taking part in the investigation

IRB Review
The IRB will review recruitment and advertising materials to ensure that:

- they do not state or imply a certainty of favorable outcome or other benefits beyond what is outlined in the consent document and the protocol
- they do not include exculpatory language
- they do not emphasize the payment or the amount to be paid, by such means as larger or bold type
- payments are not designed to accelerate recruitment by being tied to the rate or timing of enrollment (i.e., “bonus payments”)
- do not promise “free treatment” when the intent is only to say participants will not be charged for taking part in the investigation
- the mode of communication is consistent with the material provided
- for FDA-regulated research:
13.2 PAYMENTS FOR PURPOSES OF RECRUITMENT

The IRB will review payment arrangements among sponsors, organizations, investigators and those referring research subjects to determine whether those arrangements are permissible. The amount of payment, the proposed method and timing of disbursement may neither be coercive nor pose undue influence.

A finder’s fee is payment of any type made to an individual in exchange for referral or recruitment of a subject into a biomedical research study. Such payments generally are offered to medical residents, physicians, nurses or other health care personnel in a position to identify patients who may qualify for enrollment in a research study. The policy of the American Medical Association is that offering and accepting payment for referring patients to research studies and not for the provision of any medical service is unethical (AMA Policy E-6.03). In concurrence with the AMA policy, the use of finder’s fees to recruit research subjects in a UB affiliated research study is strictly prohibited.

Payments designed to accelerate recruitment that were tied to the rate or timing of enrollment (“bonus payments”) are permitted only if paid to compensate for additional recruitment costs (e.g., paid staff effort, advertising).

Other forms of payments for purposes of recruitment will be reviewed by the IRB on a case-by-case basis.

13.3 SUBJECT COMPENSATION

The intent of compensation to research subjects is for their time and inconvenience, not for the risk associated with their research participation. Excessive monetary or other incentives that would be interpreted as inappropriate, posing undue influence, or are coercive may not be offered. The terms of all forms of compensation, including the scheduling of the compensation, must be described in the protocol and the consent document. Subject compensation should not be considered as or referred to as a “benefit” of participation in the research.

Payments to subjects should generally be pro-rated and not be contingent upon the subject completing the entire study. Payments to subjects who withdraw from the study may be paid at the time they would have completed participation in the study (or completed a segment of the study) had they not withdrawn, unless doing so creates a coercive situation. Payment of a small incentive for study completion is acceptable providing that the incentive amount does not pose undue influence and is not coercive. The IRB will determine whether the amount paid as a bonus for completion is reasonable and not so large as to unduly induce subjects to stay in the study when they might otherwise withdraw.

The amount and schedule of payments to subjects must be presented to the IRB for review and approval. The IRB will review the amount of payments and the proposed method of payment, including timing of payments, to assure that these factors do not pose undue influence and are not coercive. The IRB will also consider whether the potential subjects are adequately informed regarding the amount of and requirements for compensation.
Subjects may be compensated in a variety of ways including, but not limited to:
- Financial remuneration for participation-related expenses (e.g., travel, parking, or babysitters)
- Financial remuneration for participation-related time and inconvenience
- Merchandise (e.g., gifts, toys, or vouchers)
- Education credit(s)

**IRB Review**

The IRB will review compensation plans to ensure that:

- The amount of payment and the proposed method and timing of disbursement neither is coercive nor presents undue influence.
- Credit for payment accrues as the study progresses and not be contingent upon the participant completing the entire study.
- Any amount paid as a bonus for completion is reasonable and not so large as to unduly induce participants to stay in the study when they would otherwise have withdrawn.
- All information concerning payment, including the amount and schedule of payments, is set forth in the consent process.
- In reviewing a proposal to give human subjects payment or incentives to refer other subjects (e.g., family member, friend), the IRB must consider whether or not this procedure could negatively affect the subject’s relationship with the other individual, and whether or not this procedure introduces a new risk or raises the risk level of the study.

**13.4 DECEPTION AND INCOMPLETE DISCLOSURE**

In most studies, the subject is informed of the purpose of the research and the procedures involved as part of the consent process. In some studies, however, some deception or incomplete disclosure may be involved during the consent process in order to prevent biasing the results.

The IRB will consider the merit of the investigation against the risks posed by the deception or incomplete disclosure, why deception or incomplete disclosure is necessary, how the potential benefits justify its use, whether debriefing is required and, if so, how it will be conducted.

Deception can only be permitted where the IRB documents that a waiver of the informed consent requirements is justified under the criteria present in the Common Rule and 38 CFR 16.116(d).

Generally, the employment of deception by an investigator(s) for the purpose of securing subject participation and/or to prevent potentially biased reporting of data/information by the subject is permissible provided all of the following conditions exist:

a. Deception is necessary due to the lack of alternative procedures for data collection that do not involve deception
b. The deceptive procedures will not place subjects at significant financial, physical, legal, psychological, or social risk
c. The data collection/experiment will be followed by careful debriefing sessions where the subjects are fully informed of the nature and purpose of the deception. In rare instances, where revealing the deception increases risk, the IRB will document the need to waive debriefing
d. The procedures for deception will meet the guidelines established by the discipline of the investigator in its professional code of ethics

**Debriefing**

In reviewing projects utilizing deception or incomplete disclosure, the IRB will consider whether appropriate measures are in place to debrief the subjects. Debriefing is appropriate when it contributes to the subject’s welfare, i.e., when it corrects painful or stressful misperceptions, or when it reduces pain, stress, or anxiety concerning his/her performance in the research, etc. In instances when debriefing may not be appropriate such as in instances where the debriefing itself would increase risk to the subjects, the IRB may determine that debriefing is not to be used.

### 13.5 CERTIFICATES OF CONFIDENTIALITY

Certificates of Confidentiality (CoC) are issued by the National Institutes of Health (NIH) and other Department of Health & Human Services (DHHS) agencies to protect identifiable research information from forced or compelled disclosure. They allow the investigator and others who have access to research records to refuse to disclose identifying information on research subjects in civil, criminal, administrative, legislative, or other proceedings, whether federal, state, or local.

CoCs may be granted for studies collecting information that, if disclosed, could have adverse consequences for subjects, such as damage to their financial standing, employability, insurability, or reputation. By protecting researchers and institutions from being compelled to disclose information that would identify research subjects, CoCs help to minimize risks to subjects by adding an additional level of protection for maintaining confidentiality of private information.

CoCs protect subjects from compelled disclosure of identifying information but do not prevent the voluntary disclosure of identifying characteristics of research subjects. Researchers, therefore, are not prevented from voluntarily disclosing certain information about research subjects, such as evidence of child abuse or a subject’s threatened violence to self or others. If however, a researcher intends to make such voluntary disclosures, the consent form should clearly indicate this. Furthermore, Certificates of Confidentiality do not prevent other types of intentional or unintentional breaches of confidentiality. Therefore, other appropriate mechanisms and procedures may need to be in place to protect the confidentiality of the identifiable private information to be obtained in the proposed research.

Any research project that collects personally identifiable, sensitive information and that has been approved by an IRB is eligible for a CoC. Federal funding is not a prerequisite for a Certificate. For projects that were previously approved with Certificates of Confidentiality, investigators must submit, at the time of renewal, a copy of the Certificate of Confidentiality with the submission materials for IRB review.

### 13.6 PILOT STUDIES

Pilot studies involving human subjects require IRB review and approval before they are conducted. A pilot experiment is usually a precursor to a full-scale study. Pilot studies are usually conducted with a smaller sample size than a full study and are generally intended to test experimental procedures and to obtain information useful for conducting power calculations. As such, a pilot project usually exposes human research subjects to many of the same experiences and ensuing risks as a full-scale study.
13.7 PROGRAM EVALUATION OR QUALITY ASSURANCE STUDIES

Typically, a program evaluation or quality assurance measure does not fall under the oversight of the IRB. However, if the project is conducted with the goal of publishing findings or otherwise contributing to generalizable knowledge, the project may qualify as research and require IRB review.

13.8 CASE REPORTING

13.8.1 Overview

Case studies generally involve the collection and presentation of detailed information about a particular subject or small group to highlight an interesting condition, treatment, presentation, or outcome. When considering a case study, the IRB will consider whether the proposed case study or series of cases constitutes “research” (see Section 4.5: Determination of ‘Human Subject Research’). A retrospective case study that reports the observation of a single subject is generally not considered research because there is no intent to test a hypothesis via systematic analysis, or add to a body of knowledge. However, when a series of subject observations are compiled in such a manner that would allow possible extrapolation of the results into a larger population, this could likely represent research and require IRB review.

13.8.2 Humanities Projects and Case Reporting

Humanities projects sometimes qualify as “research” and which involve “human subjects” as defined in the federal regulations would require IRB review under UB HRPP guidelines. Under those guidelines, a project must intend-to generate conclusions that can be applied in or be predictive of similar circumstances. The IRB will determine on a case-by-case basis whether a case study of a single individual constitutes human subject research.

13.8.3 Medical Case Reporting

Clinical experiences are often the genesis of research questions and the design and development of clinical research trials. In an academic/medical center it is not unusual for unique and interesting clinical cases to be written up as case reports for publication in medical journals or presentation at medical or scientific meetings. The following information provides guidance on when publication/presentation of case report(s) constitutes human subject research requiring prospective IRB approval.

Federal regulations for the protection of human subjects define research as a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge [45 CFR 46.102(d)]. In general, the review of medical records for publication of case reports of typically three or fewer patients is not considered human subject research and does not typically require IRB review and approval because case reporting on a small series of patients does not involve the formulation of a research hypothesis that is subsequently investigated prospectively and systematically for publication or presentation. Reporting or publication is not typically envisioned when one interacts clinically with the subject.
When larger series of patients are being reported, investigators usually begin to ask specific research questions and formal systematic collection of data occurs, moving these activities closer to prospectively designed research. Boundaries between case reporting and formal medical records research may be unclear for a series of one’s own patients. Investigators should submit larger case series reports to the IRB for a determination when uncertainty exists about whether formal and systematic collection of human subject research is occurring.

It should be noted that teaching, and soliciting colleagues’ advice on clinical care of a specific patient or groups of patients during presentation of a case at departmental conferences does not require IRB review. Generalized commentary by a clinician on the outcome of their clinical care of patients in accepted venues for discussion of clinical management is also not considered research requiring IRB review, if there is no prospective research plan and no formal systematic and prospective collection of information. This type of communication may occur at hospital or practice meetings, in continuing education venues, or in editorials, where the comments are explicitly identified as personal experience and not formal clinical research.

Patient confidentiality should be respected in all clinical situations involving identifiable medical information from patients. In addition to UB HRPP policies and guidelines, the investigator is responsible for being in compliance with the policies of the site where the research is being conducted. Where requirements differ, the more stringent of the policies must be adhered to. In general, the following guidelines apply:

- Names, dates of birth, social security numbers, and other codes or combination of identifiers, which might easily identify someone should never be used
- Unique family trees or pedigrees should be masked or disguised
- Photographs should be appropriately masked
- Being sensitive to the “small cell problem” – the existence of individuals with such unique or unusual diagnoses or illnesses that might make it possible for the individuals be identified

It is recommended that written permission be obtained to allow publication or electronic dissemination of pictures or other information (e.g., videos, voice recordings, or transcripts). When photographs will only be used in confidential medical records or as part of direct clinical care of a patient (e.g., photograph of a characteristic rash which would be retained in a record for documentation or shown to colleagues in the provision of clinical care), it is appropriate and acceptable to obtain and document verbal permission.

13.9 PROSPECTIVE RESEARCH INVOLVING RETROSPECTIVE REVIEW OF RECORDS (e.g., MEDICAL OR EDUCATION RECORDS)

Formal prospective research involving records review (e.g., medical or education records) to answer specific research questions constitutes systematic record research on identifiable human subjects and does require IRB review and approval prior to initiation.

Investigators are permitted to abstract and retain only the minimum relevant information from the records. Investigators should discard links to human subjects when the research has been completed and published, or when relevant research goals requiring links to individuals are accomplished. In general, links to identifiable subjects should not be retained indefinitely.
13.10 ORAL HISTORIES

The term oral history interview has been used to describe a process whereby a person obtains information from a subject about the subject’s life and events that the subject witnessed or participated in. In many cases, conducting an oral history interview constitutes research with human subjects. The IRB will determine whether particular projects meet the definition of research with human subjects on a case-by-case basis after receiving sufficient information from the investigator. When a definitive determination cannot be made that a particular oral history project is not research with human subjects, the IRB will err on the side of caution and require prospective review of the project.

Some oral history interviews are conducted solely for the purpose of adding to the historical record and preserving information. This type of interview does not contribute to generalizable knowledge in that no analysis is conducted in order to draw conclusions, inform policy, or generalize findings. In such cases, no IRB review would be needed.

Other oral history interviews are conducted with the intent of contributing to knowledge through analysis of the information gathered to drawing conclusions, inform policy, or generalize findings. In these cases, the project does constitute research and would require IRB review.

13.11 OBSERVATIONAL RESEARCH

Research that involves the observation of people, in either a public or private setting requires IRB review for a determination whether it is human subject research. Observational research involving sensitive aspects of subjects’ behavior, or in settings where subjects have a reasonable expectation of privacy, does not qualify for exempt status. Observation of children does not qualify for exempt status if the researcher participates in or influences the observed activities.

13.12 STUDENT PRACTICA, INTERNSHIPS, AND RESEARCH PROJECTS

Generally, student projects involving human subjects fall into one of two categories:

- **Research Projects** (directed or independent), such as honors or graduate theses, which employ systematic data collection with the intent to contribute to generalizable knowledge
- **Research Practica**, the goal of which is to provide research training

Research projects require prospective IRB review and approval. IRB approval will not be granted retrospectively.

Research practica, on the other hand, generally do not require IRB review. A research practicum is a course of study that involves the supervised practical application of previously studied theories of research method. Schools frequently offer courses that require students to undertake projects in which other people are interviewed, observed, or otherwise serve as subjects. The purpose of these course projects is to train students and provide them with a closer view of social, educational, or psychological processes, and an opportunity to practice various research methods. Such projects typically do not lead to generalizable knowledge and are not undertaken with that goal in mind. Therefore, they do not meet the DHHS definition of research and IRB review and approval are not required. Projects conducted as research practica and later
submitted for IRB approval will generally not be granted approval but will be considered on a case-by-case basis.

13.13 SURVEYS, QUESTIONNAIRES, INTERVIEW MATERIALS, OR OTHER TESTING INSTRUMENTS

Surveys, questionnaires, and interviews can be used for both research and non-research purposes, sometimes simultaneously. When the intent of any portion of the data collection is for contribution to generalizable knowledge, the IRB must prospectively review and approve the project. The study instruments used to collect the data must be submitted as a part of the written project documentation for the IRB to review. The project may be reviewed by the expedited process or may be granted exempt status when applicable criteria are met.

If the materials ask for information which, according to local law, would require reporting to outside entities (e.g., elder or child abuse), these reporting requirements should be clearly stated in the confidentiality section of the consent document.

13.14 USE OF HUMAN CADAVER TISSUES OR CELLS

The regulation of human subject research by IRBs pertains to living human subjects. Consequently, when a research subject is deceased, such research is generally not covered by IRB regulations. Thus, if research is being performed on deceased individuals or on information specifically pertaining to the deceased individual (e.g., medical record), IRB approval is not required. However, if the research on the deceased subject extends to include information obtained about living individuals (e.g., genetic information that could be related to family members) then the research is subject to IRB review.

13.15 ENROLLMENT EXCEPTIONS

In rare instances, the IRB may allow the enrollment of a single individual who does not meet the enrollment criteria of an IRB-approved protocol. The investigator may submit a written request for a one-time enrollment exception as a protocol modification request to the IRB. The request should include justification for the exception that is presented in terms of how the exception serves the best interests of the potential study subject. Obtaining prior IRB approval for an enrollment exception modification meets compliance requirements and therefore is not considered to be a protocol deviation/violation or instance of non-compliance. The IRB Chair will evaluate the request for appropriate level of review.

When the IRB approval is granted for an enrollment exception, the data should be collected according to the IRB approved protocol and included in the scientific evaluation of the study.

**Important notes:**
- Prior IRB approval is required before a one-time single individual exception to the enrollment criteria of an approved protocol can be made, and
- For sponsored studies, an enrollment exception usually requires the additional approval of the study sponsor
14. THE INFORMED CONSENT PROCESS

14.1 OVERVIEW

The informed consent process is an ongoing exchange of information between the research staff and the subject that begins when a potential research subject is initially informed about the research, often at the time of recruitment, and continues throughout the course of the study. It includes subject recruitment materials, question/answer sessions, methods and materials used to obtain the subject’s consent to participate in the research, and any other communication between the subject and research staff that explains or clarifies the research to be conducted.

Obtaining consent for participation in a research study is a critical point of entry for subjects and must be carried out only by individuals who are suitably trained. If investigators are not the ones obtaining consent, they are responsible for delegating the responsibility only to individuals who are not only familiar with the research project but also meet HRPP education and training requirements. The ultimate responsibility for ensuring that proper consent is obtained, even when the task is delegated to another individual, rests with the investigator.

In order for the IRB to evaluate the consent process to ensure that it is adequate, the investigator must describe consent procedures and provide all consenting documents as a part of the project’s application for IRB review.

14.2 IRB REQUIREMENTS REGARDING INDIVIDUALS WHO WILL OBTAIN CONSENT

The IRB must be informed of the individuals designated by the investigator to obtain consent. Personnel who are obtaining consent must be specifically indicated on the HS-1A Application Form as “research staff who obtains consent.” These individuals must meet HRPP education and training requirements (see Section 3: Education and Training).

14.3 PRESENTATION OF STUDY INFORMATION

Study information must be presented in a manner that is understandable to the subjects so that they can make an informed decision whether to participate. Subjects should be allowed sufficient time to consult with family and/or friends before making their decision regarding participation. Subjects must also have the opportunity to ask questions and have their questions answered prior to making an enrollment decision as well as at any time during the course of the study.

In situations where the ability of the subject to understand the consent document is in question (e.g., if the document includes complex scientific information or if the subject may be educationally or cognitively impaired), additional considerations and procedures may be required.

For clinical research studies, the presentation of the research consent document should be a separate process from the hospital admission and hospital consent process so it is clear to the subject that participation in the research is a separate issue.
14.4 USE OF IRB APPROVED CONSENT DOCUMENTS

In all instances, IRB approved consent, permission, and assent documents must be used in the consenting process. When approved, the IRB stamps and indicates the approval period on the document. Consent documents that subjects sign must bear a legible, dated IRB approval that is currently valid. If consent will be obtained orally (in person or by phone) or by email, the script/text to be used and method for documenting consent requires IRB approval prior to use.

14.4.1 Templates for Consenting Documents

The UB IRBs have developed templates for written consent, permission, and assent documents that provide investigators with guidance in development of the forms. Use of the templates helps ensure that all required elements are incorporated into the document(s) and facilitates IRB review.

14.4.2 Sponsor-prepared Sample Consent Documents

While Investigators may utilize sample or draft consent documents developed by a sponsor or cooperative study group, the UB IRB has final authority regarding approval of the consent document that is presented to prospective study subjects covered under UB’s HRPP.

14.4.3 Revision of Consenting Documents During the Study

Study projects often change during the course of a study which may require revisions to the consenting document(s). The revised consenting document(s) must be submitted to the IRB for review using the Amendment Form. The revised document(s) may not be used until IRB approval has been obtained.

14.5 PROVIDING ENROLLED SUBJECTS WITH IMPORTANT NEW INFORMATION

Subjects enrolled in a research study should be kept informed of any new information relative to the study that might affect their decision to continue participation. Whenever possible, this information should be presented to them in written form and subjects should be asked to sign a copy of the notice/form indicating their receipt of the information. When the new information requires a change to the consent document, the enrolled subject may need to be re-consented. Any new or revised documents that will be presented to subjects require IRB review and approval prior to use.

14.6 ELEMENTS OF CONSENT

14.6.1 Basic Elements of Consent

Consenting documents or other methods used to obtain consent must include the basic requirements of DHHS 45 CFR 46.116 and, for studies regulated by the FDA, 21 CFR 50.25 unless a waiver or alternation of the document has been approved by the IRB. Studies subject to FDA regulations must also meet the requirements of FDA 21 CFR 50.20, as applicable. IRBs have the authority to make the determination regarding the adequacy of the information in consent documents.
Elements for consent documents under DHHS 45 CFR 46.116 and FDA 21 CFR 50.25 are essentially the same. The requirements under DHHS 45 CFR 46.116 are as follows (any significant FDA differences are noted in italics):

- A statement that the study involves research, an explanation of the purposes of the research, expected duration of the subject’s participation, description of the procedures to be followed, and identification of any procedures which are experimental
- A description of any reasonably foreseeable risks or discomforts to the subject
- A description of any benefits to the subject or to others which may reasonably be expected from the research
- A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject
- A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained. (FDA studies must also state the “...possibility that the Food and Drug Administration may inspect the records.”)
- For research involving more than minimal risk, an explanation as to whether any compensation or medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained
- Information regarding whom to contact for pertinent questions about the research and research subjects’ rights and whom to contact in the event of a research-related injury to the subject
- A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled

In order to approve a non-exempt project, the IRB must determine that the above elements are appropriately disclosed to each participant or legally authorized representative as a part of the consent process unless a waiver of consent has been approved in conjunction with the study.

### 14.6.2 Additional Elements of Consent

When appropriate, the federal regulations indicate that one or more of the following elements information shall be provided to each subject:

- A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable
- Anticipated circumstances under which the subject’s participation may be terminated by the investigator without regard to the subject’s consent
- Any additional costs to the subject that may result from participation in the research
- The consequences of a subject’s decision to withdraw from the research and procedures for orderly termination of participation by the subject
- A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject, and
- The approximate number of subjects expected to participate in the study
When reviewing a project, the IRB will consider the need for inclusion of any of these additional elements of consent. In addition to the requirements listed above, the IRB may further require the inclusion of any of the following:

- A provision for subjects to be given a copy of the consent form, if the consent is written
- Identification of the sponsor in sponsor-initiated studies
- If blood samples will be drawn, information regarding the amount of blood that will be drawn
- If subjects are being followed for survival, indication of the investigator’s intent to do so
- If material such as tumor tissue, bone marrow, blood, etc. will be turned into a commercial product, statement that the subjects may not benefit from the development of the commercial product
- The amount of compensation, and whether payment will be made incrementally or paid in full upon completion
- When applicable, information that compensation of $600 or more paid to subjects within one calendar year is required to be reported to the IRS
- A disclosure statement if the investigator is being directly compensated for conducting the study or has a significant financial conflict of interest

### 14.6.3 Projects Involving FDA Investigational Drugs, Agents or Biologics

If the project involves an FDA investigational drug, agent, or biologic, additional IRB consent requirements include, when applicable, that:

- The document must contain a statement that the drug, agent or biologic is “investigational” or “not FDA-approved”
- No claims may be made which state or imply, directly or indirectly, that the drug, agent or biologic is safe or effective for the purpose(s) under investigation or that the product is in any way superior to another product
- The document must describe any plans for randomization
- The document must describe any plans for use of a placebo and the probability of the subject receiving an active or inert substance
- For phase I studies, the consent document must disclose that the purpose of the research includes examining the safety and toxicity of the drug, agent, or biologic. For phase II and phase III studies, the consent document must disclose that the purpose of the research includes examining the drug, agent, or biologic for safety and efficacy (effectiveness)
- The document must include the conditions for breaking the code if the study is blinded

### 14.6.4 Projects Involving FDA Investigational Devices

If the project involves an FDA investigational device, additional IRB consent requirements include, when applicable, that:

- No claims may be made which state or imply, directly or indirectly, that the device is safe or effective for the purposes under investigation or that the device is in any way superior to any other device
- The consent document must contain a statement that the device is “investigational,” or that it is “not FDA approved.”
14.7 WAIVER OF CONSENT REQUIREMENTS

Under DHHS 45 CFR 46.116, the IRB may waive or alter the requirements for obtaining informed consent provided the IRB finds and documents that:

- The research is not FDA-regulated;
- The research involves no more than minimal risk to the subjects;
- The waiver or alteration will not adversely affect the rights and welfare of the subjects;
- The research could not practicably be carried out without the waiver or alteration; and
- Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

-or-

- The research is not FDA-regulated;
- The research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine: (i) public benefit or service programs; (ii) procedures for obtaining benefits or services under those programs; (iii) possible changes in or alternatives to those programs or procedures; or (iv) possible changes in methods or levels of payment for benefits or services under those programs; and
- The research could not practicably be carried out without the waiver or alteration.

For FDA-regulated research, the exceptions to informed consent requirements at 21 CFR 50.23 generally require that:

- The subject is confronted with a life-threatening situation
- Informed consent is not possible because of an inability to communicate with, or obtain legally effective informed consent from, the subject
- Time is not sufficient to obtain consent from the subject’s legally authorized representative
- No alternative method of approved therapy is available that provides equal or greater likelihood of saving the subject’s life

14.8 DOCUMENTING CONSENT

14.8.1 Overview

In general, informed consent must be documented unless the IRB has determined that it can be waived under DHHS 45 CFR 46.117(6) or FDA 21 CFR 56.109(c). For studies that involve FDA regulated products, investigators are responsible for adhering to any other FDA guidelines regarding documentation of consent that are applicable to the type of research being conducted including the dating of the consent document by the subject or the subject’s legally authorized representative. In all cases, the subject or the subject’s representative should be given adequate opportunity to read the consent document and have questions answered before the document is signed.

The consent signature(s) should be obtained as follows:
The subject or the subject’s legally authorized representative is asked to sign and date the consent document.

The person obtaining the subject’s consent will sign and date the document, if required by the study protocol, the IRB, or study sponsor.

A witness to the subject’s signature will sign and date the document, if required by the study protocol, the IRB, or study sponsor.

In all cases, signatures on the consent document may only be dated by the individuals who sign the document.

The subject or the subject’s legally authorized representative will be given a copy of the consent document unless waived per DHHS 45 CFR 46.117(c) or FDA 21 CFR 50.27.

A copy of the documentation of consent must be retained in the stated repository.

### 14.8.2 Missing Signatures or Dates on Consent Documents

In all cases, signatures and dates on consent documents may only be provided by the individual(s) who sign the documents. If a signature or date is later found to be missing, procedures are as follows:

- **If a subject’s signature is later found to be missing** on a consent document, this information must be documented in the subject’s file and in the study records, as appropriate. The information should not be filled in. The IRB must be notified immediately upon discovery of the omission that the consenting document is missing the subject’s signature. The IRB will instruct the investigator on how to proceed. Measures should be taken to prevent future omissions of subject signatures on consenting documents.

- **If a date is later found to be missing** on a consent document, the information must be documented in the subject’s file and in the study records, as appropriate. The information should not be filled in. The IRB must be notified promptly upon discovery of the omission that the consenting document is missing the signature date. The IRB will instruct the investigator on how to proceed. Measures should be taken to prevent future omissions of the signature date.

### 14.8.3 Waiver of Written Documentation of Consent

IRB policy and federal regulations [DHHS 45 CFR 46.11] generally require written documentation of informed consent. The requirement may be waived by the IRB if the research is not FDA-regulated and:

- The only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject’s wishes will govern; or

- The research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.

If a principal investigator wishes a waiver of the requirement for a signed consent document and meets the requirements, he/she should request and provide justification for a waiver as part of a submission to the IRB.
Waiving the requirement for obtaining a signed consent form does not waive the requirement for informed consent. Subjects must be informed of the nature of the research, and their consent (or the consent of their legal representatives) must be obtained whenever appropriate. The IRB must be provided with a written description of the information that will be provided to subjects. The IRB may require the use of an IRB approved information statement when it waives the requirement for written documentation of informed consent. An information statement essentially contains all elements of a consent document and may include the signature and date of signature of the individual obtaining consent and the investigator's signature and date of signature, but does not include a signature line for the subject.

14.8.4 Requirements for Documentation of Consent When Some or All Elements of Consent are Waived

If only some elements of informed consent are waived, documentation of partial consent may still be required, depending on the type of study. If all elements of consent are waived, documentation of consent is also waived.

14.8.5 Documenting the Time of Consent

In some instances, it may be critical to document not only the date but also the time when consent was obtained. In such instances, the “time of signature” may be added to the signature area of the consent document.

14.9 USE OF NON-ENGLISH CONSENT FORMS

14.9.1 Overview

For studies that anticipate enrollment of research subjects who do not read/speak English, the investigator is responsible for providing a version of the entire consent document in a language that is understandable to the subject.

All non-English consent forms, recruitment tools, questionnaires, surveys, and/or any other study documents that provide information to the subject or that the subject will complete must be approved by the IRB before use. As with the consent document, translation of any other study documents should occur after the English version has received IRB approval. The investigator bears the responsibility of verifying the accuracy of the translation of the IRB approved documents. The protocol should specify the credentials of the translator to perform the translation. Expedited review of foreign language versions may be possible if the protocol and the full English language consent document have already been approved by the IRB.

The investigator is also responsible for addressing any cultural norms that might affect the consent process. Information regarding how these issues will be addressed should be provided to IRB as part of the protocol at the time of review.

The IRB will consider which of the procedures at DHHS 45 CFR 46.117(b) is appropriate for documenting informed consent in protocols requiring translated consent documents.

The following are consent procedures for non-English language subjects:
• In most cases, a witness must be present during consent procedures. In studies where the consent documents are in the subject’s native language and the individual obtaining consent is fluent in the subject’s native language, requirements for a witness will be determined on a case-by-case basis.

• An IRB-approved translated consent document shall be presented to the subject and/or to the subject’s legally authorized representative (LAR) in the subject’s native language. An individual who is fluent in both English and the subject’s language may assist the person obtaining consent. When obtaining clinical consent, investigators should engage an appropriate medical translator to perform the consent process.

• Signing non-English Consent Forms
  o The subject and/or the subject’s legally authorized representative must sign and date the consent document
  o The person obtaining consent (as authorized by the PI and as listed on the HS-1A Application Form) must sign and date the consent document, and
  o In situations where an interpreter is involved in the consent process, that individual must also sign the consent document. That individual may also serve as the witness.

• Copies of the consent document(s) will be given to the subject or the subject’s LAR

• When a translator is used, the individual obtaining consent should document in the research records that consent was obtained using a translator. This documentation should include the name of the translator and a statement of the translator’s belief that the subject understood the study and the consent process prior to signing the consent document.

• A copy of the signed consent document must be retained in the stated repository

Other considerations for consenting non-English language subjects:

• A member of the research staff fluent in the subject’s language should be available not only at the time of consent, but also throughout the course of the study to answer questions and ensure ongoing understanding. If such a staff member is not available, a translator fluent in both English and the subject’s language should be available to answer questions and ensure ongoing understanding.

The investigator is responsible for complying with both the UB IRB policies regarding foreign language consent as well as any interpretation and/or translator services policies that apply at the site/institution where the research will be conducted.

14.9.2 Consent of Non-English Speaking Subjects Encountered Unexpectedly

If a non-English speaking subject is encountered unexpectedly, investigators should carefully consider the ethical and legal ramifications of enrolling subjects when a language barrier exists.

The following guidelines should be used only in rare instances when a non-English speaking subject is encountered “unexpectedly” and the investigator determines that a suitable translator is available.

In such instances, investigators may rely on an oral translation of the English language consent document if it will be presented by an individual fluent in the subject’s native language. When obtaining clinical consent, investigators should engage an appropriate medical translator to perform the consent process. Extra care must be taken in the consent process to ensure that the subject has adequately understood the study procedures, risks, benefits, etc. If there is no individual on hand who is qualified to translate and convey the consent document information and
adequately answer questions relating to the study protocol, the subject may not be enrolled until/unless an appropriate translator becomes available.

Consent procedures:
- A witness must be present during consent procedures
- The full IRB approved English language consent document should be presented verbally to the subject in their native language. All of the subject’s questions shall be answered. An individual fluent in the subject’s language (preferably a member of the research staff) should be available not only at the time of initial consent, but also throughout the study to answer questions and ensure ongoing understanding
- If the subject agrees to participate in the research study:
  - The subject will sign and date the consent document,
  - The witness to the consent process will sign and date the consent document, and
  - The person obtaining consent, will then sign and date the consent document.
- Copies of the signed consent documents will be given to the subject
- Copies of the signed consenting documents will be retained in the stated repository
- It should be documented in the research records that consent was obtained using a translator. This documentation should include the name of the translator and a statement of the translator’s belief that the subject understood the study and the consent process prior to signing the consent document.

**14.9.3 Use of Short Form Consent Documents**

Whenever possible, subjects who do not speak English should be presented with a full consent document written in a language understandable to them. Although use of a short form is not typically advised, DHHS 45 CFR 46.117(b)(2) permits oral presentation of informed consent information in conjunction with a short form written consent document (stating that the elements of consent have been presented orally to the subject or the subject’s legally authorized representative) and a written summary of what is presented orally. The written summary must embody the basic and required additional elements of disclosure and be reviewed by the IRB for this purpose. A witness to the oral presentation is required, and the subject must be given copies of the short form document and the summary.

When this procedure is used with subjects who do not speak English:
- A witness who is fluent in both English and the language of the subject must be present during consent procedures, and
- The oral presentation and the short form written document must be in a language understandable to the subject or the subject’s legally authorized representative, and
- The IRB-approved English language consent document may serve as the summary

At the time of consent:
- The short form document should be signed by the subject or the subject’s legally authorized representative, and
- The summary (i.e., the English language consent document) should be signed by the person obtaining consent as authorized by the PI and as indicated on the HS-1A Application Form; and
- The short form document and the summary must be signed by the witness. When the person obtaining consent is assisted by a translator, the translator may serve as the witness.
For studies that involve FDA regulated products, investigators are responsible for adhering to any other FDA guidelines regarding documentation of consent that are applicable to the type of research being conducted including the dating of the consent document by the subject or the subject’s legally authorized representative.

The IRB must receive all foreign language versions of the short form document as a condition of approval. Review of these versions may be conducted by the expedited process if the protocol, the full English language consent document, and the English version of the short form document have already been approved by the IRB.

It is the responsibility of the IRB, not the investigator, to determine which of the procedures at DHHS 45 CFR 46.117(b) is appropriate for documenting informed consent in protocols that it reviews.

A copy of the summary and copy of the short form will be given to the subject or the legally authorized representative. Copies of the signed documents must be retained in the stated repository.

In order to allow the use of the short form of consent documentation, the IRB must determine that:

- The consent document states that the elements of disclosure required by regulations have been presented orally to the participant or the participant’s legally authorized representative.
- A written summary embodies the basic and required additional elements of disclosure.
- There will be a witness to the oral presentation.
- For participants who do not speak English, the witness is conversant in both English and the language of the participant.
- The participant or the participant’s legally authorized representative will sign the consent document.
- The witness will sign both the short form and a copy of the summary.
- The person actually obtaining consent will sign a copy of the summary.
- A copy of the signed short form will be given to the participant or the legally authorized representative.
- A copy of the signed summary will be given to the participant or the legally authorized representative.

### 14.10 CONSENT OF ILLITERATE SUBJECTS

Illiterate populations pose a particular challenge. When a study is not greater than minimal risk, the IRB may approve a verbal consent process that waives the signed documentation of consent and provides the elements of consent verbally to potential participants in their native language. When a signed consent document is required, the following procedures should be followed.

A person who speaks and understands English but does not read and write can be enrolled in a study as long as the person is competent and able to indicate consent by other means. The person must:
• Retain the ability to understand the concepts of the study and evaluate the risk and benefit of being in the study when it is explained verbally, and
• Be able to indicate consent to study entry.

Consent procedures:
• A witness must be present during consent procedures
• The IRB approved, full description, English language consent document must be presented verbally to the subject. All of the subject’s questions shall be answered
• If the subject agrees to participate in the research study:
  o If the subject is unable to sign his/her name, it may be necessary for him/her to indicate consent by “making his/her mark” on the signature line (e.g., make an “X” on the signature line),
  o The witness to the consent (required) shall sign and date the consent document, and
  o The person obtaining consent, shall then sign and date the consent document
  o The subject shall be given a copy of the “signed and dated” consent document
• The method used for communicating with the prospective subject and the specific means by which the prospective subject communicated agreement to participate in the study must be documented, in writing, by the individual who obtained consent, directly on the signature page of the consent document as well as in the research records. This documentation should include the name of the witness and a brief signed statement of the witness’s belief that the subject understood the study and the consent process
• The original signed document shall be retained in the stated repository

If a PI anticipates enrollment of illiterate persons into a study, this information should be clearly indicated in the submitted project documents. When illiterate persons who do not speak English are to be enrolled, and signed documentation of consent is required, the above procedures can be appropriately tailored for the population and described in the submitted project documents. In these cases, the consent process should be conducted in the native language of the participants.

**14.11 CONSENT OF PHYSICALLY INCAPACITATED INDIVIDUALS**

A person who can understand and comprehend the spoken or written word, but is physically unable to talk or write, can be entered into a study if he/she has the ability to understand the concepts of the study and evaluate the risks and benefits of being in the study when it is explained, and is able to indicate consent to study entry by other means.

Consent procedures:
• A witness must be present during the consent process
• It will be documented in the research records how consent was obtained and how understanding by the subject was determined. This documentation should include the name of the witness and a statement of the witness’s belief that the subject understood the study and the consent process prior to indicating consent to participate
• The means by which the subject indicated consent to study participation will be documented
• The witness must sign and date the consent document
• The subject shall be given a copy of the “signed” and dated consent document

Copies of the signed documents must be retained in the stated repository.
14.12 CONSENT INVOLVING ADULT DECISIONALLY INCAPACITATED SUBJECTS

14.12.1 Overview

The UB HRPP holds the ethical position that the use of surrogate permission with decisionally incapacitated adults should generally follow the federal regulations for research involving children and the protections they provide. This policy does not apply to the conduct of emergency research under the FDA regulations 21 CFR 50.24. The IRBs may consider for approval enrollment of decisionally incapacitated adults, with the permission of an LAR, into research that has:

- Minimal risk (regardless of the likelihood of benefit to the subject)
- Greater than minimal risk research, if direct benefit to the subject is anticipated
- Greater than minimal risk research with no direct benefit to subjects, but potentially yielding knowledge about the subject’s disease/condition, however, the risk must be determined to present only a minor increase over minimal
- Greater than minimal risk research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of decisionally incapacitated adults

14.12.2 Capacity Assessment

In general, an adult subject is assumed to have the capacity to make an informed decision regarding participation as a research volunteer. In accordance with standard clinical procedures, a subject may be determined to lack capacity only if the following are determined to be deficient:

- The ability to understand and appreciate the nature and consequences of enrolling in research, including the benefits and risks
- The ability to understand the meaning of personal participation in the study
- The ability to reach and communicate an informed decision

Decisional incapacity may be temporary, permanent, progressive, or fluctuating. The fact that a person has been determined to lack capacity to make other decisions (e.g., is deemed unable to make decisions regarding personal asset holdings) does not establish lack of capacity for making a decision about research participation, nor does a determination of a lack of capacity to make a research enrollment decision mean that the person lacks capacity to make any other decision.

In studies involving a subject population whose capacity is known to be impaired, or is highly likely to be impaired, the submitted project documents must describe adequate procedures for making and documenting this determination. The submitted project documents must include procedures for informing persons who are determined to have decisional incapacity of that determination prior to enrollment in a study and procedures to document that this has occurred. In addition, the submitted project documents must include procedures for informing subjects that they may be enrolled in the research only with permission of an LAR. Such information should be given to subjects in the presence of the LAR. Research study designs must include appropriate procedures for the continuing/periodic capacity assessment of decisionally incapacitated subjects and their continued willingness to participate.
14.12.3 Legally Authorized Representatives

A research subject must be legally able to give informed consent; otherwise, the consent of the subject’s LAR, on their behalf, may be accepted.

LAR consent for participation in a research study should be employed only to the extent that it is consistent with the intent of DHHS 45 CFR 46.116, and FDA 21 CFR 50.20 and all other federal and state laws and regulations pertaining to protecting human subjects participating in research.

Federal regulations DHHS 45 CFR 46.116 and FDA 21 CFR 50.20 allow a “legally authorized representative” to give consent on behalf of a decisionally incapacitated adult subject, and defer to state law for the definition. New York law (Public Health Law Article 24-A) allows LAR permission, noting that a Legally Authorized Representative (LAR) is an individual or judicial or other body authorized to give permission on behalf of a prospective adult subject for the subject’s participation in the procedure(s) involved in the research. The role of the LAR is to assist the subject, as necessary, in understanding the research procedures and to ensure that the subject’s rights and welfare are protected.

LAR consent must be obtained in the same manner and extent as for adults with capacity (i.e., sufficient information provided to the representative, adequate understanding of the information by the representative, and voluntary agreement to enrollment on behalf of the subject).

The following are considered to qualify as LARs acting on behalf of decisionally incapacitated adults in New York State (listed in descending order of priority):

- A health care agent properly designated on a health care proxy form
- A court-appointed guardian or committee under the New York Surrogates Court Procedure Act Article 17-A
- The spouse
- An adult son or daughter
- A parent
- An adult brother or sister; or
- A close friend, who is an adult (18 years or older) who has a close personal relationship with the subject and provides a signed written statement (in a format approved by the IRB) to the PI that they are a close friend of the subject and that they have maintained such regular contact with the subject as to be familiar with the subject’s activities, health, religious or moral beliefs, and some means of corroborating such familiarity.

When a person with priority on this list is not reasonably available, not willing to make a decision, or not competent to make a decision regarding research participation, the authority falls to the person of the next highest priority. Once identified, the identity of the surrogate will be documented in the research records.

When research is occurring in a jurisdiction outside of New York State that specifies a different priority for LARs, the local laws will be followed. When a locality has no priority for LARs, the order in this document will be followed.

Use of LARs does not apply to the conduct of emergency research under Food and Drug Administration (FDA) regulations [21 CFR 50.24].

14.12.4 Assent by Decisionally Incapacitated Adult Subjects
When an adult subject is not capable of providing consent but is capable of providing assent, the submitted project documents must describe adequate provisions for soliciting and documenting the assent of the subject in addition to obtaining the permission of the authorized representative.

Assent of decisionally incapacitated adult subjects is required unless specifically waived by the IRB. “Failure to object” is not considered to be assent and resistance to a research procedure in a non-verbal subject is an indication of the subject’s disapproval.

For minimal risk studies, the IRB may waive the assent requirement under circumstances in which consent may be waived in DHHS 45 CFR 46.116. For FDA regulated studies, FDA 21 CFR 50.23 and 24 apply. The IRB may also waive the requirement for assent if it determines that it is not a necessary condition for protecting subjects because the capability of the subjects is so limited that they cannot reasonably be consulted (e.g., when the subject is in a coma or in an acute psychotic state). To the extent possible, and in consideration of the subject’s condition, the subject will be informed of the enrollment and the procedures involved. For all research, the adult subject’s objection to participation will be honored (i.e., the subject will not be enrolled into the research or will be withdrawn from the research if already enrolled).

In considering assent requirements, the IRB shall take into account the subjects’ expected medical, social and psychological state. When the IRB determines that assent is required, it may also consider whether adequate provisions have been made to document assent procedures.

**14.12.5 Consent of Adult Subjects Who Regain Capacity**

Adequate provision must be made for soliciting the consent of each adult subject who is capable of giving consent. If an adult subject who has been enrolled in research by the permission of a surrogate regains capacity during the course of participation, then consent must be obtained from that person before continuing research-related activities. Research study designs must include appropriate procedures for the continuing/periodic capacity assessment of decisionally incapacitated adult subjects.

**14.12.6 Anticipated Loss of Decisional Capacity by Adult Subjects Enrolled In Research**

In cases where adult subjects will be capable of providing consent to enroll but will likely lose that capacity as the study progresses (e.g., in progressive dementia research), the submitted project documents must make provision for the subject to designate a legally authorized representative upon enrollment or at the earliest appropriate time while the subject still has capacity. In these cases, the subjects should be asked to provide guidance to the LAR about the conditions under which the subject would and would not want to participate in the event of loss of capacity. Until/unless the subject loses capacity, the designated representative is not empowered to make decisions about the subject’s participation in research.

**14.12.7 Documentation of LAR Consent**

If consent is obtained in person, the LAR’s consent signature will be obtained as follows:

- The LAR shall sign and date the consent document
- When possible, the subject shall sign and date assent
- The person obtaining consent may also sign and date the document
A witness to the subject's signature shall also sign and date the document if required by the study protocol, the IRB, or study sponsor.

The LAR must be given a copy of the signed and dated consent document.

Documentation of any assessments of cognitive capacity or assessments of the capacity to consent, identification of the authorized representative, as well as the consent, permission, and assent documents, as applicable, must be kept within the stated repository.

14.13 PERMISSION AND ASSENT FOR CHILDREN

14.13.1 Definitions (for research purposes):

- **Minor:** In New York State, persons who are less than 18 years of age
- **Children:** Individuals who unless emancipated or otherwise legally authorized, have not yet reached the age at which they may legally consent to the procedures in research. Where a local jurisdiction does not specifically address consent to participate in research, the age at which one can consent to medical procedures will be used. If neither age is specified, the IRB may make this determination based on the customs of the area where the research is to be conducted.
- **Parent:** A child's biological or adoptive parent
- **Guardian:** An individual who is authorized under applicable state or local law to consent on behalf of a child for general medical care. In the absence of parents, if state or local law do not specify who may act as a guardian, the persons and priorities listed for LARs may be used to determine this.
- **Parental Permission:** The agreement of parent(s) or the guardian for the child to participate in research.
- **Assent:** The child's affirmative agreement to participate in the research. The absence of an objection may not be construed as assent.

14.13.2 Overview

When children are involved as research subjects, a legally valid consent to participate in research cannot be achieved by obtaining the signature of the subject alone. In most circumstances, both permission from one or both parents/legal guardians and the assent of the child must be obtained before the research subject can be enrolled.

If the research does not involve more than minimal risk, or if it does involve greater than minimal risk but there is prospect of direct benefit to the child, the IRB may determine that the permission of one parent is sufficient. For research involving greater than minimal risk with no prospect of direct benefit, permission must be obtained from both parents. When the IRB determines that the permission of both parents is necessary, the permission of one parent is sufficient if one parent is deceased, unknown, incompetent, not reasonably available, or when one parent has legal responsibility for the care and custody of the child. The IRB makes the final determination regarding signature requirements for the permission document; the determination will be based on the level of risk involved.

14.13.3 Waiver of Parental Permission

- For FDA-regulated studies, permission of parents or guardians may not be waived.
For studies which are not FDA-regulated, permission of parents or guardians must be obtained unless relevant regulations at DHHS 45 CFR 46 116 or 46.408 are met. In general, parental permission may be waived or altered by the IRB:
- By meeting regulatory criteria for waivers or alteration of consent
- The IRB determines that the protocol is designed for a condition or subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects provided that another appropriate mechanism for protecting the children is substituted

### 14.13.4 Permission of Parents or Guardians

Permission by parents or guardians will be documented in a manner similar to that used to document informed consent for adults. In general, parental permission must be appropriately documented unless it is determined that it can be waived under the Common Rule or FDA regulations. For studies that involve FDA regulated products, investigators are responsible for adhering to the FDA guidelines for the type of research being conducted.

If signed permission is obtained in person, the parental permission signature will be obtained as follows:
- The parent(s) is asked to sign and date the parental permission document
- The person obtaining consent shall also sign the document if required by the study protocol, the IRB, or study sponsor,
- A witness to the parent’s signature may also sign the document if required by the submitted project documents, the IRB, or study sponsor
- The parent may be given a copy of the document

When signed permission is not obtained in person:
- If permission is not obtained in person, appropriate documentation shall consist of the date permission was granted, the means by which permission was obtained, and the person obtaining permission (i.e., the investigator or authorized investigator designee) must date and sign the documentation

A copy of the signed permission or signed documentation of permission must be retained in the stated repository.

In all cases, signatures on the consent document may only be dated by the individuals who sign the document. If the dates or signatures on the document are later found to be missing, this information should be reported to the IRB and managed as indicated in Section 14.8.2: Missing Signatures or Dates on Consent Forms.

### 14.13.5 Assent of the Child

Generally, in addition to parental permission, the assent of the child must be obtained. Children should be asked about their willingness or “assent” to participate. Information about the research study must be presented to children at their level taking into consideration age, maturity, and psychological state, so they can understand what is requested of them. The same basic elements of the consent document discussed in Section 14.6: Elements of Consent apply to the assent document.
For research with very young children who do not have the capacity to understand the research, typically only parental permission is needed.

For older children, generally both parental permission and child assent are required. Two consenting documents are advisable, one written for the child at the basic level (the assent document) that may be a script for oral presentation or for reading, and a more detailed document (the Parental Permission document) for the parent or guardian’s understanding and signature. The parental permission document must include all elements of the consent document (see Section 14.6: Elements of Consent for required elements of consenting documents).

The IRB generally requires that the forms for parental permission be separate from those that are used to obtain child subject assent so that the child is free of parental influences and allowed to make their own decision about participation in research. This separate assent form includes the use of larger fonts and simplified language in written consent documents for children who can read and, for very young children, a script to be read to them or a presentation made to them for their verbal assent.

Although separate permission and assent documents are generally recommended, for older adolescents between the ages of 14 and 17, a single form that both the adolescent and parent(s) sign may be used. The consent document containing all the required elements would have a signature page that includes places for both the parent and the adolescent’s signatures. When one document is used, the information may be presented to both the parent and the adolescent, however, signatures should be obtained separately to reduce the likelihood of parental pressure on the adolescent to participate.

Statements such as “your parent has agreed to allow you to take part in the research study” may not be used since this may imply parental pressure to participate.

In considering assent requirements, the IRB shall take into account the subjects’ expected medical, social and psychological state. When the IRB determines that assent is required, it may also consider whether adequate provisions have been made to document assent procedures.

### 14.13.6 Waiver of Child Assent

In accordance with 45 CFR 46 Subpart D, the assent of the child must be obtained unless the IRB determines that one or more of the following conditions are met:

- Conditions are met for waiving consent for adults, or
- A child or all children involved in the study are incapable of assenting based on age, maturity or psychological state, or
- The capability of a child or all children involved in the study is so limited that they cannot reasonably be consulted.
- The research holds out prospect of direct benefit that is important to the health or well-being of the children that is available only in the research context.

When the above conditions are met the IRB will determine and document if and when assent is to be a requirement of all, some or none of the children in a study. When assent may be waived for only some children who will participate in a study, the IRB will determine and document that only some children are not required to provide assent.
14.13.7 Documenting Child Assent

The IRB will determine whether assent will be documented and the process used to document assent based on considerations such as the child's age, maturity, and degree of literacy. If adolescents are involved in research where a consent document would be used for adult subjects, a similar form should be used to document the adolescent's assent.

If young children are involved who are unable to read the assent form, documentation should take a form that is appropriate for the purpose of recording that assent took place. The IRB may determine that documentation of assent is not warranted.

14.13.8 When a Child Reaches the Legal Age of Consent While Enrolled in a Study

When a child who was enrolled in research with parental/guardian permission subsequently reaches the legal age of consent to participate in the procedures involved in the ongoing research, the subject's participation is no longer regulated by the requirements of DHHS 45 CFR 46.408 regarding parental or guardian permission and subject assent.

Unless the IRB determines that the requirement for obtaining informed consent can be waived, the investigator should seek and obtain the legally effective informed consent for the now adult subject for any ongoing interactions or interventions with the subjects. The prior parental permission and child assent are not equivalent to legally effective informed consent for the now-adult subject.

14.13.9 Legally Authorized Representative (LAR) for Children/Minors in New York State

The Legally Authorized Representatives (LARs) for children/minors in New York State are listed in descending order of priority as follows:

1. the parent or parents of the child
2. the judicially-appointed guardian(s) of the child, if the guardian has been appointed and if medical decisions are within the scope of the guardianship
3. in certain cases, the Commissioner of Social Service

(Source: New York Civil Liberties Union: Teenagers, Health Care & the Law)

14.13.10 Minors in New York State Who May be Able to Give Legally Effective Informed Consent

In New York State, under very specific conditions, minors may provide their own consent. This includes emancipated minors (i.e., individuals who have not yet attained the age of legal competency as defined by state law, but have a legal status conferred upon them as if they had by virtue of assuming adult responsibilities such as self-support, marriage, or procreation). Because of their age, such individuals are considered to be "vulnerable" and may require special protections.

14.13.11 Process to Determine Which Individuals Qualify as Children/Guardians/Legally Authorized Representatives for Research Conducted Outside New York State
If research on children is being conducted outside New York State, the determination of which individuals legally qualify as “children”, “guardians”, or “legally authorized representatives” will be made in the following order of priority:

1. If the out-of-state site’s own IRB is reviewing the study for that site’s activities, the UB IRB will typically accept that the IRB is approving activities that are in compliance with its own state’s requirements regarding minors, legally authorized representatives and guardians and therefore needs no further description in the local protocol.

2. If the research is to be conducted outside New York State, the PI is responsible for finding out the applicable information regarding age of consent, guardian, and LAR information and providing the information in the protocol. The source of the information must also be provided in the protocol for verification purposes. The source of information should come from one of the following (in order of priority):
   a) Publicly available legal documentation applicable to the jurisdiction in question that defines the age of consent, guardianship, and LAR information, as it pertains to research participation.
   b) Publicly available legal documentation applicable to the jurisdiction in question that defines the age of consent, guardianship, and LAR information, as it pertains to activities that are similar to research participation (e.g., consent to medical treatment).
   c) A copy of the determination from an Ethics Committee, or its equivalent, that has reviewed the project. The determination should indicate that cultural norms for the age of consent, LAR and guardianship were taken into consideration when reviewing the project.
   d) A consultation from an individual who is familiar with the cultural context and community attitudes of the area/country/site in which the research will be conducted. Documentation of the consultation that includes pertinent information must be provided to the UB IRB. The protocol should identify the individual who will be consulted on issues regarding consent, guardianship, and LAR, as appropriate, during the course of the study. When appropriate, means of verifying this information must be provided in the protocol.

The UB IRB has the authority to make its own determination whether the research can be approved based on the information provided.

### 14.14 WARDS OF THE STATE

The special protections for children set forth in 45 CFR 46 Subpart D include additional limitations on some research involving children who are wards of the state or any other agency, institution, or entity. When the research involves greater than minimal risk to the subjects with no prospect of direct benefit to individual subjects [45 CFR 46.406], or requires DHHS Secretarial approval [45 CFR 46.407], the research must either be related to their status as wards, or else be conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards [45 CFR 46.409]. The IRB requires, for each child who is a ward in these studies, the appointment of an advocate in addition to any other individual acting on behalf of the child as a guardian or *in loco parentis*.
When an advocate has been identified, but before he/she begins to act in this role for a specific study, IRB must make the following determinations:

- The advocate is an individual who has the background and experience to act in, and agrees to act in, the best interests of the child for the duration of the child’s participation in the research
- The advocate is not associated in any way (except in the role as advocate or member of the IRB) with the research, the investigators, or the guardian.

A specific member may be designated by the board to make these determinations for any/all advocates associated with a specific study.

If the IRB is unable to make the above determinations, it may request that information be provided by the researcher, the advocate or any other persons so that they can be made.

14.15 CONSENT GUIDELINES FOR GENETIC RESEARCH

Many clinical research projects involve obtaining a sample of blood or tissue for genetic analysis. The storage of the sample, its coding, storage, transfer to others and means by which the results linked to that sample are disclosed are important issues and have consequences for patient privacy and confidentiality. The information, if disclosed, may cause discriminatory decisions regarding insurance or employment matters. In developing the informed consent for the use of genetic materials, it is important to clarify what samples are to be used, how these will be coded, a description of any disclosures of results, the duration of storage, and how the data will be secured.

A separate consent document is recommended for a genetic substudy. This will permit individuals to consent to participation in the main study but not consent for genetic substudy. In addition to all required elements of informed consent discussed earlier in this section, the following are specific additional considerations that must be addressed in the consent document for studies collecting genetic information:

- **Purpose of the study**: The purpose for collecting the genetic information must be stated
- **Procedures**: The procedures for how the genetic sample will be collected, who will handle the sample, where the sample will be stored, how long the sample will be kept, and whether the subject may be contacted in the future about the sample must be stated
- **Risks and benefits**: The risks and benefits associated with collecting and storing the sample must be stated. In addition, any potential risk associated with disclosure of genetic information must be stated
- **Confidentiality of the patient information**: The mechanisms that will be used to protect the confidentiality of the sample including any plans to destroy the sample in the future must be included
- **Commercialization**: Subjects must be made aware of any potential for commercial benefit from results obtained with their sample. If so, it must be clearly stated that the subject will not be a recipient of any financial reward

**Description of how samples will be coded**

When describing the mechanisms used to protect the confidentiality of the samples/data, the proper terminology and/or description should be used to promote understanding and avoid confusion. There are a number of ways to code samples. The method selected depends upon the information being collected and the degree of confidentiality and security that will be provided. When describing data and coding methods, HIPAA terminology (see Section 11.1 for HIPAA
terminology) should be used when possible for purposes of consistency and clarity (e.g., anonymous data, coded data (identifying or non-identifying), or de-identified data).

14.16 CONSENT GUIDELINES FOR RESEARCH INVOLVING PREGNANT WOMEN OR FETUSES PRIOR TO DELIVERY

Informed consent requirements [45 CFR 46.204]:
- The consent document clearly explains the reasonably foreseeable impact of the research on the fetus, and
- Consent will be obtained from the appropriate individuals as follows:
  - The pregnant woman or her legally authorized representative if:
    - The research holds out the prospect of direct benefit to the pregnant woman, or,
    - The research holds out the prospect of a direct benefit both to the pregnant woman and the fetus, or
    - The research does not hold out the prospect of direct benefit for the woman or the fetus, but the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means
  - The pregnant woman and the father if:
    - The research holds out the prospect of a direct benefit solely to the fetus unless the father is unavailable, incompetent, or temporary incapacitated, or the pregnancy resulted from rape or incest
    - The father's consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest. In cases where the father is not reasonably available, a statement to this effect must be signed by the mother.

Generally, for children who are pregnant, assent and permission are obtained in accord with the provisions of the DHHS 45 CFR 46 Subpart D: Protections for Children Involved as Participants.

14.17 CONSENT GUIDELINES FOR RESEARCH INVOLVING NEONATES

Neonates of Uncertain Viability: After delivery, and until it has been ascertained whether the neonate is viable, the neonate may not be involved in research unless all of the following conditions are met:
- The research holds out the prospect of enhancing the probability of survival of the neonate to the point of viability, and any risk is the least possible for achieving that objective, or
- The purpose of the research is the development of important biomedical knowledge which cannot be obtained by other means and there will be no added risk to the neonate resulting from the research

Informed consent requirements [45 CFR 46.205]:
- The consent document shall explain the reasonably foreseeable impact of the research on the neonate.
- Informed consent shall be obtained from either parent of the neonate or, if neither parent is able to consent because of unavailability, incompetence, or temporary incapacity, consent shall be obtained from either parent's legally authorized representative. If the
pregnancy resulted from rape or incest, the father’s consent or that of his legally authorized representative need not be obtained.

**Nonviable neonates:** After delivery, a nonviable neonate may not be involved in research unless all of the following conditions are met:

- Vital functions of the neonate will not be artificially maintained
- The research will not terminate the heartbeat or respiration of the neonate
- There will be no added risk to the neonate resulting from the research
- The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means

Informed consent requirements *(45 CFR 46.205)*:

- The informed consent of both parents of the neonate will be obtained. However, if either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of one parent will suffice. If the pregnancy resulted from rape or incest, the consent of the father is not needed.
- The consent of a legally authorized representative of either or both of the parents of a nonviable neonate will not suffice

**Viable Neonates:** Viable neonates are considered to be children and will be treated as such under UB HRPP policy (see Section 10.4: Research Involving Children).

### 14.18 SUBJECT WITHDRAWAL

As part of the consent process, investigators should inform participants what will happen to the data that has been collected about them, if they choose to withdraw from the study or if the investigator withdraws them from the study. Participants will be told that once they withdraw from the study no additional information will be collected about or from them, and whether or not data collected up to the time of their withdrawal may continue to be used by the investigator.

The investigator may obtain the participant’s subsequent consent for continued limited participation in study follow up when withdrawal occurs.

### 14.19 CONSENT FOR CONTINUED USE OF DATA AFTER SUBJECT WITHDRAWAL

Investigators should generally inform participants as a part of the consent process whether they intend to either: (1) retain and analyze already collected data relating to the subject up to the time of subject withdrawal; or (2) honor a research subject’s request that the investigator destroy the subject’s data or that the investigator exclude the subject’s data from any analysis.

With regard to data retention when participants withdraw from a clinical trial the following procedures must be followed and the IRB will ensure as a part of its review that:

- When a participant withdraws from a study, the data collected on the participant to the point of withdrawal remains part of the study database and may not be removed. The consent document cannot give the participant the option of having data removed.
- A Researcher may ask a participant who is withdrawing whether the participant wishes to provide continued follow-up and further data collection subsequent to their withdrawal.
from the interventional portion of the study. Under this circumstance, the discussion with
the participant distinguishes between study-related interventions and continued follow-up
of associated clinical outcome information, such as medical course or laboratory results
obtained through non-invasive chart review, and address the maintenance of privacy and
confidentiality of the participant’s information.

- The Researcher must obtain the participant’s consent for this limited participation in the
  study (assuming such a situation was not described in the original consent document).
  The IRB must approve the consent document.
- If a participant withdraws from the interventional portion of a study and does not consent
to continued follow-up of associated clinical outcome information, the Researcher must
not access for purposes related to the study the participant's medical record or other
confidential records requiring the participant's consent. However, a Researcher may
review study data related to the participant collected prior to the participant's withdrawal
from the study, and may consult public records, such as those establishing survival status.
15. RESPONSIBILITIES OF INVESTIGATORS AND FACULTY SPONSORS

15.1 INVESTIGATOR RESPONSIBILITIES

15.1.1 Overview

Investigators are responsible for conducting their research activities in compliance with federal and state regulations, Institutional requirements, and ethical principles and standards appropriate for their discipline. While investigators may delegate responsibilities to other members of the staff, the ultimate responsibility for the overall conduct of the study rests with the investigator even when those responsibilities have been delegated. Investigators must always regard the protection of the rights and welfare of research subjects as their primary concern. In general, investigators are responsible for the research plan, training and education of the research staff, meeting IRB requirements, obtaining informed consent of subjects, reporting and recordkeeping.

15.1.2 The Research Plan

- Understanding the definition of human research and seeking guidance when unsure whether the research meets that definition
- Designing and implementing research that is consistent with the ethical principles delineated in the Belmont Report
- Submitting to the IRB a comprehensive and well-written protocol
- Conducting the research according to the IRB approved protocol
- Employing sound study design in accordance with the standards of the discipline so that the research will likely develop or contribute to generalizable knowledge
- Judging the research design to be sound enough to meet its objectives before submitting the project to the IRB for review
- When investigators do not design the research themselves, judging the research design to be sound enough to meet its objectives before agreeing to enroll subjects
- Possessing appropriate credentials to conduct the research
- Possessing sufficient time to conduct and complete the research
- Ensuring that the research staff for the project has appropriate credentials to perform their functions in the study
- Ensuring that all units collaborating with the investigator, but are not under the investigator's direct supervision, are aware of their roles in the research project and their responsibilities to the research subjects
- Ensuring that adequate space, personnel, services and equipment required for conducting the proposed research properly and safely are and will remain available to complete the project. If resources should become unavailable that puts subjects at risk if they continue to participate, the investigator is responsible for stopping the research
- Ensuring that there is access to an adequate population to allow recruitment of the necessary number of subjects to complete the study
- Ensuring that any investigator or co-investigator’s conflict of interest that might affect the relationship with the research subject or the outcome of the research are properly disclosed and managed
- Ensuring that the choice and recruitment of subject population results in an equitable distribution of the burdens and benefits of the research
• Minimizing risks to research subjects by using procedures that are consistent with sound research design, preventing exposure of subjects to unnecessary risks and, whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.
• Ensuring that any risks to human subjects are reasonable in relation to the anticipated benefits (if any) to the individual, and the importance of the knowledge that is expected to be gained
• Ensuring that appropriate safeguards are included to protect the rights and welfare of human subjects who are likely to be vulnerable to coercion or undue influence (e.g., children, prisoners, pregnant women, decisionally impaired individuals, educationally or economically disadvantaged persons)
• Submitting a data and safety monitoring plan to the IRB as part of the submitted project documents
• Implementing reporting mechanisms that enable monitoring of the safety and rights and welfare of subjects enrolled in the research as appropriate to the research being conducted
• Implementing mechanisms for monitoring the data during the conduct of the research to ensure the safety of subjects and integrity of the data as appropriate to the research being conducted
• Conducting the research in compliance with HRPP policies
• Complying with federal regulations for the protection of human subjects as appropriate including, as applicable:
  o Department of Health & Human Services (DHHS) regulations: 45 CFR 46 including Subparts B-D
  o Food and Drug Administration (FDA): 21 CFR 56 and 21 CFR 50 as well as FDA regulations based on use of FDA regulated products: drugs [21 CFR 312], devices [21 CFR 812], or biologics [21 CFR 600]
  o Protection of subjects’ privacy and confidentiality according to applicable HIPAA policies
  o Policies from other federal agencies
• Complying with any state or local laws for the protection of human subjects

15.1.3 Training and Education

• Meeting HRPP requirements for initial and continuing education and ensuring that members of the research staff also meet those requirements
• Ensuring that all research staff and others assisting in the conduct of the research study are informed of the following as appropriate to the research being conducted and to the individual’s role on study:
  o study procedures
  o informed consent requirements
  o steps to be taken to reduce potential risks
  o potential events/problems associated with study participation
  o event/problem reporting requirements
  o how to respond to subject questions, complaints, or concerns
  o data collection and record-keeping requirements
15.1.4 IRB Requirements

- Ensuring that all research involving human subjects is submitted to the appropriate IRB and that approval is obtained prior to initiation of the research.
- Complying with all applicable IRB policies, requirements, procedures, decisions, and conditions
- Conducting research in strict accordance with the current IRB-approved research project (except where a change may be necessary to eliminate an apparent immediate hazard to a given human research subject)
- Reporting events/problems to the IRB as described in Section 17: Reportable Events and Problems
- Submitting to the IRB and obtaining approval for any changes or amendments prior to initiation of those changes
- Submitting requests for renewal in a timely fashion so that IRB approval does not expire
- Ensuring that enrollment does not continue and all project activity ceases if IRB approval of the project expires, is suspended, or terminated (see Section 7.3.2: Continuing/Renewal Review and Section 8.7.4: Suspensions and Terminations of IRB Approval)
- Ensuring that, for research involving the use of protected health information (PHI), appropriate HIPAA mechanisms are submitted to and approved by the IRB prior to use of PHI

15.1.5 Informed Consent (unless requirements for consent or documentation of consent have been waived)

- Obtaining prospective informed consent
- Documenting Informed consent and parental permission/child assent, as applicable, in accordance with federal regulations and IRB policy and as approved by the IRB unless the IRB has granted a waiver of the informed consent or documentation of informed consent
- Ensuring that human research subjects are kept informed of any new information that may affect their willingness to continue to participate in the research study
- Ensuring that subjects can contact the investigator or research team with any questions or concerns

15.1.6 Reporting and Recordkeeping

- Ensuring that subjects’ questions, concerns, and complaints are properly addressed and that documentation of the resolution to any complaints or concerns is retained in the project files
- Maintaining current and accurate records of research data, outcomes, and events/problems to permit an ongoing risk/benefit assessment of study participation
- Reporting progress of approved research to the IRB as often and in the manner prescribed by the IRB (e.g., timely submission of properly completed Applications for Continuing Review)
- Reporting promptly to the IRB (and the sponsor, when applicable) any serious event/problem (SEP) according to the guidelines in Section 17: Reportable Events and Problems
• Reporting any significant changes in the risk/benefit assessment in regard to study participation
• If a Data Safety Monitoring Board (DSMB) has been established for a clinical trial, submitting copies of the DSMB’s reports to the IRB for review
• Notifying the IRB if the Principal Investigator will be leaving UB or one of its affiliated institutions (see Section 7.3.5: When an Investigator Leaves the Institution)
• Submitting a Completed/Closed Notification – Final Report when a study is completed or closed
• Ensuring that the human subject documentation for the project is properly retained for at least 3 years after the project is completed or closed

15.2 ADDITIONAL INVESTIGATOR RESPONSIBILITIES

The investigator is responsible for securing any additional approvals required by the institution or site where the research will be conducted (e.g., for use of specific equipment or to use facilities during certain hours). Investigators are reminded of this responsibility in IRB application and approval process guidelines.

15.3 RESPONSIBILITIES OF FACULTY SPONSORS

All student and resident researchers are required to have a faculty sponsor. The faculty sponsor is responsible for advising the student throughout the process of protocol development, submission to the IRB and subsequent review, as well as in the implementation of the research project.

Faculty sponsors are also responsible for:
• Meeting education and training requirements as determined by UB’s Human Research Protection Program (HRPP)
• Ensuring that their student researchers meet HRPP education and training requirements
• Ensuring that their student researchers are aware of and meet their responsibilities as investigators
• Ensuring the student project is closed in a timely fashion
• Ensuring that the human subject documentation for the project is properly retained for at least 3 years after the student project is completed or closed
16. CONFLICT OF INTEREST AND SIGNIFICANT OBLIGATIONS

16.1 OVERVIEW

An investigator's financial or non-financial interests and obligations may create a conflict of interest that compromises or has the appearance of compromising his/her professional judgment and independence in the design or conduct of research. Federal regulations that require IRBs to ensure that the rights and welfare of human research subjects are protected extend to the protection of those individuals from investigators whose research conduct may be compromised by a conflict of interest. Federal regulations also prohibit IRB members who have a conflict of interest in a research project from participating in any review of that project except to provide information or answer questions at the request of the IRB.

16.2 UNIVERSITY AT BUFFALO INVESTIGATOR CONFLICT OF INTEREST POLICY

The UB Investigator Conflict of Interest Policy sets forth the requirements and guidelines for:

- The disclosure of outside financial interests and obligations by investigators at the University at Buffalo who engage in University activities funded by any external entity or are funded internally through specified internal programs
- The review of investigator disclosures by designated University officials
- The identification, reporting, and resolution of conflicts of interest

The following working definitions capture the substance of the policy while focusing on its application to research:

- **Conflict of Interest:** A conflict of interest exists when an investigator's significant financial interest or significant external obligation could directly and significantly affect his/her professional judgment in exercising his/her duties or responsibilities in the administration and management of a research project.

- **Significant Financial Interest:** Anything of monetary value to the investigator or the investigator's spouse and/or dependent children that may compromise or have the appearance of compromising the investigator's professional judgment and independence in the design or conduct of research. This includes, but is not limited to:
  - Salary, royalties or other payments for services (e.g., consulting fees or honoraria) that, when aggregated for the investigator and the investigator's spouse and dependent children over the next twelve months, are expected to equal or exceed $5,000;
  - Equity interests (e.g., stocks, stock options, warrants or other ownership interests) that meet both of the following criteria: equals or exceeds $5,000 in value as determined through reference to public prices or other reasonable measures of fair market value; Intellectual property rights (e.g., patents, copyrights and royalties from such rights).

- **Significant External Obligation:** Relationships or activities with outside entities, such as positions held by the investigator (or the investigator's spouse or dependent children) as an officer, trustee, director, employee or professional consultant, that may adversely affect, or have the appearance of adversely affecting, the investigator's professional judgment and independence in the design or conduct of research.
16.3 DISCLOSURE REQUIREMENTS FOR UB INVESTIGATORS, CO-INVESTIGATORS AND OTHER KEY STUDY PERSONNEL

The UB Investigator Disclosure Policy requires UB investigators, co-investigators and other key study personnel (individuals responsible for the design, conduct, or reporting of the research) to disclose their financial interests and non-University obligations as well as the financial interests and non-University obligations of their immediate family (i.e., spouse and dependent children) by completing and submitting to the appropriate dean or vice president an Annual Disclosure of Significant Financial Interests and Significant Obligations. The Annual Disclosure form must be updated at least annually; updating is required sooner if a new conflict of interest or significant obligation arises. Disclosure criteria do not vary by funding or regulatory oversight.

The following financial interests must be disclosed:
- Ownership interest, stock options, or other financial interest related to the research of any value unless it meets the following four tests:
  - The value of the interest when aggregated for the immediate family does not exceed $5,000
  - The interest is publicly traded on a stock exchange
  - The value of the interest does not exceed 5% interest in any one single entity when aggregated for the immediate family
  - No arrangement has been entered into where the value of the ownership interests will be affected by the outcome of the research
- Compensation related to the research of any amount unless it meets the following two tests:
  - The value of the compensation when aggregated for the immediate family does not exceed $5,000 in the past year
  - No arrangement has been entered into where the amount of compensation will be affected by the outcome of the research
- Proprietary interest related to the research of any value including, but not limited to, a patent, trademark, copyright or licensing agreement

16.4 DISCLOSURE REQUIREMENTS FOR UNAFFILIATED INVESTIGATORS, CO-INVESTIGATORS AND OTHER KEY STUDY PERSONNEL

Under UB HRPP policy, unaffiliated investigators, co-investigators and other key study personnel (individuals responsible for the design, conduct, or reporting of the research) satisfy the financial conflict of interest requirement through their own institutions, including, if a significant financial conflict of interest exists, management of the conflict. The name of the institution and office that retains the unaffiliated investigator’s financial disclosure information must be provided to the UB IRB on the HS-1A Application Form.

16.5 INVESTIGATOR RESPONSIBILITIES FOR REPORTING CONFLICT OF INTEREST INFORMATION TO THE IRB

At the time of initial and continuing review, the PI must list in the financial disclosure section of the HS-1A Application Form all key study personnel (i.e., investigators, co-investigators and any other individuals responsible for the design, conduct, or reporting of the research) and indicate:
- For UB investigators, co-investigators, and key study personnel: the UB office where each individual’s current Annual Disclosure of Significant Financial Interests and Significant Obligations is retained
- For unaffiliated investigators: the name of their home institution and contact information for an official who retains their financial disclosure information

16.6 RESPONSIBILITY FOR CONFLICT OF INTEREST DETERMINATIONS

The appropriate UB dean or vice president (or their designee) acts as the University’s designated official responsible for reviewing investigator financial disclosure statements in the context of each research project and for determining whether a conflict of interest, or appearance of conflict of interest, exists. In addition, the designated official will determine what conditions or restrictions, if any, should be imposed by the institution to manage, reduce or eliminate such conflicts. The appropriate dean or vice president’s office is responsible for assisting investigators in identifying areas of potential concern and, whenever possible, for instituting remedies that permit the affected research to proceed. If a conflict of interest cannot be resolved, the designated official will inform the investigator and the IRB that the conflict could not be resolved. The evaluation criteria do not vary by funding or regulatory oversight.

16.7 IRB RESPONSIBILITIES REGARDING CONFLICT OF INTEREST

UB IRBs request a financial conflict of interest determination for all PIs, co-PIs, and key study personnel at the time of initial and continuing review for projects that are funded/sponsored by a for-profit organization. For UB PIs, co-PIs, and key study personnel who indicated on the HS-1A Application Form that they have filed an Annual Disclosure with a UB office, the IRB staff contacts the appropriate dean or vice president’s office (as indicated on the HS-1A Application Form) to request a conflict of interest determination. The appropriate office completes and returns the conflict of interest determination indicating one of the following: (1) there is no conflict, (2) there is a conflict but an agreement has been reached to successfully manage the conflict, or (3) there is a conflict of interest that has not been possible to resolve.

Unaffiliated investigators who are listed in the HS-1A Application Form as having satisfied the requirements for financial conflict of interest for the research being conducted at their own institutions must provide the IRB with the name and contact information for an official at the institution that holds their documentation of financial disclosure.

When the research is sponsored by not-for-profits through a grant, Sponsored Projects Services is responsible for contacting appropriate UB offices for COI determinations with respect to conflict of interest determinations for UB personnel.

The IRB may review a project before receiving a conflict of interest determination. However, IRB approval will not be granted until a determination has been made that there is no conflict, or if a conflict exists, that it has been managed in a manner acceptable to the IRB. The IRB may require the inclusion of a statement in the consent document indicating the existence and nature of an investigator’s financial conflict of interest. The IRB will determine whether the description in the consent document may be presented in general terms or whether specific financial information should be disclosed.
The convened IRB has the authority to make the final determination whether the financial interest and its management, if any, allows the research to be approved.

16.8 IRB MEMBER AND OUTSIDE REVIEWER CONFLICT OF INTEREST OR SIGNIFICANT OBLIGATION

Any member or outside reviewer with a potential conflict of interest or significant obligation must disclose that information to the IRB Chair. This policy applies to all types of projects reviewed by the IRB regardless of level or type of IRB review including review by a convened IRB, Review by expedited procedures, review of unanticipated problems involving risks to participants or others and review of non-compliance with regulations or laws or the requirements of the IRB or EC.

IRB members or consultants are defined as having a “Financial Interest Related to the Research” and must disclose a potential conflict of interest whenever they have a financial interest in the sponsor, product or service being tested.

Potential non-financial conflicts of interest that must be disclosed include when the IRB member or consultant is related (i.e. a spouse or family member) to a member of the research team.

16.8.1 IRB Member Conflict of Interest or Significant Obligation

Whenever an IRB member receives materials to review, it is his/her responsibility to assess whether he/she has a potential conflict of interest or significant obligation using the criteria described in Section 16.3: Disclosure Requirements for UB Investigators, Co-Investigators and Other Key Study Personnel with regard to any of the projects assigned to him/her for review. If so, that information must be disclosed to the IRB Chair as soon as possible.

When the IRB chair is informed of a member’s potential conflict of interest, he/she will determine whether the situation constitutes a conflict of interest based upon whether an independent observer could reasonably question the IRB member’s actions or decisions based on factors other than the rights, welfare and safety of the subjects. If it is determined that a conflict of interest exists, the member may not review the affected project. That individual must recuse him/herself from any deliberations and voting on that project. If an IRB member realizes at a full board meeting that he/she may have a conflict of interest in a given project, this information should be disclosed to the Chair immediately and that IRB member must recuse him/herself from any deliberations and voting on that project (see also Sections 8.8 and 16.8: IRB Member and Outside Reviewer Conflict of Interest of Significant Obligation).

In instances when a member has a conflicting interest or significant obligation but his/her expertise is necessary, he/she may provide information to the IRB provided the following requirements are met:

a. The chair was notified of his/her conflicting interests, and
b. The individual is excluded from discussion of the project except to provide information requested by the IRB, and
c. The individual is required to leave the meeting room when voting takes place, and
d. The chair is responsible for ensuring that requirements “b” and “c” above are met.
The IRB member with a conflict of interest will not be counted as part of the quorum for review and approval of the project. If the quorum fails, the IRB may not take further action or vote on the project until a quorum is established.

16.8.2 Outside Reviewer Conflict of Interest or Significant Obligation

If the Chair determines that no IRB member has adequate knowledge or experience to provide an in depth review of a project, the Chair may engage an outside reviewer with appropriate expertise and experience to conduct the review. In instances when an outside reviewer has a conflicting interest or significant obligation but his/her expertise is necessary, he/she may provide information to the IRB provided the following requirements are met:

a. The chair was notified of his/her conflicting interests, and
b. The individual is excluded from discussion of the project except to provide information requested by the IRB, and
c. The individual is required to leave the meeting room when voting takes place, and
d. The chair is responsible for ensuring that requirements “b” and “c” above are met
17. REPORTABLE EVENTS AND PROBLEMS

17.1 INTRODUCTION

Federal regulations DHHS 45 CFR 46.103 (b)(5), FDA 21 CFR 56.108(b)(1), and FDA 21 CFR 312.66 require written procedures for ensuring prompt reporting to the IRB of events and problems involving harm or risk of harm to subjects or others (‘others’ refers to investigators, research staff, or other individuals who were affected or who may be affected by the event or problem).

Different agencies and institutions use different terms for events and problems that often cause confusion with regard to what events/problems investigators need to report and how they should be reported. For example, a “serious adverse drug experience” under FDA regulations, or a “protocol deviation/violation,” or “serious adverse event” may or may not be an “unanticipated problem involving risks to subjects or others” under DHHS regulations.

In order to avoid misunderstandings associated with variations in terminology, the reporting of events and problems under UB HRPP policy is based on the nature of the event or problem rather than according to specific terminology.

In general, the types of events and problems that must be reported to the IRB are those that involve one or both of the following:

- harm to subjects or others
- increased risk to subjects or others, whether or not actual harm has occurred

UB HRPP guidelines for reporting these events and problems meet regulatory requirements for reportable events including recent OHRP requirements for reporting events and problems that OHRP refers to as “Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events.”

17.2 DEFINITIONS FOR PURPOSES OF THIS POLICY

The following definitions are provided for use in the application of this policy:

- **On-site (internal/local) event/problem**: an event/problem experienced by subjects enrolled by a UB investigator or UB affiliated investigator or experienced by subjects enrolled in studies for which a UB IRB acts as the IRB of record
- **Off-site (external) event/problem**: an event/problem experienced by subjects enrolled by investigators at other institutions engaged in the research project
- **Related or possibly related to the research**: there is a reasonable possibility that the event/problem, incident, experience, or outcome may have been caused by the procedures involved in the research
- **Protocol deviations/violations**: any departures from or changes to the study design or procedures that are under the investigator’s control that have not been reviewed and approved by the IRB
- **Serious event/problem (SEP)**: any event/problem that is “serious” as determined by a “yes” response to any question in Chart 1-Section 17.4.2: Determining a Serious Event/Problem (SEP) Chart
Non-Serious events/problems: any event/problem that is “non-serious” as determined by a “no” response to all questions in Chart 1-Section 17.4.2: Determining a Serious Event/Problem (SEP) Chart

Unanticipated: an event/problem that was unforeseen at the time of its occurrence

Unexpected: an event/problem occurring in one or more subjects in a research project that is not identified by nature, severity or frequency in the research protocol or consent document and is not consistent with the known or foreseeable risk of unfavorable events associated with the procedures involved in the protocol, investigator brochure and approved consent document or the expected natural progression of any underlying disease, disorder, or condition of the subject experiencing the event/problem.

17.3 PROCESS FOR REPORTING EVENTS AND PROBLEMS

Whenever an investigator becomes aware of or is notified of an event/problem, whether it occurs on-site or off-site, the investigator is responsible for determining whether the event/problem is required to be reported to the IRB and, if it is, to report it in an appropriate and timely manner.

The steps in this section outline:
- How an investigator determines whether an event/problem is reportable
- The required timeframe for reporting an event/problem
- The manner in which reporting should occur

Requirements for reporting “on-site” events/problems and off-site events/problems are covered separately as follows:
- **On-site**: Section 17.4: Investigator Responsibilities and Procedures for Reporting On-Site Events and Problems
- **Off-site**: Section 17.5: Investigator Responsibilities and Procedures for Reporting Off-Site Events and Problems.

17.4 INVESTIGATOR RESPONSIBILITIES AND PROCEDURES FOR REPORTING ON-SITE EVENTS AND PROBLEMS

The investigator is responsible for ensuring that events/problems are reported to the local IRB as outlined in this document and, as applicable, the monitoring entity (e.g., the research sponsor, a coordinating or statistical center, an independent medical monitor, or a DSMB/DMC) as required under the monitoring provisions described in the IRB-approved protocol or the sponsor/investigator agreement.

17.4.1 Procedures for Reporting “On-Site” Events and Problems

Whenever an “on-site” event/problem is identified, the investigator is responsible for reporting the event/problem according to the following Steps:

**Step 1**: Determine whether the event/problem is “Serious” or “Non-Serious”  
(See Chart 1-Section 17.4.2: Determining a Serious Event/Problem (SEP Chart))

**Step 2**: A. Report the “Serious” Events/Problems (SEPs) as described in Section 17.4.3: Reporting On-Site “Serious” Events/Problems
- or -
B. Report the “Non-Serious” Events/Problems as described in Section 17.4.4: Reporting On-site “Non-Serious” Events/Problems

**Step 3:** Submit Follow-Up Reports for previously submitted Serious Events/Problems (SEPs) whenever a change in the status of the event/problem occurs as described in Section 17.4.5: Step 3 - Submitting Follow-Up Reports for On-Site “Serious” Events/Problems (SEPs)

### 17.4.2 Step 1: Determining On-Site “Serious” Events/Problems (SEPs) Chart

Investigators will use the **Determining a “Serious” Event/Problem (SEP) Chart** to determine whether an event/problem is “serious” or “non-serious.”

- “Serious” events/problems are determined by a “yes” response to “any” question (a-f) in Chart 1 below: Determining a Serious Event/Problem (SEP)
- “Non-serious” events/problems are determined by a “no” response to “all” questions (a-f) in Chart 1 below: Determining a Serious Event/Problem (SEP)

<table>
<thead>
<tr>
<th><strong>DETERMINING A “SERIOUS” EVENT/PROBLEM (SEP) CHART</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>a.</strong> Did the event/problem cause actual harm or does it suggest that the research places the subjects or others at greater risk of physical, psychological, economic, or social harm than was previously known or recognized (even though no such harm actually occurred)? <strong>Examples:</strong> theft or loss of stored research data, a subject complaint indicates unexpected risks, unexpected subject incarceration or withdrawal poses increased risks to the subject or others, etc.</td>
</tr>
</tbody>
</table>
| **b.** Did the event/problem significantly impact the integrity of the research data? **Examples:**  
  - breach or increase to the risk of breach of confidentiality than was previously known  
  - unplanned destruction of study records |
| **c.** Do any of the following apply to the event/problem?  
  - resulted in death (except when death is the endpoint of the study),  
  - is life-threatening (placed the subject at immediate risk of death from the event as it occurred),  
  - required hospitalization or prolongation of existing hospitalization,  
  - resulted in a persistent or significant disability or incapacity, or  
  - resulted in a congenital anomaly or birth defect |
| **d.** Based on appropriate clinical judgment:  
  - does the event/problem jeopardize the subject’s health, or  
  - has it required or may require medical or surgical intervention to prevent one of the other outcomes listed in “c” above? |
| **e.** Was this event a deviation from the approved investigational plan initiated in order to protect the life or physical well-being of a subject in an emergency situation? |
| **f.** Was this event a deviation from the approved investigational plan initiated in order to eliminate an apparent hazard to a subject in an emergency situation? |

(Chart 1)
17.4.3 Step 2-A: Reporting On-Site “Serious” Events/Problems (SEPs)

Note: To report “Non-Serious” event/s/problems, see below - Section 17.4.4: Step 2-B- Reporting On-Site “Non-Serious” Events/Problems)

Investigators are responsible for reporting SEPs according to the nature of the event/problem and according to the timeframes indicated on the On-Site “Serious” Events/Problems Reporting Chart (Chart 2 below).

### ON-SITE “SERIOUS” EVENTS/PROBLEMS (SEPs) REPORTING CHART

<table>
<thead>
<tr>
<th>Type of Report</th>
<th>When to Report</th>
<th>How to Report</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deaths - except when death is the endpoint of the study</td>
<td>Within 24-hours of knowledge or notification</td>
<td>Serious Events / Problems (SEPs) – Initial Report form</td>
</tr>
<tr>
<td>Life-threatening i.e., events/problems that place the subject at immediate risk of death from the event as it occurred</td>
<td>Within 72-hours of knowledge or notification</td>
<td>Serious Events / Problems (SEPs) – Initial Report form</td>
</tr>
<tr>
<td>Required hospitalization or prolongation of existing hospitalization</td>
<td>Within 72-hours of knowledge or notification</td>
<td>Serious Events / Problems (SEPs) – Initial Report form</td>
</tr>
<tr>
<td>Resulted in persistent or significant disability or incapacity</td>
<td>Within 72-hours of knowledge or notification</td>
<td>Serious Events / Problems (SEPs) – Initial Report form</td>
</tr>
<tr>
<td>Resulted in congenital anomaly or birth defect</td>
<td>Within 72-hours of knowledge or notification</td>
<td>Serious Events / Problems (SEPs) – Initial Report form</td>
</tr>
<tr>
<td>Based on appropriate clinical judgment, the event required or may require medical or surgical intervention to:</td>
<td>Within 72-hours of knowledge or notification</td>
<td>Serious Events / Problems (SEPs) – Initial Report form</td>
</tr>
<tr>
<td>• prevent a life-threatening event/problem (the subject is at immediate risk of death from the event as it occurred)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Required hospitalization or prolongation of existing hospitalization</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Resulted in persistent or significant disability or incapacity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Resulted in congenital anomaly or birth defect</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DSMB Report that indicates a change in the risk/benefit assessment. Examples:</td>
<td>Immediately, upon receipt of the DSMB report</td>
<td>Send a copy of the DSMB report by mail, email, or fax to the IRB with a cover memo to accompany the report</td>
</tr>
<tr>
<td>• interim analysis indicates that an arm of the research study is of no therapeutic value,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• safety monitoring indicates that a particular side effect is more severe or occurs more frequently than initially expected</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Suspensions or Terminations in Multi-Site studies -- initiated by the Sponsor or PI/IRB of other institutions</td>
<td>Within 72-hours of PI knowledge or notification – IF based on change in risk/benefit</td>
<td>If Sponsor initiated, provide a copy of the suspension or termination notice. If initiated by other PI</td>
</tr>
</tbody>
</table>
### Deviation from the approved investigational plan initiated in order to protect the life or physical well-being of a subject in an emergency situation

Within 5 days of the emergency

Serious Events / Problems (SEP) – Initial Report form

### Deviation from the approved investigational plan initiated in order to eliminate an apparent hazard to a subject in an emergency situation

Within 5 days of the emergency

Serious Events / Problems (SEPs) – Initial Report form

### Increased Risk of Harm to subjects or others than was previously known or recognized (whether or not actual harm has occurred). Risks may be physical, psychological, economic, or social:

**Examples:**
- Theft or loss of stored research data
- A subject complaint indicates unexpected risks
- Unexpected subject withdrawal poses increased risks to the subject or others

Within 10 working days of knowledge or notification

Serious Events / Problems (SEPs) – Initial Report form

### Breach of Confidentiality that caused harm or places subjects or others at increased risk of harm (physical, psychological, economic, or social harm (even if actual harm has not occurred).

Within 10 working days of knowledge or notification

Serious Events / Problems (SEPs) – Initial Report form

### Significant impact on the integrity of the research data

Example:
- Unplanned destruction of study records
- Withdrawal of subject(s) impacts data integrity or causes inability to complete the study
- Incarceration of an enrolled subject, in a study not approved for participation of prisoners, where ceasing all study involvements or interventions with the now-incarcerated prisoner-subject may increase risks to his/her health or safety.

Within 10 working days of knowledge or notification

Serious Events / Problems (SEPs) – Initial Report form

### Unanticipated Adverse Device Effects

Any serious adverse effect on health or safety of any life-threatening problem or death caused by, or associated with, an FDA regulated device, if that effect problem or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application, or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

Within 10 working days of knowledge or notification

Serious Events / Problems (SEPs) – Initial Report form

### Any event/problem that would cause the sponsor to modify the investigator’s brochure, consent document, or would prompt other action by the IRB to assure protection of subjects.

Within 10 working days of knowledge or notification

Serious Events / Problems (SEPs) – Initial Report form

### Change in FDA safety labeling or withdrawal from marketing of a drug, device, or biologic used in a research protocol due to serious events/problems.

Example: FDA recalls or destructions

Within 10 working days of knowledge or notification

Memo explaining the circumstances requiring recall or destruction

### Relationship.

Otherwise, within 10 working days of knowledge or notification

or IRB, provide a memo explaining the circumstances leading to the suspension or termination.
Monitoring entity determines that an Unanticipated “Serious” Event/Problem exists. The investigator determines that an event/problem is not a “Serious Event/Problem” – however, the monitoring entity subsequently determines that the event/problem IS a “Serious Event/Problem.”

Within 10 working days of receipt of notification from the monitoring entity.

Memo indicating the circumstances of the determination by the monitoring entity.

Any other “Serious” Event/Problem not described above

Within 10 working days of knowledge or notification

Serious Events / Problems (SEPs) – Initial Report form

“Serious” Events/Problems Follow-Up Reports (Follow-Up Reports are required when changes to a previously reported event occurs)

Examples:
- when the reported relationship is changed (e.g., unrelated to related, unknown to related), or
- there is a change in outcome (a subject suffering a stroke subsequently dies), or
- when a reported risk of breach of confidentiality changes to an actual breach

As the information becomes known

Serious Events / Problems (SEPs) – Follow-Up Report form

17.4.4 Step 2-B: Reporting On-Site “Non-Serious” Events/Problems

(to report “Serious Events/Problems, see Step 2-A: Section 17.4.3 above)

The following types of “non-serious” events/problems must be reported to the IRB on the Amendment Form, as they occur, according to the instructions in Chart 3 below:
- “Non-serious” events that effected the study (i.e., events/problems that require changes to the study in order to prevent further occurrences)
- “Non-serious” events/problems that impacted on the rights and welfare of the subjects

Non-serious events that did not effect the study or impact on the rights and welfare of the subjects are not required to be reported to the IRB.

Investigators are responsible for reporting “non-serious” events and problems according to the nature of the event/problem and according to the manner and timeframes indicated on Chart 3 below:

<table>
<thead>
<tr>
<th>ON-SITE “NON-SERIOUS” EVENTS/PROBLEMS REPORTING CHART</th>
</tr>
</thead>
<tbody>
<tr>
<td>(“Non-serious” as determined by a “No” response to ALL questions in Chart 1 in Section 17.4.2)</td>
</tr>
<tr>
<td><strong>Type of Report</strong></td>
</tr>
<tr>
<td>“Non-serious” events/ problems that required changes in order to prevent future occurrences</td>
</tr>
<tr>
<td>“Non-serious” events/ problems that impacted on subjects rights or welfare</td>
</tr>
<tr>
<td>“Non-serious” events/problems that DID NOT require changes to the study and DID NOT impact on subject rights or welfare</td>
</tr>
</tbody>
</table>
17.4.5 **Step 3: Submitting Follow-Up Reports for On-Site “Serious” Events/Problems (SEPs)**

When a change to a previously reported “serious” event/problem occurs, investigators are required to notify the IRB of the change using the *Serious Events/Problems (SEP) Follow-Up Report Form:*

- Examples of when a follow-up report is required:
  - when the reported relationship is changed (e.g., unrelated to related, unknown to related), or
  - when there is a change in outcome (a subject suffering a stroke subsequently dies), or
  - when a reported risk of breach of confidentiality changes to an actual breach

17.5 **INVESTIGATOR RESPONSIBILITIES AND PROCEDURES FOR REPORTING “OFF-SITE” EVENTS AND PROBLEMS**

17.5.1 **Safety Reports**

Safety Reports (SR) are issued by the FDA or the study sponsor to inform all researchers using the same pharmacological compound about serious events/problems that have occurred in patients/subjects. These Safety Reports regarding external events/problems should be reviewed by the UB Investigator for a determination whether they need to be reported to the UB IRB.

The UB Investigator is responsible for determining whether SR event/problem is a SEP according to *Chart 1: Determining a “Serious” Event/Problem Chart (Section 17.4.2)* that is unanticipated and related or possibly related to participation in the research or is otherwise associated with the research. If it is, the investigator must send written notification to the UB IRB indicating the circumstances of the event/problem along with a copy of the report within 5 working days of Investigator knowledge or notification. SR events/problems that do not meet the criteria in Chart 1 for being “serious” do not need to be reported to the UB IRB.

17.5.2 **Other Types of Notifications Regarding Off-Site SEPs**

Multi-site studies have procedures in place to inform the collaborating researchers about serious events/problems that have occurred at the various sites. These reports regarding “off-site events/problems” should be reviewed by the “local Investigator” for a determination whether they need to be reported to the UB IRB.

The UB Investigator is responsible for determining whether an off-site event/problem is a SEP according to *Chart 1: Determining a “Serious” Event/Problem (Section 17.4.2)* that is unanticipated and related or possibly related to participation in the research or is otherwise associated with the research. If it is, the investigator must notify the UB IRB in writing indicating the circumstances along with a copy of the report within 5 working days of Investigator knowledge or notification. Off-site events/problems that do not meet the criteria in Chart 1 for being “serious,” do not need to be reported to the UB IRB.
17.5.3 What the Investigator Must Submit to the IRB to Report an Off-Site SEP

When an investigator determines that a Safety Report or other notification from a collaborating site constitutes an SEP that is unanticipated and related or possibly related to participation in the research or is otherwise associated with the research, the investigator is responsible for submitting to the IRB the following information along with a copy of the off-site report (e.g., a Med-Watch, IND safety report, or other form of notification) within 5 working days of investigator knowledge or notification:

- Title of the research project
- Investigator’s name
- IRB project number
- Indication of when the event occurred
- Description of the event
- Pertinent subject history, when appropriate
- Basis for determination that the event/problem is a SEP that is unanticipated and related or possibly related to participation in the research or is otherwise associated with the research

17.6 INVESTIGATOR RESPONSIBILITIES FOR REPORTABLE EVENTS/PROBLEMS AT THE TIME OF CONTINUING REVIEW

At the time of Continuing Review, the Investigator is responsible for completing the Application for Continuing Review that includes required information and documentation regarding reportable events and problems.

17.7 IRB REVIEW OF EVENTS AND PROBLEMS

17.7.1 Overview

The IRB will review non-serious events/problems that are reported on the Amendment Form as described in Section 7.3.3: Amendments/Modifications to an Approved Project

When a report of any serious event/problem (SEP) is received by the IRB, the IRB Chair or designee will initially assess the report to determine whether the reported event is a SEP and whether it was unanticipated, and related or possibly related to participation in the research or is otherwise associated with the research.

The chair or designee may:

- Determine that immediate action is necessary to protect the safety and well-being of the subject(s). In such instances, the chair may temporarily suspend the research pending full board review.
- Determine that the event is a SEP that is unanticipated and related or possibly related to participation in the research or is otherwise associated with the research, and must be referred to the full board for review.
- Determine that the reported event/problem does not meet one or more of the SEP criteria, i.e., the event is determined to be “not-serious,” or “anticipated” or “not related to the study.” At the discretion of the chair, these events/problems may be reviewed by an
expedited procedure or they may be referred to the full board. If reviewed by expedited procedures, the chair or designee may make the following determination:
  o To accept the report with no further action necessary
  o To require minimal corrective measures

Written notification to the investigator from the Chair or Chair designee may include:
  o Project title
  o IRB assigned number
  o Statement of the determination regarding “serious” or “non-serious”
  o Indication of level of review (expedited or full board)
  o If reviewed through expedited procedure, a statement of current status including, when appropriate, an indication of corrective measures required and timeframe for investigator response

When corrective measures are required, the Chair or chair designee will evaluate the investigators response and may continue to follow-up with the investigator until the corrective measures have been resolved.

17.7.2 Full Board Review of SEPs

When review of a SEP is referred to the full board, the documents are distributed to members as follows:

- If a primary reviewer system is used, documents distributed to primary reviewers will include the protocol and consent documents in effect at the time of the event, the investigator’s report of the SEP, and any other pertinent documentation as determined by the IRB chair or administrator.
- If a primary reviewer system is not used, documents distributed to all IRB members include the protocol and consent documents in effect at the time of the event, the investigator’s report of the SEP and any other pertinent documentation as determined by the IRB chair or administrator.

In its review of the report, the IRB will:

- Consider whether the SEP represents new information that alters the IRB’s previous determinations, particularly with respect to risks to subjects or others and determine what action(s), if any, must be taken in order for the study to continue to meet requirements for IRB approval under regulations at DHHS 45 CFR 46.111 and FDA 21 CFR 56.111.
- Determine whether the event/problem constitutes a SEP that is unanticipated and related or possibly related to participation in the research or is otherwise associated with the research.

IRB actions that may be taken include:

- Acceptance of the report with no further action necessary
- Requirement of corrective measures that include, but are not limited to:
  o notifying current subjects when such information may relate to their willingness to continue participation in the study
  o modifying the protocol
  o modifying the consent process
  o providing additional information to past subjects
  o re-consenting current subjects prior to their continuing participation in the study
- Modification of the continuing review schedule
- Monitoring of the research
Monitoring of the consent process
Suspension or Termination of the research (see Section 8.7.4 Suspensions and Terminations of IRB Approval)
Referral to other organizational entities

Any proposed changes to a research project in response to a serious event/problem (SEP) must be reviewed and approved by the IRB before being implemented, except when necessary to eliminate apparent immediate hazards to subjects.

The investigator will be notified of the IRB’s determination as indicated in Section 6.4: Notifications of IRB Determinations.

17.7.3 IRB and HRPP Responsibility for Further Reporting of SEPs

The IRB Chair is responsible for reporting all on-site SEPs that are unanticipated and related or possibly related to participation in the research or is otherwise associated with the research to the IO/HRPP Administrator. The report of the incident will include the following information:
- Name of the institution (e.g., university, hospital, foundation, or school) conducting the research
- Title of the research project and/or grant proposal
- Name of the principal investigator
- IRB assigned project number and identifying number of any applicable federal award(s) (grant, contract, or cooperative agreement)
- Detailed description of the serious event/problem (SEP);
- Description of the actions the IRB is taking or plans to take (e.g., suspend subject enrollment, terminate the research, require increased monitoring of the research, or require revision of the protocol or consent document)

IO/HPP Administrator is responsible for reporting these serious events/problems (SEPs) to OHRP, FDA (when the research is FDA-regulated), other federal agencies (when the research is overseen by those agencies and they require reporting separate from that to OHRP) and other university offices, as needed, within 10 working days. The IO/HPP Administrator report to federal authorities will typically include the IRB’s actions in response to the SEP. The IO/HPP Administrator is responsible for ensuring that the IRB receives a copy of the report. The IRB will retain a copy of the report in the study file.

17.7.4 IRB Considerations of Reportable Events/Problems at the Time of Continuing Review

As a part of the continuing review process, the IRB will review all reported events/problems associated with a project to ensure that the criteria for IRB approval under DHHS regulations at 45 CFR 46.111 c and FDA 21 CFR 56.111 continue to be satisfied. The IRB will consider whether the events/problems represent new information that has emerged that might alter the IRB’s previous determinations, particularly with respect to risk to subjects or others.
18. Complaints and Non-Compliance

18.1 INTRODUCTION

As part of its responsibility to protect the rights and welfare of human subjects in research, the UB HRPP provides written procedures to receive, review, and take appropriate action in response to complaints, concerns, and allegations of non-compliance related to its human subject research. This includes procedures for ensuring prompt reporting of any serious or continuing non-compliance with the regulations or the requirements or determinations of the IRB to appropriate institutional officials and relevant federal department or agency heads, when applicable (e.g., the Office for Human Research Protection and when applicable, the Food and Drug Administration, and the funding agency).

In order to comply with these various responsibilities, the HRPP and its IRBs have adopted procedures for receiving, handling, and reporting complaints, concerns, and allegations of non-compliance.

[Note: All concerns, complaints, reportable events and problems, and audit reports are assessed to determine whether they require management under non-compliance procedures.]

The process begins with an assessment by the IRB chair or chair designee of the nature, severity, and validity of the complaint, concern, or allegation of non-compliance. The assessment process is a critical piece in the determination of the proper management of the issues since:

- Most complaints or concerns will not rise to the level of alleged or actual non-compliance and can be resolved outside of the non-compliance process,
- Some, but not all, allegations of non-compliance will prove to be supported,
- The initial assessment may determine that the nature of the complaint, concern, or allegation of non-compliance is beyond the purview of the IRB and needs to be referred to another Institutional official, office, or department

At any point during the assessment process, the IRB chair or full board may initiate an administrative hold for all or part of the affected research while conducting the fact-finding necessary to make a determination regarding the nature, severity and validity of the complaint or allegation of non-compliance. Such holds are not considered suspensions or terminations and thus, are not subject to the reporting and other requirements for suspensions or terminations described in Section 8.7.4 Suspensions and Termination of IRB Approval.

The procedures in this section address how these and related situations will be addressed and managed.

Investigators and their research teams are expected to cooperate with internal efforts to investigate and resolve the matter. Failure to do so may be considered by the IRB to be an instance of non-compliance.

When investigating or reviewing complaints, concerns, and allegations of non-compliance, the IRB chair and any involved IRB members are subject to the conflicts of interest policy for IRB members set forth in Section 16.8.1 IRB Member Conflict of Interest or Significant Obligation of this document.
The HRPP staff will make every effort to resolve or refer concerns, complaints, and allegations of non-compliance promptly and will be handled confidentially to the extent possible and as warranted by the situation. The privacy of the complainant will be maintained to the extent possible, when privacy is a concern. No individual shall be discriminated against or be subject to reprisal for reporting any complaint, concern, or possible non-compliance. Any attempt to retaliate against a person for reporting such issues may itself be considered serious non-compliance with HRPP policy.

18.2 COMPLAINTS AND CONCERNS

Research subjects, investigators, study staff, and others may communicate any complaints or concerns about a research study, including (but not limited to): their participation in a study, their involvement with the principal investigator or other member of the research team, the IRB, or other institutional officials.

Individuals who receive any complaint or concern involving UB human subject research (e.g., any investigator, compliance staff, or other Institutional official) should promptly inform the appropriate IRB office to ensure timely and coordinated response.

Upon notification, the IRB Administrator or Chair/Chair designee will make a preliminary assessment to determine the nature, severity, and validity of the complaint or concern. If necessary, the IRB chair/chair designee may gather background or additional information necessary in order to make a proper assessment on how to proceed. Investigation by the IRB staff may include, among other things, additional conversations with the person bring the complaint, interviews with related parties, and a review of relevant study documents and files that may involve a fact-finding site review of the associated projects.

In general, complaints and concerns will be managed as follows:

- If the preliminary assessment of the complaint/concern does not rise to the level of an allegation of non-compliance, the IRB Administrator, staff, or IRB Chair/Chair designee may coordinate management of the issues
- If the preliminary assessment of the complaint/concern indicates that it may represent an instance of non-compliance, it will be managed in accordance with the procedures described in the “Non-Compliance” Section 18.3 of this document
- If the concern/complaint involves issues beyond the purview of the IRB, those issues may be referred to other Institutional processes, as appropriate. (Examples of when this might occur include, but are not limited to: issues that involve research integrity, the institution’s conflict of interest policies, scientific misconduct, the institution’s data security policies, or legal action against the researcher, the IRB, or the institution.)

18.3 NON-COMPLIANCE

18.3.1 Overview
Anyone may submit a report or an allegation of non-compliance with regard to human subject research to the IRB verbally or in writing. All allegations will be reviewed in a timely manner and, to the extent possible, will be handled confidentially. No individual shall be discriminated against or be subject to reprisal for submitting an allegation of non-compliance under this policy. Any attempt to retaliate against a person for reporting an allegation of non-compliance may itself be considered non-compliance with HRPP policy.

Federal regulations require that institutions have written procedures for ensuring prompt management of any instances of serious or continuing non-compliance. This section describes the UB’s HRPP policies and procedures for addressing all reports and allegations of non-compliance related to its human subject research which includes the management and reporting of instances of serious or continuing non-compliance.

18.3.2 Definitions for purposes of this policy:

- **Non-compliance**: failure to comply with applicable federal or state regulations or the requirements or determinations of the UB IRB which includes UB HRPP and Institutional policies related to the protection of human research subjects.
- **Allegation of non-compliance**: an unproven assertion of non-compliance.
- **Continuing non-compliance**: a pattern of multiple instances of non-compliance by the same investigator that, when taken together, evidence a lack of understanding of or commitment to conducting research in a manner that abides by ethical principles or fulfills regulatory requirements. The “pattern” of non-compliance may involve multiple instances within one study or may involve similar instances of non-compliance over any number of different studies conducted by the same investigator. Continuing non-compliance may refer to patterns of non-compliance that are intentional as well as those that are not intentional.
- **Finding of non-compliance**: an allegation or report of non-compliance that is substantiated by the IRB
- **Minor non-compliance**: non-compliance that is not “serious” or “continuing non-compliance”
- **Serious non-compliance**: non-compliance that, in the judgment of the IRB, increases risks or decreases benefits to the subject or to any individual involved or affected by the research, or that compromises the study’s scientific integrity or the validity of the research data.

18.3.3 Investigator responsibility for reporting events and problems that may represent instances of non-compliance

The investigator is responsible for submitting to the IRB all reportable events as indicated in Section 17: Reportable Events and Problems. These self-reported events/problems are reviewed as described in Section 17.7: IRB Review of Events and Problems. During the review process, it may be determined that a reported event represents an instance of minor non-compliance or serious or continuing non-compliance; when this occurs, procedures for the management of non-compliance will be applied.

The investigator is also responsible for self-reporting directly to the IRB any events/problems that he/she believes may represent serious or non-continuing compliance. While the proper self-
reporting of events/problems to the IRB is compliant with HRPP requirements, the nature of the events/problems reported may themselves constitute serious or continuing non-compliance.

18.4 REPORTS AND ALLEGATIONS OF “POSSIBLE” NON-COMPLIANCE

18.4.1 Receipt of the report or allegation

Until a determination is made that a report or allegation of non-compliance is “supported,” the matter will be considered a “possible” instance of non-compliance.

Reports of possible non-compliance should be directed to the IRB in writing. If a verbal report is received, the IRB may request a written report.

Any individual may submit a report or allegation of non-compliance. All reports or allegations of non-compliance will be directed to the IRB chair/chair designee. The recipient of the report or allegation will document as much relevant information as possible that may include:

- Date of receipt of the report
- Method of report (e.g., in writing or verbal)
- Name of individual making the report and contact information, when possible
- The individual’s contact information
- Description of the possible non-compliance issue
- Any supporting details or documentation that the complainant will provide
- Name of person “receiving” the information

The IO/HRPP Administrator will be notified of the report of allegation of non-compliance.

18.4.2 Initial screening

Within 10 business days of receipt of the report, the IRB chair/chair designee will make an assessment to determine the nature, severity, and validity of the report. If necessary, the IRB chair/chair designee will conduct a fact-finding investigation. As warranted by the situation, the IRB administrative staff, HRPP staff, IRB members, or outside reviewers with special expertise may be involved in the investigation. Additional information regarding the report may be obtained by the IRB chair/chair designee, through various methods including:

- Interview or written inquiry directed to the investigator, or other study personnel,
- Request for relevant research records from the PI or study personnel,
- Requests for information from other related sources, or
- Other means necessary to obtain information needed to make a determination.

Throughout the investigation, the identity of a complainant will not be divulged to the investigator unless the complainant has given permission to do so.

Through the investigational and assessment process, findings may indicate that the report or allegation of non-compliance is:

- **Not supported: No findings of non-compliance. No corrective measures are required**
- **Not supported: No findings of non-compliance but corrective measures are required that will be managed outside of non-compliance procedures**
Supported: Finding of minor non-compliance that can be managed between the investigator and the IRB Chair/Chair designee

Supported: Finding of possible serious or continuing non-compliance

When the findings indicate that the report or allegation may represent serious or continuing non-compliance, the matter will be presented for full board consideration as described in Section 18.5 Full Board Review of Reports and Allegations of Possible Serious or Continuing Non-Compliance.

Involves issues beyond the purview of the IRB. Either some or all of the issues involved in the report or allegation of non-compliance may be referred to other Institutional processes, as appropriate. (Examples of when this would occur include, but are not limited to, matters involving research integrity, the Institution’s conflict of interest policies, scientific misconduct, or the Institution’s data security policies)

18.4.3 Examples of corrective actions that may be required by the IRB:
- Modification to the research protocol and/or consent document(s)
- Additional education or training by the investigator or research staff
- Investigator submission of periodic status reports
- Consent monitoring
- Re-consenting of subjects
- Modification of the continuing review schedule
- Monitoring of the research
- Notifications of subjects (current, past, or both) regarding new information revealed by the report or allegation of possible serious or continuing non-compliance
- Referral by the IRB to other institutional or other entities for action

18.4.4 Notifications

The IRB will be notified at full board meetings of any findings related to reports or allegations of non-compliance.

The IRB chair/chair designee will use his/her discretion in determining the timing of disclosures to the investigator and to complainants and the level of detail that will be provided.

The IRB chair/chair designee will notify the investigator of any final determinations that are made.

A. Written notification to investigators:

Written notification letters to investigators from the IRB chair/chair designee will include the following information, as appropriate to the specific situation:
- Project title
- IRB assigned number
- Description of the report or allegation of non-compliance
- Statement that the project was investigated for the nature, severity, and validity of the report or allegation
Statement that the project was found to represent possible serious or continuing non-compliance and will be referred to the full board for consideration. Indication that additional information may be sought in order to facilitate an adequate presentation and review at the full board meeting.

Statement of the findings and determinations (including any required corrective measures and timeframe for investigator response).

When the findings indicate the possibility of serious or continuing non-compliance:
   a) indication that the matter will be referred to the full board for consideration,
   b) indication that additional information may be sought in order to facilitate an adequate presentation and review at the full board meeting, and may include a request for the PI to attend the meeting to answer questions.

When a response is required from the investigator, the IRB chair/chair designee will evaluate the response and may continue to follow-up with the investigator until corrective measures or other related issues have been resolved.

A copy relevant documentation of findings and written notifications to the investigator will be retained in the project’s IRB file.

**B. Notification to complainants**

Written notification to the complainant from the IRB chair/chair designee may include:
   - Date of receipt of the allegation of non-compliance
   - Brief description of the allegation
   - Statement of the IRB’s determination

A copy of the notification to the complainant will be retained in the project’s IRB file.

**18.5 FULL BOARD REVIEW OF REPORTS AND ALLEGATIONS OF POSSIBLE SERIOUS OR CONTINUING NON-COMPLIANCE**

**18.5.1 Overview**

In order to consider the report or allegation of possible serious or continuing non-compliance, IRB members will receive a description of the report or allegation and relevant study documents that may include: the protocol, consent document, and other documentation as determined by the IRB Chair or Administrator. At the discretion of the Chair, the investigator or others with special expertise may be invited to attend the full board meeting to answer questions regarding the matter. The IO/HRPP Administrator will be notified of all full board meetings where reports or allegations of possible serious or continuing non-compliance will be discussed.

**18.5.2 Full Board Determinations**

The board will review information and findings provided by the Chair and Administrator(s). Possible full board determinations include:

- **To Table/Defer review until additional information is obtained:**
   The process of obtaining additional information may involve, but is not limited to:
   - The IRB Chair or Administrator requesting additional information from the investigator, complainant, research staff, or others
Temporary suspension of study activities pending receipt of additional information
A request for a for-cause site visit (audit) to be conducted (see Section 19.2.3: Site Visits). Findings of the site-visit will be presented to the full-board
- **Not supported:** The report or allegation of possible serious or continuing non-compliance is not supported and no corrective measures are required
- **Not supported:** the report or allegation of possible serious or continuing non-compliance is determined to be not-supported but corrective measures are required that will be managed outside of non-compliance procedures
  [Examples: the PI will be instructed to submit the issue as reportable event or problem (see Section 17 Reportable Events and Problems) for management under those procedures.]

The board will determine whether the investigator’s responses may be managed by the IRB Chair or Administrator or whether the response must be considered by the full board. The follow-up to the corrective measures will be managed accordingly until the issues are resolved.
- **Supported:** report or allegation of possible serious or continuing non-compliance is supported and corrective measures are required
  The board will determine what the corrective measures are and whether the investigator’s responses may be managed by the IRB Chair or Administrator or whether the response must be considered by the full board. The follow-up to the corrective measures will be managed accordingly until the issues are resolved.
- **Supported:** report or allegation of possible serious or continuing non-compliance is supported – some or all research activities will be suspended
  o The IO/HRPP Administrator will be notified immediately of the full board’s determination to suspend some or all research activities and he/she will coordinate the Institutional response to appropriate internal and external constituencies.
- **Supported:** report or allegation of possible serious or continuing non-compliance is supported – some or all research activities will be terminated
  o The IO/HRPP Administrator will be notified immediately of the full board’s determination to terminate the project and he/she will coordinate the Institutional response to appropriate internal and external constituencies.
- **Supported:** report or allegation of possible serious or continuing non-compliance is determined to be supported - other actions the IRB may take
  o Suspension of other active projects of the investigator,
  o Withholding of approval for future projects if an investigator’s serious or continuing non-compliance affects those projects or if the serious or continuing non-compliance issues remain unresolved

The management of these “other actions” will be determined on a case-by-case basis.

**18.5.3 Examples of Corrective Actions That May be Required by the IRB:**
- modification to the research protocol and/or consent document(s)
- additional education or training by the investigator or research staff
- Investigator submission of periodic status reports
- Consent monitoring
- Re-consenting of subjects
- Modification of the continuing review schedule
- Monitoring of the research
• Notifications of subjects (current, past, or both) regarding new information revealed by the report or allegation of possible serious or continuing non-compliance
• Referral by the IRB to other institutional or other entities for action

18.5.4 Notifications:

• **Written notification to the IO/HRPP Administrator regarding full board determinations related to reports or allegations of serious or continuing non-compliance:** the IO/HRPP Administrator will be notified promptly, in writing, of any full board determinations related to reports or allegations of serious or continuing non-compliance. If the full board determination is to suspend any or all of the study’s activities or to terminate the study, the IO/HRPP Administrator will coordinate the Institutional notifications to appropriate internal and external constituencies.

• **Written notification to Investigators:**
  Written notification letters to investigators from the Chair/Chair designee will include the following information, as appropriate to the specific situation:
  - Project title
  - IRB assigned number
  - Description of the report or allegation of non-compliance
  - Statement that the project was investigated for the nature, severity, and validity of the report or allegation
  - Statement that the project was found to represent possible serious or continuing non-compliance and was referred to the full board for consideration.
  - Statement of the findings and determinations (including any required corrective measures and timeframe for investigator response)
  - If the study is suspended, a statement indicating the full board’s determination to suspend all or some study activities (if, some, indicate which activities), any requirements for lifting the suspension, and timeframe for investigator response (see also Section 8.7.4: Suspensions and Terminations of IRB Approval)
  - If the study is terminated, a statement indicating the full board’s determination to terminate the study and the basis for the action
  - Indication that, if the investigator disagrees with a determination of the IRB, he/she may submit a written appeal requesting reconsideration of the decision (as described in Section 8.7.5 Appeal of IRB Determinations)

When a response is required from the investigator, the IRB chair/chair designee will evaluate the response and may continue to follow-up with the investigator until corrective measures or other related issues have been resolved.
A copy relevant documentation of findings and written notifications to the investigator will be retained in the project’s IRB file.

• **Written notification to Complainants:**
  When written notification will be provided to the complainant, notification from the IRB chair/chair designee may include:
  - Date of receipt of the allegation
  - Brief description of the allegation
18.6 RESPONSIBILITIES FOR FURTHER REPORTING OF IRB DETERMINATIONS REGARDING SUPPORTED SERIOUS OR CONTINUING NON-COMPLIANCE

In cases of supported findings of serious or continuing non-compliance, the Chair or IRB Administrator will prepare a summary report within 10 business days of the determination that will be provided to:
- The IO/HRPP Administrator
- the Human Research Protection Program
- the full board

The report will include:
- Project title
- IRB assigned number
- Name of the Principal Investigator
- Circumstances of the initial receipt of information including whether the event/report was self-reported by the investigator or was an allegation by another person
- Process for determining that reported or alleged event/problem represented serious or continuing non-compliance
- IRB determinations and actions taken

18.7 FOR-CAUSE SITE VISIT (AUDIT)

When the full board requests that a “for-cause” audit of a project be conducted, the audit will be conducted by the QA/QI Administrator and another individual (if specific expertise is warranted). The IRB Chair, IRB Administrator, and IO/HRPP Administrator will receive copies of the audit findings. The for-cause site visit (audit) will be conducted as outlined in Section 19.2.3 Site Visits.

18.8 RECORDKEEPING

Records of the fact-gathering process and findings, review by the IRB, and IRB determinations or recommendations shall be maintained in a confidential section of the IRB files for the project. Minutes of IRB meetings at which the non-compliance issues were discussed will be recorded and maintained as detailed in Section 8.9: Meeting Minutes: Documentation of IRB Findings and Actions.

18.9 MANAGEMENT OF COMPLAINTS OR ALLEGATIONS OF NON-COMPLIANCE NOT WITHIN THE PURVIEW OF THE IRB

Instances of serious or continuing non-compliance that do not fall within the purview of the UB IRBs will be referred to the IO/HRPP Administrator for management. The referral will include any relevant information and will be managed on a case-by-case basis in consultation with the VPRED.
19. QUALITY ASSURANCE/QUALITY IMPROVEMENT ACTIVITIES

19.1 OVERVIEW

The goal of UB’s HRPP Quality Assurance/Quality Improvement (QA/QI) program is to work collaboratively with members of UB’s research community to ensure that the rights and welfare of research subjects are being properly protected in accordance with federal regulations, ethical principles, and Institutional and IRB policies. The QA/QI Administrator, in collaboration with other members of the HRPP staff, coordinates the QA/QI efforts.

Definitions for purposes of this section:

- **Quality Assurance (QA):** A planned and systematic process that provides confidence in an outcome for its intended purpose. QA cannot guarantee a quality result or product but helps to assure the process toward that goal.
- **Quality Improvement (QI):** The effort to assess and take measures to improve the level of performance of a program, process, or institution

19.2 QUALITY ASSURANCE (QA) ACTIVITIES

19.2.1 Overview

UB’s HRPP QA activities primarily involve, but are not limited to:

- Development and initiation of training and education support for the IRB, investigators, research teams, and the UB research community
- Conducting site visits of IRB approved research projects:
  - Routine site visits that include audits of study procedures and recordkeeping
  - Fact-finding assessments and for-cause visits conducted for any or all of the following reasons:
    - as a result of suspected or known problems in the conduct of human subject research,
    - to determine the nature, seriousness, or validity of complaints, concerns, or allegations of non-compliance
- QA assessments requested by the Principal Investigator
- Reviewing Investigator self-assessment results

19.2.2 Training and Education Support

*(See also, Section 3: Education and Training)*

The goal of the QA/QI training and education effort is to support UB’s research community by developing and delivering training on human research compliance issues that are responsive to researcher needs and relevant to the performance of routine research tasks.

The QA/QI training sessions are designed to complement CITI training. While CITI provides general information regarding human research protection, the QA/QI training sessions provide
specific information that will help researchers to be compliant with UB IRB requirements in the course of the daily conduct of their research.

Training on compliance with UB IRB requirements for the protection of human subjects is provided as follows:

- Training sessions are provided on a regular basis and are open to the UB research community,
- Training sessions for specific research groups scheduled by special request
- To support investigators in the initiation of corrective measures as a result of site visit findings, or as otherwise indicated by the IRB
- To support specific IRB needs (e.g., training of new IRB member to complement CITI training, or as part of ongoing IRB member training)
- To provide guidance on identified problem issues or areas of interest (e.g., HRPP Topics newsletters on specific topics)
- Other training or education initiatives, as needed

19.2.3 Site Visits

19.2.3.1 Introduction

The QA/QI Administrator, or other representative(s) from the HRPP Program, may conduct site visits of studies based on “routine,” “fact-finding,” or “for-cause” criteria as follows:

- Routine site visits are intended to be opportunities to identify deficiencies, collaborate with investigators to resolve them, and to provide educational support. Routine site visits also provide information about best practices that may be shared with other researchers.
- Fact-finding assessments and for-cause site visits may be conducted for any or all of the following reasons:
  - as a result of suspected or known problems in the conduct of human subject research,
  - to determine the nature, seriousness, or validity of complaints, concerns, or allegations of non-compliance

If, at any time during a site visit, findings indicate the necessity for immediate action to protect the safety and welfare of research subjects or others, the Chair and IRB Administrator will be contacted immediately so appropriate action may be taken.

19.2.3.2 Routine Site Visits

A. Introduction

Studies may be selected for routine site visits for reasons including, but not limited to:

- as part of routine QA/QI activities
- because the study does not undergo some degree of formal routine on-site monitoring by the study sponsor
- the study involves enrollment of a vulnerable population/group
- the study design has a potential for increased risk to study subjects
- the study is complex and involves unusual levels or types of risks to subjects
- the Investigator requests an on-site review for one or more of his/her studies

B. Routine site visit procedures
• The investigator is sent a written notification that a routine site visit will be conducted.

• Routine visits are generally conducted within 1-3 weeks of investigator notification. The written notification to the investigator includes:
  o Reason for the site visit
  o Proposed site visit date
  o Outline of the scope of the site visit
  o Identification of who will be conducting the site visit
  o Indication of who will receive the site visit report

Although the written notification outlines the general scope of the site visit, the QA/QI Administrator or other HRPP representatives reserve the right to review other documents and procedures as deemed necessary.

• Preparation for the site visit: Prior to the site review, the QA/QI Administrator may study the IRB files for the projects in order to become familiar with the protocol and to identify any issues that should be considered during the site review.

• On the day of the visit:
  o The QA/QI Administrator will meet with the PI or the PI’s designee to explain the site review process and answer questions the PI may have
  o Records and procedures review may include examination of any or all of the following:
    ▪ research records, including consent documents, protocol amendments, and serious events/problems (SEP) reports
    ▪ research procedures
    ▪ recordkeeping
    ▪ data security
    ▪ allocation of responsibilities
    ▪ the informed consent process, including observation of subject consent
    ▪ any other relevant procedures, materials, or documents
  o Observation of the informed consent process: The QA/QI administrator or other HRPP representatives have the authority to observe the informed consent process to assess whether procedures are being conducted as specified in the protocol. Observation of the consent process may occur on the day of the site visit or an appointment may be arranged with the investigator to observe the consenting of a subject at another time. The observation would occur only if the subject to be observed provides permission to be observed.
  o An exit interview may be held with the PI or his/her designee to review the site visit observations and to answer questions.

• The site visitor (usually the QA/QI administrator) will prepare a report outlining the findings of review. The site visit report may include:
  o Investigator name
  o Project title and IRB assigned number
  o Date of site visit and reason for site visit
  o Statement of findings
  o Indication of any suggested corrective actions and suggested timeframe for PI response
  o Name of person conducting the site visit
  o Other pertinent information

• Distribution of the site visit report:
  Generally, a copy of the draft report is sent to the PI for comments or clarifications. Relevant responses received from the PI by a due date (specified in the draft report cover
letter/email), will be included in the report that is sent to the PI, IRB Chair, IRB Administrator, IO/HRPP Administrator, and others on a case-by-case basis. Upon their review, the need for additional corrective measures may be identified and be required of the PI. At the discretion of the Chair, the report may be referred to the full board for informational purposes or for additional consideration. See Section 19.2.3.5 for full board review of site visit findings.

- The PI will be notified, in writing (usually in the cover letter/email for the site visit report), regarding the outcome of the site visit and current status.

19.2.3.3 Fact-Finding assessments

Fact-finding assessments are conducted in order to determine the nature, seriousness, or validity of complaints, concerns, or allegations of non-compliance. Fact-finding assessments may be conducted at the request of the IRB, IRB Chair, the VPRED, or IO/HRPP Administrator and may or may not involve an on-site visit. A for-cause site visit may be conducted as a result of a fact-finding assessment that indicates an in-depth investigation is warranted.

In general, findings will be provided to the individual(s) who requested the assessment. Further management of the issues is on a case-by-case basis according to nature of the findings. See also: Section 18 Complaints and Non-Compliance

19.2.3.4 For-cause Site Visits

A. Introduction

For-cause site visits are conducted to provide an in-depth investigation of suspected or known problems in the conduct of human subject research. For-cause site visits are conducted at the earliest possible time following knowledge or notification of the problem.

For-cause site visits may be conducted at the request of the IRB, IRB Chair, VPRED, or IO/HRPP Administrator. The IRB, IRB Chair, VPRED, and IO/HRPP Administrator will be notified of all for-cause site visits.

B. For-cause site visit procedures

- The investigator may or may not be notified in advance that a for-cause site visit will be conducted, depending on the nature of the suspected or known problem
- Preparation for the site visit: the QA/QI Administrator may study the relevant IRB project files in order to become familiar with the protocol and to identify issues that should be considered during the site review.
- On the day of the visit:
  - The QA/QI Administrator may meet with the PI or the PI’s designee to explain the reason for the site visit and the site review process and answer questions the PI may have
  - Records and procedures review may include examination of any or all of the following:
    - current and previously approved versions of the study protocol
    - current and all previously approved stamped consent forms
    - initial and continuing review approval letters
    - protocol amendment request forms and corresponding approval letters
    - serious events/problems (SEP) reports
    - FDA and sponsor required documentation and correspondence
- data security
- Review of subject records may include, but are not limited to:
  - signed consent documents
  - source documentation
  - logs or checklists
  - narrative forms and/or notes-to-file (when applicable)
- any other relevant procedures, materials, or documents
  - Observation of subject consent: The QA/QI administrator or other HRPP representatives have the authority to observe the informed consent process to assess whether procedures are being conducted as specified in the protocol. Observation of the consent process may occur on the day of the site visit or an appointment may be arranged with the investigator to observe the consenting of a subject at another time. The observation would occur only if the subject to be observed provides permission to be observed.
  - An exit interview may be held with the PI or his/her designee to review the site visit findings and to answer questions.
- A report outlining the findings of review will be prepared. The site visit report may include:
  - Investigator name
  - Project title and IRB assigned number
  - Date of site visit and reason for site visit
  - Statement of findings
  - Suggestions for corrective actions and suggested timeframe for response
  - Name of person conducting the site visit
  - Other pertinent information
- The site visit report: A report of findings will be presented to the full board for consideration

19.2.3.5 Review by the full board of site visit findings

The board may determine that:
- No further action is required: the Chair or Chair designee will notify the PI, in writing, describing the outcome of the IRB’s determination as described in Section 6.4: Notifications of IRB Determinations
- Additional information or additional corrective measures are required: The Chair or Chair designee will notify the PI in writing of the IRB’s requirements and a timeframe for response. When the required information is received or the corrective measures have been resolved, the matter will be brought back to the full board. Alternatively, the board may give the Chair the authority to review and approve the PI’s response. Upon receipt of the investigator’s response, the Chair may request additional information, approve the investigator’s response as submitted, or refer the matter back to the IRB for further review. The Chair or Chair designee will notify the investigator and others (as appropriate), in writing, of any determination as described in Section 6.4: Notifications of IRB Determinations
- Suspension or termination of the research is warranted. The Chair or Chair designee will notify the investigator and others (as appropriate) of the board’s determination as described in Section 6.4: Notifications of IRB Determinations.
19.2.4 Investigator Self-Assessment Form

The Quality Improvement through Self-Assessment form was developed for use by Investigators to help them to assess the quality and level of compliance of their research and recordkeeping procedures with regulatory, Institutional, and IRB policies and to assist them in preparation for a site visit. The QA/QI Administrator may also use the self-assessment tool for QA/QI purposes, or in lieu of, or preliminary to, a site visit.

19.2.4.1 Investigator-Initiated (Voluntary) Self-Assessment

Investigators may voluntarily choose to self-evaluate a project’s level of compliance by conducting a self-assessment using the Quality Improvement through Self-Assessment form.

Investigator-initiated self-assessment forms are not required to be submitted to the QA/QI Administrator or the IRB for review. If, however, the investigator or research team would like collaborative review, the form may be submitted to the QA/QI Administrator for a compliance review. The QA/QI Administrator may provide guidance or training to the investigator and the research staff to address deficiencies. The IRB and others will not receive copies of the findings unless the investigator requests that they be sent or unless the findings reveal deficiencies in the protection of human subjects that require reporting. Management of deficiencies may be conducted according to procedures described above for routine site visits.

19.2.4.2 Required Self-Assessment

An investigator may be required to complete part or all of the Quality Improvement through Self-Assessment form as part of a fact-finding process or in lieu of, or preliminary to, a site visit. The investigator will be instructed to complete and return the form to the QA/QI Administrator within a specified timeframe, generally within 2-3 weeks. The form may be completed by the investigator or by a member of the research staff designated by the investigator.

The QA/QI Administrator will verify the submitted information by comparing the investigator’s responses to IRB records and/or the investigator’s records. Management of the findings will be on a case-by-case basis according to the purpose the required self-assessment (e.g., fact-finding or in lieu of, or preliminary to, a site visit).

19.2.4.3 Management of Required-Self-Assessment Findings

Management of the findings will be according to the purpose for the required self assessment, as follows:
- Fact-finding (see Section 19.2.3.3 Fact-Finding Assessments)
- In lieu of or in preparation for a routine site visit (See Section 19.2.3.2 Routine Site Visits)
- As part of the conduct of a for-cause site visit (see Section 19.2.3.4 For-Cause Site Visits)

19.2.5 Subject Survey: Assessment of Subjects’ Research Experience

Subject surveys may be conducted as part of a fact-finding process of for quality assurance or quality improvement purposes. The QA/QI Administrator, IRB Chair, or full board, may direct the PI to send a survey to subjects who participated in the study. The survey would be comprised of questions related to the research experience. The survey results would be returned directly to the QA/QI Administrator for evaluation.
Management of the findings will be according to the purpose for the subject surveys as follows:
- Fact-finding (see Section 19.2.3.4 Fact-Finding Assessments)
- Quality Assurance/Quality Improvement purposes (See Section 19 Quality Assurance / Quality Improvement Activities)

19.2.6 Recordkeeping and Documentation
Documentation of correspondence and records of fact-finding and site visit findings are maintained by the QA/QI Administrator. When appropriate, copies of the report will be included in the specific IRB project file.

19.2.7 File Retention Period
Documentation for protocol-specific fact-finding assessments and site reviews will be maintained for a minimum of 3 years after study closure. The QA/QI Administrator will maintain a record of site visit documentation. A periodic review the records will be conducted to determine whether the retention period has expired. Elimination of records will be undertaken only after consultation with the IRB Chair and IRB Administrator(s).

19.3 QUALITY IMPROVEMENT (QI) ACTIVITIES

19.3.1 Overview
The goal of QI activities is to improve human subject protection processes by monitoring them in a systematic manner, identifying strategies to correct deficiencies, and maintaining any improvements that are achieved.

QI activities address areas that need improvement that have been identified through:
- QA audits that measure compliance levels with HRPP requirements
- Collaboration with HRPP staff
- Concerns and observations expressed by members of the UB research community (e.g., investigators, research staff, and research volunteers)

19.3.2 The Quality Improvement Cycle - Select Quality Improvement Activities
The quality improvement cycle incorporates QA findings with QI activities into an ongoing process that may be applied to any number of HRPP activities. The QA/QI Administrator will implement ongoing programmatic quality improvement initiatives in order to:
- Improve specific functions or processes
- Provide a means for improvement and successful change to take place
- Provide a structure to continue to evaluate and improve functions and processes
Steps of the Quality Improvement Cycle:

A. Identify
- Select the focus:
  - Identify and select the activity to be assessed
- Map the current process
  - Detail the order of steps in the activity from beginning to end
- Measure performance
  - Measure current performance
- Identify problem areas that answer such questions as:
  - Are there any times between steps when nothing is being accomplished?
  - Are there unnecessary steps
  - Are there overlapping processes?
  - Where does it appear that things are backing up or slowing down?

B. Plan
- Research and develop solutions
  - Define or clearly state the problem including the possible causes and effects
  - Determine what might be done to improve the process or make it more efficient
  - Determine how you will know that the process has been improved
- Develop a plan
  - Determine what needs to be done to implement the solution(s)
  - Determine how long it will take to implement the solution
  - Determine whether there is adequate support (e.g., from management, staff, monetary, equipment, or other)
  - Determine the plan for follow-up once the solutions have been implemented.

C. Implement
• Implement the plan

D. Evaluate
• Re-measure the performance
• Assess the measurements
• Determine whether the activity warrants continuing QI
• Evaluate the effectiveness of the plan
  o Determine whether causes to the problem have been eliminated or decreased
  o If there are no clear indicators of improvement, consider the reasons for this
  o Determine whether adjustments to the plan are needed and adjust, as necessary

19.3.3 Recordkeeping and Documentation
Documentation of QI activities will be maintained by the QA/QI Administrator for a minimum of 3 years.
<p>| <strong>Anonymous Data</strong> | Information recorded or collected without any of the 18 personal identifiers, or pieces of the identifiers, related to an individual, relatives of the individual, household members or employers as defined by HIPAA regulations, and no code is assigned which would permit data to be traced to an individual, relative, household member, or employer. |
| <strong>Assent (to participate in research)</strong> | Agreement by an individual not competent to give legally valid informed consent (e.g., a child or cognitively impaired person) to participate in research). The absence of an objection may not be construed as assent. |
| <strong>Assurance (Federal)</strong> | A formal written, binding commitment that is submitted to a federal agency in which an institution promises to comply with applicable regulations governing research with human subjects and stipulates the procedures through which compliance will be achieved. (See also “Federalwide Assurance”) |
| <strong>Autonomy</strong> | A principle of the Belmont Report that pertains to respect for a person’s right to consider alternatives, make choices, and act without the undue influence or interference of others. |
| <strong>Belmont Report</strong> | A report issued by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research in 1979. The Report describes three basic principles relevant to the ethics of human subject research: Respect for Persons, Beneficence, and Justice. |
| <strong>Beneficence</strong> | A principle of the Belmont Report that pertains to an obligation to protect persons from harm. The principle of beneficence can be expressed in two general rules: (1) do not harm; and (2) protect from harm by maximizing possible benefits and minimizing possible risks of harm. |
| <strong>Biologic</strong> | Any therapeutic serum, toxin, anti-toxin, or analogous microbial product applicable to the prevention, treatment, or cure of diseases or injuries. |
| <strong>Certificate of Confidentiality</strong> | A Certificate of Confidentiality (CoC) is issued by the National Institutes of Health (NIH) and other Department of Health &amp; Human Services (DHHS) agencies to protect identifiable research information from forced or compelled disclosure. |
| <strong>CFR</strong> | Acronym for “Code of Federal Regulations” |
| <strong>Child</strong> | For research purposes: A person who has not attained the legal age for consent for treatment or procedures involved in research under the applicable law of the jurisdiction in which the research will be conducted (e.g., 18 years in the State of New York). |
| <strong>CITI</strong> | Acronym for “Collaborative Institutional Training Initiative” |</p>
<table>
<thead>
<tr>
<th><strong>Class I, II, III Devices</strong></th>
<th>Classification by the Food and Drug Administration of medical devices according to potential risks or hazards.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical Trial</strong></td>
<td>A clinical trial is a research study to answer specific questions about vaccines or new therapies or new ways of using known treatments. Clinical trials (also called medical research and research studies) are used to determine whether new drugs or treatments are both safe and effective. Carefully conducted clinical trials are the fastest and safest way to find treatments that work in people. Trials are in four phases. (See also “Phases 1-4 Clinical Trial”)</td>
</tr>
</tbody>
</table>
| **Code of Federal Regulations (CFR)** | A codification of the general and permanent rules published in the Federal Register by the Executive departments and agencies of the Federal government. The Code is divided into 50 titles that represent broad areas subject to Federal regulation. The titles that most frequently apply to human subjects research are:  
  - 45 CFR – Department of Health and Human Services  
  - 21 CFR – Food and Drug Administration |
| **Coded Data**                | o **Identifying code**: code that explicitly contains any of the 18 identifiers defined by HIPAA regulations, or pieces of those identifiers, or any non-identifying code that could be used in combination with other information directly accessible by the researcher to identify the associated individual.  
  o **Non-identifying code**: under the Privacy Rule, a non-identifying code is one that does not contain any of the 18 identifiers defined by HIPAA regulations, or pieces of those identifiers, and cannot be used in combination with other information directly accessible by the researcher to identify the associated individual. |
<p>| <strong>Coercion</strong>                  | The act of compelling a person or manipulating him/her to behave in an involuntary way (whether through action or inaction) by use of threats, intimidation or some other form of pressure or force. These methods are used as leverage to force the person to act in the desired way. |
| <strong>Cognitive Capacity</strong>        | For research enrollment purposes, this pertains primarily to the level of ability of an individual to understand the choice(s) presented, the implications of choosing one alternative rather than another, and to make and communicate a choice regarding participation in a research study. |
| <strong>Collaborative Institutional Training Initiative (CITI)</strong> | CITI provides a comprehensive selection of web-based training modules on human research subject protection. |</p>
<table>
<thead>
<tr>
<th>Common Rule</th>
<th>Also known as DHHS 45 CFR 46, the Common Rule outlines the requirements of federally supported research with regards to human subject protections and places the responsibility of these protections on institutions, their Institutional Review Boards (IRBs), and investigators. It is the “common” set of regulations for the protection of human subjects in research agreed to by 17 federal agencies in 1991.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Confidentiality</td>
<td>Confidentiality pertains to the treatment of information that an individual has disclosed in a relationship of trust and with the expectation that it will not be divulged to others in ways that are inconsistent with the understanding of the original disclosure without permission.</td>
</tr>
<tr>
<td>Conflict of Interest</td>
<td>A conflict of interest occurs when individuals involved with the conduct, reporting, oversight, or review of research have financial or other interests from which they can benefit depending on the results of the research and therefore could directly and significantly affect the individual’s professional judgment in exercising his/her duties or responsibilities in the administration and management of the research project.</td>
</tr>
<tr>
<td>Continuing Non-compliance</td>
<td>A pattern of multiple instances of non-compliance by the same investigator that, when taken together, evidence a lack of understanding of or commitment to conducting research in a manner that abides by ethical principles or fulfills regulatory requirements. The “pattern” of non-compliance may involve multiple instances within one study or may involve similar instances of non-compliance over any number of different studies conducted by the same investigator. Continuing non-compliance may refer to patterns of non-compliance that are intentional as well as those that are unintentional.</td>
</tr>
<tr>
<td>Continuing Review</td>
<td>Periodic review by the IRB of active research for the purpose of determining whether the research project continues to meet the requirements for IRB approval. Continuing review must occur at least annually, as determined by the IRB.</td>
</tr>
<tr>
<td>Control Group</td>
<td>Generally, the group of test subjects left untreated or unexposed to some procedure and then compared with treated subjects in order to validate the results of the test.</td>
</tr>
<tr>
<td>Covered Entity</td>
<td>A legal entity defined by HIPAA regulations as having to comply with the regulations, currently defined as a health plan, a health care clearinghouse, or health care provider who transmits health information in connection with a transaction for which DHHS has adopted a standard, or any other entity designated as part of a covered function within a hybrid entity.</td>
</tr>
<tr>
<td><strong>Data and Safety Monitoring Board (DSMB)</strong></td>
<td>An independent committee composed of community representatives and clinical research experts, which reviews data while a clinical trial is in progress to ensure that participants are not exposed to undue risk. A DSMB may recommend that a trial be stopped if there are safety concerns or if the trial objectives have been achieved.</td>
</tr>
<tr>
<td><strong>Data and Safety Monitoring Plan (DSMP)</strong></td>
<td>A plan that provides assurance that the investigation has a system for proper oversight and monitoring of the conduct of the study and the data generated by the study.</td>
</tr>
<tr>
<td><strong>Debriefing</strong></td>
<td>Giving subjects previously undisclosed information about the research project following completion of their participation in research involving deception.</td>
</tr>
<tr>
<td><strong>Deception Study</strong></td>
<td>A research study that incorporates in the design a technique for intentionally misleading a human subject during the course of the study in order to prevent biasing the results. Generally, the subject is debriefed after the study ends or after their participation ends.</td>
</tr>
<tr>
<td><strong>Decisionally Impaired/Incapacitated</strong></td>
<td>Individuals who have a diminished capacity for judgment and reasoning due to developmental, psychiatric, organic, or other disorders that affect cognitive or emotional functions. Other individuals who may be considered decisionally impaired/incapacitated (with limited decision-making capacity) are individuals under the influence of or are dependent on drugs or alcohol, those suffering from degenerative diseases affecting the brain, terminally ill patients, and persons with severely disabling physical disabilities. Decisional impairment/incapacity may be temporary, permanent, progressive, or fluctuating.</td>
</tr>
<tr>
<td><strong>Declaration of Helsinki</strong></td>
<td>A code of ethics for clinical research approved by the World Medical Association in 1964 and widely adopted by medical associations in various countries. It has subsequently been revised several times.</td>
</tr>
<tr>
<td><strong>Deferred/Tabled Study</strong></td>
<td>The convened IRB may table/defer review of a project if additional information is required before a considered judgment may be made or if additional expertise is required in order to conduct adequate review.</td>
</tr>
<tr>
<td><strong>De-Identified Data or Tissue Samples</strong></td>
<td>Protected Health Information (PHI) that has been de-identified by removing all HIPAA specified identifiers related to an individual, relatives of the individual, household members, or employers.</td>
</tr>
<tr>
<td><strong>DHHS</strong></td>
<td>Acronym for “Department of Health and Human Services”</td>
</tr>
<tr>
<td><strong>Diagnostic Procedure</strong></td>
<td>A method or technique used to identify or to see the nature of a disease or disorder. It is also used to determine what type of disease is present.</td>
</tr>
<tr>
<td><strong>DSMB</strong></td>
<td>Acronym for “Data &amp; Safety Monitoring Board”</td>
</tr>
<tr>
<td><strong>DSMP</strong></td>
<td>Acronym for “Data &amp; Safety Monitoring Plan”</td>
</tr>
<tr>
<td><strong>Endpoint</strong></td>
<td>Overall outcome that the protocol is designed to evaluate. Common endpoints are severe toxicity, disease progression, or death.</td>
</tr>
<tr>
<td><strong>Engagement in Human Subject Research</strong></td>
<td>An entity is engaged in human subject research when its employees or agents (i) intervene or interact with living individuals for research purposes; or (ii) obtain individually identifiable private information for research purposes. [45 CFR 46.102(d),(f)]</td>
</tr>
<tr>
<td><strong>Exempt Status</strong></td>
<td>Upon review of an initial project submission, the IRB may determine that the research project that involves no more than minimal risk to human subjects may be exempt from having to meet all the requirements of DHHS 45 CFR 46 and DHHS 21 CFR 56. The exempt status determination is made by IRB, not the investigator.</td>
</tr>
<tr>
<td><strong>Existing Data</strong></td>
<td>Data that existed prior to the IRB approval date to use that data.</td>
</tr>
<tr>
<td><strong>Expedited Review</strong></td>
<td>Review of proposed research by a designated reviewer rather than by the convened (full board) IRB. Federal rules permit expedited review for certain types of minimal risk research [DHHS 45 CFR 46.110 and FDA 21 CFR 56.110].</td>
</tr>
<tr>
<td><strong>Experimental</strong></td>
<td>Term often used to denote a therapy (drug, device, procedure, etc.) that is unproven or not scientifically validated with respect to safety and efficacy.</td>
</tr>
<tr>
<td><strong>Faculty Sponsor</strong></td>
<td>The faculty sponsor is responsible for advising the student throughout the process of protocol development, submission, and review, as well as in the implementation of the research project. All student and resident researchers are required to have a faculty sponsor.</td>
</tr>
<tr>
<td><strong>Family Educational Rights and Privacy Act</strong></td>
<td>See “FERPA”</td>
</tr>
<tr>
<td><strong>FDA</strong></td>
<td>Acronym for “Food &amp; Drug Administration”</td>
</tr>
<tr>
<td><strong>Federalwide Assurance (FWA)</strong></td>
<td>A compliance agreement accepted and approved by OHRP (Office of Human Research Protection) for institutions engaged in non-exempt human subject research conducted or supported by DHHS. Under an FWA, an institution commits to DHHS that it will comply with the requirements set forth in 45 CFR Part 46, as well as other terms of the Assurance.</td>
</tr>
<tr>
<td><strong>FERPA</strong></td>
<td>Acronym for the “Family Educational Rights and Privacy Act.” A Federal law that protects the privacy of student education records. The law applies to all schools that receive funds under an applicable program of the U.S. Department of Education. FERPA defines the rights of students and parents concerning the reviewing, amending and disclosing educational records.</td>
</tr>
<tr>
<td><strong>Food and Drug Administration (FDA)</strong></td>
<td>An agency of the Federal government established by Congress in 1912 and presently part of the Department of Health and Human Services (DHHS). The FDA is responsible for protecting public health by assuring the safety, efficacy, and security of human drug, biological products, medical devices, and products that emit radiation. DHHS regulations apply to all human subject research including those regulated by the FDA.</td>
</tr>
<tr>
<td><strong>Full Board Review</strong></td>
<td>Pertains to review of a research project at a convened meeting of the IRB where a majority of the membership of the IRB is present and includes at least one member whose primary concerns are in nonscientific areas.</td>
</tr>
<tr>
<td><strong>FWA</strong></td>
<td>Acronym for “Federalwide Assurance”</td>
</tr>
<tr>
<td><strong>Generalizable Knowledge</strong></td>
<td>Knowledge that is expressed in theories, principles, and statements of relationships that can be widely applied to our experiences. Generalizable knowledge is usually created to share with others through presentations and publications.</td>
</tr>
<tr>
<td><strong>Guardian</strong></td>
<td>Definition for research purposes: An individual who is authorized under state or local law to consent on behalf of a minor for general medical care.</td>
</tr>
<tr>
<td><strong>Health Information (HIPAA term)</strong></td>
<td>Information in any form or medium (paper, electronic, verbal, and images such as x-rays or sonograms) that relates to a living or deceased individual’s past, present, or future physical or mental health or condition, or to the provision or payment of healthcare to an individual.</td>
</tr>
<tr>
<td><strong>Health Insurance Portability and Accountability Act (HIPAA)</strong></td>
<td>The Health Insurance Portability and Accountability Act of 1996 establishes a set of national standards for the protection of certain health information that apply to the use and disclosure of individuals’ health information, called Protected Health Information (PHI), for various purposes including research. It also sets standards for individuals’ privacy rights to gain access to, be informed of, and control how their health information is used.</td>
</tr>
<tr>
<td><strong>HIPAA</strong></td>
<td>Acronym for the “Health Insurance Portability and Accountability Act”</td>
</tr>
<tr>
<td><strong>HIPAA Authorization</strong></td>
<td>An individual’s written permission to allow the use or disclosure of specified Protected Health Information (PHI) for a particular purpose. The contents of the Authorization comply with requirements stipulated by HIPAA regulations.</td>
</tr>
<tr>
<td><strong>HRPP</strong></td>
<td>Acronym for “Human Research Protection Program”</td>
</tr>
<tr>
<td><strong>HUD</strong></td>
<td>Acronym for “Humanitarian Use Device”</td>
</tr>
<tr>
<td><strong>Human Research Protection Program (HRPP)</strong></td>
<td>A systematic and comprehensive approach by an organization to ensure the protection of the rights and welfare of human research participants recruited to participate in research.</td>
</tr>
<tr>
<td>Human Subject</td>
<td></td>
</tr>
<tr>
<td>---------------</td>
<td></td>
</tr>
<tr>
<td>• The DHHS defines a “human subject” as a living individual about whom an investigator (whether professional or student) conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information.</td>
<td></td>
</tr>
<tr>
<td>• The FDA defines a “human subject” as an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. In the case of research involving a device, a human subject includes an individual on whom or on whose specimen a device is used.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Humanitarian Use Device (HUD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A device that is intended to benefit patients in the treatment and diagnosis of diseases or conditions that affect or are manifested in fewer than 4,000 individuals in the United States per year.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hybrid Entity (HIPAA term)</th>
</tr>
</thead>
<tbody>
<tr>
<td>An entity comprised of functions which are considered covered by the HIPAA regulations, and other functions which are not.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>IDE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acronym for “Investigational Device Exemption”</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Identifying Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>See “Coded Data”</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Incapacity</th>
</tr>
</thead>
<tbody>
<tr>
<td>With regard to an individual’s ability to make a decision to consent to participate in research – the term refers to the inability of an individual to understand information presented, to appreciate the consequences of participating or not participating, and to make a choice.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Inclusion Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>A set of conditions that must be met in order for an individual to be eligible for participation in a research project.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Incomplete Disclosure</th>
</tr>
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<tbody>
<tr>
<td>See “Deception Study”</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>IND</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acronym for “Investigational New Drug” Application”</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Individually Identifiable Health Information (IIHI) (HIPAA term)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A subset of health information that identifies the individual in a manner defined by the HIPAA regulations, or that can reasonably be used to identify the individual.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Informed Consent</th>
</tr>
</thead>
<tbody>
<tr>
<td>A process by which an individual voluntarily confirms his/her willingness to participate in a research project after having been informed of all aspects of the research project that are relevant to the individual’s decision to participate. Informed consent is usually documented by means of a written, signed, and dated informed consent form, which has been approved by an IRB.</td>
</tr>
</tbody>
</table>
### Informed Consent Process

The informed consent process is an ongoing exchange of information between the research staff and the subject that begins when a potential research subject is initially informed about the research, often at the time of recruitment, and continues throughout the course of the study. It includes subject recruitment materials, question/answer sessions, methods and materials used to obtain the subject’s consent to participate in the research, and any other communication between the subject and research staff that explains or clarifies the research procedures.

### Institutional Official/Human Research protection Program Administrator (IO/HRPP Administrator)

The individual who is responsible for ensuring the effective administration and implementation of UB’s Human Research Protection Program (HRPP).

### Institutional Review Board (IRB)

An independent committee comprised of scientific and non-scientific members appointed by the institution and established according to federal requirements to ensure the protection of the rights and well-being of research subjects through its authority to approve, modify, or disapprove proposed research projects and through its continued review of ongoing research projects.

### Interaction

Communication or interpersonal contact between the investigator and the subject.

### Intervention

Physical procedures by which data are gathered (e.g., venipuncture) or manipulations of the subject or the subject’s environment that are performed for research purposes.

### Investigational Device Exemption (IDE)

An IDE allows an investigational device to be used in a clinical study in order to collect safety and effectiveness data required to support requests to legally market the device.
| **Investigational Drug** | Includes those substances in any of the clinical stages of evaluation which have not been released by the FDA for general use or cleared for sale in interstate commerce. An investigational drug may also be defined by one of the following:  
- A drug in any of the clinical stages of evaluation (Phase I, II, and III) which has not been released by the FDA for general use or cleared for sale in interstate commerce  
- Any commercially available drug proposed for a new use  
- A new dosage form or method of administration  
- A commercially available drug which contains a new component such as an excipient, coating or menstruum  
- Any new combination of two or more commercially available drugs  
- A combination of commercially available drugs in new proportions |
<p>| <strong>Investigational Medical Device</strong> | An investigational medical device is a device not yet approved for marketing by the FDA. |
| <strong>Investigational New Drug Application (IND)</strong> | An IND application (FDA Form 1571) is a request for authorization from the Food and Drug Administration (FDA) to administer an investigational drug or biological product to humans. Such authorization must be secured prior to interstate shipment and administration of any new drug or biological product that is not the subject of an approved New Drug Application or Biologics/Product License Application (21 CFR 312). |
| <strong>Investigator</strong> | See “Principal Investigator” |
| <strong>in vitro</strong> | Used to refer to processes that are carried out outside the living body, usually in the laboratory, as distinguished from in vivo. |
| <strong>in vivo</strong> | Processes carried out in the living body rather than in a laboratory, such as the absorption of a drug by the human body. |
| <strong>IRB</strong> | See “Institutional Review Board” |
| <strong>Justice</strong> | A principle of the Belmont Report requiring that the risks of research be equitably distributed and not unduly involve persons from groups unlikely to be among the beneficiaries of subsequent applications of the research. |
| <strong>Key Study Personnel</strong> | The investigator, co-investigator and other personnel responsible for the design, conduct or reporting of the research (see also “Research Staff”) |
| <strong>LAR</strong> | Acronym for “Legally Authorized Representative” |
| <strong>Legally Authorized Representation (LAR)</strong> | An individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject’s participation in the procedure(s) involved in the research. |</p>
<table>
<thead>
<tr>
<th><strong>Life Threatening</strong></th>
<th>Any diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted and diseases or conditions with potentially fatal outcomes, where the endpoint of clinical trial analysis is survival.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Medical Device</strong></td>
<td>A diagnostic or therapeutic article that does not achieve any of its principal intended purpose through chemical action within or on the body.</td>
</tr>
<tr>
<td><strong>Minimal Risk</strong></td>
<td>In the context of research: the probability and magnitude of harm or discomfort anticipated in the proposed 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.</td>
</tr>
<tr>
<td><strong>Monitoring of research</strong></td>
<td>The collection and analysis of data as the project progresses to assure the appropriateness of the research, its design and subject protections.</td>
</tr>
<tr>
<td><strong>Non-Compliance</strong></td>
<td>A failure to comply with applicable federal or state regulations or the requirements or determinations of the UB IRB which includes UB HRPP and Institutional policies related to the protection of human research subjects.</td>
</tr>
<tr>
<td><strong>Non-identifying Code</strong></td>
<td>See &quot;Coded Data&quot;</td>
</tr>
<tr>
<td><strong>Non-significant Risk (NSR)</strong></td>
<td>An NSR investigational medical device is a device that has been determined not to present significant risk to the patient. NSR device studies should not be confused with the concept of &quot;minimal risk,&quot; a term utilized in the IRB regulations to identify certain studies that may be approved through an &quot;expedited review&quot; procedure. (See also: &quot;Significant Risk Device&quot;)</td>
</tr>
<tr>
<td><strong>Nuremberg Code</strong></td>
<td>A code of research ethics developed following the trials of Nazi war criminals following World War II widely adopted as a standard during the 1950s and 1960s for protecting human subjects.</td>
</tr>
<tr>
<td><strong>Office for Human Research Protection (OHRP)</strong></td>
<td>A federal government agency within the Department of Health and Human Services (DHHS) charged with the protection of human subjects participating in research. It issues assurances and oversees compliance with regulatory guidelines by research institutions.</td>
</tr>
<tr>
<td><strong>Off-site Event/Problem</strong></td>
<td>An event/problem experienced by subjects enrolled by investigators at other institutions engaged in the research project.</td>
</tr>
<tr>
<td><strong>OHRP</strong></td>
<td>Acronym for “Office for Human Research Protection”</td>
</tr>
<tr>
<td><strong>On-site Event/Problem</strong></td>
<td>An event/problem experienced by subjects enrolled by a UB investigator or UB affiliated investigator or experienced by subjects enrolled in studies for which a UB IRB acts as the IRB of record.</td>
</tr>
<tr>
<td><strong>Oral History Interview</strong></td>
<td>A process whereby information is obtained from an individual about the person’s life and events that the person witnessed or participated in. Some oral history Interviews require IRB and approval prior to initiation.</td>
</tr>
<tr>
<td>Term</td>
<td>Definition</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Outside Reviewer</td>
<td>An outside reviewer is a non-voting reviewer of research projects generally asked by the IRB Chair to review projects because of their area(s) of experience and expertise.</td>
</tr>
<tr>
<td>Parent</td>
<td>A child’s biological or adoptive caregiver.</td>
</tr>
<tr>
<td>Parental Permission</td>
<td>The agreement of one or both parents or a guardian for a child to participate in research (45 CFR 46.402(c)).</td>
</tr>
<tr>
<td>Phase 1, 2, 3, 4 Clinical Drug Trials</td>
<td>Different stages of testing drugs in humans, from first application in humans (Phase 1) through limited and broad clinical tests (Phase 3), to post marketing studies (Phase 4).</td>
</tr>
<tr>
<td>PHI</td>
<td>See “Protected Health Information”</td>
</tr>
<tr>
<td>PI</td>
<td>Acronym for “Principal Investigator”</td>
</tr>
<tr>
<td>Pilot Study</td>
<td>Usually a precursor to a full-scale study. Pilot studies are usually conducted with a smaller sample size than a full study and are generally intended to test experimental procedures and to obtain information useful for conducting power calculations.</td>
</tr>
<tr>
<td>Placebo</td>
<td>A placebo is an inactive pill, liquid, or powder that has no treatment value. In clinical trials, experimental treatments are often compared with placebos to assess the treatment's effectiveness.</td>
</tr>
<tr>
<td>PPRA</td>
<td>Acronym for “Protection of Pupil Rights Amendment”</td>
</tr>
<tr>
<td>Principal Investigator (PI)</td>
<td>An individual who conducts an investigation, i.e., the person under whose immediate direction research is conducted, or, in the event of an investigation conducted by a team of individuals, the responsible leader of that team. There may also be co-principal investigators.</td>
</tr>
</tbody>
</table>
| Prisoner                      | For research purposes, the term “prisoner” includes any individual who is:  
  - Involuntarily confined or detained in a penal institution,  
  - Sentenced to serve time in a penal institution under a criminal or civil statute,  
  - Detained in other facilities (e.g., for drug detoxification or treatment of alcoholism)  
  - Detained pending arraignment, trial or sentencing.  
  [45 CFR 46.303(c)]  
The regulations that apply to prisoner enrollment in human subject research studies also apply to subjects already enrolled in a study who become incarcerated. Federal regulations do not differentiate between detention, jail or prison. People incarcerated in any of these places are considered prisoners. |
<p>| Prisoner Representative       | A member of an IRB who has appropriate background and experience to represent the interests and concerns of an individual who is involuntarily confined to an institution [45 CFR 46.304(b)].                                                                                                                                                                                                                                           |</p>
<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Privacy</td>
<td>For purposes of the HIPAA Privacy Rule, privacy means an individual’s interest in limiting who has access to his/her personal health care information</td>
</tr>
<tr>
<td>Protected Health Information (PHI)</td>
<td>PHI is a HIPAA term that means individually identifiable health information that is created or received by a covered entity and is transmitted by electronic media, maintained in electronic media, or transmitted or maintained in any other form or medium, including verbal or written form. PHI excludes education records covered by the Family Educational Rights and Privacy Act (FERPA) and Employment Records held by a covered entity in its role as employer.</td>
</tr>
<tr>
<td>Protection of Pupil Rights Amendment (PPRA)</td>
<td>PPRA is intended to protect the rights of parents and students in programs funded by the United States Department of Education. As it pertains to research, PPRA law states that surveys, questionnaires and instructional materials may be inspected by parents or guardians. The law further states that parental permission must be obtained to allow minors to participate in a survey revealing certain types of information, e.g., mental and psychological problems, income, sexual behavior and attitudes, illegal behavior, political affiliations, and close family relationships.</td>
</tr>
<tr>
<td>Protocol</td>
<td>The formal plan of a research project that describes the objectives, design, methodology, statistical considerations, and organization of the study.</td>
</tr>
<tr>
<td>Quality Assurance (QA)</td>
<td>A planned and systematic process that provides confidence in an outcome for its intended purpose. QA cannot guarantee a quality result or product but helps to assure the process toward that goal.</td>
</tr>
<tr>
<td>Quality Improvement (QI)</td>
<td>The effort to assess and take measures to improve the level of performance of a program, process, or institution.</td>
</tr>
<tr>
<td>Quorum (for IRB meeting)</td>
<td>A quorum for a valid IRB meeting consists of more than half of the total number of full voting members listed on the IRB roster. An additional requirement for a valid IRB meeting is the presence of at least one member whose primary concern is non-scientific.</td>
</tr>
<tr>
<td>Research</td>
<td>DHHS definition: A systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.</td>
</tr>
<tr>
<td>Research Practica</td>
<td>Student projects for which the goal is to provide research training.</td>
</tr>
<tr>
<td>Research Staff</td>
<td>The term “research staff” includes: investigators, co-investigators, all individuals who obtain consent, study/research managers and coordinators, data collectors, recruiters, interviewers, and statisticians. See also “Key Study Personnel”</td>
</tr>
<tr>
<td>Respect for Persons</td>
<td>See “Autonomy”</td>
</tr>
<tr>
<td><strong>Serious Event/Problem (SEP) (UB HRPP term)</strong></td>
<td>Any event or problem that meets the requirements for being “serious” according to UB HRPP specified criteria. In general, “serious” events/problems are those which caused harm or increase the risk of harm (whether or not actual harm has occurred) or jeopardize subject rights and welfare. The risks may be physical, psychological, economic, or social.</td>
</tr>
<tr>
<td><strong>Serious non-compliance</strong></td>
<td>Non-compliance that, in the judgment of the IRB, significantly increases risks or decreases benefits to the subject or to any individual involved or affected by the research, or that significantly compromises the study's scientific integrity or the validity of the research data.</td>
</tr>
<tr>
<td><strong>Significant Risk Device (SR)</strong></td>
<td>An SR investigational medical device is one that has been determined to present a potential for serious risk to the health, safety, or welfare of the subject and (1) is intended as an implant; or (2) is used in supporting or sustaining human life; or (3) is of substantial importance in diagnosing, curing, mitigating or treating disease, or otherwise prevents impairment of human health; or (4) otherwise presents a potential for serious risk to the health, safety, or welfare of a subject. (See also: Non-Significant Risk Device)</td>
</tr>
<tr>
<td><strong>SOP</strong></td>
<td>Acronym for “Standard Operating Procedures.” Detailed written procedures for the uniform performance of a function.</td>
</tr>
<tr>
<td><strong>Standard Treatment (Standard of Care)</strong></td>
<td>A treatment currently in wide use that is considered to be effective in the treatment of a specific disease or condition.</td>
</tr>
<tr>
<td><strong>Systematic Investigation</strong></td>
<td>An attempt to answer a research hypothesis where the qualitative and/or quantitative data are organized in a consistent manner and where a conclusion can be drawn from the findings.</td>
</tr>
<tr>
<td><strong>Tabled Study</strong></td>
<td>See “Deferred/Tabled Study”</td>
</tr>
<tr>
<td><strong>Test Article</strong></td>
<td>Any drug (including a biological product for human use), medical device for human use, human food additive, color additive, electronic product, or any other article subject to regulation under the act or under sections 351 and 354-360F of the Public Health Service Act (42 U.S.C. 262 and 263b-263n) and 21 CFR 50.3(j).</td>
</tr>
<tr>
<td><strong>Therapy</strong></td>
<td>Interventions that are applied solely to enhance the well being of an individual patient who is sick. The interventions are procedures commonly accepted by the medical community and represent the standard of care.</td>
</tr>
<tr>
<td><strong>Unanticipated</strong></td>
<td>An event that was unforeseen at the time of its occurrence</td>
</tr>
<tr>
<td><strong>Undue Influence</strong></td>
<td>Abuse of position of trust or authority in order to induce a person to do or refrain from doing something to the advantage of the person exerting the influence. The Common Rule prohibits investigators from using unfair measures or influence for purposes of enrolling persons in research (45 CFR 46.116).</td>
</tr>
</tbody>
</table>
**Unexpected Event/Problem**

An event/problem occurring in one or more subjects in a research protocol that is not identified by nature, severity or frequency in the research protocol or informed consent document and is not consistent with the known or foreseeable risk of adverse events associated with the procedures involved in the protocol, investigator brochure and approved informed consent document or the expected natural progression of any underlying disease, disorder, or condition of the subject experiencing the adverse event.

**Voluntary**

Free of coercion, duress, or undue inducement. Used in the research context to refer to a subject's decision to participate (or to continue to participate) in a research activity.

**Vulnerable Subjects in Research**

Individuals who lack the capacity to provide informed consent or whose willingness to participate in research may be unduly influenced by others.